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

4-05
25 May 2005

DRAFT ASSESSMENT REPORT

APPLICATION A470

FORMULATED BEVERAGES

DEADLINE FOR PUBLIC SUBMISSIONS: 6pm (Canberra time) 6 July 2005
SUBMISSIONS RECEIVED AFTER THIS DEADLINE
WILL NOT BE CONSIDERED
(See 'Invitation for Public Submissions' for details)

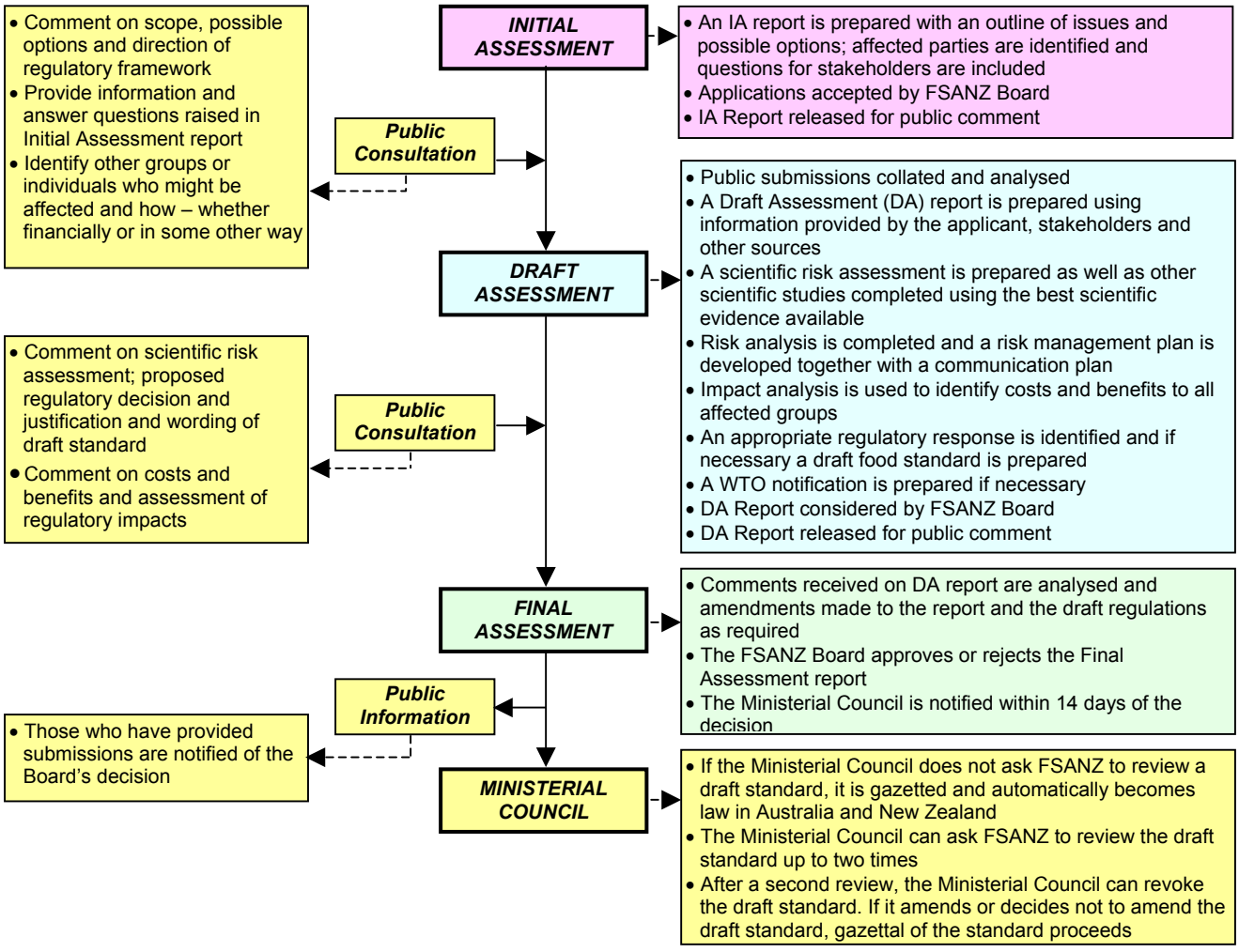
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

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

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

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

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



INVITATION FOR PUBLIC SUBMISSIONS

FSANZ has prepared a Draft Assessment Report for Application A470; and prepared a draft variation to the *Australia New Zealand Food Standards Code* (the Code).

FSANZ invites public comment on this Draft Assessment Report based on regulation impact principles and the draft variation to the Code for the purpose of preparing an amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in preparing the Final Assessment for this Application. Submissions should, where possible, address the objectives of FSANZ as set out in section 10 of the FSANZ Act. Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information and provide justification for treating it as commercial-in-confidence. Section 39 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions must be made in writing and should clearly be marked with the word 'Submission' and quote the correct project number and name. Submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2222
www.foodstandards.gov.au

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
www.foodstandards.govt.nz

Submissions need to be received by FSANZ by 6pm (Canberra time) 6 July 2005.

Submissions received after this date will not be considered, unless agreement for an extension has been given prior to this closing date. Agreement to an extension of time will only be given if extraordinary circumstances warrant an extension to the submission period. Any agreed extension will be notified on the FSANZ Website and will apply to all submitters.

While FSANZ accepts submissions in hard copy to our offices, it is more convenient and quicker to receive submissions electronically through the FSANZ website using the Standards Development tab and then through Documents for Public Comment. Questions relating to making submissions or the application process can be directed to the Standards Management Officer at the above address or by emailing slo@foodstandards.gov.au.

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

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Executive Summary and Statement of Reasons

Food Standards Australia New Zealand (FSANZ) received an Application from the Australian Beverages Council Limited (formerly the Australasian Soft Drink Association) on 26 June 2002 seeking the development of a new standard in the *Australia New Zealand Food Standards Code* (the Code) for formulated beverages (FB).

FB are described as non-alcoholic, water-based, flavoured beverages containing claimable amounts of a range of vitamins and minerals. Currently only three vitamins (vitamin C, folate and beta-carotene) are permitted to be added to general purpose beverages including juices and fruit drinks containing at least 25% fruit juice. Application A470 is seeking permissions for the addition of 23 vitamins[1] and minerals, a range of food additives excluding caffeine and carbon dioxide, and the use of some fruit-based ingredients and sugar[2].

This Draft Assessment discusses issues on the regulation of FB and proposes a preferred regulatory option. FSANZ seeks comment on this Draft Assessment, particularly in relation to the expected impact(s) of the proposed regulatory options from all interested parties. Comments received will assist in the preparation of a Final Assessment, including a recommended regulatory approach for FB.

Regulatory Problem

Currently there are no specific provisions in the Code for the addition of vitamins and minerals to FB. Consequently, any possible public health benefits and/or safety risks have not yet been assessed so that consumer confidence can be assured. There are potential hazards to consumers of FB from over-exposure to some vitamins and minerals and from excess energy (kilojoules) consumption. Most consumers would be unaware of any potential risks associated with the consumption of FB. Hence an assessment of FB is essential to protect public health and safety.

In addition, Australian beverage manufacturers are currently unable to manufacture FB, unless they utilise the existing Formulated Supplementary Sports Foods (FSSF) Standard. This is incongruous with the intent of the FSSF Standard, which is designed to regulate special-purpose food. These products, however, can be lawfully manufactured in New Zealand under the *New Zealand Dietary Supplements Regulations 1985* (NZDSR). New Zealand manufacturers are able to produce FB and sell them in Australia in accordance with the Trans Tasman Mutual Recognition Arrangement.

This situation results in a serious inequity between the New Zealand and Australian beverage industries. Furthermore, the Australian beverage industry is prevented from innovating and developing new products in response to emerging consumer demands. This system of regulations also is inconsistent with the intent of the Code to create a single set of food regulations in Australia and New Zealand.

[1] Note both retinol and carotene forms of vitamin A are considered separately increasing the total number of vitamins and minerals assessed to 24.

[2] For the purpose of this report, the term 'sugar' as it relates to FB refers to total sugars i.e. monosaccharides and disaccharides.

Objectives

In the context of FSANZ's statutory objectives, which includes having regard to Ministerial policy guidance, the specific objectives of Application A470 are to:

- protect the public health and safety of consumers of FB; and

- ensure a regulatory system which promotes efficiency and competitiveness for all sections of the FB industry.

Risk Assessment

A risk assessment has been conducted in relation to the addition of vitamins and minerals to FB. Both potential benefits and risks have been considered. A Nutrition Assessment (at Attachment 5) has been undertaken to assess the potential nutrition and health need of the addition of vitamins and minerals to FB.

The potential for FB to result in a health risk associated from the over-consumption of the requested vitamins and minerals has also been examined (at Attachment 6).

The methodology used for dietary modelling of the vitamins and minerals is described in Attachment 7. The requested food additives for addition to FB have also been examined. A detailed report outlining the nature of any potential hazard and a characterisation of the risk is provided in Attachment 8.

Risk Management

This Draft Assessment Report considers a number of issues relevant to the regulation of FB including the purpose and definition of FB, the appropriateness of FB as a vehicle for voluntary fortification and the labelling of FB.

Regulatory Options and Impact Analysis

There are three proposed regulatory options for addressing this Application:

- Option 1 - Maintain Status Quo i.e. no explicit permissions for FB in the Code.

- Option 2 - Amend the Code to permit the addition of a defined set of vitamins and minerals to FB (as detailed in the table on Page 9) excluding cordials, in addition to a restriction on the total sugar content of FB.

- Option 3 – Amend the Code to permit the addition of vitamins and minerals to FB and cordials as requested by the Applicant without any other specific compositional requirements.

For each regulatory option, an impact analysis has been undertaken to assess potential costs and benefits to the identified affected parties.

Consultation

The Initial Assessment Report for this Application was released for public comment from 15 January to 26 February 2003 (six weeks). A total of 19 submissions were received and are summarised at Attachment 10. Issues raised in submissions are discussed in this report. FSANZ now seeks public comment on this Draft Assessment Report in order to proceed to Final Assessment.

Conclusion

Option 2 delivers net-benefits in comparison with Option 1.

Option 2 fulfils the specific objectives of this Application. The health and safety of consumers is protected through limits on the level of fortification to ensure safe levels of consumption, and by excluding specific nutrients that could be potentially hazardous, or where their safety cannot be verified. The main benefit offered under Option 2 is the elimination of the opportunity cost incurred by a large part of Australian industry, which cannot supply the domestic market under the current regulatory arrangements. This situation is resolved in Option 2 by allowing the manufacture of FB in Australia.

Option 3 provides greater net-benefits to industry compared with Option 1. These benefits to industry also exceed the benefits from Option 2, because under Option 3 manufacturers may draw from a broader range of vitamins and minerals for future development of FB, eliminating the time and cost of obtaining regulatory approval and facilitating faster innovation. However, Option 3 could potentially impose large costs on consumers, in comparison with Option 1, by allowing specific nutrients that may have adverse health impacts. In addition, by not limiting the levels of vitamins and minerals in FB, this could possibly cause overexposure to these nutrients, and potential harm to consumers. Option 3 does not achieve the objective of protecting public health and safety, and is thus rejected.

Overall, Option 2 is the preferred regulatory option.

Proposed Regulatory Approach

On the basis of public health and safety, and having regard to Ministerial policy guidance, the promotion of fair trading and the desirability for an efficient and competitive food industry, FSANZ is proposing the following regulatory approach for FB:

- classification of FB as a general-purpose food;
- inclusion of a definition for FB in the Code, in association with a maximum limit of 24% fruit ingredients;
- exclusion of cordials as FB;
- restriction of total sugar content of FB to 7.5 g/100 ml;
- application of generic labelling requirements to FB;
- permissions for the range of food additives requested by the Applicant (as detailed in Attachment 9); and

- permissions for the addition of vitamins and minerals in amounts to allow 'source' (10% Recommended Dietary Intake (RDI)) and/or 'good source' (25% RDI) claims with the exception of vitamin C (100% RDI) per 600 ml reference quantity as outlined in the table below:

Vitamin / Mineral	Maximum Claimable Amount Per 600 ml Reference Quantity	No Public Health and Safety Concerns	Consistent with FSANZ's s.10 (2)(c), s.10(2)(d) and s.10(2)(e) Objectives*
Beta-carotene	200 µg	✓	✓
Thiamin	0.28 mg	✓	✓
Riboflavin	0.43 mg	✓	✓
Niacin	2.5 mg	✓	✓
Folate	50 µg folic acid	✓	✓
Vitamin B_6	0.4 mg pyridoxine	✓	✓
Vitamin B_{12}	0.5 µg	✓	✓
Vitamin C	40 mg in total of L-ascorbic acid and dehydroascorbic acid	✓	✓
Vitamin D	2.5 µg	✓	✓
Vitamin E	2.5 mg alpha-tocopherol equivalents	✓	✓
Pantothenic Acid	1.3 mg	✓	✓
Calcium	200 mg	✓	✓
Iodine	38 µg	✓	✓
Iron	3 mg	✓	✓
Magnesium	80 mg	✓	✓
Selenium	17.5 µg (inorganic and organic forms)	✓	✓

* FSANZ Act section 10(2)(c) the desirability of an efficient and internationally competitive food industry.
FSANZ Act section 10(2)(d) the promotion of fair trading in food.
FSANZ Act section 10(2)(e) any written policy guidelines formulated by the Ministerial Council.

Statement of Reasons

FSANZ recommends that the proposed draft variations to the Code (Attachment 1), incorporating defined vitamin and mineral permissions, specific compositional requirements, and a definition for FB, be approved for the following reasons:

- the regulation of FB provides assurance for consumers regarding the protection of public health and safety by:

  - permitting the safe addition of vitamins and minerals to FB;
  - permitting the addition of vitamins and minerals to FB where an inadequacy or deficiency exists; and
  - setting a prescribed limit on the total sugar content of FB;

- regulation of FB ensures certainty for industry balanced against the need to provide consumer choice and prevent consumers being misled regarding the nutritional quality of the product;

- the variations to the Code meet FSANZ's statutory obligations and are consistent with Ministerial policy guidance on voluntary fortification;

- the permitted range of vitamins and minerals is consistent with the principles of minimum effective regulation and the promotion of fair trading;

- the variations to the Code provide an effective regulatory framework within which industry can work efficiently and competitively;

- the inclusion of permissions for FB in the Code promotes equity by providing a regulation which enables the manufacture of FB in Australia;

- the explicit recognition of FB in the Code provides greater certainty for industry and reduces both the costs of compliance and enforcement; and

- the regulation impact assessment concludes that the preferred regulatory option of permitting net benefits from permitting FB outweigh any potential costs to affected parties.

1. Introduction

FSANZ received an Application from the Australian Beverages Council Limited[3] on 26 June 2002 requesting the development of a new standard in the Code for formulated beverages (FB).

FB are described as non-alcoholic, water-based, flavoured beverages containing claimable amounts of a range of vitamins and minerals. They are examples of recent innovative drinks that represent a growing sector of the global food market. Currently only three vitamins (vitamin C, folate and beta-carotene) are permitted to be added to general-purpose beverages including juices and fruit drinks containing at least 25% fruit juice as compared with the Application A470 request for 23 vitamins[4] and minerals. Permissions for a range of food additives, excluding caffeine and carbon dioxide, the use of some fruit-based ingredients and sugar are also being sought.

This Draft Assessment Report discusses issues regarding the regulation of FB and proposes a preferred regulatory option and draft variations to the Code (Attachment 1). FSANZ seeks comments on this Draft Assessment Report, particularly in relation to the expected impact(s) of the proposed regulatory options from all interested parties. Comments received will assist in the preparation of the Final Assessment.

A glossary of commonly used acronyms in this Report is at Attachment 2.

1.1 Nature of Application

Specifically, the Applicant is seeking permissions for FB as follows:

1. the addition of vitamins and minerals, in amounts to allow 'source' (10% recommended dietary intake (RDI)) and/or 'good source' (25% RDI) claims with the exception of vitamin C at 100% RDI per 600 ml reference quantity as outlined in the table below;

2. sugar at unspecified amounts;

3. fruit juice, puree concentrates, orange peel extract and/or comminuted fruit; and

4. a range of food additives (57 in total) currently permitted in the Code excluding caffeine and carbon dioxide .

Vitamin / Mineral	Maximum Claimable Amount Per 600 ml Reference Quantity
Vitamins	
Vitamin A	187.5 μg
Thiamin	0.275 mg
Riboflavin	0.425 mg
Niacin	2.5 mg
Folate	50 μg folic acid
Vitamin B_6	0.4 mg pyridoxine
Vitamin B_{12}	0.5 μg

[3] Formerly known as the Australasian Soft Drink Association Limited.
[4] Note both retinol and carotene forms of vitamin A are considered separately increasing the total number of vitamins and minerals assessed to 24.

Vitamin / Mineral	Maximum Claimable Amount Per 600 ml Reference Quantity
Vitamin C	40 mg in total of L-ascorbic acid and dehydroascorbic acid
Vitamin D	2.5 μg
Vitamin E	2.5 mg alpha-tocopherol equivalents
Biotin	7.5 μg
Pantothenic Acid	1.25 mg
Minerals	
Calcium	200 mg
Chromium	50 μg (inorganic forms)
Copper	0.75 mg (inorganic and organic forms)
Iodine	37.5 μg
Iron	3 mg
Magnesium	80 mg
Manganese	1.25 mg (inorganic and organic forms)
Molybdenum	62.5 μg (inorganic forms)
Phosphorus	250 mg
Selenium	17.5 μg (inorganic and organic forms)
Zinc	3 mg

1.1.1 Basis of the Application

The Applicant requested the creation of a standard for FB, as a general-purpose food, partly as a means of addressing the purported disadvantage that Australian beverage manufacturers are experiencing with the importation of FB from New Zealand under the *Trans-Tasman Mutual Recognition Arrangement* (TTMRA). Currently in New Zealand such beverages can be manufactured to the New Zealand *Dietary Supplements Regulations 1985* (NZDSR)[5], and exported and sold legally in Australia under the TTMRA. There is no explicit standard permitting manufacture of FB in Australia for sale on the Australian market. Some FB are being manufactured as special-purpose food under Standard 2.9.4 – Formulated Supplementary Sports Foods (FSSF) of the Code. However, this Standard is not intended to regulate FB and industry's preference is for explicit FB regulations. The Applicant also cited consumer demand for FB as underpinning the basis of their request.

1.1.2 Amendments to the original Application

Since the lodgement of Application A470 there have been a number of subsequent amendments. These amendments have ranged from minor changes addressing typographical errors to more substantial compositional changes. In terms of the latter, the original Application sought permissions for vitamins and minerals equivalent to those permitted for formulated supplementary sports foods (FSSF) in Standard 2.9.4 of the Code. These permissions have since been revised to 25% RDI with the exception of vitamin C, at 100% RDI per 600 ml reference quantity. The Applicant also withdrew the request for carbon dioxide as a permitted ingredient together with the addition of cyclamate and quinine as food additives. A more detailed summary of the amendments to Application A470 is at Attachment 3.

[5] http://www.legislation.govt.nz/browse_vw.asp?content-set=pal_regs

1.1.3 Requests for additional information

Although work on this cost-recovered Application commenced immediately, the statutory timeframe has been suspended on three separate occasions pending receipt of information requested from the Applicant.

This additional information, requested by FSANZ under section 34 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), was necessary to enable a comprehensive, robust assessment of the Application to be completed.

These information requests primarily related to obtaining information on: FB consumption and usage data; product substitution; and proposed marketing strategies. FSANZ also sought clarification as to the requested vitamin and mineral permitted forms and food additives.

The statutory timeframe for the Application was suspended for a total of 460 days as FSANZ sought this additional information from the Applicant.

1.1.4 Extension of statutory timeframe

In addition to the suspension associated with the requests for additional information, the timeframe for Application A470 was also extended as a result of the following:

- ANZFA to FSANZ transition period. All Applications being assessed by FSANZ at 30 June 2002 were given an extension of three months to the statutory timeframe as part of the changeover from the Australia New Zealand Food Authority (ANZFA) to FSANZ;

- delay in receipt of fees which resulted in an additional 73 days being added to the statutory timeframe for Application A470; and

- extension of the statutory timeframe by six months as permitted by section 35(2) of the FSANZ Act. This was due to the complexity and volume of work required to be completed, particularly in relation to the risk assessment of the 23 vitamins and minerals, and the numerous food additives being requested.

The current revised completion date for Application A470 is 22 August 2005.

2. Regulatory Problem

Currently there are no specific provisions in the Code for the addition of vitamins and minerals to FB. Consequently, any possible public health benefits and/or safety risks have not yet been assessed so that consumer confidence can be assured. There are potential hazards to consumers of FB from over-exposure to some vitamins and minerals and from excess energy (kilojoules) consumption. Most consumers would be unaware of any potential risks associated with the consumption of FB. Hence an assessment of FB is essential to protect public health and safety.

In addition, Australian beverage manufacturers are currently unable to manufacture FB, unless they utilise the existing Formulated Supplementary Sports Foods (FSSF) Standard.

This is incongruous with the intent of the FSSF Standard which is designed to regulate special-purpose food. These products, however, can be lawfully manufactured in New Zealand under the NZDSR. New Zealand manufacturers are able to produce FB and sell them in Australia in accordance with the TTMRA. This situation results in a serious inequity between the New Zealand and Australian beverage industries.

Furthermore, the Australian beverage industry is prevented from innovating and developing new products in response to emerging consumer demands. This system of regulations also is inconsistent with the intent of the Code to create a single set of food regulations in Australia and New Zealand.

3. Objectives

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out, in order of priority, in section 10 of the FSANZ Act. These are:

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

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

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

In having regard to the above five matters, FSANZ does so initially without assigning precedence to any one particular matter. However, FSANZ will on a case-by-case basis, balance these matters and assign them appropriate weightings, given the relevant considerations for a particular application or proposal.

In the context of FSANZ's statutory objectives, which includes having regard to Ministerial policy guidance, the specific objectives of Application A470 are to:

- protect the public health and safety of consumers of FB; and
- ensure a regulatory system which promotes efficiency and competitiveness for all sections of the FB industry.

4. Background

4.1 Regulatory Framework

4.1.1 Australia

In Australia, foods are regulated under the Code and therapeutic goods are regulated under the Commonwealth *Therapeutic Goods Act 1989*.

4.1.2 New Zealand

In New Zealand[6], foods are predominately regulated under the Code, however in some instances foods are being manufactured in accordance with the NZDSR. Products of a therapeutic nature are regulated as medicines under the New Zealand *Medicines Act 1981* or as 'dietary supplements[7]' under the NZDSR.

4.1.2.1 New Zealand Dietary Supplements Regulations 1985

The NZDSR were made under the New Zealand *Food Act 1981*, and commenced in August 1985. In contrast to Australia, these regulations created a separate regulatory category for dietary supplements in addition to those for foods and medicines/therapeutic goods.

In Australia, these 'dietary supplements' could be regarded as foods i.e. food-type dietary supplements (FTDS) [8] or medicines/therapeutic products depending on the nature of the product.

Details of the permissions for vitamins and minerals contained in the NZDSR are outlined in the table below:

Vitamins	Maximum Daily Dose (for adult) – if specified	Minerals	Maximum Daily Dose (for adult) – if specified
Vitamin A or retinol	3000 μg	Calcium	
Vitamin B1 or thiamin		Chlorine	
Vitamin B2 or riboflavin		Chromium	
Niacin or nicotinic acid	100 mg	Copper	5 mg
Pantothenic acid		Fluorine	
Vitamin B_6 or pyridoxine		Iodine	
Vitamin B_{12} or cyanocobalamin or hydroxycobalamin	50 μg	Iron	24 mg
Vitamin C or ascorbic acid		Magnesium	
Vitamin D or calciferol	25 μg	Manganese	

[6] Prior to 20 December 2001, foods in New Zealand were regulated by the New Zealand *Food Regulations 1984*.

[7] The NZDSR define a dietary supplement as *any amino acids, edible substances, foodstuffs, herbs, minerals, synthetic nutrients, and vitamins sold singly or in mixtures in controlled dosage forms as cachets, capsules, liquids, lozenges, pastilles, powders, or tablets, which are intended to supplement the intake of those substances normally derived from food*.

[8] The term food-type dietary supplement (FTDS) is used to emphasise that the products under consideration are regarded as foods. It encompasses those food type products that are manufactured or imported under the New Zealand *Dietary Supplements Regulations 1985* but are referred to as 'dietary supplements'.

Vitamins	Maximum Daily Dose (for adult) – if specified	Minerals	Maximum Daily Dose (for adult) – if specified
Vitamin D or cholecalciferol	25 μg	Molybdenum	
Vitamin E		Phosphorus	
Biotin		Potassium	
Vitamin K		Selenium	150 μg
Vitamin K1 or phytomenadione		Sodium	
Vitamin K or menaphthone		Zinc	15 mg
Folic acid	300 μg		

Advice from the New Zealand Government[9] is that the NZDSR were designed to regulate controlled dosage supplements such as tablets and capsules. Furthermore, the NZDSR were intended to cover products not regulated by the food regulations rather than provide a choice of regulatory regimes for the food industry. More recently, the New Zealand Government[10] has indicated that the NZDSR *are not underpinned by a comprehensive risk-based methodology and therefore do not reflect today's best regulatory practice*.

The New Zealand Government[10] has foreshadowed changes to the NZDSR including a preference for the regulation of fortified foods, currently regulated as 'dietary supplements' to be regulated under the Code. The rationale underpinning this preference includes:

- meeting risk management and safety concerns;
- enhancing consumer confidence; and
- contributing to a fair trading environment between New Zealand and Australia.

This preference is consistent with the intent of the *Agreement between the Government of Australia and the Government of New Zealand concerning a Joint Foods Standards System* to establish a single market for food in Australia and New Zealand, underpinned by a single set of food regulations in both countries.

4.1.3 Trans Tasman Mutual Recognition

The *Trans Tasman Mutual Recognition Act 1997* gives effect to the TTMRA in Australia. The TTMRA commenced on 1 May 1998 in Australia and New Zealand to promote closer economic relations and trade between Australia and New Zealand. Under the TTMRA, a range of products, including food, which can be produced in or imported and be legally sold in one country, may be lawfully imported into and sold in the other country, without the necessity of compliance with further requirements imposed by or under the law of the jurisdiction.

The exemptions set out in the *Trans Tasman Mutual Recognition Act 1997*, prescribe legislation that must be complied with irrespective of compliance with the laws of the originating jurisdiction.

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[9] New Zealand Food Safety Authority submission to Proposal P235 – Review of Food-Type Dietary Supplements Initial Assessment Report dated 30 August 2002.

[10] New Zealand Food Safety Authority Discussion Paper No. 01/04 (July 2004) *Proposed Changes to the Dietary Supplements Regulations 1985*.

Specifically, a special exemption applies to the *Therapeutic Goods Act 1989*. This means that New Zealand products captured under the *Therapeutic Goods Act 1989* must comply with that Act irrespective of whether that product complies with the laws of New Zealand. Consequently, products that complied with the NZDSR*, Food Regulations 1984,* or *Medicines Act 1981* that are not considered to be 'therapeutic goods' within the meaning of the *Therapeutic Goods Act 1989* may be lawfully imported from New Zealand and sold in Australia.

4.1.4 Joint Australia and New Zealand Therapeutic Goods Agency

Australia and New Zealand are in the process of establishing a bi-national agency that will regulate therapeutic goods in both Australia and New Zealand. The joint scheme is expected to commence by July 2006. When legislation for therapeutic goods is developed, it is expected that FTDS will be regulated by the Code.

4.1.5 International regulations

4.1.5.1 Codex Alimentarius

Codex has no specific texts that address FB other than its *General Principles for the Addition of Essential Nutrients to Foods* (CAC/GL 09-1987, Amended 1991), which provides guidance to countries in establishing their own regulatory approach to fortification of conventional foods.

4.1.5.2 Overseas regulations

There is a lack of international consistency in the regulation of FB. Although FB can be defined as '*dietary supplements'* under the NZDSR, the regulation of these products, where permitted in overseas jurisdictions, occurs under general provisions for the addition of vitamins and minerals to foods. No overseas regulation pertaining specifically to FB has been identified, although the Applicant advises that many countries, including a number of countries in Asia, allow for the production of vitamin and mineral enhanced beverages. Where they exist internationally, dietary supplements regulations refer to complementary medicines/therapeutic-type dietary supplements (e.g. tablets, capsules etc.), rather than beverages.

While there is no regulatory approach internationally for the addition of vitamins and minerals specific to FB, both Canada and the United States have respectively proposed or extant policies in relation to fortification. A review of the Health Canada policy[11] on fortification was released in early 2005. The proposed approach allows for an expanded range of fortified products through discretionary fortification and does not preclude beverages except for those containing alcohol. The United States Food and Drug Administration[12] does not consider it 'appropriate to fortify fresh produce; meat, poultry, or fish products; sugar; or snack foods such as candies and carbonated beverages'.

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[11] Health Canada (2005) *Addition of Vitamins and Minerals to Foods 2005 – Health Canada's Proposed Policy and Implementation Plans*

[12] USFDA: Title 21, *Food and Drugs: Fortification Policy*. 45 Federal Register 6323 (1980), as amended at 58 Federal Register 2228 (1993)(codified at 21 CFR §104.20).

Similarly, the European Commission (EC)[13] proposes to restrict the addition of vitamins and minerals to certain foods such as alcohol and fresh produce such as fruits, vegetables, meat, poultry, fish etc. The EC purport that products with an 'undesirable' nutrient profile (i.e. high in sugar, fat and/or salt) will be dissuaded from adding vitamins and minerals due to their inability to meet the proposed nutrition and health claims criteria.

4.2 Ministerial Policy Guidance

In accordance with the section 10 objectives of the FSANZ Act (see Section 3 above), in developing or varying a standard, FSANZ must have regard to a number of specific matters including any written policy guidelines formulated by the Ministerial Council.

Since completion of the Initial Assessment of Application A470, the Ministerial Council has adopted policy guidance on fortification of food with vitamins and minerals, and nutrition, health and related claims, both being of direct relevance to consideration of Application A470. The Ministerial Council has also commenced policy development work in relation to the addition of substances other than vitamins and minerals to food.

4.2.1 Fortification with vitamins and minerals

In May 2004, the Ministerial Council adopted a Policy Guideline on the *Fortification of Food with Vitamins and Minerals*[14] (Policy Guideline). The Policy Guideline includes 'High Order' Policy Principles, which are FSANZ's statutory objectives, and are supplemented by separate 'Specific Order' Policy Principles and 'Additional Policy Guidance' for both mandatory and voluntary fortification. The 'High Order' Policy Principles restate the objectives of the FSANZ Act and take precedence over the policy guidance specifically provided on voluntary fortification.

The Policy Guideline contains seven 'Specific Order' Policy Principles that FSANZ must have regard to when considering voluntary fortification. The first 'Specific Order' Policy Principle lists five conditions that can be used as a basis for permitting voluntary fortification. Of relevance to Application A470 is where there is:

- a need for increasing the intake of a vitamin or mineral demonstrated by evidence of deficiency or inadequate intake; or
- generally accepted scientific evidence that an increase in a vitamin and/or mineral can deliver a health benefit.

In response to the Policy Guideline, FSANZ is in the process of developing the *Fortification Implementation Framework*[15]. This Framework is an internal document, which details FSANZ's decision making, in light of the Policy Guideline, on the addition of vitamins and minerals to food.

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[13] Commission of the European Communities *Proposal for a Regulation of the European Parliament And Council on The Addition of Vitamins and Minerals and of Certain other Substances to Foods* COM(2003) 671 final. Brussels

[14] Policy Guideline on the Fortification of Food with Vitamins and Minerals. Available from Food Regulation Secretariat , <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Food+Regulation+Secretariat-1>

[15] The draft Fortification Implementation Framework is available at www.foodstandards.gov.au

Given FSANZ is required to have regard to the Policy Guideline in its broader consideration of Application A470, Australian Beverages were invited to respond to the Policy Guideline, particularly in terms of the 'Specific Order' Policy Principles for voluntary fortification to ensure procedural fairness had been afforded to the Applicant.

4.2.2 Nutrition, health and related claims

In December 2003, the Ministerial Council referred a *Policy Guideline on Nutrition, Health and Related Claims*[16] to FSANZ for the development of a new standard to permit a broader range of claims.

FSANZ has commenced work on Proposal P293 - Nutrition, Health and Related Claims, which is the means by which FSANZ will, having regard to ministerial policy guidance, develop a Standard for the regulation of nutrition, health and related claims and an appropriate management system to support enforcement of the Standard.

Claims relating to the vitamin and/or mineral content of a food are currently regulated in Standard 1.3.2 – Vitamins and Minerals of the Code. At this stage, the review of the criteria for vitamin and mineral content claims has been excluded from consideration in Proposal P293. However, other claims (e.g. nutrition function and health claims) in relation to fortified foods including FB, do fall within the regulatory framework for nutrition, health and related claims. Therefore FB will be subject to the existing requirements for nutrition and health claims (i.e. Standard 1.2.8 – Nutrition Information Requirements, the Code of Practice on Nutrient Claims on Food Labels and in Advertisements (CoPoNC) and Transitional Standard 1.1A.2 – Health Claims), and will in time be required to meet the provisions of the new Standard.

4.2.3 Addition of substances other than vitamins and minerals

Recently the Ministerial Council initiated work on developing policy guidance on 'the addition of substances other than vitamins and minerals'. Further information on this is available from the Food Regulation Secretariat[17]. Although Application A470 is not seeking permissions for the addition of 'substances other than vitamin and minerals' to FB, ultimately policy guidance on this matter will have implications in the broader consideration of FTDS (see Section 4.4.1), the scope of which previously included FB.

4.3 Relevant Standards in the Code

The generic regulations contained in Chapter 1 of the Code, that apply to all foods, and regulations in Chapter 2 that are specific to various commodities, are of particular relevance to the assessment of FB.

The most relevant regulations in Chapter 1 are:

- Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions which contains the Schedule of permitted forms of vitamins and minerals;

[16] Policy Guideline on Nutrition, Health and Related Claims. Available from Food Regulation Secretariat , <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Food+Regulation+Secretariat-1>

[17] Australian Department of Health and Aging, Food Regulation Secretariat http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Food+Regulation+Secretariat-1

- Standard 1.2.8 – Nutrition Information Requirements which sets out the labelling requirements for the provision of nutrition information including nutrition claims;

- Standard 1.3.1 – Food Additives which regulates the use of food additives in production and processing and currently includes specific additive permissions for fruit juices, drinks and water based flavoured drinks; and

- Standard 1.3.2 – Vitamins and Minerals, which regulates the addition of vitamins and minerals to food, and the claims which can be made about the vitamin and mineral content of food.

Standard 1.3.2 establishes minimum and maximum claim limits for permitted vitamins and minerals whereby the minimum is 10% of the RDI per serve and the maximum is up to 1250% of the RDI per serve. In effect this deters the addition of vitamins and minerals in amounts that exceed the maximum claim limit. Where necessary however, absolute maximum amounts are established for those few vitamins and minerals where there is a potential public health and safety risk.

Currently, Standard 1.3.2 permits the addition of the carotenoid forms of vitamin A (i.e. beta-carotene), vitamin C and folic acid in moderate amounts to beverages that contain at least 25% fruit- or vegetable juice; and the addition of vitamin C in moderate amounts to fruit-based cordials. In addition, Standard 1.3.2 sets out the conditions and criteria for claims in relation to the vitamin and mineral content of food, including 'source' (10% RDI) and 'good source' (25% RDI) claims.

The relevant regulation in Chapter 2 is:

- Standard 2.6.2 – Non-alcoholic Beverages and Brewed Soft Drink, which regulates the majority of non-alcoholic, water-based beverages and includes product definitions, compositional and labelling requirements.

Other pertinent Standards in Chapter 2 that merit consideration include:

- Standard 2.6.4 – Formulated Caffeinated Beverages (FCB) which allows for the addition of certain vitamins and minerals to FCB and details specific labelling requirements; and

- Standard 2.9.4 – Formulated Supplementary Sports Foods (FSSF) defines and regulates the composition, including permissions for broad range of vitamins and minerals, and labelling of foods specially formulated to assist sports people in achieving specific nutritional or performance goals. FSSF must be labelled as 'Unsuitable for children under 15 years of age and pregnant women: Should only be used under medical or dietetic supervision'.

4.4 Other Relevant FSANZ Activities

4.4.1 Proposal P235 – Review of Food-Type Dietary Supplements

Prior to receipt of this Application, FB were considered within the scope of Proposal P235 – Food-Type Dietary Supplements.

The aim of this Proposal is to develop regulations in Australia and New Zealand in recognition of the growing market for foods containing added substances with health-related properties. FTDS often contain substances such as vitamins, minerals, non-culinary herbs and other extracts where the presence or amounts are beyond the current permissions in the Code, but are permitted under the NZDSR.

The Proposal P235 Initial Assessment Report was previously released for public comment on 26 June 2002. However, its progress has been deferred pending development of policy guidance from the Ministerial Council in relation to the addition of substances other than vitamins and minerals.

The development of policy guidance on the addition of vitamins and minerals to food provides a framework to progress Application A470 independently of Proposal P235.

4.4.2 Application A424 – Fortification of Calcium to Foods

In March 2005, FSANZ completed a First Review of Application A424 – Fortification of Foods with Calcium that is seeking to amend Standard 1.3.2 – Vitamins and Minerals of the Code, to permit the voluntary addition of calcium to fruit- and vegetable juices and drinks, soups and savoury biscuits. The First Review reaffirmed FSANZ's previous approval to permit the addition of calcium to the requested foods. FSANZ has notified the Ministerial Council of its decision at First Review.

4.5 Current Formulated Beverage Market and Product Range

In June 2003, FSANZ commissioned surveys in both Australia and New Zealand to assist in the assessment of Application A470 and Proposal P235. The objectives were two-fold. Firstly, to identify those products available which are consumed as food but are marketed or formulated as FTDS; and secondly, to examine the FTDS industry focusing on structure and market share. For both countries, beverages comprised the largest category. More recently (March/April 2005), FSANZ staff conducted surveys to determine the current FB product range in both Australia and New Zealand. Using the results from the 2003 FTDS Surveys as a base line, products were assessed in terms of availability, composition and claims.

A summary of the key findings in relation to the FB market and product range is discussed below. For specific details on the current product range refer to Attachment 4.

4.5.1 Formulated beverages market

4.5.1.1 International

FB are the latest in a series of innovative, non-alcoholic, water-based drinks that represent a growing sector of the global food market.

Current market trends indicate a shift away from beverages that are 'nutritionally inferior' towards healthier alternatives. This shift is reflected by consumers limiting soft drink intake, looking for functional beverages, being conscious of fat and sugar levels, and meeting health recommendations such as 6-8 glasses of water a day[18].

[18] Commercial-in-confidence industry data.

Sales of FB, FCB and other 'fortified' beverages in the United States (US), one of the most established overseas markets, have experienced a growth from a niche market in 1997 to an estimated $US8 billion today and an expected $US12 billion per year by 2007[19]. The majority of this growth has been attributed to 'energy drinks' and vitamin-enhanced beverages.

FB sales worldwide have grown at rates in excess of 10% per year. Market intelligence suggests some recent slowing in these growth rates. In 2005 growth should be a little less than 10% per year, slowing to around 5% over the next five years[20]. Notwithstanding this decline in growth, the FB category is seen as 'relatively underdeveloped' with capacity for continuing expansion[20]. FB follow other innovative, non-alcoholic water-based beverages, especially the energy drinks and sports drinks, and while growth in these products was strong in the past, these markets have now matured[20]. Based on current market trend data[21] showing consumers want products that are healthy, convenient and good value for money, there appears to be enormous potential for market growth of FB.

Internationally, the FB market is concentrated and much of the market is dominated by a few multinational companies, principally the traditional soft drink bottlers. Innovative, non-alcoholic, water-based drinks have increasingly attracted the attention of the multinational soft drink bottlers, looking for new growth areas to maintain their competitiveness as their traditional carbonates sector has matured. They have invested heavily in the FB sector by acquisition, new product development and extension of existing brands. Notwithstanding this activity, there remains a significant, though minor, share of the market that is supplied by small and medium sized companies.

4.5.1.2 New Zealand

The current regulatory arrangements have allowed the New Zealand non-alcoholic beverage industry to respond to international market trends and develop innovative products. New Zealand manufacturers are noted as early adopters of overseas trends and the local market has responded well to the offering. Enhanced fruit drinks first appeared in New Zealand stores in 1996, while the 'sports water' category was developed in 2001. In 2002 the New Zealand domestic market was valued at around $NZ15 million[22]. Today, one company continues to be the market leader, with competition from other major beverage manufacturers plus a number of smaller manufacturers. Until recently, a distinctive feature of the New Zealand market had been the locally owned status of the market leader; which is now a division of a multinational subsidiary. Imports of FB onto the New Zealand market are negligible.

This solid manufacturing activity provided a base to expand into exports, valued at around $NZ35 million in 2004, of which $NZ32 million is exported to Australia[23].

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[19] An Australasian Standard for Formulated Water-Based Non-Alcoholic (Functional) Beverages – The Economic Benefits. The Allen Consulting Group, July 2002.
[20] Functional Soft Drinks – An International Perspective. Leatherhead Food International, November 2003.
[21] What's Hot Around the Globe, ACNeilsen Global Services, December 2004 – used in the Retail World article.
[22] The New Zealand Market for Food-Type Dietary Supplements. Food Concepts & Design Limited (NZ), June-August 2003.
[23] Statistics New Zealand – Overseas trade exports for calendar years 1995-2004. Reference number JOA7632.

The 2005 FB Survey identified ten products, compared with nine in the 2003 FTDS survey. There are five new products while four have been withdrawn from the market. Thus, there appears to have been a plateau in the number of products on the New Zealand market. Only one imported product was found on the New Zealand market in 2005.

4.5.1.3 Australia

The FB market in Australia is relatively small but is experiencing growth.

Structurally, the market is comprised of several large to medium companies with an increasing number of smaller players entering the field. It is continuing to evolve with repositioning and take-overs of existing FB. This evolution also involves a lot of opportunistic activity, with importers, distributors and manufacturers experimenting with new products to gauge consumer acceptance. Consequently, there is a considerable 'churning' of these types of products.

Unlike the New Zealand market, the Australian FB market has changed somewhat since 2003. In the 2003 Australian FTDS survey, only three products were identified that would be classified as FB. All three products were imported from New Zealand via the TTMRA. In the 2005 FB Survey the FB product range had significantly increased to 20. Of these, only four are being imported from New Zealand. The remaining products are either being manufactured under Standard 2.9.4 – Formulated Supplementary Sports Foods or appear to be non-compliant with the Code. Whilst the composition of the FB manufactured and labelled as FSSF include some of the vitamin and mineral permissions permitted under Standard 2.9.4, manufacturers do not utilise the amino acid and other ingredients permissions in these formulations.

The market for FB produced under Standard 2.9.4 is valued at approximately $A10 million for 2004 (*personal communication* Tony Gentile 2005). Whilst some local companies have produced niche FB under this Standard, the larger multinational beverage manufacturers in Australia believe the mandatory advisory labelling requirements are particularly onerous and adversely affect consumer perceptions and marketing of FB. They also quote resistance from retailers to stock any item that is 'not suitable for children' because the retailers believe they could be legally liable if such a product was sold to a child.

In addition to the local production estimate of $A10 million, a further $A40 million worth of FB is estimated to be imported from New Zealand.

4.5.2 Formulated beverage products

4.5.2.1 New Zealand

As previously reported, the 2005 New Zealand Survey identified a total of 10 products in the marketplace that would be classified as FB. The ingredients ranged from FB consisting of water, flavouring and no added sugar to FB with greater than 5% fruit juice and added sugar. These formulations have remained relatively constant compared with the ingredient listings of the 2003 Survey products.

The energy and macronutrient composition per 100 ml varies between FB, however it has not changed significantly since the 2003 Survey. The protein and fat contents of all FB surveyed were less than 1 g per 100 ml. FSANZ has classified FB into four categories and provided a summary of the energy and total sugar content in the Table below:

FB Product Range	Total Sugar (%)	Energy (kJ per 100 ml)
Water, flavouring + no added sugar	0	2
Water, flavouring + added sugar	2.3	41
2-5% fruit juice +/- added sugar	2.5-3.2	43-59
> 5% fruit juice + added sugar	9.7-11.3	171-196

In 2005, ten vitamins (vitamin A, thiamin, niacin, pantothenic acid, vitamin B_6, folic acid, vitamin B_{12}, biotin, vitamin C and vitamin E) are present in FB. The same vitamins were being used in 2003, except for biotin. There has been an increase in the use of thiamin, niacin, pantothenic acid, vitamin B_6, folic acid, vitamin B12 and vitamin E. The average number of vitamins added in 2005 is 5.7 per product, with niacin, pantothenic acid and vitamin B_6 being the most commonly used vitamins. In 2003, the most commonly added vitamins were vitamin C, together with niacin and vitamin B_6. The percentage of the RDI per serve of a FB ranged from 10-350% in the 2005 products. Most products contained between 10-40% of the RDI for a specific vitamin.

The addition of minerals to FB has increased slightly since 2003. In 2005 six different minerals (calcium, iron, magnesium, potassium, sodium, and zinc) are used, compared with three in 2003. All ten products contain added sodium in quantities ranging from 3-20 mg per 100 ml.

In 2003, three products contained herbal extracts (guarana, ginkgo leaf and echinacea), however all these products have since been withdrawn from the market. One new product contains a green tea extract.

Serving sizes have increased from 200-400 ml in 2003 to 200-710 ml in 2005. Six of the products identified in 2005 stated a serving size of 200 ml, with five of these products sold in packages containing 800 ml or more. In addition five of the products provided maximum recommended daily intakes or serves on their product labels. The maximum intake range equated to 1600-4800 ml per day for adults and 800-1600 ml per day for children.

Many of the FB carry claims, the majority of these are vitamin content claims, while other claims pertain to the benefits with respect to antioxidant intake, hydration and energy.

4.5.2.2 Australia

The 2005 Australian Survey identified a total of 20 products in the marketplace that would be classified as FB, compared with only three products from the 2003 survey, two of which are still available. Like the New Zealand products, FB sold in Australia range from beverages consisting of water, flavouring and no added sugar to beverages with greater than 5% fruit juice and added sugar. The majority (14) contain 2-5% fruit juice with or without added sugar.

The energy and macronutrient composition per 100 ml varied between the beverages, however it has not changed significantly since the 2003 FTDS survey. The protein and fat contents of all FB surveyed were less than 1 g per 100 ml.

FB Product Range	Total Sugar (%)	Energy (kJ per 100 ml)
Water, flavouring + no added sugar	0	2
Water, flavouring + added sugar	2.3	41
2-5% fruit juice +/- added sugar	2.2-5.4	38-94
> 5% fruit juice + added sugar	10.8-11.0	182-194

Ten different vitamins make up the vitamin profile of the FB sold in Australia in 2005 (vitamin A, thiamin, niacin, pantothenic acid, vitamin B_6, folic acid, vitamin B_{12}, biotin, vitamin C and vitamin E) with the addition of vitamin A and biotin since 2003. Niacin, pantothenic acid, vitamin B_6 and vitamin B12 are the most commonly added vitamins, with an average of 4.8 vitamins added per product. Biotin is added by three manufacturers to ten products. The percentage of the RDI provided per serve of a FB ranged from 10-350% in the 2005 products, with vitamin C, niacin and vitamin B_6 provided in some products in amounts greater than 100% per serve.

Seven minerals are added to FB currently sold in Australia. These are calcium, potassium, sodium, magnesium, zinc, iron and iodine. All twenty FB contain added sodium in quantities ranging from 2-25 mg per 100 ml.

Herbal extracts have not been commonly added to FB sold in Australia. In 2003, no product contained herbal extracts, and in 2005, only one FB has added Aloe extract.

The serving size range has remained constant between 2003 and 2005 at 200-710 ml, however the average serving size has increased from 370 ml in 2003 to 480 ml in 2005. Five products provided maximum recommended daily intakes or serves on their product label, ranging from 600-3600 ml per day for adults. Only one product provided a recommendation for children, which equated to 800 ml per day.

Like the New Zealand products, many of the FB sold in Australia make claims, the majority being vitamin content claims. While other claims pertain to benefits of the beverages with respect to antioxidant intake, glycaemic index rating, healthy body, hydration and energy.

4.6 Consumer Research on Food-Type Dietary Supplements

In June 2003, FSANZ commissioned consumer research in both Australia and New Zealand to assist future decision-making on issues related to FTDS including Application A470. Specifically, the purpose of the research was to examine consumers' awareness, familiarity, understanding and use of FTDS and related labelling elements such as the term 'dietary supplement', nutrition content claims and other nutritional and non-nutritional information including 'percentage daily intake' and trigger/advisory statements.

A summary of the research findings is provided below. A copy of the full report '*A qualitative consumer study related to food-type dietary supplement labelling*' is available on the FSANZ website[24].

[24] http://www.foodstandards.gov.au/mediareleasespublications/publications/consumerstudyrelatedtofoodtypedietarysupplementlabellingjuly2003/

A total of 10 focus groups were conducted. The sample was skewed to include more people who are health conscious or who have special health needs compared to less health conscious people. The research demonstrated that participants were unable to distinguish between general-purpose foods carrying nutrition content claims and FTDS labelled 'dietary supplement', because they are almost exclusively influenced by content claims and because manufacturers display the term 'dietary supplement' in a way which renders it difficult to discern.

Awareness and use of FTDS was low. There were very few concerns about over-consumption of supplements (in terms of vitamins, minerals, non-culinary herbs and botanicals) and therefore participants were very open to the concept of supplementation of foods in almost all processed food categories. They did, however, want labels that distinguish between foods that intrinsically contain particular nutrients and foods that contain extrinsic or 'added' nutrients. They also wanted claims to be more quantified through the use of comparative percentages or exact amounts. Content claims such as 'source' and 'good source' were viewed as advertorial in nature and imprecise, which therefore meant they were treated with scepticism, even though they were considered to be truthful. There was no awareness that such terms are regulated.

The term 'dietary supplement' was described in both positive and negative terms because consumers were confused as to whether the intent was to caution consumers or to market the product. The addition of a trigger statement directing consumers to the Nutrition Information Panel (NIP) was not well supported, nor was a cautionary statement about FTDS or a percentage daily intake column in the NIP, because none of them were seen as being necessary.

The report highlighted the need to inform and educate consumers about labels relating to FTDS as consumers' current understanding of supplementation and nutritional information is such that informed choices cannot be made. The addition of more information on labels to reflect supplementation will not be meaningful to consumers unless accompanied by education.

5. Relevant Issues

5.1 Risk Assessment

A risk assessment has been conducted in relation to the addition of vitamins and minerals to FB. The Applicant has requested the addition of the following vitamins and minerals up to a level of 25 % of the RDI per 600 ml (reference quantity): vitamin A, beta-carotene, thiamin, riboflavin, niacin, folate, vitamin B_6, vitamin B_{12}, vitamin D, vitamin E, biotin, pantothenic acid, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorus, selenium and zinc. The Applicant has also requested the addition of vitamin C at 100% of the RDI per 600 ml.

In the case of the requested vitamin and mineral additions, there is a potential for both benefits and risks depending on the nutritional status of the population and the level of dietary intake of the vitamins and minerals. Both potential benefits and risks have been considered in determining the suitability of the addition of vitamins and minerals to FB.

A nutrition assessment has been undertaken to assess the potential nutrition and health need in support of vitamin and mineral additions to FB. 'Nutrition and health need' encompasses two concepts: i) nutritional need, referring to inadequate intakes or deficiency states; or ii) 'health benefits'.

In addition, the nutrition assessment has also assessed the potential health risk from an increase sugar and energy intakes of the population that may occur with FB consumption. A detailed report is provided in Attachment 5 – Nutrition Assessment and is summarised below.

The potential for FB to result in a health risk associated from the over-consumption of the requested vitamins and minerals has also been examined. A detailed report is provided in Attachment 6 – Risk Assessment – Micronutrients[25], and is summarised below.

The methodology used for dietary modelling of the vitamins and minerals is described in Attachment 7 – Dietary Modelling Methodologies for Nutrient Intake Assessment.

In the case of food additives, the technological justification for the use of these food additives is considered in Attachment 9 – Food Technology Report. Once the technical justification has been established, the potential for health risks associated with the use of the food additives in FB has been examined. A detailed report that examines the nature of any potential hazard, an estimate of the dietary exposure from the substitution of FB for other available beverages, and a characterisation of the risk is provided in Attachment 8 – Risk Assessment – Food Additives, and is summarised below.

5.1.1 Nutrition Assessment

The purpose of the nutrition assessment is to determine the nutrition and health need for adding the requested vitamins and minerals to FB, and to examine the health risks to the broader Australian and New Zealand populations from the sugars and energy content of FB. The overarching approach to the nutrition assessment has been the consideration of the requested vitamins and minerals in the context of FSANZ's statutory objectives, including having regard to the Policy Guideline.

The Policy Guideline permits the voluntary addition of vitamins and minerals to food *where there is a need for increasing the intake of a vitamin or mineral in one or more population groups demonstrated by actual clinical or sub-clinical evidence of deficiency or by data indicating low levels of intake*. For an assessment of the 'nutrition and health need', the first step was to determine if there is a nutritional need, by assessing the extent of existing inadequate vitamin and mineral intakes, or alternatively the extent of vitamin and mineral deficiencies within Australia and New Zealand. If the vitamin or mineral intake was identified as being inadequate, or the vitamin or mineral status assessed as being deficient, then that vitamin or mineral was regarded as having demonstrated nutritional need and was not further considered in relation to health benefit.

The Policy Guideline also states that voluntary fortification can be permitted where there is *generally accepted scientific evidence that the fortification can deliver a health benefit*. This potential for a 'health benefit' was investigated for those vitamins and minerals that do not have an existing level of inadequacy or deficiency, as a second step in the assessment of 'nutrition and health need'.
The process used to assess the nutrition and health need for a vitamin or mineral is illustrated in Figure 1 below. It also shows the results of this process for each of the requested vitamins and minerals. The results were based on the following criteria at each step:

[25] For the purpose of this report the term 'micronutrient' is used for vitamins and minerals

- Step 1: - Inadequate intakes were defined as the situation where 3% or more of the whole population or two sub-population groups have an intake of a vitamin or mineral at a level below the Estimated Average Requirement (EAR)[26]. Six vitamins and minerals could not be assessed on the basis of inadequacy as they had no EAR (beta-carotene, biotin, pantothenic acid, chromium, manganese) or because dietary intake data was not available for this assessment (molybdenum).

  A level of deficiency was established for a vitamin or mineral if there was scientific evidence to show that clinical or sub-clinical deficiency states were prevalent in Australian and New Zealand populations.

- Step 2: - The potential for a 'health benefit' was determined by criteria established by FSANZ in relation to the levels of generally accepted scientific evidence; the full details of these criteria can be found in Attachment 5.

Figure 1: Assessment of Nutrition and Health Need

<table>
<tr><th colspan="2" rowspan="2">Vitamin / Mineral</th><th>Step 1</th><th colspan="2">Step 2</th><th rowspan="2">Existence of a Nutrition and Health Need</th></tr>
<tr><th>Nutrition Need</th><th colspan="2">Health Benefit</th></tr>
<tr><td rowspan="10">Group 1</td><td>Riboflavin</td><td rowspan="10">> 3% of population intakes were below the EAR,

OR

Evidence of deficiency existed</td><td rowspan="10"></td><td rowspan="10"></td><td rowspan="10">Identified as having a nutrition and health need</td></tr>
<tr><td>Folate</td></tr>
<tr><td>Vitamin B_6</td></tr>
<tr><td>Vitamin D</td></tr>
<tr><td>Vitamin E</td></tr>
<tr><td>Calcium</td></tr>
<tr><td>Iodine</td></tr>
<tr><td>Iron</td></tr>
<tr><td>Magnesium</td></tr>
<tr><td>Selenium</td></tr>
<tr><td rowspan="13">Group 2</td><td>Zinc</td></tr>
<tr><td>Vitamin A (retinol)</td><td rowspan="6">< 3% of population had intakes below the EAR,

AND

No evidence of deficiency</td><td rowspan="13">Assessed for the potential to deliver a health benefit

(none met FSANZ criteria for a 'health benefit')</td><td rowspan="13"></td><td rowspan="13">No nutrition and health need identified</td></tr>
<tr><td>Thiamin</td></tr>
<tr><td>Niacin</td></tr>
<tr><td>Vitamin B_{12}</td></tr>
<tr><td>Vitamin C</td></tr>
<tr><td>Copper</td></tr>
<tr><td>Phosphorus</td><td rowspan="7">Unable to assess for inadequacy,
AND
No evidence of deficiency</td></tr>
<tr><td>Beta-carotene</td></tr>
<tr><td>Chromium</td></tr>
<tr><td>Biotin</td></tr>
<tr><td>Pantothenic acid</td></tr>
<tr><td>Manganese</td></tr>
<tr><td>Molybdenum</td></tr>
</table>

Figure 1 shows that Group 1 met all criteria for demonstration of a nutrition and health need. Therefore, the vitamins and minerals with a nutrition and health need in support of their addition to FB are as follows:

[26] The EAR is a value representing the median requirement for a vitamin or mineral. The details on the specific EARs that were allocated to each vitamin and mineral can be found in Attachment 5.

Vitamins	Minerals
Riboflavin	Calcium
Folate	Iodine
Vitamin B_6	Iron
Vitamin D	Magnesium
Vitamin E	Selenium
	Zinc

As a final component of the nutrition assessment, FSANZ reviewed the energy and sugar content of FB and their potential impact on the overall diet. A potential risk was identified, that intakes of sugar-containing beverages (including those with a natural sugar content) would increase as a result of FB expanding the beverage sector of the market. There is evidence to show that consumption of standard sugar-containing beverages (e.g. soft drinks) can significantly increase the overall intake of energy within the diet and thus contribute to weight gain. Therefore, a potentially higher beverage intake resulting from the approval of Application A470 will likely increase the intake of sugar and energy in the Australian and New Zealand populations, and is a potential health risk.

5.1.2 Risk Assessment – Micronutrients

5.1.2.1 Micronutrients without risk for the general population

For the following vitamins and minerals, it is concluded that addition to FB at a level of 25% of the RDI / 600 ml (100% of RDI per 600 ml for vitamin C) would raise no public health and safety concerns for any sector of the population: beta-carotene, thiamin, riboflavin, niacin, folate, vitamin B_6, vitamin B_{12}, vitamin C, vitamin D, vitamin E, pantothenic acid, calcium, magnesium, phosphorus and selenium.

5.1.2.2 Micronutrients with some risk for sensitive subpopulations

For the following minerals, it is concluded that while the general population is without risk, there may be a risk for certain sectors of the population:

Copper: Individuals with Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis may respond adversely to copper in FB at a level of 0.75 mg per 600 ml.

Iodine: Individuals with thyroid disorders or a long history of iodine deficiency may respond adversely to iodine in FB at a level of 37.5 μg per 600 ml.

Iron: Individuals who are homozygous for hereditary haemochromatosis are susceptible to iron overload, even at normal dietary iron intakes, and are generally advised to avoid iron-supplements and highly iron fortified foods. As the majority of individuals with this condition are not diagnosed until sufficient iron has accumulated to produce adverse effects, the addition of iron to FB at a level of 3 mg per 600 ml serve may be a concern to these individuals.

5.1.2.3 Micronutrients with some risk for specific age groups

For the following vitamins and minerals, there are potential risks for specific age groups if they were permitted to be added to FB:

Vitamin A: The dietary modelling results suggest that young children consuming FB may have excess intakes of retinol for several years and therefore be at risk of hepatoxicity. For all other age groups and life-stages, there is no appreciable risk posed by excess intake of retinol. There are potential safety concerns for children up to the age of 3 years, and maybe up to 6 years, with the addition of retinol to FB at a level of 187.5 μg in a 600 ml serve.

Manganese: An upper level of intake (UL) could not be established because of limitations with the human data and considerable uncertainty with the animal toxicity studies. The available data suggests that the margin between the intake level producing adverse effects in humans and animals and the estimated intake from food is very small. Based on the severity of the potential adverse effect (neurotoxicity), additional oral exposure to manganese beyond the levels normally present in food and beverages could pose a public health and safety risk. Therefore, there are potential safety concerns with the addition of manganese to FB at a level of 1.25 mg in a 600 ml serve.

Zinc: Dietary modelling indicated that children up to 8 years of age, who are consumers of a diet high in zinc, are predicted to exceed the UL for zinc. For adolescents up to the age of 18 years, who are consumers of a diet high in zinc, the intake is predicted to be 80% of the UL of zinc. Chronic zinc toxicity is associated with symptoms of copper deficiency. These adverse effects include anaemia, neutropaenia and impaired immune response. Furthermore, the potential contribution from other sources (e.g. dietary supplements) have not been taken into consideration in the dietary intake assessment. The intake of zinc may therefore be underestimated for children and adolescents up to the age of 18 years and, for this group, FB at a level of 3 mg per 600 ml serve pose a public health and safety risk.

5.1.2.4 Micronutrients with insufficient data to assess risk

For the following vitamins and minerals there was insufficient data to characterise the potential risk:

Biotin and Chromium: Due to insufficient data on potential adverse effects and only limited food composition data it was not possible to establish an UL for biotin and chromium or to undertake a complete dietary intake assessment. In the absence of sufficient information, it is currently not possible to evaluate the safety of the addition of biotin and chromium to FB.

Molybdenum: An UL has been established based on reproductive effects in rats. While some food composition data are available for molybdenum, it is insufficient to undertake a complete dietary intake assessment at this present time. In the absence of sufficient information, it is not currently possible to evaluate the safety of the addition of molybdenum to FB.

5.1.2.5 Assessment of permitted forms

For pantothenic acid, biotin, chromium, manganese, molybdenum and selenium, currently there are no forms permitted in Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions. The requested permitted forms for pantothenic acid, copper and selenium have been included in evaluations of their toxicity, and are considered to be acceptable as permitted forms.

5.1.3 Risk Assessment – Food Additives

A risk assessment has been conducted on 57 food additives/additive groups requested by the Applicant to be added to FB. All of these food additives are currently permitted in Standard 1.3.1 – Food Additives.

5.1.3.1 Hazard identification and characterisation

FSANZ has not performed an independent hazard identification and characterisation of the 57 food additives, but has relied upon the assessment reports from the Joint FAO/WHO Expert Committee on Food Additives (JECFA). JECFA has established numerical Acceptable Daily Intakes (ADI)[27] for some, and established an ADI 'not specified'[28] for many in this group. For several, there was not enough data available to perform an assessment.

5.1.3.2 Dietary exposure assessment

Dietary exposure assessments were conducted only on those food additives with a numerical ADI, i.e., those where there was a potential for safety concerns if the exposure significantly increased. For the majority of the food additives, the dietary exposure either did not change or changed very little when FB were included in the modelling.

5.1.3.3 Risk Characterisation

Food additives which have an ADI 'not specified' or an ADI which is sufficiently high to allow GMP use for the additive in food

For the additives with an ADI 'not specified', dietary exposure assessments were not conducted, since these food additives are considered to have low toxicity and would not be expected to pose a public health and safety risk as a result of their use in FB.

Food additives that have a numerical ADI

For the additives for which a numerical ADI existed, dietary exposure assessments were conducted. The risk characterisation concluded that the addition of the following food additives to FB at the requested concentration would pose no public health and safety risk: tartrazine, quinoline yellow, sunset yellow, azorubine, amaranth, ponceau 4R, allura red, indigotine, brilliant blue, fast green, brilliant black, brown HT, sorbates, sulphites, calcium disodium EDTA, sucrose acetate isobutyrate, glycerol ester of wood rosin, and dioctyl sodium succinate.

In the case of annatto, benzoates, acesulphame potassium (ace K), saccharin and alitame, the dietary exposure assessment predicted that there could be an increase in exposure as a result of their use in FB.

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[27] JECFA defined the ADI *as an estimate of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk*

[28] JECFA defined the term '*ADI not specified' to mean that, on the basis of available data (chemical, biochemical, toxicological, and other), the total daily intake of the substance, arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not represent a hazard to health.*

This apparent increase is the result of the assumptions made about which beverages were substituted with FB in the dietary model used, and the current permissions in these particular beverages. Even taking into account these apparent increases in exposure, no public health and safety concerns were raised.

5.1.4 Risk assessment summary

5.1.4.1 Vitamins and minerals

The table below summarises the findings of the nutrition assessment and the risk assessment in relation to the addition of vitamins and minerals to FB.

Risk Assessment findings on the requested vitamin and mineral additions

Vitamin and Mineral	Outcomes of the Nutrition Assessment	Outcomes of the Risk Assessment - Micronutrients	Eligibility for Addition to FB (Combined outcomes of the Nutrition Assessment and Risk Assessment – Micronutrients)
Vitamins			
Vitamin A (retinol)			
Beta-carotene		✓	
Thiamin		✓	
Riboflavin	✓	✓	✓
Niacin		✓	
Folate	✓	✓	✓
Vitamin B_6	✓	✓	✓
Vitamin B_{12}		✓	
Vitamin C		✓	
Vitamin D	✓	✓	✓
Vitamin E	✓	✓	✓
Biotin		*Not assessed*	
Pantothenic acid		✓	
Minerals			
Calcium	✓	✓	
Chromium		*Not assessed*	
Copper		✓	
Iodine	✓	✓	✓
Iron	✓	✓	✓
Magnesium	✓	✓	✓
Manganese			
Molybdenum		*Not assessed*	
Phosphorus		✓	
Selenium	✓	✓	✓
Zinc	✓		

Whilst iodine and iron meet the nutrition assessment criteria and do not raise public health and safety concerns for the general population, there were concerns identified for sensitive subpopulations in relation to these nutrients. Risk management strategies may be considered necessary to protect these vulnerable individuals.

5.1.4.2 Macronutrients

In the context of the overall diet, there is the possibility that beverage intakes will increase as a result of FB expanding this sector of the market. This increased beverage intake is likely to increase the intake of sugar-containing beverages in the diet, and therefore increase the intake of energy via increased sugar consumption. This impact on the diet is a risk that may require management if FB are permitted to contain added vitamins and minerals.

5.1.4.3 Food additives

On the basis of currently available information, it can be concluded that the addition of the requested 57 food additives/additive groups to FB would not raise any public health and safety concerns.

5.2 Risk Management

On the basis of FSANZ's risk assessment the following sections discuss approaches to managing any identified public health and safety risks, and other broader issues requiring consideration in the development of regulations for FB.

5.2.1 Target group of formulated beverages

The Applicant identified the target group for these products as 'those consumers who are looking for these types of beverages', citing that their Application is in response to Australian consumers who are purchasing FB imported from or through New Zealand. The indicative age range of the target group appears to be adults aged 20-39 years old, with industry data provided by the Applicant showing this group accounts for approximately 70% of the total volume consumed of one leading FB product.
The Applicant has indicated that the marketing of FB would be aimed at adults, showing FB to be more interesting tasting beverages which contain low levels of vitamins and minerals. Industry research reports that quenching thirst is a key reason for selecting FB for both men and women, but more so for women. Women consumers of FB are also seeking more energy and health, where men tend to be more likely to seek rehydration from these products.

Market intelligence suggests the drivers for FB would be their appeal to young people (16-34 years) who are aware of the fashionable image and compatibility with their lifestyle, rising consumer interest in the role of diet in health and a growing desire to take a more active role in promoting and optimising personal health and wellbeing.

In response to the Initial Assessment Report, submitters identified various target groups including those who currently consume soft drinks, current supplement users who may substitute FB for supplements, the 'worried well' with disposable cash, and children and youth who are influenced by advertising and popularity.

The incidental target group for FB appear to be children and teenagers. Whilst the Applicant has advised FB will not be targeted towards children, industry data on a leading brand of FB reports 20% volume consumption by 12-19 year olds. In addition, FSANZ is aware that some manufacturers are actively promoting water-based beverages with added vitamins and minerals to children, with products being developed and labelled specifically for children.

One product currently available in Australia is labelled as a 'sportswater for kids'. Another Australian FB manufacturer has announced that they will be launching a 'junior' product aimed at children aged 5-12 years old in July 2005. A marketing campaign by one New Zealand manufacturer uses colourful cartoon images of youths and language such as 'cool', 'wickedest' and 'funky' including promotions and giveaways to promote their product.

5.2.2 Characterising the product category of formulated beverages

5.2.2.1 Purpose

At Initial Assessment, the nature of Application A470 made it necessary to consider the purpose of FB, particularly as the Applicant had not ascribed any particular purpose to FB other than to respond to consumer demand. They had however requested vitamin and mineral permissions generally exceeding those permitted in general-purpose food.

Determining the appropriate 'purpose' category for FB is fundamental to the assessment of the Application as it directs the appropriate regulatory approach particularly as policy guidance on the addition of vitamins and minerals to food excludes special purpose food.

Currently the Code distinguishes two broad categories of purpose:

- General-purpose food i.e. food that is widely available for consumption by the general community (the vast majority of foods); and

- Special-purpose food i.e. food that is produced to satisfy particular dietary requirements which exist because of a particular physical or physiological need, and/or specific diseases and disorders. Part 2.9 of the Code contains the standards for special-purpose food e.g. infant formula and foods, formulated meal replacements and FSSF.

At Initial Assessment a third category of 'supplemental' purpose was also discussed. This purpose was identified during the development of a standard for FCB (Application A394) in 2001 and sits outside the conventional nutritional paradigm. The development of the Policy Guideline, which places fortification with vitamins and minerals predominantly in a nutritional paradigm, means consideration of 'supplemental' purpose is no longer appropriate.

The Initial Assessment Report suggested that FB were not special-purpose food, as they did not address situations of particular physiological need. Submitters at Initial Assessment agreed with this, with the majority supporting regulation as a general-purpose food.

The Applicant has subsequently amended Application A470 and is now seeking lower levels of vitamin and mineral additions to FB (i.e. 25% RDI with the exception of vitamin C, at 100% RDI, per a 600 ml reference quantity). As such, it is appropriate that FB are regulated as general-purpose food. Consequently, any permission to add vitamins and minerals to FB will be incorporated in Standard 1.3.2 of the Code.

5.2.2.2 Definition

At Initial Assessment, the need to clearly define FB was raised as a key issue to ensure that the product category of FB is unambiguously described and does not inadvertently act as a means to circumvent other, more appropriate food standards. It was suggested that the definition could include reference to elements of composition and/or purpose. As FB are to be considered as general-purpose food, composition therefore represents the most suitable defining feature for FB.

In their submission to the Initial Assessment Report, the Applicant provided a suggested definition for FB of 'a water-based product, that may be sweetened and/or flavoured; may or may not contain juice; and that contains a mix of added vitamins and/or minerals'.

Other industry submitters supported a definition that would encompass a wide range of non-alcoholic water-based beverage products, including FCB and both carbonated and non-carbonated water-based drinks including those with flavours and fruit ingredients. The original Application however specifically excluded caffeinated beverages, and since Initial Assessment the Applicant has withdrawn carbonated drinks from the scope of the Application.

In August 2004, the Applicant provided further information in relation to the likely range of products that may be produced as FB. These included:

- sugar sweetened waters (may contain a blend of sugar/non-nutritive sweeteners);
- unsweetened waters (with no added sweeteners);
- non-nutritive sweetened waters;
- sugar sweetened or non-nutritive sweetened, still fruit drinks and fruit juice drinks with juice added as an ingredient;
- unsweetened, flavoured, still fruit drinks and fruit juice drinks with juice added as an ingredient; and
- fruit juice/drink cordials which may contain nutritive and non-nutritive sweeteners.

'Water-based beverage' is currently not defined in the Code but rather is recognised within the definition of a non-alcoholic beverage in Standard 2.6.2 – Non-alcoholic Beverages and Brewed Soft Drink as *a water-based beverage which may or may not contain other foods, except for alcoholic beverages*. From this context its broad composition can be inferred to include products whose ingredient composition ranges from mostly water to, those fruit drinks[29] containing mostly juice with a small amount of added water.

Given the proposed composition of FB as described by the Applicant above, FB can be considered to be a sub-category of water-based beverages, which may or may not include fruit ingredients. Therefore, FSANZ is proposing the following definition for inclusion in Standard 2.6.2.

[29] The Code requires fruit drink to contain at least 5% (except in the case of passionfruit which requires 3.5%) specified fruit ingredients.

Formulated Beverage is:

> non-carbonated, water-based flavoured beverage that contains added vitamins and/or minerals, prepared from one or more of the following:
>
> - water; and
> - fruit juice; and
> - fruit purée; and
> - concentrated fruit juice; and
> - concentrated fruit purée; and
> - comminuted fruit; and
> - orange peel extract; and
> - mineral water; and
> - sugar.

This definition allows for ingredient composition as requested by the Applicant noting that the Code considers non-nutritive sweeteners and flavourings as food additives. Permissions for food additives are discussed in Section 5.2.6.

5.2.2.3 Per cent fruit juice composition

The above definition although considered explicit in terms of compositional description does not necessarily distinguish FB from other water-based beverages currently regulated in the Code. For instance, there is a potential overlap of FB with other beverages such as fruit drinks, particularly those containing at least 25% fruit ingredients that are permitted to contain a small number of added vitamins in Standard 1.3.2 according to the modified restoration[30] principle.

As discussed previously, it is important that FB are unambiguously described and do not inadvertently act as a means to circumvent other, more appropriate food standards. As FSANZ is not proposing to require additional labelling specific to FB, a compositional requirement to distinguish FB from other fruit drinks is appropriate.

For this reason FSANZ is proposing a maximum limit for fruit ingredients of 24% so that FB are clearly distinguished from other fruit juice based products. This should also assist consumers to discern FB from other fruit drinks.

5.2.3 Appropriateness of food vehicle

It is important that consideration be given to the suitability of the requested food vehicle i.e. water-based beverages in terms of its nutritional appropriateness as a vehicle for voluntary fortification.

Submitters to the Initial Assessment Report varied in their comments about whether the composition of the food vehicle should be taken into account. The complementary medicine sector believed that the composition of the food vehicle was important particularly given the potential for FB to be consumed in large amounts.

[30] The principle of modified restoration is described in the Fortification Policy Guideline.

In contrast, some industry submitters believed that the food vehicle composition was of no regulatory concern as the NIP would declare the nutritional quality of the product, however another manufacturer believed it would be important to keep the energy content of these beverages low and to encourage water intake. The public health and government sectors believed that the composition of the food vehicle was important to consider particularly given the rising prevalence of obesity and dental erosion from chronic intake of acidified beverages.

Based on the FB definition above, the following beverage types could be used as potential vehicles for voluntary fortification:

- water ± sugar ± non-nutritive sweeteners;
- fruit juice drinks ± sugar ± non-nutritive sweeteners; and
- cordials ± sugar ± non-nutritive sweeteners.

The Policy Guideline states that permission to voluntarily fortify *should not promote consumption patterns inconsistent with the nutrition policies and guidelines of Australia and New Zealand* and *should not promote increased consumption of foods high in salt, sugar or fat.*

In accordance with the Policy Guideline, FSANZ's Fortification Implementation Framework recognises that the nature of the food vehicle can have nutritional consequences which warrant consideration when assessing any new proposed voluntary fortification measure.

On this basis, FSANZ will focus primarily on the total sugar and energy content of the above beverage types when assessing the appropriateness of the potential food vehicle.

5.2.3.1 Total sugar and energy content of formulated beverages

The table below shows the total sugar and energy content for commonly consumed water-based beverages and FB currently on the market in both Australia and New Zealand.

Beverage Category	**Sugar (g/100 ml)**	**Energy (kJ/100 ml)**
Carbonated, sugar based soft drinks*	9.1 – 14.8	155 - 282
Fruit Juices*	5.3 – 14.1	103 - 256
Fruit Juice Drinks*	9.4 – 15.2	164 – 259
Cordials (ready to drink)*	9.7 - 14.8	166 - 196
FB water, flavoured +/- added sugar‡	0.0 – 2.3	2-41
FB 2-5% Fruit Juice‡	2.0 - 5.4	38 - 34
FB > 5% Fruit Juice‡	9.7 - 11.3	171 - 196

* = Data derived from *AUSNUT Special Edition (2) – Australian Food and Nutrient Database for Nutrient Labelling: Release 2* Australia New Zealand Food Authority (2002)

‡ = Data derived from FSANZ's market research (Section 4.6)

Although not all FB contain high levels of sugar, products of this type are contained within the present scope of the Applicant's request. The table above shows that some FB currently contain sugar levels similar to amounts found in carbonated soft drinks, cordials and fruit juices and drinks.

If the addition of vitamins and minerals to FB increases these products nutritional attractiveness and thus marketability, there is potential to increase the sugar and energy intake of the population and is therefore inconsistent with policy guidance.

5.2.3.1.1 Serving size of formulated beverages

As indicated in Section 4.5.2, the serving sizes of FB are generally larger than the standard serving size for soft drinks, juices and cordials. Market intelligence indicates that the intended purpose of FB is to provide a thirst quenching beverage and to aid hydration, hence the larger serving size. This is reflected in the Applicant's request that the reference quantity for FB be 600 ml.

One currently available FB, targeted at children, and available as a 500 ml serve, claims to have one third of the sugar content when compared with carbonated soft drinks. This comparison, however, is on a 100 ml basis but given the increased serving serve (i.e. 500 ml) as opposed to 375 ml (i.e. one standard can of soft drink), the difference is less apparent.

If consumers substitute FB for carbonated soft drinks, juices and cordials, the potential exists to increase intakes of sugar and energy due to the larger serving size of FB.

5.2.3.1.2 Risk of overweight and obesity

The increased consumption of sweetened drinks, such as soft drinks, is now recognised as an important, independent risk factor for the development of obesity in school aged children (Krebs-Smith, 2001; Ludwig *et al*., 2001; Somerset, 2003; Berkey *et al*., 2004; James *et al*., 2004). It is widely acknowledged that childhood obesity is reaching epidemic proportions[31]. Since 1985, it is estimated that there has been nearly a 1% annual increase in the rates of overweight and obesity in children aged seven to 11 years in Australia (*personal communication*, Boyd Swinburn 2005).

As part of its risk assessment, FSANZ examined the potential nutritional impact of FB, including macronutrient intakes, on the population. In the Nutrition Assessment (at Attachment 5), it is concluded that there is a *risk of increased energy intakes within Australian and New Zealand diets from proposed FB permissions (via increased sugar-containing beverage consumption).* In assessing the appropriateness of the food vehicle, it is apparent that there is potential for FB to increase both the sugar and energy intake of the population.

In order to effectively manage this risk, especially in children, FSANZ is proposing to restrict the amount of sugar in FB (refer to Section 5.2.4.2.). This will help ensure that FB do not promote the increased consumption of food high in sugar and thus is in accordance with FSANZ's statutory objective of protecting public health and safety and subsequently the 'Specific Order' Policy Principles for voluntary fortification.

5.2.3.1.3 Potential to mislead consumers as to the nutritional quality of the fortified food

As part of its assessment in determining the appropriateness of the food vehicle, FSANZ has examined the potential for consumers to be misled as to the nutritional quality of the fortified food.

[31]World Health Organization (2005) *Obesity and Overweight* http://www.who.int/dietphysicalactivity/publications/facts/obesity/en/print.html Accessed 20 April 2005.

This is in accordance with FSANZ's second and third priority statutory objectives and the Specific Order' Policy Principle for voluntary fortification which states that *the fortification of a food, and the amount of fortificant in the food, should not mislead the consumer as to the nutritional quality of the fortified food.*

As part of FSANZ's 2003 FTDS consumer research, consumers' perceptions on the importance of the composition of the food vehicle were investigated. Most participants did not object to the addition of vitamins and minerals to various food categories, with the exception of those food categories specifically marketed to teenagers and children because of their reduced likelihood to read labels or to be 'unfairly' persuaded to buy the products. A minority view was that added vitamins and minerals should not be permitted in 'unhealthy' foods given the potential for consumers to be misled by an emphasis on the positive attributes of the vitamins and minerals without being able to balance the potentially negative attributes such as energy and total sugar content.

In the Nutrition Assessment (at Attachment 5), it was concluded that there is a risk that consumers could be misled as to the nutritional quality of FB. Some FB have similar or higher amounts of sugar when compared to many soft drinks. The addition of vitamins and minerals can enhance their nutritional attractiveness of FB, resulting in many consumers being unaware that they are consuming significant amounts of sugar and energy due to the larger serving sizes and high sugar content of some FB. This assessment supports the concerns raised by many submitters in response to the Initial Assessment for Application A470, and the views expressed by participants in FSANZ's consumer research.

A compositional restriction on the amount of sugar permitted in FB should minimise the risk of consumers being misled as to the nutritional quality of FB.

5.2.3.2 Cordial Consumption in Australia and New Zealand

The Applicant has requested cordials be included in the scope of the Application. In determining the suitability of cordial as a potential food vehicle, FSANZ has considered:

- the potential target group;
- possible public health and safety risks;
- consumers' perceptions; and
- submitters' comments as to the nutritional quality of fortified food.

National Nutrition Survey data has been used to determine which population groups consume cordial. The percentage of each population group and the mean and 95th percentile intakes of cordials for consumers of cordials, are presented in Figures 2 and 3, respectively. In general, a larger proportion of children drink cordials, however teenagers consume the largest volume of cordials for the population groups assessed.

Figure 2: Percentage of Australian and New Zealand population groups consuming cordial, as recorded in the 1995/1997 National Nutrition Surveys

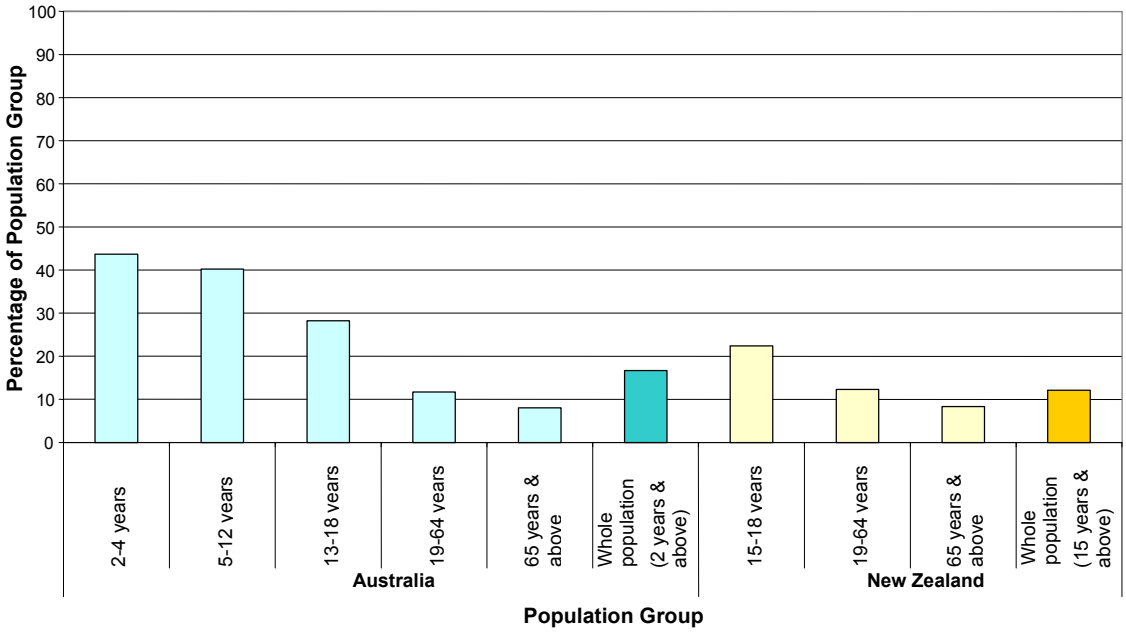
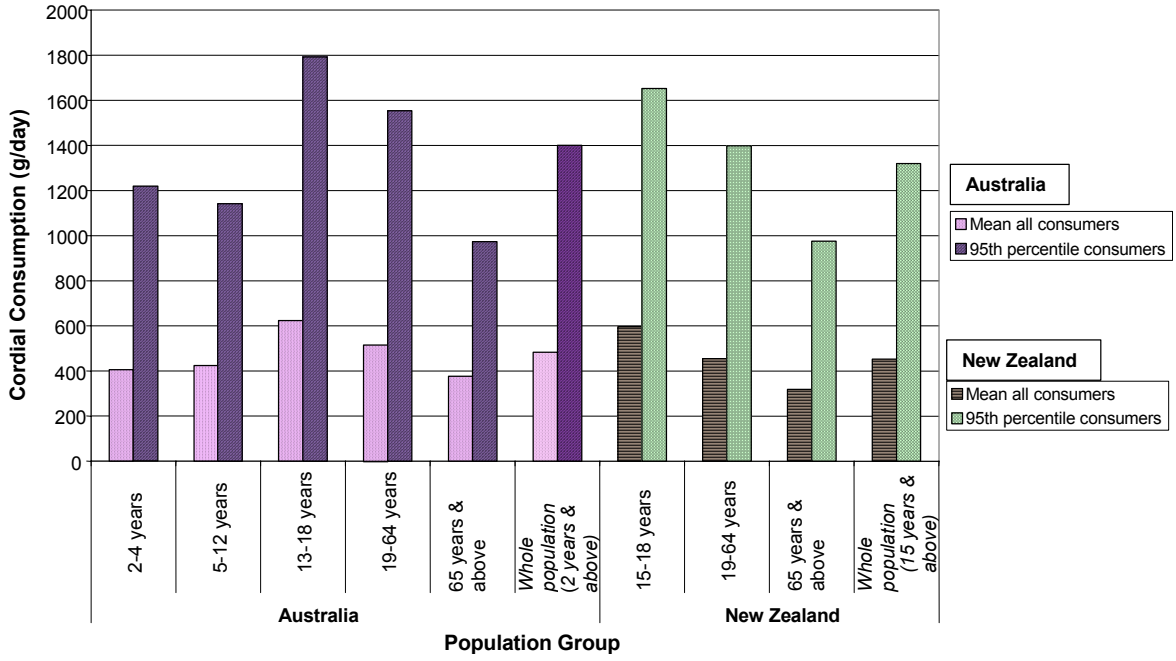
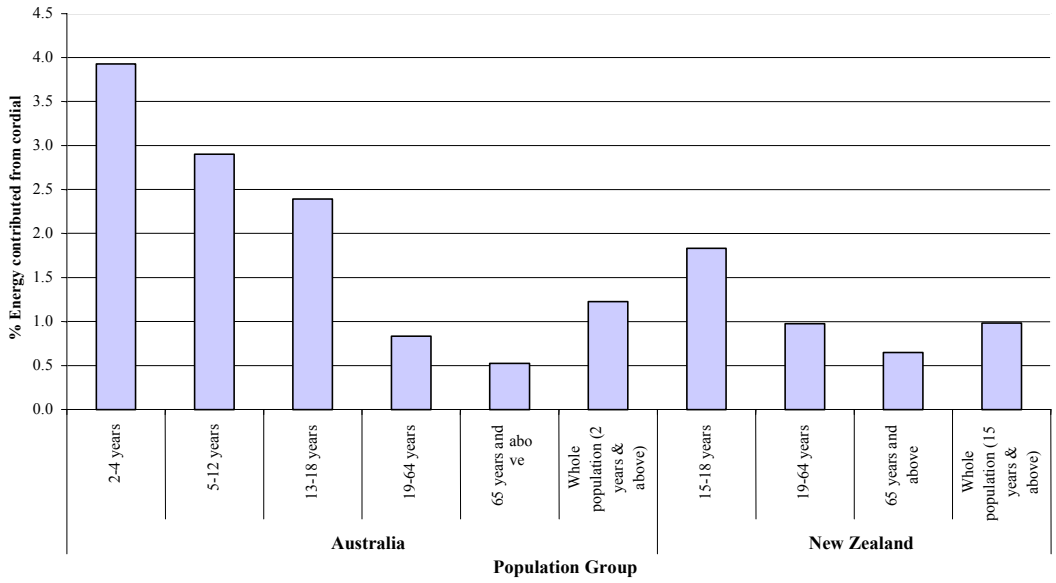


Figure 3: Mean and 95th percentile consumption of cordials for Australian and New Zealand consumers of cordials, as recorded in the 1995/1997 National Nutrition Surveys



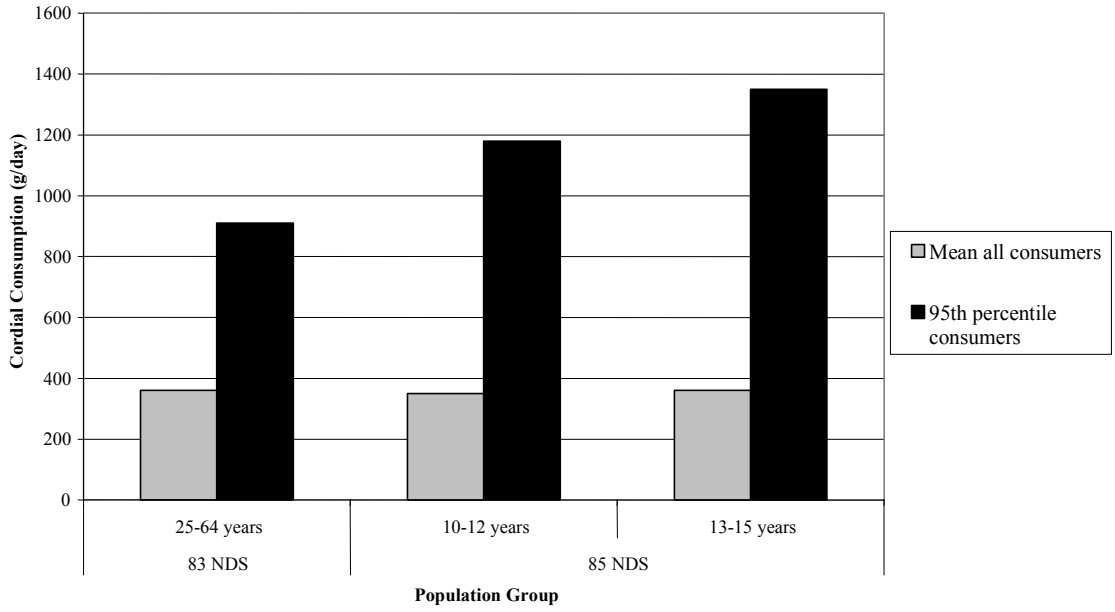
Using the FSANZ 1995/1997 National Nutrition Survey data, FSANZ has assessed the energy contribution from cordials as a percentage of the total energy intake for the Australian and New Zealand population groups as shown in Figure 4. This shows that the contribution of cordial to total energy intake is greatest in younger age groups.

Figure 4: Percentage of energy contributed from cordial consumption in the Australian and New Zealand diet as recorded in the 1995/1997 National Nutrition Surveys



FSANZ also sought to determine consumption trends with respect to cordial intakes. FSANZ compared the estimated mean and 95th percentile consumption of cordials from the 1983 National Dietary Survey of adults and the 1985 National Dietary Survey of school children (83 NDS and 85 NDS respectively) with the 1995 National Nutrition Survey. The population sub-groups examined were 25-64 years for the 83 NDS and 10-12 years and 13-15 years for the 85 NDS. The mean and 95th percentile for cordial consumption 1983/1985 National Dietary Surveys is shown in Figure 5 below.

Figure 5: Mean and 95th percentile consumption of cordials for Australian consumers of cordials as recorded in the 1983/1985 National Dietary Surveys



Comparison of the estimated cordial consumption between 1983/1985 to 1995 suggests that cordial consumption has increased in the period between the surveys. However, it is important to note that the data are not directly comparable due to the different methodologies used and the different age groups assessed. Therefore this information is only indicative. However, in support of this apparent trend, the 2003 FSANZ survey[32] on the consumption of intense sweeteners also showed an increase in cordial consumption (both sugar sweetened and intense sweetened) from 1994 until 2003 for consumers aged 12-39 years.

Children and teenagers have been identified as a potential incidental target group for FB (Section 5.2.1). FSANZ's Product Surveys shows that some products that could potentially fall under the FB category are specifically targeted towards children. As cordials are one of the beverage types requested by the Applicant as a potential vehicle for voluntary fortification, it is likely that children and teenagers would be the main target group for this type of FB.

As previously discussed in Section 5.2.3.1.2, the increased consumption of sweetened drinks is recognised as a risk factor for the development of obesity in school aged children. Given that the addition of vitamins and minerals to cordials could potentially increase the nutritional attractiveness and thus marketability of these products, there is potential to increase cordial consumption in children and teenagers. FSANZ recognises that cordial consumption may also inadvertently result in potentially larger quantities of vitamins and minerals being unintentionally consumed through varied preparation of cordials.

At Initial Assessment submitters expressed concern regarding the appropriateness of cordial as a suitable food vehicle. Their concerns were based on cordials being particularly targeted towards children and the research linking the consumption of high sugar beverages to increased rates of childhood obesity. These concerns are similar to the views expressed by participants in the FSANZ 2003 FTDS consumer research survey who believe that vitamins and minerals should not be added to food categories specifically marketed to teenagers and children. The level of community concern regarding the appropriateness of cordial as a potential food vehicle, has previously led an Applicant to withdraw cordial from their Application (Application A424 - Fortification of Foods with Calcium).

On the basis of the potential target group i.e. children, the identified public health and safety risks and stakeholder concerns, FSANZ has determined that cordials are not appropriate food vehicles for voluntary fortification.

5.2.3.2.1 Conclusion

In assessing the appropriateness of the food vehicle, FSANZ has examined the potential for FB to adversely impact on public health and safety. Specifically, FSANZ has assessed the issues identified in the Nutrition Assessment including total sugar and energy content, and serving size of FB. In addition, FSANZ has considered the potential for the requested FB product range to mislead consumers as to the nutritional quality of the fortified food. On this basis, FSANZ is proposing to restrict the sugar content of FB and exclude cordial from the scope of the Application.

[32] FSANZ (2004) *Consumption of Intense Sweeteners in Australia and New Zealand. Benchmark Survey 2003.* Evaluation Report Series No.8.

5.2.4 Composition of formulated beverages

5.2.4.1 Vitamin and Mineral Additions

The regulatory controls applied to the addition of vitamins and minerals are firstly guided by the determination of the 'purpose' category as discussed in Section 5.2.2.1 above. As FB are considered general-purpose foods, the Policy Guideline is directly relevant to decisions on the regulatory control of the vitamin and mineral additions to FB.

As previously discussed (section 4.2.1) the Policy Guideline consists of 'High Order' Policy Principles that are FSANZ's section 10 objectives, which take precedence over the 'Specific Order' Policy Principles for voluntary fortification. FSANZ's *Fortification Implementation Framework* provides the context for standards development in relation to voluntary fortification particularly as it relates to FSANZ's statutory obligations.

5.2.4.1.1 Public Health and Safety

The protection of public health and safety is paramount to the consideration of permitting the voluntary addition of vitamins and minerals to FB. The protection of public health and safety is the primary objective of the FSANZ Act. Additionally, public health and safety underpins the Policy Guideline which provides direction in relation to the need for fortification as well as assuring safety of any potential fortification.

The first 'Specific Order' Policy Principle *states that the voluntary addition of vitamins and minerals should be permitted only:*

- *Where there is a need for increasing the intake of a vitamin or mineral in one or more population groups demonstrated by actual clinical or sub-clinical evidence of deficiency or by data indicating low levels of intake.*

or

- *Where data indicates that deficiencies in the intake of a vitamin or mineral in one or more population groups are likely to develop because of changes taking place in food habits.*

or

- *Where there is generally accepted scientific evidence that an increase in the intake of a vitamin and/or mineral can deliver a health benefit.*

or

- *To enable the nutritional profile of foods to be maintained at pre-processing levels as far as possible after processing (through modified restoration).*

or

- *To enable the nutritional profile of specific substitute foods to be aligned with the primary food (through nutritional equivalence).*

The first and third conditions of this 'Specific Order' Policy Principle are the most relevant to consideration of Application A470.

In addition, the Policy Guideline also states that *permissions to fortify should ensure that the added vitamins and minerals are present in the food at levels which will not have the potential to result in detrimental excesses or imbalances of vitamins and minerals in the context of total intake across the general population.*
FSANZ's risk assessment has on the basis of 'need' and safety determined that the following vitamins and minerals can be permitted for addition to FB in the amounts requested by the Applicant. These are:

Vitamins	Minerals
Riboflavin	Calcium
Folate	Iodine
Vitamin B_6	Iron
Vitamin D	Magnesium
Vitamin E	Selenium

FSANZ's risk assessment did identify certain sensitive subpopulation groups who may be at increased risk from the addition of copper, iodine and iron to FB.

The risk assessment found that for certain sensitive individuals, the addition of copper to FB would pose a risk. As FSANZ is not proposing to allow the addition of copper to FB, this issue does not require further consideration.

In the case of iodine, the risk assessment indicates that the addition of iodine to FB is predicted to have only a relatively small impact on dietary iodine intake for the general population. However individuals with thyroid disorders or a long history of iodine deficiency may respond adversely to levels of intake that are safe for the general healthy population. For these individuals, the addition of iodine is not considered to pose any additional risks, as the iodine content of FB will be labelled. Furthermore FSANZ is currently progressing a proposal considering the mandatory fortification of food with iodine (Proposal P230). This issue will be further investigated as part of this Proposal currently at Draft Assessment.

Similarly, FSANZ risk assessment identified that the addition of iron to FB poses no appreciable risk to public health and safety for the general population. However, individuals who are homozygous for hereditary haemochromatosis are susceptible to iron overload even at normal dietary iron intakes and are generally advised to avoid iron-supplements and highly iron fortified foods. As the majority of individuals with this condition are not diagnosed until sufficient iron has accumulated to produce adverse effects, the addition of iron to FB may pose an increased risk of iron toxicity for those undiagnosed individuals.

FSANZ's Nutrition Assessment demonstrated that there is an inadequate intake of iron in the Australian and New Zealand populations. Both Australian and New Zealand nutrition guidelines recommended consumption of iron containing foods to reduce the incidence of iron deficiency anaemia particularly in adolescent girls and women[33,34,35].

[33] National Health and Medical Research Council (2003) *Dietary Guidelines for Australian Adults*.
[34] New Zealand Ministry of Health (1998) *Food and Nutrition Guidelines for Healthy Adolescents: A background paper*.
[35] New Zealand Ministry of Health (2003) *Food and Nutrition Guidelines for Healthy Adults.*

On this basis, FSANZ considers the potential health gain from permitting the addition of iron to FB outweighs the risk to those vulnerable individuals who, prior to being diagnosed, will not know to modify their diet. For those diagnosed individuals, the addition of iron will be labelled and therefore they can make an informed choice.

Therefore, FSANZ is not proposing any additional risk management strategies in relation to the addition of iodine or iron to FB.

5.2.4.1.2 Fair Trade and Industry Competitiveness

In accordance with FSANZ's statutory objectives, i.e. the 'High Order' Policy Principles, consideration has also been given to other matters including the promotion of fair-trading and the desirability of an efficient and competitive food industry. This includes applying the principle of minimum effective regulation as required by the Council of Australian Governments (COAG)[36] and the New Zealand Code of Good Regulatory Practice.

Currently permissions exist in the Code for the addition of certain vitamins to other water-based beverages e.g. Standard 1.3.2 permits the addition of vitamin C, folate and carotene forms of vitamin A (e.g. beta-carotene) to fruit drinks. These products could be viewed as fulfilling a similar primary function to FB i.e. hydration.

Standard 2.6.4 permits the addition of thiamin, riboflavin, niacin, vitamin B_6, vitamin B_{12} and pantothenic acid to FCB. The quantities of these permitted vitamins are significantly higher than those being requested for Application A470. Whilst FCB are compositionally different when compared to fruit juice drinks, by virtue of the addition of caffeine and carbon dioxide, FB can be considered to be an alternative substitute for all categories of water-based beverages including fruit drinks and FCB.

Although the Code distinguishes these products for regulatory and enforcement purposes, from the perspective of both the beverage industry and consumers, these products could all be considered quite similar.

Also from FSANZ's 2005 Product Surveys, the majority of FB in Australia and New Zealand currently contain the following B vitamins: thiamin; riboflavin; niacin; folate; pantothenic acid; vitamin B_6; and vitamin B_{12}.

Therefore, in the interest of minimum effective regulation, industry competitiveness and fair-trading, and in the absence of public health and safety concerns, FSANZ is proposing to also permit the addition of the following vitamins to FB in the amounts requested by the Applicant:

Vitamins
Beta-carotene
Vitamin C
Thiamin
Niacin
Pantothenic acid
Vitamin B_{12}

[36] COAG, *Principles and Guidelines for National Standard Setting and Regulatory Action by Australia and New Zealand Food Regulatory Ministerial Council and Standard Setting Bodies*. (1995, amended 2004).

5.2.4.1.3 Permitted forms

The Schedule to Standard 1.1.1 of the Code lists the permitted forms of vitamins and minerals. There are currently no permitted forms for pantothenic acid and selenium. FSANZ's risk assessment found the requested permitted forms for pantothenic acid (calcium pantothenate and dexpanthenol) and selenium (seleno methionine, sodium selenate, sodium selenite) to be acceptable. As FSANZ is proposing the addition of these nutrients to FB, the above permitted forms will be included in the Schedule to Standard 1.1.1.

5.2.4.1.4 Conclusion

On the basis of public health and safety, and having regard to Ministerial policy guidance, the promotion of fair trading and the desirability for an efficient and competitive food industry, FSANZ is proposing to permit the addition of the following vitamins and minerals to FB in the amounts requested by the Applicant:

Vitamins	Minerals
Riboflavin	Calcium
Folate	Iodine
Vitamin B_6	Iron
Vitamin D	Magnesium
Vitamin E	Selenium
Beta-carotene	
Vitamin C	
Thiamin	
Niacin	
Pantothenic acid	
Vitamin B_{12}	

5.2.4.2 Sugar content

As discussed in Section 5.2.3.1 there is potential for the consumption of FB to increase the sugar and energy intakes of the population. In order to effectively manage this risk, especially as it relates to children, FSANZ is proposing to restrict the amount of sugar permitted in FB.

Subclause 7(3) of Standard 1.2.8 – Nutrition Information Requirements stipulates a daily intake reference value for sugar of 90 g. On the basis of the requested reference quantity of 600 ml and in the light of current public health recommendations encouraging moderate sugar intake, 50% of the daily intake reference value for total sugar has been applied to the requested reference quantity of 600 ml. This equates to 45 g of sugar per 600 ml, or 7.5 g of sugar per 100 ml of FB.

From the 2005 Product Surveys, the proposed restriction on sugar will most likely impact on those FB that contain greater than 5% fruit juice and added sugar. Presently there are three FB available in Australia and four in New Zealand that contain greater than 7.5 g sugar per 100 ml.

The proposed restriction on the sugar content of FB minimises the potential risk of increased energy and sugar intakes in the population. It also provides consistency with the Policy Guideline by reducing the likelihood that FB will promote the increased consumption of foods high in sugar.

FSANZ therefore is proposing a maximum limit of 7.5 g per 100 ml of sugar in FB.

5.2.4.3 The use of formulated beverages as ingredients in other foods

In the Code, individual foods can be used as ingredients in mixed foods except in the case of Standard 2.6.4 – Formulated Caffeinated Beverages which prohibits the mixing of FCB with other non-alcoholic beverages. The reason for this prohibition was that, without the accompanying labelling statements that advised appropriate conditions of use, there could be a risk to groups such as children from the unregulated use of FCB as ingredients in other non-alcoholic beverages.

At Initial Assessment, the issue of FB being used as ingredients in mixed foods was raised with the vast majority of submitters supporting a prohibition of their use in other foods.

The Policy Guideline explicitly states that *regard should be had to the policy in the development of regulatory measures applying to the mixing of foods where one, or both of the foods may be fortified.* As previously discussed, FB present a case in point where unless unambiguously described, they could provide an avenue for inappropriate products being fortified to make use of the broader vitamin and minerals permissions available. This could also be the case for using FB as ingredients in other foods.

Consequently, FSANZ is proposing a prohibition on the mixing of FB with other beverages as a means of effectively quarantining the permissions for addition of a broad range of vitamins and minerals to those products that are intended to be FB.

5.2.5 Labelling of formulated beverages

Labelling provisions are included within the Code as a means of achieving three main objectives: to protect public health through the management of risk, to provide adequate information to the consumer to facilitate informed choice, and to prevent misleading conduct.

The Policy Guideline states that *there should be no specific labelling requirements for fortified food, with the same principles applying to non-fortified food*. Therefore, the generic labelling requirements contained in Chapter 1 of the Code will apply to FB.

This Section discusses the application of the generic labelling requirements to FB as well as specific labelling issues raised at Initial Assessment.

5.2.5.1 Vitamin and mineral content claims

The Applicant has requested that FB be permitted to carry claims of 'source' or 'good source' for vitamins and minerals. These claims are permitted under clause 6 of Standard 1.3.2 – Vitamins and Minerals providing that the added vitamin or mineral is a permitted form; and is present in a 'claimable food[37]' in amounts of no less than 10 % RDI per reference quantity for a 'source' claim. Clause 7 of Standard 1.3.2 permits a 'good source' claim where no less than 25 % RDI is present in a reference quantity of a food.

[37] 'Claimable food' is defined in Standard 1.3.2.

FB will be considered a 'claimable food' under Standard 1.3.2. Therefore, vitamin and mineral claims will be permitted for FB in accordance with clause 6 and 7 of the Standard. The permission for claims is consistent with other general-purpose food. In accordance with clause 9 of Standard 1.3.2, FB will be required to also include the proportion of the RDI per serve.

5.2.5.2 Nutrition, health and related claims

Nutrition claims, other than vitamin and mineral content claims, are currently regulated either by Standard 1.2.8 or the *Code of Practice on Nutrient Claims on Food Labels and in Advertisements* (CoPoNC).

Currently, there is a general prohibition on health claims on food labels or in advertising under Transitional Standard 1.1A.2 of the Code (except for the permitted pilot health claim regarding maternal folate consumption and a reduced risk of foetal neural tube defects, such as spina bifida).

The regulation of nutrition, health and related claims are being reviewed under Proposal P293, which is currently at Draft Assessment. Until such time as Proposal P293 is finalised, the existing provisions of Standard 1.2.8, CoPoNC and the general prohibition on health claims will apply to all food, including FB.

5.2.5.3 Percentage daily intake

At Initial Assessment, it was suggested that if an average quantity of a nutrient in a serve is declared in a nutrition information statement such as a NIP, Standard 1.2.8 – Nutrition Information Requirements would permit that quantity to be expressed as a percentage of a reference daily value, which in the case of vitamins and minerals is the RDI. It was noted that if this approach were considered appropriate for FB, expressions of content up to multiples of the RDI would be possible and that such information may lead consumers to believe that these products should play a more significant role in the diet than may be warranted.

Since Initial Assessment, the requested vitamin and mineral permissions have been revised downwards to 25% of the RDI with the exception of vitamin C, at 100% of the RDI per 600 ml reference quantity. Multiples of the RDI are therefore no longer an issue and restricting vitamin and mineral claims to quantitative declarations only is not considered necessary.

5.2.5.4 Prescribed name

Prescribed names are provided in the Code primarily for use by enforcement agencies in the identification and regulatory classification of foods.

At Initial Assessment, submitters were asked whether the generic provisions in Standard 1.2.2 – Food Identification Requirements that require a label to contain *...a name or description of the food sufficient to indicate the true nature of the food* would adequately allow for the identification of FB. Eleven submitters commented on the use of a prescribed name. The five food industry submitters who responded all considered that there is no need for FB to have a prescribed name. Their rationale being that a prescribed name would have no meaning to consumers and that claims, ingredients and nutrition information panels would be sufficient to identify FB.

The remaining six submitters (two complementary medicine industry, two public health, one consumer and one government) were in favour of a prescribed name for identification and enforcement purposes so FB can be distinguished from other beverages such as soft drinks.

The Applicant requested that the term 'formulated beverage' not be prescribed. FB currently manufactured under the NZDSR are required to label products as 'dietary supplement'. The FB manufactured in Australia to the current sports food standard are also required to label products as 'Formulated Supplementary Sports Food'. The additional labelling requirement reflects the nature of these sports foods as special-purpose food.

Given the classification of FB as general-purpose foods, for consumption by the general population, FSANZ does not consider a prescribed name for FB to be necessary for the purpose of identification for consumers and/or enforcement agencies.

5.2.5.5 Mandatory labelling statements for FB

Where appropriate, mandatory labelling statements are used to manage risk. Such statements can alert consumers to the compositional nature of a product and/or identify population groups for which particular products are not recommended.

At Initial Assessment, submitters were invited to comment on whether FB should be labelled with statements that advise against the use of FB as substitutes for a healthy diet or as providing health benefits. Of the ten submitters who provided comments, those received from the industry sector (5) did not support the use of these statements, viewing them as unnecessary, unreasonable and applicable to all food products. The remaining five submitters (one complementary medicine industry, two public health, one consumer and one government), all supported the use of such statements. One public health submitter who considered the information as essential to ensure informed consumer choice, suggesting additional statements such as: 'a healthy diet provides other essential components as well as vitamins and minerals'. The complementary medicine industry submitter considered the advisory statement appropriate and consistent with complementary medicines and other food categories.

As part of the 2003 FTDS consumer research, participants were exposed to a number of labelling elements including a statement which cautioned against regarding FTDS as 'magic bullets' – *this product should be consumed in the context of a healthy, balanced diet*. The statement was generally viewed as either obvious, condescending, or meaningless. For some, the statement was seen as a good way of cautioning vulnerable shoppers, such as those less experienced, and children, who may inadvertently consume excessive amounts of a supplemented product. Overall, however the statement was regarded as an idealistic health education message rather than a motivator to further investigate the products claim(s).

The risk assessment has not identified any population groups considered at risk from FB consumption. The proposed permitted vitamins and minerals to be added to FB are considered to be at moderate levels and are consistent with permissions for other general-purpose food. These fortified foods are not required to carry any additional advisory statements in relation to dietary advice and/or food selection. FSANZ considers that the information contained in the NIP and the ingredient listing, together with the permitted vitamin and mineral claims should ensure sufficient information is available to enable consumers to assess the appropriateness of FB when making food/beverage choices.

In light of the above comments, FSANZ is of the opinion that mandatory advisory statements are not necessary for FB.

5.2.5.5 Conclusion

In accordance with the policy guidance, FSANZ is not proposing any specific labelling requirements for FB. Therefore, the generic labelling requirements contained in Chapter 1 of the Code will apply.

5.2.6 Food additives

A detailed Food Technology Report is provided at Attachment 9.

The use of food additives is regulated by Standard 1.3.1 – Food Additives, with permissions provided by Schedules 1 to 4. Schedule 1 of this Standard permits the use of food additives at specified levels in specific foods. Maximum permitted levels are prescribed for additives where risk assessment indicates a need to restrict usage levels to protect public health and safety. Schedule 2 lists food additives that may be used to levels determined by Good Manufacturing Practice (GMP) where permitted by Schedule 1. Schedule 3 lists colours that are permitted to GMP levels where permitted in Schedule 1. Schedule 4 lists colours that are restricted to 70 mg/kg for liquids and to 290 mg/kg for solid foods and which may be further restricted by Schedule 1. Schedule 5 lists the permitted technological functions to be performed by food additives as distinct from processing aids (Standard 1.3.3) and vitamins and minerals (Standard 1.3.2).

The Applicant has requested permission for use of a wide range of food additives in FB. Some of these requests are covered by the general permissions in Schedule 2 of Standard 1.3.1 and colours have been requested for use in accordance with Schedules 3 and 4. The levels requested for other additives are compliant with the permissions currently available for non-alcoholic beverages in Schedule 1 under the categories of 14.1.2.2 – Fruit and vegetable juice products and of 14.1.3 – Water-based flavoured drinks. A comparison of the requested food additive permissions for A470 and the current permissions for food additives in comparable products is included in the appendix to Attachment 9.

It is important to note that there are some differences in food additive permissions sought for FB and those currently permitted for comparable products, and the restrictions that need to be maintained. These are listed below:

- no permissions sought for quinine;
- no permissions sought for cyclamate;
- no permissions sought for carbon dioxide;
- permissions for acesulphame potassium at 3,000 mg/kg comparable to water-based flavoured drinks;
- permissions for sodium and calcium propionate for fruit and vegetable juices and fruit and vegetable juice products only at GMP;
- permission for calcium disodium EDTA for products containing fruit flavouring, juice or pulp or orange peel extract only; and
- permission for annatto extracts for fruit and vegetable products only.

The majority of submitters to the Initial Assessment agreed with the requested list of additives, believing they were appropriate for their technological purposes and were the same as approvals for other beverages.

However, one public health submitter raised concerns about sensitive individuals with asthma, hyperactivity and chronic allergy reactions to benzoic acid, sulphites and annatto. The approvals for benzoates and sulphites are requested to be the same as for the commonly produced and consumed water-based flavoured drinks. These preservatives have an accepted technological function of preserving the drinks and they have been assessed as safe. Concerned consumers can avoid such drinks by checking the ingredient list on the labels. Annatto currently has specific approval for fruit and vegetable juice products and therefore could only be considered for comparable FB that contain such fruit ingredients.

Concerns were also raised that the maximum permitted level of calcium disodium EDTA of 33 mg/kg is more than the Acceptable Daily Intake (ADI, 2.5 mg/kg bw/day for a young child of less than 13 kg, if they consumed 1 litre of FB per day over a life time). However, the situation for calcium disodium EDTA is again consistent with current approvals for water-based flavoured drinks and fruit drinks. The permission is only for products containing fruit flavouring, juice or pulp or orange peel extract. This use is technologically justified to chelate metal ions from solution to ensure flavour retention in FB.

5.2.6.2 Conclusion

The requested food additives are technologically justified for their proposed use in FB in the same way as they are technologically justified for their current use in comparable fruit and vegetable juice products and water-based flavoured drinks.

On the basis of the dietary exposure assessment for food additives (at Attachment 8) which concludes that the requested 57 food additives/additive groups to FB would not raise any public health and safety concerns, FSANZ is permitting their addition to FB.

5.2.7 Other issues raised in submissions

At Initial Assessment, submitters were asked to comment on number of issues which, at the time, were considered to have direct relevance to the regulation of FB. These were the use of a maximum one-day quantity and the addition of non-culinary herbs. In light of the subsequent amendments to the Application and the fact that the Applicant is not seeking the inclusion of non-culinary herbs to FB, these issues are no longer considered relevant to the consideration of this Application.

No other relevant issues were raised by submitters in response to the Initial Assessment Report.

5.2.8 Risk management summary

In summary, FSANZ is proposing the following regulatory approach for FB:

- classification of FB as a general-purpose food;
- inclusion of a definition for FB in the Code, in association with a maximum limit of 24% of fruit ingredients;

- exclusion of cordials as FB;
- restriction of total sugar content to 7.5 g/100 ml;
- application of generic labelling requirements to FB;
- permissions for the range of food additives requested by the Applicant (as detailed in Attachment 9); and
- permissions for the addition of vitamins and minerals in amounts to allow 'source' (10% RDI) and/or 'good source' (25% RDI) claims with the exception of vitamin C (100% RDI) per 600 ml reference quantity as outlined in the table below:

Vitamin / Mineral	Maximum Claimable Amount Per 600 ml Reference Quantity	No Public Health and Safety Concerns	Consistent with FSANZ's s.10 (2)(c), s.10(2)(d) and s.10(2)(e) Objectives*
Vitamins			
Beta-carotene	200 µg	✓	✓
Thiamin	0.28 mg	✓	✓
Riboflavin	0.43 mg	✓	✓
Niacin	2.5 mg	✓	✓
Folate	50 µg folic acid	✓	✓
Vitamin B_6	0.4 mg pyridoxine	✓	✓
Vitamin B_{12}	0.5 µg	✓	✓
Vitamin C	40 mg in total of L-ascorbic acid and dehydroascorbic acid	✓	✓
Vitamin D	2.5 µg	✓	✓
Vitamin E	2.5 mg alpha-tocopherol equivalents	✓	✓
Pantothenic Acid	1.3 mg	✓	✓
Minerals			
Calcium	200 mg	✓	✓
Iodine	38 µg	✓	✓
Iron	3 mg	✓	✓
Magnesium	80 mg	✓	✓
Selenium	17.5 µg (inorganic and organic forms)	✓	✓

* FSANZ Act section 10(2)(c) the desirability of an efficient and internationally competitive food industry.
FSANZ Act section 10(2)(d) the promotion of fair trading in food.
FSANZ Act section 10(2)(e) any written policy guidelines formulated by the Council for the purposes of this paragraph and notified to the Authority.

6. Regulatory Options

At Initial Assessment, two regulatory options were proposed either to maintain status quo or include regulations specific to FB in the Code. However, since this time FSANZ has determined, on the basis of its assessment, the need for an additional option. Therefore FSANZ is proposing the following three regulatory options at Draft Assessment:

6.1 Option 1 – Maintain *Status Quo*

Under this Option, there would be no change to the current regulatory arrangements for FB. FB would continue to be manufactured under the NZDSR and sold in New Zealand and/or exported to Australia. In Australia, without specific FB provisions in the Code, beverage manufacturers would have to continue manufacturing FB using the existing FSSF Standard (with specific mandatory labelling requirements), which is not intended to regulate FB.

6.2 Option 2 – Amend the Code to permit the addition of a defined set of vitamins and minerals to FB (excluding cordials) with additional specific compositional requirements.

Under this Option, FB would be permitted with a defined set of vitamin and minerals (that do not present any public health and safety concerns), in addition to a restriction on the sugar content of FB. This Option would allow Australian manufacturers to access the FB market without having to utilise the existing FSSF Standard. In addition, Australian and New Zealand manufacturers would be able to compete equitably.

6.3 Option 3 – Amend the Code to permit the addition of vitamins and minerals to FB and cordials as requested by Applicant without any other specific compositional requirements.

Similar to Option 2, this Option permits Australian and New Zealand Manufacturers to manufacture FB and compete equitably. However, Option 3 includes permission for the addition of a broader range of vitamins and minerals without additional compositional restrictions being imposed.

7. Impact Analysis

7.1 Affected Parties

The parties affected by this Application are:

- the non-alcoholic beverage industry in Australia with the capability to manufacture FB, importers of FB into Australia, and the non-alcoholic beverage industry in New Zealand that currently manufactures FB;
- consumers of FB in Australia and New Zealand; and
- agencies of the State and Territory governments in Australia and of the New Zealand government that are responsible for enforcing food regulation.

7.2 Data Collection

The impact analysis has been informed by market intelligence on FB provided by the Applicant, interviews with the Applicant on current conditions in the Australian market, research commissioned and undertaken by FSANZ into the FB product range available in Australia and New Zealand, and by official statistics supplied by the Australian Bureau of Statistics and Statistics New Zealand.

7.3 Impact Analysis

7.3.1 Option 1 - Maintain Status Quo

7.3.1.1 Impacts on Australian Industry

Currently there are no specific provisions in the Code for FB. However, some manufacturers are using the FSSF Standard to produce FB, which, as noted previously, is intended for products specially formulated to assist sports people in achieving specific nutritional or performance goals. It imposes strict labelling requirements including the mandatory advice that such products are 'Not suitable for children under 15 years of age or pregnant women: Should only be used under medical or dietetic supervision'. These labelling requirements have been acceptable to only a few Australian companies that produce distinctive products for niche markets and account for one-fifth of the Australian FB market. For most of the non-alcoholic beverage market, however, these labelling requirements are unacceptable.

The Applicant, representing the major beverage manufacturers in Australia, believes that the mandatory labelling advice is unsuitable for FB as a generally available consumer product: it would diminish consumer perceptions, marketing and distribution of the products. Hence the lack of a specific FB permission in the Code, unencumbered by mandatory labelling requirements, is a serious impediment to Australian industry. Some indication of the lost manufacturing opportunity to Australian industry is indicated by the size of FB imports from New Zealand (under the TTMRA) that are not required to carry any specific labelling advice, of around $A40 million in 2004.

Another indication of the lost manufacturing opportunity would be the future growth in the Australian FB market that Australian industry cannot participate in. Market intelligence indicates growth of 10% p.a. would be possible and may be conservative in the next few years, fading to around 5% p.a. in five years time. These growth rates are significantly stronger than for the general soft drinks market, of a little over 1% p.a., reflecting the difference between a small developing market and a large mature market. On the basis of such future growth, the Australian FB market could be expected to double over the next ten years. Under current regulatory arrangements this burgeoning market in Australia will not be accessible to most local non-alcoholic beverage producers.

The lost manufacturing opportunity also includes forgone exports. A local manufacturing base would support additional production for export, valued by the Applicant at between $A9 million and $A30 million per year.

Around 80% of the Australian market is supplied by imports from New Zealand (under the TTMRA), which benefits the importers and distributors of these products.

The Australian non-alcoholic beverage industry is concerned by the lost manufacturing opportunities associated with forgone production because of the inequity in the current regulatory arrangements. While Australian industry is disadvantaged, New Zealand industry is advantaged through its ability to manufacture and its access to the Australian market that for the most part is unhindered by competition from Australia.

Importers benefit under the current regulatory arrangements because most of Australia's FB market is supplied by imports from New Zealand. The extent the benefit would be small compared with the lost manufacturing opportunities of the non-alcoholic beverage industry.

7.3.1.2 Impacts on New Zealand Industry

In contrast to Australia, the New Zealand regulatory arrangements have not constrained their industry's ability to respond to international market trends, but rather has facilitated this expansion. New Zealand manufacturers are noted as early adopters of overseas trends. The non-alcoholic beverage manufacturers developed a number of FB and one company in particular was highly innovative and now dominates this product category. The local market has responded well to the offering. FB have grown from a small market in 2000 to around $NZ17 million in 2004. This solid manufacturing activity provided a base to expand into exports, valued at $NZ35 million free-on-board (f.o.b.) in 2004, of which $NZ32 million f.o.b. is exported to Australia. The regulatory arrangements in New Zealand have been beneficial to the local New Zealand non-alcoholic beverage industry.

Under this option, the New Zealand industry will continue to be at a greater advantage when compared to the Australian industry in their ability to market FB in both countries and internationally without significant competition from Australia.

7.3.1.3 Impacts on Consumers

The current regulatory arrangements permit consumers in Australia and New Zealand access to a market in FB, of around $A50 million and $NZ17 million respectively in 2004. Most FB are manufactured by multinational food and beverage companies and would be available in many other countries. Australian and New Zealand consumers are therefore participating in a recent innovation in non-alcoholic beverages that is a global phenomenon. The FB market, though small compared with the general market for beverages, is of sufficient size to offer a range of products, and consumers will be aware that they are able to exercise real choice in selecting their preferred product. Hence the current regulatory arrangements are supportive of consumers who have an interest in or desire to consume FB.

Australian consumers are unlikely to be aware that most FB are imported from New Zealand. They also are unlikely to perceive any restrictions on their FB purchases that may be associated with current regulations that inhibit local manufacture of these products.

Some Australian consumers have an assurance of the safety of the FB they purchase, because one-fifth of the Australian market is manufactured by local companies under the FSSF standard in the Code. The remainder of consumers in Australia and New Zealand are not provided with an equivalent level of assurance. The NZDSR, that permits the sale of the majority of FB, does set maximum daily doses for some vitamins and minerals, but it does not take into account their total daily intake by consumers, leaving open the possibility that consumption of FTDS could involve over-exposure and potential harm. Most consumers would be unaware of any potential risks associated with their consumption of FTDS and FB in particular.

7.3.1.4 Impacts on Government Enforcement Agencies

For the government sector, maintenance of the *status quo* means a continued discrepancy between Australian and New Zealand food law, not a broad united approach, which has the potential to undermine the joint food standards system. It also creates greater ambiguity for Australian enforcement agencies if two different regulatory measures are to be retained.

For example, an enforcement officer has to decide whether a product: complies with the FSSF standard; is a known import from New Zealand (under the TTMRA); or is simply non-compliant with the Code. This confusion takes time and resources to resolve, and over many products and various sites could result in significant costs to the enforcement agencies of the States and Territories. The priority that the enforcement agencies attach to monitoring and enforcing to correct product labelling of FB will depend on the resources assigned to this activity. Thus while potential the cost could be significant, in reality the cost is likely to be small.

The ambiguity surrounding the food drug interface will continue as will the inappropriate application of the existing FSSF standard to FB.

By maintaining the status quo, it is likely that the Australian Government in particular will continue to experience political pressure and lobbying from the Australian beverages industry regarding the inequity of manufacturing opportunities.

In New Zealand the regulatory arrangements might be as confusing as those in Australia, with an enforcement officer having to decide whether a product complies with: the FSSF Standard; the NZDSR; or is simply non-compliant with the Code. If most FB comply with the NZDSR, as is likely to be the case, then the potential for confusion is much reduced.

7.3.2 Option 2 – Amend the Code to permit the addition of a defined set of vitamins and minerals to FB with additional specific compositional requirements.

Option 2 would affect the current range of FB on the market in Australia and New Zealand. Some products currently produced under the NZDSR would have to be reformulated to comply with the compositional requirements for FB in the Code. For example, the removal of non-permitted vitamins and/or minerals. All products would have to be reformulated to reduce to amounts of added vitamins and minerals, although for most added vitamins and minerals the reduction would be small. Some products would have to be reformulated to reduce the sugar content.

7.3.2.1 Impacts on Australian Industry

The compositional restrictions generally would not affect consumer perceptions of FB and hence in general Australian industry could compete effectively with the current range of New Zealand imports. The exception would be the few New Zealand imports with a higher sugar content which, in some circumstances, might have a market advantage.

The impact of the new permissions would be immediate. Many Australian companies already have developed FB which could be quickly introduced onto the Australian market. This includes the major beverage manufacturers, some of whom had imported small volumes of FB from their New Zealand associated companies to establish a presence on the Australian market.

They would be expected to switch to local manufacture (to avoid high transport costs) and vigorously promote their products. Australian industry would immediately seek to compete in earnest with the New Zealand market leader of FB that currently dominates the market. The result of this competition would not simply be a redistribution of market share between Australian and New Zealand producers. The competition could trigger growth of FB. The Australian market has lagged behind international consumer trends in FB and hence it offers opportunities for development as Australia catches up to international consumer levels. Market intelligence described the Australian FB market as "extremely small, underdeveloped and fragmented" and "still in its infancy", indicating substantial upside to further development. When global FB markets developed beyond the infancy stage, they grew at rates in excess of 20% p.a. Hence the market intelligence outlook for Australia of 10% p.a. in the next few years, fading to 5% p.a. in five years, is both possible and likely to be conservative. Overall the impact would be beneficial to the Australian non-alcoholic beverage industry.

Those businesses that currently manufacture FB under the FSSF Standard would have the choice to continue under that Standard or to comply with the new Standard.

The Applicant suggests that a solid manufacturing base in Australia would provide a platform to export FB to Asia, estimated at between $A9 million and $A30 million per year.

Importers could lose some business with the likely loss of some market share from New Zealand suppliers. However this could be a short-term phenomenon. Over the longer-term a smaller share of a growing market could still provide net-benefits to importers. **Distributors** of imported products could similarly lose business in the short term, although this loss would be offset by gains in business by distributors of locally produced FB.

7.3.2.2 Impacts on New Zealand Industry

Under this Option New Zealand beverage companies could elect to continue to produce FB under the NZDSR, or to produce under the new permissions in the Code. If they elect to continue to produce under the NZDSR, there will be no impact on New Zealand industry. If they elect to produce under the new permissions in the Code, then the majority of FB would need to be reformulated. A few products would have to remove zinc and vitamin A. The majority of FB would have to reduce the amounts of added vitamins and minerals, although in most cases the reduction would be small and the added nutrients could still be claimed on the label. These changes would be modest and involve a once-off adjustment cost. However the permission restricting sugar content could be significant to those FB with higher sugar levels and might adversely affect their continuing acceptance by consumers.

It is difficult to predict what industry's response would be to the new permissions in the Code. Previously, in similar circumstances, industry elected to produce under a new food standard rather than the NZDSR. The New Zealand government also has given in-principle support to repeal the food aspects of the NZDSR and for FTDS (which include FB) to be regulated under the Code. However, the prospect of incurring costs to reformulate existing products, and of the higher sugar content FB losing some of their appeal, in all probability would sway New Zealand industry in the short term at least to continue to produce under the NZDSR. In the longer term the NZDSR would continue to facilitate innovation, compared with the restrictions in the new permissions in the Code that would place limits on the nature of new products, providing an incentive to New Zealand industry to continue to produce FB under the NZDSR.

If New Zealand were to retain the NZDSR there could be come ramifications for trans-Tasman trade. New Zealand FB that do not comply with the proposed standard would still be able to be sold on the Australian market under the TTMRA. This is because under the TTMRA goods that can be legally sold in New Zealand can be legally sold in Australia, irrespective of any different standards or requirements relating to sale or manufacture of goods in Australia.

The major beverage manufacturers that had supplied small volumes of FB to their associated companies in Australia would discontinue these small additional volumes of production, and avoid their company incurring unnecessary and high transport costs. This action would have only a marginal effect on the New Zealand non-alcoholic beverage industry because the volumes have been small.

The major impact of Option 2 would be on the products of the market leader that dominates the FB markets in Australia and New Zealand. It would immediately face strong competition in Australia from local producers and inevitably face some loss of market share to the local producers, entailing a reduction in export earnings to New Zealand. However the competition could trigger a surge in growth of the Australian FB market, consistent with information from market intelligence. A smaller share of a strongly growing market, over a five or ten year period, could still deliver net-benefits to New Zealand.

The activities of New Zealand's small producers in exporting to Australia, if they have, are too small to be separately identified in the importer register or official statistics. Nonetheless a dynamic Australian FB market may prove attractive to small producers with niche products.

7.3.2.3 Impacts on Consumers

The most likely scenario for Option 2 would be that the Australian industry would produce FB under the new permissions in the Code while New Zealand industry would continue to produce under the NZDSR. In New Zealand the consumer impacts will be unchanged from the status quo. In Australia it is probable that consumers will not perceive any immediate change in the range and nature of FB on the market.

The new permissions would facilitate greater competition in the Australian market. Over time, as the FB market is expanded, Australian consumers would benefit from greater product choices, not only from ongoing innovation between existing players but also from the activities of potential entrants. A possible high level of advertising associated with this competition would inform a broader group of consumers, and it is likely that new consumers of FB would appreciate their properties.

Consumers of products covered by the Code will be protected from a range of risks and potential harm. Sugar content will be restricted and hence FB will not contribute to the potential problem of obesity nor the chronic diseases associated with obesity. Consumers will be protected from any nutrients, where potential safety concerns exist. The new permissions will place limits on the amount of vitamins and minerals that can be added, protecting consumers from the potential harm that can occur with over-exposure to these nutrients. The Australian industry has no option but to abide by the Code, and hence where there is an inadequate intake in the population of certain nutrients, its products will benefit consumers, compared to the status quo.

7.3.2.4 Impacts on Government Enforcement Agencies

In Australia the requirements of the two pertinent provisions in the Code – the new FB permission and the FSSF Standard – would be clear and easy to enforce. However imports from New Zealand, which are manufactured under the NZDSR, could still be an issue. It is unclear as to whether or not New Zealand imports would comply with the new permissions rather than relying on the NZDSR and TTMRA, however it is hoped that in keeping with the spirit of the joint Code this would occur. The New Zealand Government has also given in-principle agreement to repeal the food aspects of the NZDSR and for FTDS (including FB) to be regulated under the Code. As noted previously, the NZDSR were in fact designed to regulate controlled dosage supplements such as tablets and capsules. Further, the original intention of the NZDSR was to encompass those products not regulated by the (then) New Zealand *Food Regulations 1984*, rather than provide a choice of regulatory options for the food industry. From the assessment in the preceding industry section, there are circumstances which favour New Zealand businesses switching from the NZDSR to the FB permission in the Code. However the situation is ambiguous and overall enforcement costs in Australia are likely to be much the same as under the *status quo*.

It is acknowledged that the enforcement burden may be greater in New Zealand as the new permissions are more restrictive than the NZDSR in relation to compositional requirements. They would require some effort to become familiar with new regulations and, in enforcement, determine which of two very different regulatory regimes apply to any given FB product.

7.3.3 Option 3 – Amend the Code to permit the addition of vitamins and minerals to FB as requested by the Applicant without any other specific compositional requirements.

7.3.3.1 Impacts on Industry

The set of vitamin and mineral permissions would be sufficiently broad that:

- no FB currently on the market in Australia and New Zealand would require reformulation; and
- future innovations in FB would be unrestricted in practically all cases in the choice and amount of nutrients to add to beverages.

New Zealand industry could easily move from the NZDSR to the Option 3 permissions, with little cost, and over the short term would probably do so. Competition in the Australian market would be intense, as outlined in the previous option, with the exceptions that there would be no regulatory-driven difference between products produced in Australia and New Zealand. Australian industry would benefit from access to the local market. While New Zealand industry would lose some market share, a smaller share of a growing market could still deliver net-benefits.

Importers could lose some business with the likely loss of some market share from New Zealand suppliers. However this could be a short-term phenomenon. Over the longer-term a smaller share of a growing market could still provide net-benefits to importers. **Distributors** of imported products could similarly lose business in the short term, although this loss would be offset by gains in business by distributors of locally produced FB.

7.3.3.2 Impacts on Consumers

The range and character of FB under Option 3 would be similar to what is already on the market, so consumers would perceive no immediate impact at all in moving from Option 1 to Option 3. Option 3 would facilitate greater competition and growth in the Australian market and over time Australian consumers would benefit from expanded product choices.

However, the broad set of permissions under Option 3 includes nutrients that:

- could adversely affect consumers' health at exposure levels that are possible within a normal diet; or
- are not known to be safe as ingredients in food on currently available information; or
- do not fulfil a health need.

The set of permissions is too broad to provide an assurance of safety to the public. These permissions would not be subject to compositional restrictions, increasing the possibility of overexposure of the added nutrients. These health risks could occur where future FB innovations include a broader set of vitamins and minerals, or increased amounts of vitamins and minerals. In addition the absence of a restriction on sugar content of FB would contribute to the problem of obesity and the chronic diseases associated with obesity. In these circumstances consumers potentially could incur significant costs to their health and well-being.

7.3.3.3 Impacts on Government Enforcement Agencies

The set of vitamin and mineral permissions would be sufficiently broad that industry in New Zealand and Australia would be expected to adopt it as the single standard for FB, in preference to the NZDSR or the FSSF Standard. In these circumstances, enforcement would be a simpler activity than under Option 1 and fewer resources would be required.

8. Consultation

8.1 Public Consultation

8.1.1 Initial Assessment

FSANZ received a total of 19 written submissions in response to the A470 Initial Assessment Report during the public consultation period of 15 January 2003 to 26 February 2003. Of these, 14 were from Australia, two from New Zealand and three represented Australasian interests.

Thirteen submissions were received from the industry sector, including three submissions from the complementary medicine industry. There were also three submissions from government, two from public health organisations and/or professionals and one from a consumer group.

Submitters' views were evenly divided between the two proposed regulatory options maintaining the status quo and supporting an amendment. One submitter did not state any preferred regulatory approach.

A summary of submissions received is at Attachment 10. Where appropriate, issues raised in submissions have been addressed in Section 5 of this Report. Whilst submitters' comments form an integral part of the assessment process, FSANZ notes that in some instances comments may not be as relevant as when raised in 2003.

Draft Assessment

FSANZ is now seeking comment in relation to this Draft Assessment Report. Comments received in response to this Report will be used to assist in the development of a Final Assessment Report.

Submitters are invited to provide comments in relation to the:

- issues discussed in Section 5 of this Report; and
- proposed regulatory options, and potential impacts in relation to these regulatory options.

8.2 World Trade Organization (WTO)

Australia and New Zealand are members of the WTO and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the Agreement between the Government of Australia and the Government of New Zealand Concerning a Joint Food Standards System, FSANZ is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

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

There are no international regulations governing FB rather these products appear to be included in countries fortification policies more broadly. This approach is reflected in the FB permissions proposed to be contained within Standard 1.3.2 – Vitamins and Minerals of the Code.

Amending the Code to permit FB is unlikely to have a significant effect on trade. However, unless the repeal of the NZDSR occurs, FSANZ recognises that there are potential trade implications. Therefore, notification of the proposed FB regulations will be made to the WTO in accordance with the WTO Technical Barrier to Trade Agreement.

9. Conclusion and Recommendation

Option 2 permits the addition of a defined set of vitamins and minerals, which do not pose any public health and safety concerns, to FB (excluding cordials) in addition to a restriction on total sugar content. Option 2 delivers net-benefits in comparison with Option 1 (*Status Quo*).

The main benefit offered under Option 2 is the elimination of the lost manufacturing opportunity incurred by a large part of Australian industry which cannot supply the domestic market under the current regulatory arrangements. This situation is resolved in Option 2 by allowing the manufacture and sale of FB.

Option 2 would facilitate a period of strong competition and growth in the Australian market, to the benefit of Australian and New Zealand industries over the longer term. In the short term, New Zealand industry would lose some part of its share of the Australian market, but over time, the growth in the FB market would more than compensate for the loss. A smaller share of a strongly growing market could still provide net-benefits to New Zealand industry over the longer term.

Consumers are unlikely to perceive any immediate difference if Option 2 is introduced, because the New Zealand product range probably will not change and the Australian products will claim a similar range of nutrients. Over time, with competition between suppliers and expansion of the Australian market, Australian consumers will benefit in comparison with Option 1 in terms of greater choice of FB. Consumers of those products produced under the Code would also benefit from the protection of their health and safety that Option 2 would provide, through the limits placed on the amount and range of acceptable vitamins and minerals. Some consumers may perceive this protection and consume FB with greater confidence.

Option 2 fulfils the specific objectives of this Application. The health and safety of consumers is protected through limits on the level of fortification to ensure safe levels of consumption, and by excluding specific nutrients that could be potentially hazardous, or where their safety cannot be verified.

Option 2 provides a framework for the non-alcoholic beverage industry in Australia and New Zealand to produce FB under a common standard. If the New Zealand industry continued to produce FB under the NZDSR, there would be little difference in the short term because the product range would be similar to those products allowable under Option 2. Over time and with the introduction of new FB, differences could emerge between Australian and New Zealand. However there are good reasons why New Zealand industry may elect to switch from the NZDSR to the permissions under Option 2, including the previous choices of New Zealand industry in similar circumstances and the New Zealand Government's in-principle agreement to repeal the NZDSR.

Option 3, which permits the addition of vitamins and minerals to FB as requested by the Applicant without any other specific compositional requirements, provides greater net-benefits to industry compared with Option 1. These benefits to industry also exceed the benefits from Option 2, because under Option 3 manufacturers may draw from a broader range of vitamins and minerals for future development of FB, eliminating the time and cost of obtaining regulatory approval and facilitating faster innovation. However, Option 3 could potentially impose large costs on consumers, in comparison with Option 1, by allowing specific nutrients that may have adverse health impacts. In addition, by not limiting the levels of vitamins and minerals in FB, this could possibly cause overexposure to these nutrients, and potential harm to consumers. Option 3 does not achieve the objective of protecting public health and safety, and is thus rejected.

Overall, Option 2 is the preferred regulatory option.

FSANZ recommends that the proposed draft variations to the Code (Attachment 1), incorporating defined vitamin and mineral permissions, specific compositional requirements, and a definition for FB, be approved for the following reasons:

- the regulation of FB provides assurance for consumers regarding the protection of public health and safety by:

  - permitting the safe addition of vitamin and minerals to FB;
  - permitting the addition of vitamins and minerals to FB where an inadequacy or deficiency exists; and
  - setting a prescribed limit on the total sugar content of FB;

- regulation of FB ensures certainty for industry balanced against the need to provide consumer choice and prevent consumers being misled regarding the nutritional quality of the product;

- the variations to the Code meet FSANZ's statutory obligations and are consistent with Ministerial policy guidance on voluntary fortification;

- the variations to the Code are consistent with Ministerial policy guidance on voluntary fortification and are therefore consistent with FSANZ's statutory obligations;

- the permitted range of vitamins and minerals is consistent with the principles of minimum effective regulation and the promotion of fair trading;

- the variations to the Code provide an effective regulatory framework within which industry can work efficiently and competitively;

- the inclusion of permissions for FB in the Code promotes equity by providing a regulation which enables the manufacture of FB in Australia;

- the explicit recognition of FB in the Code provides greater certainty for industry and reduces both the costs of compliance and enforcement; and

- the regulation impact assessment concludes that the preferred regulatory option of permitting net benefits from permitting FB outweigh any potential costs to affected parties.

10. Implementation and review

Following the consultation period for this document, a Final Assessment of this Application will be completed. Following the preparation of the Final Assessment Report and approval by the FSANZ Board, notification will be made to the Ministerial Council.

Following this, the proposed draft variations to the Code are expected to come into effect upon gazettal, subject to any request from the Ministerial Council for a review.

ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. List of Commonly Used Acronyms
3. Amendments to Application A470 – Formulated Beverages
4. Summary of 2005 Formulated Beverages Surveys
5. Nutrition Assessment
6. Risk Assessment - Micronutrients
7. Dietary Intake Nutrient Methodologies
8. Risk Assessment - Food Additives
9. Food Technology Report
10. Summary of Submissions

Attachment 1

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

To commence: On gazettal

[1] ***Standard 1.1.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] *omitting from the* Schedule, *from* Column 2, *in relation to Pantothenic acid –*

No permitted form specified

substituting

Calcium pantothenate
Dexpanthenol

[1.2] *omitting from the* Schedule, *from* Column 2, *in relation to Selenium –*

No permitted forms specified

substituting –

Seleno methionine
Sodium selenate
Sodium selenite

[2] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting in* Schedule 1 item 14.1.4 *the heading –*

Formulated Beverages*

[2.2] *inserting in* Schedule 1 item 14.1.4 *after the heading* Formulated Beverages* –

123	Amaranth	30	mg/kg	
160b	Annatto extracts	10	mg/kg	products containing fruit or vegetable juice only
200 201 202 203	Sorbic acid and sodium, potassium and calcium sorbates	400	mg/kg	
210 211 212 213	Benzoic acid and sodium, potassium and calcium benzoates	400	mg/kg	
220 221 222 223 224 225 228	Sulphur dioxide and sodium and potassium sulphites	115	mg/kg	
242	Dimethyl dicarbonate	250	mg/kg	
281	Sodium propionate	GMP		products containing fruit or vegetable juice only
282	Calcium propionate	GMP		
385	Calcium disodium EDTA	33	mg/kg	products containing fruit flavouring, juice or pulp or orange peel extract only
444	Sucrose acetate isobutyrate	200	mg/kg	

445	Glycerol esters of wood rosins	100	mg/kg	
480	Dioctyl sodium sulphosuccinate	10	mg/kg	
950	Acesulphame potassium	3000	mg/kg	
951	Aspartame	GMP		technological use consistent with Clause 4 only
954	Saccharin	80	mg/kg	
955	Sucralose	GMP		technological use consistent with Clause 4 only
956	Alitame	40	mg/kg	
957	Thaumatin	GMP		technological use consistent with Clause 4 only
961	Neotame	GMP		

[3] ***Standard 1.3.2*** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *inserting in alphabetical order in* Column 1 *in the* Table to clause 3 *the heading* –

Formulated Beverages

[3.2] *inserting in* Columns 2, 3 and 4 *in the* Table to clause 3 *under the heading*, Formulated Beverages –

	600 mL	folate vitamin C carotene forms of vitamin A niacin thiamin riboflavin calcium iron magnesium vitamin $\mathbf{B_6}$ vitamin B12 vitamin D vitamin E iodine pantothenic acid selenium	50 µg (25%) 40 mg (100%) 200 µg (25%) 2.5 mg (25%) 0.28 mg (25%) 0.43 mg (25%) 200 mg (25%) 3.0 mg (25%) 80 mg (25%) 0.4 mg (25%) 0.5 µg (25%) 2.5 µg (25%) 2.5 mg (25%) 38 µg (25%) 1.3 mg (25%) 17.5 µg (25%)	

[4] ***Standard 2.6.2*** *of the Australia New Zealand Food Standards Code is varied by –*

[4.1] *omitting from the* Purpose –

The Standard defines a number of products and sets certain compositional requirements for packaged water, electrolyte drinks and brewed soft drinks.

substituting –

The Standard defines a number of products and sets certain compositional requirements for packaged water, electrolyte drinks, brewed soft drinks and formulated beverages.

[4.2] *inserting in the* Table of Provisions

9 Composition of formulated beverages

[4.3] *inserting in clause 1 –*

Formulated beverage means a non-carbonated, water-based flavoured beverage that contains added vitamins and/or minerals, prepared from one or more of the following:

(a) water; and
(b) fruit juice; and
(c) fruit purée; and
(d) concentrated fruit juice; and
(e) concentrated fruit purée; and
(f) comminuted fruit; and
(h) orange peel extract; and
(i) mineral water; and
(j) sugars.

[4.4] *inserting after the* Editorial note *in clause 8 –*

9 Composition of formulated beverages

(1) A formulated beverage must contain no more than:

(a) 240 mL/L of fruit prepared from any of the sources specified in the definition for formulated beverage in paragraphs 1(b) to (g); and

(b) 75 g/L of sugars.

(2) A formulated beverage must not contain carbon dioxide.

(3) A formulated beverage must not be mixed with other beverages.

Attachment 2

Glossary Of Acronyms

ADI	Acceptable Daily Intake
ANZFA	Australia New Zealand Food Authority
ATDS	Australian Total Diet Survey
AUSNUT	Australian Food and Nutrient Database for Nutrition Labelling
CAC/GL	Codex Alimentarius Commission/General Letter
CFR	Code of Federal Regulations
COAG	Council of Australian Governments
Code	*Australia New Zealand Food Standards Code*
Codex	Codex Alimentarius Commission
CoPoNC	*Code of Practice on Nutrient Claims in Food Labels and in* Advertisements
EDTA	Ethylene-diamine-tetraacetic acid
EU	European Union
FAO	Food and Agriculture Organization
FB	Formulated Beverages
FCB	Formulated Caffeinated Beverages
FRSC	Food Regulation Standing Committee
f.o.b.	free-on-board
FSANZ	Food Standards Australia New Zealand
FSANZ Act	*Food Standards Australia and New Zealand Act 1991*
FSSF	Formulated Supplementary Sports Food
FTDS	Food-Type Dietary Supplements
GMP	Good Manufacturing Practices
JECFA	Joint Expert Committee on Food Additives
NIP	Nutrition Information Panel
NNS	National Nutrition Survey
NUTTAB	Nutrient Composition Database
NZDSR	New Zealand Dietary Supplement Regulations
Policy Guideline	Australia and New Zealand Food Regulation Ministerial Council's Policy Guideline on *Fortification of Food with Vitamins and Minerals*
RDI	Recommended Dietary Intake
RIS	Regulation Impact Statement
SPS	Sanitary and Phyto Sanitary

TBT	Technical Barriers to Trade
TGA	Therapeutic Goods Administration
TTMRA	Trans-Tasman Mutual Recognition Arrangement
UL	Upper Level of Intake
US	United States
USFDA	United States Food and Drug Administration
WHO	World Health Organization
WTO	World Trade Organization

Attachment 3

Subsequent Amendments to Application A470– Formulated Beverages

27.06.02 Original Application lodged.

11.11.02 Withdrawal of request for quinine as an additive and revised requested vitamin and mineral levels.

22.11.02 Clarification of typographical errors re: additives sulphur dioxide and sulphates and glycerol esters of wood rosin.

30.12.02 Clarification of typographical errors re: sorbic acid and sorbates; benzoic acid and benzoates and propionates.

10.04.03 Agreement to replace term 'daily dose' 'one-day quantity'.

25.04.04 Withdrawal of request for carbon dioxide as a permitted ingredient.

27.08.04 Amendment of several aspects of the Application including:

- definition of FB:
  - sugar sweetened waters
  - unsweetened water with no added sweeteners
  - non-nutritive sweetened waters – sweetened only with non-nutritive sweeteners
  - sugar sweetened, still fruit drinks and fruit juice drinks (with juice added as an ingredient) but does not include fruit juice. These may also contain non-nutritive sweeteners.
  - non-nutritive sweetened water, still fruit drinks and fruit juice drinks (with juice added as an ingredient) but does not include fruit juice.
  - unsweetened, flavoured, still fruit drinks and fruit juice drinks (with juice added as an ingredient) but does not include fruit juice. These will have no additional sweetener.
  - cordials – including fruit drink cordials and fruit juice cordials (with juice added as an ingredient) containing nutritive and non-nutritive sweeteners.
- vitamins and minerals permissions:
  - approvals per reference quantity (600 mL)
  - revised vitamin and mineral levels
  - maximum claimable amounts reduced to 25% RDI (excluding vitamin C - 100% RDI)
- Withdrawal of request for addition of cyclamate.

28.10.04 Clarification of requested food additives.

Attachment 4

Survey Results

Formulated Beverage Survey - Australia 2005

Summary

Product Name	Content Claims	Other Claims	Directions for Use	Warnings and Advisory Statements	Package Size	Serving Size
AQUAVETA Flavours: with *Lemon, Lime or Orange Juice*	Nutrient Enhanced Water. Iron , Zinc, Calcium.	Aquaveta is a refreshing source of iron, zinc & calcium. These are essential nutrients necessary for a healthy body. Enjoy! No preservatives. No artificial colours or flavours.	It is recommended to drink 700ml to replace fluid lost. Consume 1-2 bottles per day. Remove quality seal under cap. Best before: see neck of bottle.	This is a Formulated Supplementary Sports Drink, not suitable for children under 15 years of age or pregnant women. Should only be used under medical or dietetic supervision. This is not a sole source of nutrition and should be consumed in conjunction with a nutritious diet and with an appropriate exercise program.	700ml	700ml
FRUIT 2 0 *Flavours: Peach Passionfruit, Lemon Lime, Apple Cranberry*	Flavoured Spring Water with Calcium and Vitamin C	Flavoured spring water (90%) with formulated supplementary sports food (10%)			600ml	200ml

G FORCE *Flavours: Apple & Blackcurrant and Orange & Mandarin*	Fruit Drink with vitamins to go!		Push & Go cap. To open: Remove clear overcap. Push down centre of green sipper firmly to pierce the seal inside. Pull sipper up, drink and enjoy! Serve chilled, once opened keep refrigerated.	Warning: Choking risk. This cap contains small parts. Not suitable for children under 36 months.	400ml & 800ml	400ml
JODIS IQ *Flavours: Natural, Lemon Lime, Cranberry, Mandarin, Passionfruit Infusion*	Iodine Enriched Water	Don't drink just water, drink Jodis. No added sugar. Iodine is a crucial element for cell metabolism stimulation. Iodine is a building block fro thyroid hormones. Iodine is an essential nutrient required for balanced thyroid function, promoting vitality and well being.			600ml	Not Specified (assume 600ml)

MIZONE SPORTS WATER *Flavours: Mandarin, Lime, Lemon, Passionfruit, Crisp Apple*	Contains 5 essential vitamins - C, B3, B5, B6, B12.	To achieve your physical best, your body needs lots of water and MIZONE Sports Water is the easiest way to drink it. MIZONE is a pleasant, light tasting blend of purified water and fruit flavours with vitamins so it's easy to drink and it works. Vitamin B's aid in energy metabolism and antioxidant vitamin C assists with recovery and protection. With vitamins and a splash of flavour, MIZONE Sports Water will rehydrate you so you can achieve your goals.	Remove safety seal under sipper cap. Serve chilled, once opened keep refrigerated.		800ml	200ml
PLAY - *Blackcurrant Low GI Sportswater*	Fluoride, Calcium and Vitamins.	Low GI Sustained Energy. No artificial colours, flavours, sweeteners. Ultra low glycaemic index - 16			500mls	500mls
PLAY - *Fruit Fest No Added Sugar Sports Water*	Fluoride, Calcium and Vitamins. No added sugar sports water.	No added sugar. No artificial colours, flavours, sweeteners.			500mls	500mls

PLAY - *Orange Sportswater for Kids*	With fluoride calcium & vitamins. No artificial colours, flavours, sweeteners. Fluoride, Calcium, B Vitamins. Ultra low GI, low sugar. Folate. 5% juice.	Kids need to play every day. PLAY is a nutrient enhanced sportswater specifically formulated for kids. PLAY has an ultra low GI of only 16 - low GI foods provide sustained energy for active, healthy kids and avoid sugar highs and lows. PLAY has only 1/3 the sugar content of most soft drinks, fruit drinks, or cordials and only 1/2 the sugar content of most sports drinks. PLAY is enhanced with Fluoride & Calcium important nutrients for the growth and developments of strong bones and teeth. PLAY also contains Folate for healthy cell renewal, and 5 essential B Vitamins for energy. With 5% juice and no artificial colours, flavours or sweeteners PLAY delivers great tasting hydration and refreshment for kids.			500mls	500mls

POWERADE WATER *Flavours: Mandarin, Lime & Grapefruit*	With 5 essential vitamins B3, B5, B6, B9, B12	We all know how essential drinking water is to our everyday health, but for some of us, plain water is just hard to drink. Powerade Water contains purified water, with a refreshing splash of fruity flavour, 5 essential vitamins & electrolytes. Now it's easy to drink water every day. So whether your'e at work, at home or on the go, drink Powerade Water.	Please remove foil seal from under cap. Best before date-see top of bottle. Store in cool place.		750ml	400ml
SOLIS Bliss	A wellbeing drink	Pink grapefruit, cranberry and strawberry infused with calcium and B Vitamins. Contains no artificial anything.			350ml	350mL
SOLIS Cherish	A wellbeing drink.	White peach and pear infused with folate and vitamin C. Contains no artificial anything.			350ml	350ml
SPRING VALLEY ' Twist ' *Flavour - with a twist of mandarin*	With added calcium and vitmain C. Contains 10% of the RDI of Calcium and 30% of the RDI of Vitmain C.	Getting some of your essential vitamins, minerals and water is easier than ever. Just one bottle of this water contains 10% of the RDI of calcium and 30% of the RDI of vitamin C. Calcium for strong teeth and bones, and vitamin C, a powerful antioxidant which also aids in the absorption of iron. No preservatives. No artificial flavours or colours.	It is recommended to drink 3-4 bottles per day, to replace fluid lost. Consume no more than 6 bottles per day. Best Before: See neck of bottle.	This is a formulated supplementary sports drink - Not suitable for children under 15 years of age or pregnant women. Should only be used under medical or dietetic supervision. This drink is not a sole source of nutrition and should be consumed in conjunction with a nutritious diet and with an appropriate exercise program.	600ml	600ml

TEMPLE HYDRO THERAPY - *Honeydew flavour vitamin water with calcium*	No artifical anything. At last….healthy refreshment with flavour. Low glycemic index (GI) 16	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml
TEMPLE HYDRO THERAPY - *Star fruit flavour vitamin water with aloe*	No artifical anything. At last….healthy refreshment with flavour. Low glycemic index (GI) 16	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml
TEMPLE HYDRO THERAPY - *Pink grapefruit flavour vitamin water with antioxidants*	No artifical anything. At last….healthy refreshment with flavour. Low glycemic index (GI) 16	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml
TEMPLE HYDRO THERAPY - *Blood orange flavour vitamin water with calcium*	No artifical anything. At last….healthy refreshment with flavour. Low glycemic index (GI) 16	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml

TEMPLE HYDRO THERAPY - *White peach flavour vitamin water with fibre*	No artifical anything. At last….healthy refreshment with flavour. A good source of added fibre.	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml
TEMPLE HYDROTHERAPY - *Dragonfruit flavour vitamin water with iron*	No artifical anything. At last….healthy refreshment with flavour. Ultra low glycemic index (GI) 16	Indulge your mind, body and soul with Temple Hydrotherapy vitmain water. Infused with essential nutrients to nurture your body and exotic flavours to tantalise your taste buds. No artificial colour, no artificial sweeteners, no preservatives. Treat yourself.	Recommended consumption 500ml per day. For best before - see bottle.	Formulated supplementary sports food. Not suitable for children under 15 years of age or pregnant women: should only be used under medical or dietetic supervision.	500ml	500ml
THORPEDO - Advanced Hydration *Flavours: Orange, Lemon Lime, Berry, Tropical*	Ultra low GI energy water. Beat the fade.	Thorpedo Advanced Hydration provides a unique energy management system with a blend of key performance electrolytes, 6 B complex vitamins and 2 antioxidants that work in synergy with the Ultra Low GI carbohydrates to hydrate and sustain energy. So whether you're working, playing, training or competing, enjoy Thorpedo, stay hydrated and energised and feel great all day.	Best before: see neck of bottle. Shake well. Refrigerate after opening.	This is a formulated supplementary sports drink, not suitable for children under 15 years of age or pregnant women. Should only be used under medical or dietetic supervision. This is not a sole source of nutrition and should be consumed in conjunction with a nutritious diet and with an appropriate exercise program.	600ml	600ml

WATERPLUS (Bickford) *Flavours: Peach, Lemon & Lime, Lemon, Melon and Mandarin*	Antioxidants plus electrolytes plus B vitamins. Sugar free.	Antioxidants are vitamins that help protect body cells from breakdown due to the stresses of everyday life. Electrolytes are essential minerals that assist in hydration. B vitamins boost energy levels and a feeling of well being.	Remove quality seal under cap. Keep refrigerated once open.		710ml	710ml
WATERPLUS (Sanitarium) *Flavours: Peach, Lemon & Lime, Lemon, Melon and Mandarin.* Note: Bickford has since purchased product and reformulated slightly.	5 Minerals 7 vitamins. Electrolytes are essential minerals that assist in hydration. Antioxidants are vitamins that help to protect your body against harmful free radicals. Low joule.	Waterplus takes the hard work out of hydration. A refreshing blend of pure mineral water, light flavours, with vitamins and minerals. Waterplus is easy to drink. And most importantly with no sugar and only 2 calories per bottle you'll burn it off in around 30 seconds of walking. Drink Waterplus and feel the difference.	Remove quality seal under cap. Keep refrigerated once opened.		710 ml	710ml

PROPEL - Fitness Water *Flavour: Orange* Deleted Line ~ June 2004	Good source of 6 vitamins as part of daily diet. The four B vitamins in Propel aid in energy metabolism, antioxidants C & E work together to neutralize free radicals to effectively protect your body. With these 6 vitamins and a splash of flavour Propel supports your daily pursuit of fitness and well being.	Fitness Water Orange with other natural flavours. Quenches and nurtures your body. No fruit juice.	Refrigerate after opening		500mls	240ml
RIDE Flavours: Mandarin etc. Line Deleted ~ Sep 2004 replaced by Play	Low GI. Enhanced with B vitamins plus bio-available trace minerals & antioxidants - specially formulated to help convert fructose into sustained energy.	Liquid for life. Low GI Food. Delivers sustained energy. Rapid Hydration sustained energy. Ride fitness water uses all natural fructose - the low glycaemic index carbohydrate that avoids the energy highs and lows you get with ordinary sugars. With 5% juice and a splash of fruit flavour, Ride delivers great taste, hydration and energy supplement so you can ride hard all day.	Drink often , feel great.		500ml	

SLINKY Flavour: *Mandarin* Deleted Lined since ~ Sep2004	Slinky is enhanced with Carnitine, Chromate ® and Biotin - co-factors that may assist in fat metabolism. Is infused with Calcium & Folate for healthy cell renewal and B vitamins to help metabolise energy.	The world's perfect diet drink. Low GI foods can help you feel full for longer and as a result you can end up eating less over the day. Low GI Slinky is a great tasting addition to your daily hydration, exercise & lifestyle plan.	Drink often , feel great.		500ml	500ml

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Composition

Product Name	Serving Size	No. of serves per day	Energy (kJ)	Total Fat (g)	Protein (g)	Carbohydrate (g)	Sugars (g)	Vitamins (percentage RDI per serve)	Minerals (percentage RDI per serve)	Herbal Extracts
							Per 100 ml Product			
AQUAVETA	700 ml	1-2 Bottles per day	38	0	0	2.2	2.2		Sodium=2 mg Calcium=11.4mg (10%) Iron=0.2mg (10%) Zinc=0.2mg (10%)	
FRUIT 2 0	200 ml	NS	56	0	0	3.3	3.3	C=2 mg (10%)	Sodium=3mg Calcium=40mg (10%)	
G FORCE	400 ml	NS	184	<1	<1	10.8	10.8	C=35mg (350%) E=1mg (40%) B3=1mg (40%) B5=0.5mg B6=0.16mg (40%) B12=0.2ug (40%)	Sodium< 5.1mg	
JODIS IQ	600ml	NS	NS	NS	NS	NS	NS		Iodine=0.015mg Calcium=12mg Magnesium=1.5mg Potassium=0.4mg HCO3=45mg Chloride=1.5 mg Sodium=Not Specified	

MIZONE SPORTS WATER	200 ml	NS	43	0	0	2.5	2.5	C=20mg (100%) B3=1mg (20%) B5=0.5mg B6=0.16mg (20%) B12=0.1ug (10%)	Sodium=<5mg	
PLAY *Blackcurrant Low GI*	500 ml	NS	72	0	0	4.2	4	B3=2.7mg (71%) B5=0.7mg B6=0.3 mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Calcium=16mg (10%) Fluoride=0.1mg Sodium=8mg	
PLAY *Fruit Fest No Added Sugar*	500 ml	NS	94	0	0	5.6	5.4	B3=2.7mg (71%) B5=0.7mg B6=0.3 mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Calcium=16mg (10%) Fluoride=0.1mg Sodium=8mg	
PLAY *Orange Sportswater for Kids*	500 ml	NS	72	0	<1	4	4	B3=2.7mg B5=0.7mg B6=0.3 mg Folate=30ug Biotin=10ug B12=0.15ug	Calcium=28mg Fluoride=0.1mg Sodium=8mg Potassium=9mg	

POWERADE WATER	400ml	Recommended daily consumption, Adults up to 6 bottles, children between 3 and 13 up to 2 bottles.	41	0	0	2.3	2.3	B3=0.5mg (20%) B5=0.25mg B6=0.08mg (20%) B9=20ug (40%) B12=0.2ug (40%)	Sodium=12mg Potassium=14mg	
SOLIS Bliss	350 ml	NS	182	<1	<1	11	11	B1=0.6mg B3=3.5mg B5=1mg B6=0.9mg B12=1.1ug	Calcium=30mg Sodium=8mg	
SOLIS Cherish	350 ml	NS	194	<1	<1	11	11	Folate=12.5ug C=15mg	Sodium=9mg	
SPRING VALLEY 'Twist'	600 ml	Recommended 3-4 bottles per day, consuming no more than 6 bottles.	44	0	0	2.6	2.6	C=2mg (30%)	Calcium=13.3mg (10%) Sodium=3mg	
TEMPLE HYDRO THERAPY - ***Honeydew flavour vitamin water with calcium***	500ml	NS	80	<1	<1	4.7	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Calcium=16mg (10%) Sodium=2mg	

TEMPLE HYDRO THERAPY - ***Star fruit flavour vitamin water with aloe***	500ml	NS	80	<1	<1	4.7	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Sodium=2mg	Aloe extract
TEMPLE HYDROTHERAPY - ***Pink grapefruit flavour vitamin water with antioxidants***	500ml	NS	80	<1	<1	4.7	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%) E=0.2mg (10%) A=15ug (10%)	Sodium=2mg	
TEMPLE HYDRO THERAPY - ***Blood orange flavour vitamin water with calcium***	500ml	NS	80	<1	<1	4.7	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Calcium=16mg (10%) Sodium=2mg	

TEMPLE HYDRO THERAPY - ***White peach flavour vitamin water with fibre***	500ml	NS	90	<1	<1	5.4	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Sodium=2mg	
TEMPLE HYDRO THERAPY - ***Dragonfruit flavour vitamin water with iron***	500ml	NS	80	<1	<1	4.7	4.7	B3=2.7mg (135%) B5=0.7mg B6=0.3mg (94%) Folate=30ug (75%) Biotin=10ug B12=0.15ug (38%)	Iron=0.23 (10%) Sodium=2mg	
THORPEDO Advanced Hydration	600 ml	Recommend consumption 1 bottle per day	72	0	0	4.5	4.2	B3=2.7mg (162%) B5=0.6mg B6=0.3mg (110%) E=0.2mg (10%) Folate=30ug (90%) A=12.5ug (10%) Biotin=8.3ug B12=0.15ug (45%)	Sodium=25 mg Potassium=12 mg Chloride=31mg	

WATERPLUS (Bickford)	710ml	Recommended consumption: up to 4 serves per day	2	0	0	<0.1	0	B1=0.04mg (10%) B3=0.35mg (10%) B5=0.18mg (25%) B6=0.06mg (25%) B12=0.07mg (25%) C=1.4mg (25%) E=0.14mg (10%)	Magnesium=4.5mg (10%) Zinc=0.17mg (10%) Sodium=6mg Potassium=6mg	
WATERPLUS (Sanitarium) Note: Bickford has since purchased product and reformulated slightly.	710 ml	NS	2	0	0	<1	0	B1=0.04mg (25%) B3=0.4mg (25%) B5=0.2mg B6=0.06mg (25%) B12=0.1mg (25%) C=1mg (25%) E=0.1mg (10%)	Calcium=11mg (10%) Magnesium=5mg (10%) Zinc=0.2mg (10%) Sodium=6mg Potassium=6mg	
PROPEL - Fitness Water Deleted Line ~ June 2004	240 mL	NS	17.5	0	0	125%	0.83	% Daily Value C=10% E=10% B3=25% B6=25% B12=25% B5=25%	Sodium=35 mg Potassium=40mg	

RIDE Line Deleted ~ Sep 2004 replaced by Play	500 mL	NS	72	0	<1	4	4	B3=2.7mg B5=0.7mg B6=0.3mg Folate=30ug Biotin=10ug B12=0.15ug	Potassium=9mg Sodium=8mg Magnesium=17 mg Optizinc=10mg Zinc=2 mg Chromemate=100ug (niacin bound-chromium)	
SLINKY Deleted Lined since ~ Sep2004	500 mL	NS	72	0	<1	4	4	B3=2.7 mg B5=0.7 mg B6 =0.3 mg Folate=30ug Biotin=10ug B12=0.15ug	Calcium=28 mg Chromemate=100ug (niacin bound-chromium)	

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Manufacturer & Ingredients

Product Name	Manufacturer Details	Country of Origin	Distributor Details (if necessary)	Ingredients
AQUAVETA	Spring Valley Beverages 2 Beverage Drive Tullamarine Victoria 3043, Australia (Cadbury Schweppes Group)	Australia		LEMON JUICE CONTAINS: PURIFIED WATER (96%), SUCROSE, RECONSTITUTED LEMON JUICE (1%), FLAVOUR, ACID (330), MINERALS (CALCIUM GLUCONATE, CALCIUM LACTATE, FERROUS GLUCONATE, ZINC GLUCONATE), MALTODEXTRIN.
FRUIT 2 0	P&N Beverages Australia Pty Ltd 43 Mons Street Condell Park NSW 2200, Australia. PH 1800 658459	Australia		PEACH PASSIONFRUIT CONTAINS: FLAVOURED SPRING WATER (90%) [SPRING WATER, SUGAR, RECONSTITUTED PEACH AND PASSIONFRUIT JUICES (2%), FOOD ACID (330), FLAVOUR, PRESERVATIVES (211,223)], SUPPLEMENTARY SPORTS FOOD (10%) [SPRING WATER, MINERAL SALT (CALCIUM LACTATE), VITAMIN C (300)].
G FORCE	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd 13 South St Rydalmere NSW 2116, Australia. PH 1800 237727	APPLE BLACKCURRANT CONTAINS: WATER, SUGAR, RECONSTITUTED FRUIT JUICE (APPLE (5%), BLACKCURRANT (3%)), ACIDITY REGULATORS (330, 331), FLAVOURS, VITAMINS (ASCORBIC ACID (C), E, B3, B5, B6, B12), STABILISER (PECTIN)), PRESERVATIVE (202), COLOURS (123,133).
JODIS IQ		Not Specified	Jodis Australasia Pty 11 Narloo Street Perth WA 6090, Australia. www.jodiswater.com.au	NATURAL FLAVOUR, POTASSIUM SORBATE(202), SODIUM BENZOATE (211). Note: Full ingredient list not provided on label.
MIZONE SPORTS WATER.	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd 13 South St Rydalmere NSW 2116, Australia PH 1800 237727	MANDARIN FLAVOUR - PURIFIED WATER, RECONSTITUTED APPLE JUICE, FRUCTOSE, APPLE CIDER VINEGAR, MANDARIN FLAVOURING, VITAMINS (ASCORBIC ACID (C), B3, B5, B6, B12), ACIDITY REGULATOR (CITRIC ACID).

PLAY *Blackcurrant Low GI Sportswater*	Zenergy Beverages 12A/440 Collins St Melbourne Victoria 3000, Australia www.zenergybeverages.com	Australia		PURIFIED WATER, CONCENTRATED JUICES (PEACH, APPLE & GRAPE), FRUCTOSE, CALCIUM LACTATE (327), FLAVOUR (0.1%), FOOD ACID (330), PRESERVATIVES (211,223), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, SODIUM FLUORIDE, FOLIC ACID, BIOTIN, VITAMIN B12.
PLAY *Fruit Fest-No Added Sugar Sportswater*	Zenergy Beverages 12A/440 Collins St Melbourne Victoria 3000, Australia www.zenergybeverages.com	Australia		PURIFIED WATER, CONCENTRATED JUICES (APPLE, LEMON & GRAPE), CALCIUM LACTATE (327), FLAVOURS (0.1%), FOOD ACID (330), PRESERVATIVES (211,223), NIACIN(B3), PANTOTHENIC ACID (B5), VITAMIN B6, SODIUM FLUORIDE, FOLIC ACID, BIOTIN, VITAMIN B12.
PLAY *Orange Sportswater for Kids*	Zenergy Functional Beverages 15 Endeavour Drive Ocean Grove Victoria 3226, Australia	Australia		PURIFIED WATER, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), FRUCTOSE (4%), CALCIUM LACTATE (327), NATURAL ORANGE FLAVOUR (0.06%), FOOD ACID (330), POTASSIUM SORBATE (202), SODIUM BENZOATE (211), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, SODIUM FLUORIDE, FOLIC ACID, BIOTIN, VITAMIN B12.
POWERADE WATER	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		MANDARIN CONTAINS: WATER (97.3%), SUCROSE, FOOD ACID (330), TRI-POTASSIUM CITRATE, SODIUM CHLORIDE, FLAVOUR, ANTIOXIDANT (300), TRI-POTASSIUM PHOSPHATE, VITAMINS B3 (NIACIN), B5, B6, B9 (FOLIC ACID), B12.
SOLIS Bliss	Solis Beverages 40 Yeo St Neutral Bay NSW 2089, Australia PH 02 89696781	Australia		PURIFIED WATER, SUCROSE, CONCENTRATED PINK GRAPEFRUIT (3%), CRANBERRY (2%) & STRAWBERRY (2%) JUICES, FOOD ACID (330), NATURAL FLAVOURS, CALCIUM LACTATE (327) (0.2%), NATURAL COLOUR (120), NIACIN (B3), PANTOTHENIC ACID (B5), Vit B6, THIAMIN (B1), VITAMIN B12.
SOLIS Cherish	Solis Beverages 40 Yeo St Neutral Bay NSW 2089, Australia PH 02 89696781	Australia		PURIFIED WATER, SUCROSE, CONCENTRATED PEAR (24.5%) & PEACH (0.5%) JUICES, FOOD ACID (330), NATURAL FLAVOURS, VITAMIN C, FOLATE (<0.01%).
SPRING VALLEY 'Twist'	Sring Valley Beverages 2 Beverage Drive Tullamarine VIC 3043, Australia PH 1800 244054	Australia		SPRING WATER (98%), SUGAR, RECONSTITUTED MANDARIN JUICE (1%), FOOD ACID (330), MINERAL SALT (CALCIUM LACTATE), NATURAL MANDARIN FLAVOUR, VITAMIN C.

TEMPLE HYDROTHERAPY - *Honeydew flavour vitamin water with calcium*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), CITRIC ACID (330), FLAVOURS, CALCIUM LACTATE (327), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, FOLIC ACID, BIOTIN, VITAMIN B12.
TEMPLE HYDROTHERAPY - *Star fruit flavour vitamin water with aloe*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), FLAVOURS, ALOE EXTRACT, CITRIC ACID (330), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, FOLIC ACID, BIOTIN, VITAMIN B12.
TEMPLE HYDROTHERAPY - *Pink grapefruit flavour vitamin water with antioxidants*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), FLAVOUR, CITRIC ACID (330), COLOUR (120), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, ALPHA TOCOPHERYL ACETATE (VIT E), FOLIC ACID, RETINYL PALMITATE (VIT A), BIOTIN, VITAMIN B12.
TEMPLE HYDROTHERAPY - *Blood orange flavour vitamin water with calcium*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), CALCIUM LACTATE (327), FLAVOURS, CITRIC ACID (330), COLOUR (120), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, FOLIC ACID, BIOTIN, VITAMIN B12.
TEMPLE HYDROTHERAPY - *White peach flavour vitamin water with fibre*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), POLYDEXTROSE, CITRIC ACID (330), FLAVOUR, COLOUR (120), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, FOLIC ACID, BIOTIN, VITAMIN B12.
TEMPLE HYDROTHERAPY - *Dragonfruit flavour vitamin water with iron*	Carlton & United Beverages 77 Southbank Boulevard Southbank Victoria 3006, Australia PH 1800 007282	Australia		PURIFIED WATER, FRUCTOSE, CONCENTRATED JUICES (LEMON, APPLE & GRAPE), CITRIC ACID (330), FLAVOURS, COLOUR (120), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, FERROUS GLUCONATE (579), FOLIC ACID, BIOTIN, VITAMIN B12.

THORPEDO Advanced Hydration	Manufactured under licence for Thorpedo Foods Pty Ltd www.thorpedofoods.com.au	Australia	So Natural Foods Australia Ltd 80 Box Rd Taren Point NSW 2229, Australia	ORANGE FLAVOUR: PURIFIED WATER, CONCENTRATED JUICES (LEMON, APPLE, & GRAPE), FRUCTOSE (4%), ELECTROLYTES (CALCIUM LACTATE (327), SODIUM CHLORIDE, POTASSIUM CITRATE, MAGNESIUM LACTATE (329)), ORANGE FLAVOUR (0.1%), FOOD ACID (330), PRESERVATIVES (211, 223), NIACIN (B3), PANTOTHENIC ACID (B5), VITAMIN B6, VITAMIN E (ALPHA TOCOPHEROL ACETATE), FOLIC ACID, VITAMIN A (RETINOL PALMITATE), BIOTIN, VITAMIN B12.
WATERPLUS (Bickford)	Manufactured in New Zealand for: Bickfords Australia Pty Ltd 34 Starr Ave Plympton South Australia 5037, Australia	New Zealand	Bickfords Australia Pty Ltd 34 Starr Ave Plympton South Australia 5037, Australia	PEACH FLAVOUR: WATER (99%), MINERALS (POTASSIUM CITRATE, SODIUM CHLORIDE, MAGNESIUM GLUCONATE,CALCIUM LACTATE, ZINC GLUCONATE), VITAMINS (C, B3, E ACETATE, B5, B6, B1, B12), FOOD ACIDS(MALIC ACID, CITRIC ACID), PEACH FLAVOUR, ARTIFICIAL SWEETENER.
WATERPLUS (Sanitarium) Note: Bickford has since purchased product and reformulated slightly.	Sanitarium Health Food Company 124 Pah Road Royal Oak Auckland, NZ	New Zealand		LEMON LIME FLAVOUR: WATER (99%), MINERALS (MAGNESIUM GLUCONATE, CALCIUM LACTATE, POTASSIUM BICARBONATE, SODIUM CHLORIDE, ZINC GLUCONATE), VITAMINS (C, B3, E ACETATE, B5, B6, B1, B12), FOOD ACIDS (MALIC ACID, CITRIC ACID), LEMON LIME FLAVOUR, ARTIFICIAL SWEETENER.
PROPEL - Fitness Water Deleted Line ~ June 2004	Cadbury Schweppes 2 Beverage Drive Tullamarine Victoria, Australia	NS	Distributed by Gatorade Company PO Box 049003 Chicago USA	PURIFIED WATER , SUCROSE SYRUP, CITRIC ACID, NATURAL ORANGE FLAVOUR WITH OTHER NATURAL FLAVOURS, SODIUM CITRATE, POTASSIUM CITRATE, ASPARTAME, VITAMIN C (ASCORBIC ACID), VITAMIN E ACETATE, ACESULFAME POTASSIUM, NIACINAMIDE (VIT B3), CALCIUM PANTOTHENATE (VITAMIN B5), VITAMIN B12, PYRIDOXINE HYDROCHLORIDE (VITAMIN B6). PHENYLKETONURICS: CONTAINS PHENYLALANINE

RIDE Deleted Line ~ Sep 2004 replaced by Play	Zenergy Beverages 12A/440 Collins St Melbourne Victoria 3000, Australia www.zenergybeverages.com	Australia		FLAVOURED MANDARIN DRINK CONTAINS PURIFIED WATER, CONCENTRATED JUICES, (LEMON, APPLE & GRAPE), FRUCTOSE (4%), NATURAL MANDARIN FLAVOUR (0.06%), FOOD ACID(330), POTASSIUM SORBATE(202), SODIUM BENZOATE (211), MAGNESIUM LACTATE (329), L-OPTIZINC ® (ZINC L-METHIONINE), NIACIN (B3), PANTOTHENIC ACID(B5), VIT B6, CHROMEMATE (R) (NIACIN-BOUND CHROMIUM), FOLIC ACID, BIOTIN, VITAMIN B12.
SLINKY Deleted Lined since ~ Sep 2004	Zenergy Beverages 12A/440 Collins St Melbourne Victoria 3000, Australia www.zenergybeverages.com	Australia		LOW-JOULE FLAVOURED MANDARIN DRINK CONTAINS PURIFIED WATER, CONCENTRATED JUICES, (LEMON, APPLE & GRAPE), FRUCTOSE (4%), CALCIUM LACTATE(327), NATURAL MANDARIN FLAVOUR (0.06%), COLOUR (120), FOOD ACID(330), POTASSIUM SORBATE(202), SODIUM BENZOATE (211), CARNITINE, NIACIN (B3), PANTOTHENIC ACID(B5), VIT B6, CHROMEMATE ® (NIACIN-BOUND CHROMIUM), FOLIC ACID, BIOTIN, VITAMIN B12.

Formulated Beverage Survey - New Zealand 2005

Summary

Product Name	Content Claims	Other Claims	Directions for Use	Warnings and Advisory Statements	Availability	Package Size	Serving Size
AQUA SHOT *Flavours: Lime, Raspberry, Mandarin and Apple*	Active water. Picture of the flavouring fruit with 5 B-vitamin symbols attached.	If you want to grab life's opportunities, you need to be on your game. Aqua Shot is active water with a refreshing burst of fruit flavour and the boost of 5 essential vitamins, making it the tastiest way to keep hydrated, so you'll never miss a shot.	Please remove foil seal from under cap. Store in a cool place. For best before date see bottle.	Recommended daily consumption: adults up to 6 bottles; children between 3 and 13 up to 2 bottles.	Supermarkets and dairies	800ml	200ml
WATERPLUS *Flavours: Peach, Lemon & Lime, Lemon, Melon and Mandarin*	Low joule. 5 minerals. 7 vitamins. Electrolytes are essential minerals that assist in hydration. Antioxidants are vitamins that help to protect your body against harmful free radicals.	Waterplus takes the hard work out of hydration. A refreshing blend of pure mineral water, light flavours, with vitamins and minerals. Waterplus is easy to drink. And most importantly with no sugar and only 2 calories per bottle you'll burn it off in around 30 seconds of walking. Drink Waterplus and feel the difference.	Remove quality seal under cap. Keep refrigerated once opened.		Supermarkets and dairies	710ml	710ml

CHARLIE'S SPORTS WATER *Flavours: Cranberry & Raspberry, Mandarin, Lemon & Lime and Blackcurrant*	No added sugar. No artificial sweeteners. No preservatives. Vitamins charged C, B3, B5, B6, B12, E		Serve chilled, refrigerate after opening. Consume within four days of opening. Remove safety seal under sipper cap.			800ml & 3L	200ml
e2 *Flavours: Apple Crush, Orange, Lemon & Lime, Mango and Blackcurrant & Apple*	Liquid Energy. With fruit juice and vitamins. Lists 'A, B1, B5, B6, E' under the product title.	e2. The powerful fruit hit that's packed with full-on fruit flavours and vitamins. With a wicked combination of fruit juice, vitamins, minerals and electrolytes, you're drinking liquid energy, bursting with awesome flavour. Re-fuelling your body, keeping you charged. Doing the things you want to. Whenever, wherever. e2, don't run out of 'juice'.	Best before date see top of bottle. Serve chilled. Store in cool place. Refrigerate after opening.	The cap contains small parts and is therefore not suitable for unsupervised children under 36 months.		400ml & 800ml	200ml
G FORCE *Flavours: Apple & Blackcurrant and Orange & Mandarin*	Fruit drink with vitamins to go!		Push & go cap instructions. Serve chilled, once opened keep refrigerated.	Warning: Choking risk. This cap contains small parts. Not suitable for children under 36 months.		800ml	400ml

MIZONE SPORTS WATER *Flavours: Mandarin, Lime, Lemon, Passionfruit, Crisp Apple*	5 essential vitamins C, B3, B5, B6, B12. Vitamin C - assists with recovery and protection. B vitamin's - aid in energy metabolism.	Active hydration. MIZONE Sportswater is a great tasting blend of purified water and fruit flavours with the benefits of 5 essential vitmains that's easy to drink and helps you feel at your best. MIZONE Sportswater helps you rehydrate your body so you can get in your zone and achieve your goals.	Remove safety seal under sipper cap. Serve chilled, once opened keep refrigerated.	Warning: Choking risk. This cap contains small parts. Not suitable for children under 36 months.		800ml	200ml
MIZONE PEAK Performance Sportswater *Flavours: Mandarin and Lime*	5 essential vitamins plus Teavigo. Teavigo EGCG - green tea extract which helps utilise energy, increases blood flow and acts as a potent antioxidant. Iron - to help get oxygen around the body. B vitamins - aid in energy metabolism. Vitamin C - assists with recovery and protection.	It's the combination of Iron and Teavigo in MIZONE Peak Sportswater which helps you to perform at your best by keeping you hydrated and assisting you to maximise energy output.	Remove safety seal under sipper cap. Serve chilled, once opened keep refrigerated.	Warning: Choking risk. This cap contains small parts. Not suitable for children under 36 months.		650ml	650ml

POWERADE WATER *Flavours: Mandarin, Lime & Grapefruit*	With 5 essential vitamins B3, B5, B6, B9, B12	We all know how essential drinking water is to our everyday health, but for some of us, plain water is just hard to drink. Powerade Water contains purified water, with a refreshing splash of fruity flavour, 5 essential vitamins & electrolytes. Now it's easy to drink water every day. So whether you're at work, at home or on the go, drink Powerade Water.	Please remove foil seal from under cap. Best before date see top of bottle. Store in cool place.			750ml	400ml
THEXTON'S FRUIT DRINK *Flavours: Pink Grapefruit, Cranberry and Red Grape*	With vitamins A, C & E.		Store in a cool place. Refrigerate after opening. For best before date see top of bottle.			3L	200ml
CAPRI-SONNE MULTI VITAMIN *Fruit Juice Drink*	With 12% fruit juice. Enriched with 9 vitamins.		Best before: see narrow side flap.			10x 200ml	200ml

Formulated Beverage Survey - New Zealand 2005

Composition

Product Name	Serving Size	No. of serves per day	Energy (kJ)	Total Fat (g)	Protein (g)	Carbo-hydrate (g)	Sugars (g)	Vitamins (percentage RDI per serve)	Minerals (percentage RDI per serve)	Herbal Extracts
							Per 100 ml product			
AQUA SHOT	200ml	Adults - 24 maximum Children - 8 maximum	44	0	0	2.5	2.5	B3=0.5mg (10%) B5=0.25mg B6=0.08mg (10%) B9=20ug (20%) B12=0.2ug (20%)	Soduim=3mg	
WATERPLUS	710ml	Not Specified	2	0	0	<0.1	0	B1=0.04mg (25%) B3=0.4mg (25%) B5=0.2mg B6=0.06mg (25%) B12=0.1mg (25%) C=1mg (25%) E=0.1mg (10%)	Sodium=6mg Potassium=6mg Calcium=11mg (10%) Magnesium=5mg (10%) Zinc=0.2mg (10%)	
CHARLIE'S SPORTS WATER	200ml	8 serves	59.3	0.01	0.06	3.34	3.2	B3=1.0mg (20%) B5=0.5mg (20%) B6=0.16mg (20%) B12=0.1ug (10%) E=0.5mg (10%) C=20.0mg (100%)	Sodium=9mg (0.8%)	
e2	200ml	Recommended daily consumption, adults up to 2 litres, children above 3 years up to 800ml.	171	<1	<1	9.8	9.7	B1=0.06mg (10%) B3=0.5mg (10%) B5=0.3mg B6=0.08mg (10%) A=37.5ug (10%) E=0.5mg (10%)	Sodium=20mg Potassium=8.3mg Calcium=3.8mg	

G FORCE	400ml	Not Specified	177	<1	<1	10.4	10.4	C=35mg (350%) E=1mg (40%) B3=1mg (40%) B5=0.5mg B6=0.16mg (40%) B12=0.2ug (40%)	Sodium=4.7mg	
MIZONE SPORTS WATER.	200ml	Not Specified	43	0	0	2.5	2.5	C=20mg (100%) B3=1mg B5=0.5mg B6=0.16mg (20%) B12=0.1ug (10%)	Sodium=<5mg	
MIZONE PEAK Performance Sportswater	650ml	Not Specified	53	0	<1	3	2.9	C=6mg (100%) B3=0.3mg (20%) B5=0.15mg B6=0.05mg (20%) B12=0.03ug (10%)	Sodium=<5mg Iron=0.18mg (10%)	Epigallocatechin Gallate (EGCG) - Green Tea extract
POWERADE WATER	400ml	Recommended daily consumption, Adults up to 6 bottles, children between 3 and 13 up to 2 bottles.	41	0	0	2.3	2.3	B3=0.5mg (20%) B5=0.25mg B6=0.08mg (20%) B9=20ug (40%) B12=0.2ug (40%)	Sodium=12mg Potassium=14mg	
THEXTON'S Fruit Drink	200ml	Recommended daily consumption, adults up to 2 litres, children above 3 years up to 1.2 litres.	196	<1	<1	11.3	11.3	A=50ug (13%) C=8mg (40%) E=0.6mg (12%)	Sodium=12mg	

CAPRI-SONNE MULTIVITAMIN Fruit Juice Drink	200ml	Not Specified	179	<0.1	<0.1	10.2	10.2	B1=0.21mg (15%) B3=2.7mg (15%) B5=0.9mg (15%) B6=0.3mg (15%) B9=30ug (15%) Biotin=22.5ug(15%) B12=0.15ug (15%) C=9mg (15%) E=1.5mg (15%)	Sodium=<20mg (as per distributors label)	

Formulated Beverage Survey - New Zealand 2005

Manufacturer & Ingredients

Product Name	Manufacturer Details	Country of Origin	Distributor Details (if necessary)	Ingredients
AQUA SHOT	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		WATER, APPLE JUICE FROM CONCENTRATE (4.5%), FRUCTOSE, APPLE CIDER VINEGAR, FLAVOUR, FOOD ACID (330), LACTOSE, VITAMINS (B3 (NIACIN), B5, B6, B9 (FOLIC ACID), B12).
WATERPLUS	Sanitarium Health Food Company 124 Pah Road Royal Oak Auckland, NZ	New Zealand		WATER (99%), MINERALS (MAGNESIUM GLUCONATE, CALCIUM LACTATE, POTASSIUM BICARBONATE, SODIUM CHLORIDE, ZINC GLUCONATE), VITAMINS (C, B3, E ACETATE, B5, B6, B1, B12), FOOD ACIDS (CITRIC ACID, MALIC ACID), FLAVOUR, ARTIFICIAL SWEETENER.
CHARLIE'S SPORTS WATER		New Zealand	Charlie's Trading Company Ltd 125 The Strand Parnell Auckland, NZ PH 0800 126 435 office@charlies.co.nz/www.charlies.co.nz	WATER (95%), RECONSTITUTED APPLE JUICE, VITAMINS C, B3, B5, B6, B12, E, APPLE CIDER VINEGAR, FLAVOUR, FOOD ACID (330).
e2	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		BLACKCURRANT & APPLE CONTAINS: WATER, SUGAR, BLACKCURRANT JUICE FROM CONCENTRATE (2.7%), APPLE JUICE FROM CONCENTRATE (2.3%), FOOD ACID (330), FLAVOUR, MINERALS (POTASSIUM, SODIUM, CALCIUM), VITAMINS (A, NIACIN, E, B5, B6, B1), PRESERVATIVES (211, 202), COLOURS (150d, 102).
G FORCE	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand		ORANGE & MANDARIN CONTAINS: WATER, RECONSTITUTED FRUIT JUICE (ORANGE (7%), MANDARIN (3%)), SUGAR, ACIDITY REGULATORS (330, 331), FLAVOURS, VITAMINS (ASCORBIC ACID (C), E, B3, B5, B6, B12), STABILISER (PECTIN), COLOURS (160A, 123), PRESERVATIVE (202).

MIZONE SPORTS WATER	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd 99 Derby St Wilversater NSW 2128, Australia PH 1800 237 727	PURIFIED WATER, RECONSTITUTED APPLE JUICE, FRUCTOSE, APPLE CIDER VINEGAR, VITAMINS (ASCORBIC ACID (C), B3, B5, B6, B12), FLAVOURING, ACIDITY REGULATOR (CITRIC ACID).
MIZONE PEAK Performance Sportswater	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd 99 Derby St Wilversater NSW 2128, Australia PH 1800 237 727	PURIFIED WATER, RECONSTITUTED APPLE JUICE, APPLE CIDER VINEGAR, ACIDITY REGULATOR (CITRIC ACID), FLAVOURING, VITAMINS (ASCORBIC ACID (C), B3, B5, B6, B12), GREEN TEA EXTRACT (EGCG), IRON (FERROUS GLUCONATE).
POWERADE WATER	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		MANDARIN CONTAINS: WATER (97.3%), SUCROSE, FOOD ACID (330), TRI-POTASSIUM CITRATE, SODIUM CHLORIDE, FLAVOUR, ANTIOXIDANT (300), TRI-POTASSIUM PHOSPHATE, VITAMINS B3 (NIACIN), B5, B6, B9 (FOLIC ACID), B12.
THEXTON'S Fruit Drink	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ			RED GRAPE CONTAINS: WATER, SUGAR, RED GRAPE JUICE FROM CONCENTRATE (5%), FOOD ACID (330), FLAVOUR, COLOUR (150D, 122), VITAMINS (C,E,A), MINERAL SALT (452).
CAPRI-SONNE MULTIVITAMIN	Deutsche Sisi-Werke GmbH & Co. Betriebs KG, D-69009 Heidelberg, Germany	Germany	Impex International Trading Ltd P.O. Box 528 Kerikeri, NZ. PH 09 407 4277	WATER, SUGAR, LEMON JUICE (4%), ORANGE JUICE (4%), APPLE JUICE, GRAPEFRUIT JUICE, GLUCOSE-FRUCTOSE SYRUP, PINEAPPLE JUICE, PASSIONFRUIT JUICE, BANANA JUICE, KIWI JUICE, VITAMINS (C, NICOTINAMIDE, E, PANTOTHANTE, B6, THIAMIN, FOLACIN, BIOTIN, B12), NATURAL FLAVOURING (FROM CONCENTRATE).

Food-Type Dietary Supplement Survey - Formulated Beverages - Australia 2003

Summary

Product Name	Content Claims	Other Claims	Directions for Use	Warnings and Advisory Statements	Package Size	Serving Size
MIZONE SPORTSWATER	Contains 5 essential vitamins - C, B3, B5, B6, B12	Colour free and low in sugar. Vitamin B's aid in energy metabolism and antioxidant Vitamin C assists with recovery and protection.			800ml	200ml
SANITARIUM WATERPLUS	5 minerals and 7 vitamins Low joule	Electrolytes are essential minerals that assist in hydration. Antioxidants are vitamins that help tp protect your body against harmful free radicals.			710ml	710ml
PROPEL FITNESS WATER	Vitamin enhanced water beverage	In a daily diet, B vitamins aid in energy metabolism. Antioxidant Vitamin E helps neutralize free radicals. Folate is a B vitamin that is needed for healthy growth and development.			700ml	200ml

Food-Type Dietary Supplement Survey - Formulated Beverages - Australia 2003

Composition

Product Name	Serving Size	No. of serves per day	Energy (kJ)	Total Fat (g)	Protein (g)	Carbohydrate (g)	Sugars (g)	Vitamins (percentage RDI per serve)	Minerals (percentage RDI per serve)	Herbal Extracts
							Per 100ml product			
MIZONE SPORTSWATER	200ml	Not Specified	43	0	0	2.5	2.5	C=20mg B3=1mg B5 0.5mg B6 0.16mg B12 0.1ug	Sodium <5mg	
SANITARIUM WATERPLUS	710ml	Not Specified	2	0	0	<0.1	0	B1=0.04mg B3=0.4mg B5=0.2mg B6=0.06mg B12=0.1ug C=1mg E=0.1mg	Calcium=11mg Magnesium=5mg Zinc=0.2mg Sodium=6mg Potassium=6mg	
PROPEL FITNESS WATER	200ml	Not Specified	17.5	0	0	0.83	0.83	E=0.5mg B3=1mg B5=0.5mg B6=0.16mg B9=15ug B12=0.1ug	Sodium=2mg Potassium=0mg	

Food-Type Dietary Supplement Survey - Formulated Beverages - Australia 2003

Manufacturer & Ingredients

Product name	Manufacturer - full contact details	Country of origin	Distributor details (if necessary)	Ingredients
MIZONE SPORTSWATER	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd, 99 Derby St. Silverwater Nsw2128, Australia	PURIFIED WATER, RECONSTITUTED APPLE JUICE, FRUCTOSE, APPLE CIDER VINEGAR, MANDARIN FLAVOURING, VITAMINS (ASCORBIC ACID (C), B3, B5, B6, B12), ACIDITY REGULATOR (CITRIC ACID).
SANITARIUM WATERPLUS	Sanitarium Health Food Company 124 Pah Road Royal Oak Auckland, New Zealand	New Zealand	Australian Health & Nutrition Association Limited, 1 Sanitarium Drive, Berkeley Vale NSW 2261.	WATER (99%), MINERALS (MAGNESIUM GLUCONATE, CALCIUM LACTATE, POTASSIUM BICARBONATE, SODIUM CHLORIDE, ZINC GLUCONATE), VITAMINS (C, B3, E ACETATE, B5, B6, B1, B12), FOOD ACIDS (CITRIC ACID, MALIC ACID), LEMON LIME FLAVOUR, ARTIFICIAL SWEETENER.
PROPEL FITNESS WATER	Imported into New Zealand by Pepsico Australia Holdings Pty ltd, Sydney, Australia.	USA	Imported and distributed in Australia by Cadbury Schweppes Pty Ltd, 636 St Kilda Road, Melbourne, Victoria 3004, Australia.	WATER, SUCROSE SYRUP, FRUCTOSE, CITRIC ACID, NATURAL FLAVOURS, VITAMIN E ACETATE, NIACINAMIDE (B3), CALCIUM PANTOTHENATE, PYRIDOXINE HYDROCHLORIDE (B6), FOLIC ACID, VITAMIN B12.

Food-Type Dietary Supplement Survey - Formulated Beverages - New Zealand 2003

Summary

Product Name	Content Claims	Other Claims	Directions for Use	Warnings and Advisory Statements	Package Size	Serving Size
AQUANA - Alive Zest & Vigour	Water for wellbeing. Guarana, B Vitamins & natural citrus flavour.	Aquana alive brings you all the benefits of purified water and may help give zest and vigour to your life. A vital mix of purified water, B vitamins, guarana herb and a hit of natural citrus flavours. <1 Calorie/100ml Natural flavours. No colours.	Store in a cool place.		750ml	200ml
AQUANA - Strong Defend & Support	Water for wellbeing. Antioxidants & natural berry flavours.	Aquana strong brings you all the benefits of purified water and may help support your body's defences. Purified water blended with the natural protection of antioxidants, ginkgo biloba extracts and a hint of natural berry flavours. <1 Calorie/100ml Natural Flavours. No colours	Store in a cool place.		750ml	200ml
CHARLIE'S SPORTS WATER *Flavours: Lemon & Lime*	No added sugar or artificial sweetener. Contains 6 essential vitamins - C, B3, B5, E, B6, B12		Serve chilled, refrigerate after opening. Consume within four days of opening. Remove safety seal under sipper cap.	This product is not a sole source of nutrition and should be consumed in conjunction with a nutritious diet and an appropriate physical exercise program.	800ml	200ml

e2 *Flavours: Apple Mango, Watermelon, Strawberry Citrus, Mango, Apple Blackcurrant*	Liquid Energy naturally blended with apple & mango Juices With vitamins A, C & E and minerals	e2 is for people like you that exercise, work hard or just need a lift to get through the day. Vitamins A, B5, B6, C, E and Niacin are blended with fruit juices and sucrose to give a real energy boost and to put back what life takes out. Some vitamins are known to prevent the effects of free radicals. Calcium may assist in maintaining strong healthy bones. Electrolytes help in assisting hydration and giving a quicker recovery after exercise.	Drink chilled.		400ml & 1.25L	250ml
G FORCE *Flavours: Apple & Blackcurrant, Blueberrry & Raspberry, Mango & Pineapple, Orange Mandarin, Pineapple & Lime, Raspberry & Lemon*	Information not obtained	Information not obtained			800ml	400ml
MIZONE SPORTS WATER *Flavours: Mandarin, Lime, Lemon, Passionfruit, Crisp Apple*	Contains 5 essential vitamins C, B3, B5, B6, B12. Purified water and fruit flavours with vitamins. Colour free and low in sugar.	To achieve your physical best, your body needs lots of water and MIZONE Sports Water is the easiest way to drink it….Vit B's aid in energy metabolism and antioxidant Vit C assists with recovery and protection. With vitamins and a splash of flavour, MIZONE Sports Water will rehydrate you so you can achieve your goals.	Remove safety seal under sipper cap. Serve chilled, once opened keep refrigerated.		800ml	200ml

POWERADE WATER *Flavours: Mandarin, Lime & Grapefruit*	With 5 essential vitamins B3, B5, B6, B9, B12	Powerade water contains purified water, with a refreshing splash of fruity flavour, 5 essential vitamins & electrolytes.	Please remove foil seal from under cap.	Store in a cool place.	750ml	400ml
THEXTON'S Blackcurrant Drink	Quality Beverage of New Zealand. Naturally flavoured with Blackcurrant juice. Rich in Vitamin C.	OK for kids as part of a balanced diet. Blackcurrant juice has been shown to have high levels of Vitamin C and is very beneficial for your health. No Apple base.	Serve chilled. Refrigerate after opening.		1L	250ml
THEXTON'S *Flavours:Pink Grapefruit, Cranberry & Red Grape*	Quality Beverage of New Zealand. Naturally flavoured with juice. With Vitamins A, C & E plus Echinacea.	OK for kids as part of a balanced diet.	Store in a cool place. Serve chilled. Refrigerate after opening.		1L & 3L	250ml

Food-Type Dietary Supplement Survey - Formulated Beverages – New Zealand 2003

Composition

Product Name	Serving Size	No. of serves per day	Energy (kJ)	Total Fat (g)	Protein (g)	Carbohydrate (g)	Sugars (g)	Vitamins (percentage RDI per serve)	Minerals (percentage RDI per serve)	Herbal Extracts
			Per 100ml product							
AQUANA - Alive Zest & Vigour	200ml	Not Specified	0.1	0	0	0	0	C=3.8mg (20%) B6=0.1mg (10%) B3=0.5mg (10%)	Sodium=1mg	Guarana extract
AQUANA - Strong Defend & Support	200ml	Not Specified	0.1	0	0	0	0	C=5.0mg (25%) E=0.5mg (10%)	Sodium=1mg	Ginkgo leaf extract
CHARLIE'S SPORTS WATER	200ml	8 per day	59.3	0.01	0.06	3.34	3.2	C=20.0mg (100%) B3=1.0mg (20%) B5=0.5mg (20%) B6=0.16mg (20%) B12=0.1mg (10%) E=0.5mg (10%)	Sodium=9.0mg	
e2	250ml	Recommended daily consumption, adults up to 2 litres, children under 13 up to 800ml	157	0	0	10.3	9.52	A=138.9IU (14%) B1=0.04mg (14%) B3=1.06mg (14%) B5=0.3mg (14%) B6=0.089mg (14%) C=3.3mg (33%) E=0.55mg (14%)	Calcium=3.83mg Sodium=11mg Potassium=20mg	
G FORCE	400ml	NS	184	<1	<1	10.8	10.8	C=35mg (350%) E=1mg (40%) B3=1mg (40%) B5=0.5mg B6=0.16mg (40%) B12=0.2ug (40%)		

MIZONE SPORTS WATER	200ml	Not Specified	43	0	0	2.5	2.5	C=20mg (100%) B3=1mg (20%) B5=0.5mg B6=0.16mg (20%) B12=0.1ug (10%)	Sodium=<5mg	
POWERADE WATER	400ml	Recommended daily consumption, Adults up to 6 bottles, children between 3 and 13 up to 2 bottles	41	0	0	2.3	2.3	B3=0.5mg (20%) B5=0.25mg B6=0.08mg (20%) B9=20ug (40%) B12=0.2ug (40%)	Sodium=12mg Potassium=14mg	
THEXTON'S Blackcurrant Drink	250ml	Recommended daily consumption, adults up to 2 litres, children under 12 up to 1.2 litres.	225	<1g	<1g	14.2	14.2	C=45mg (280%)		
THEXTON'S	250ml	Recommended daily consumption, adults up to 2 litres, children under 12 up to 1.2 litres	188	0	0	12	11.5	A=50ug (15%) C=5mg (30%) E=0.6mg (15%)	Sodium = 20mg	Echinacea

Food-Type Dietary Supplement Survey - Formulated Beverages - New Zealand 2003

Manufacturer & Ingredients

Product Name	Manufacturer Details	Country of Origin	Distributor Details (if necessary)	Ingredients
AQUANA - Alive Zest & Vigour	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		WATER, APPLE JUICE FROM CONCENTRATE (0.5%), NATURAL FLAVOUR, GUARANA EXTRACT, VITAMIN C, VITAMIN B3, VITAMIN B6.
AQUANA - Strong Defend & Support	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		WATER, NATURAL FLAVOURS, VITAMIN C, GINKGO LEAF EXTRACT, VITAMIN E
CHARLIE'S SPORTS WATER		New Zealand	Charlie's Trading Company Ltd 125 The Strand Parnell Auckland, NZ PH 0800 126 435 office@charlies.co.nz/www.charlies.co.nz	WATER (95%), RECONSTITUTED APPLE JUICE, VITAMINS (C, B3, B5, E, B6, B12), APPLE CIDER, VINEGAR, LEMON & LIME FLAVOUR, FOOD ACID (330).
e2	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		APPLE MANGO CONTAINS: WATER, SUCROSE, APPLE AND MANGO JUICE CONCENTRATE, FOOD ACID (330), FLAVOURS, COLOURS (133, 102), MINERALS (POTASSIUM, SODIUM, CALCIUM), VITAMINS (C, A, NIACIN, E, B5, B6, B1), POTASSIUM SORBATE (202).
G FORCE	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand		APPLE & BLACKCURRANT CONTAINS: WATER, SUGAR, RECONSTITUTED FRUIT JUICE (APPLE (5%), BLACKCURRANT (3%)), ACIDITY REGULATORS (330, 331), FLAVOUR, VITAMINS (ASCORBIC ACID (C), E, B3, B5, B6, B12), STABILISER (PECTIN), PRESERVATIVE (202), COLOURS (123, 133).

MIZONE SPORTS WATER	Frucor Beverages Ltd 97 Plunket Ave Wiri Auckland, NZ PH 0800 502 929 www.frucor.com	New Zealand	Frucor Beverages Australia Pty Ltd, 99 Derby St, Wilversater, NSW 2128, Australia PH 1800 237 727	PURIFIED WATER, RECONSTITUTED APPLE JUICE, FRUCTOSE, APPLE CIDER, VINEGAR, MANDARIN FLAVOURING, VITAMINS (ASCORBIC ACID C), B3, B5, B6, B12, CITRIC ACID.
POWERADE WATER	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		MANDARIN CONTAINS: WATER (97.3%), SUCROSE, FOOD ACID (330), TRI-POTASSIUM CITRATE, SODIUM CHLORIDE, FLAVOUR, ANTIOXIDANT (300), TRI-POTASSIUM PHOSPHATE, VITAMINS B3 (NIACIN), B5, B6, B9 (FOLIC ACID), B12.
THEXTON'S Blackcurrant Drink	Rio Beverages Ltd 40 Springs Rd East Tamaki Auckland, NZ PH (09) 274 5299	New Zealand		WATER, SUGAR, RECONSTITUTED BLACKCURRANT JUICE, NATURAL FLAVOURS, FOOD ACID (330), ASCORBIC ACID, COLOURS (123, 122, 129, 133).
THEXTON'S	Coca-Cola Amatil (N.Z.) Limited The Oasis Mt Wellington Auckland, NZ	New Zealand		PINK GRAPEFRUIT CONTAINS: WATER, SUGAR RECONSTITUTED PINK GRAPEFRUIT JUICE, ACIDITY REGULATOR (330, 331), FLAVOUR, VITAMINS (C,E,A), COLOUR (163), ECHINACEA EXTRACT (0.033%).

Attachment 5

Nutrition Assessment
Application A470 – Formulated Beverages

CONTENTS

Executive Summary

The purpose of the nutrition assessment is to determine the nutrition and health need for adding the requested 24 vitamins and minerals to FB, and to examine the nutrition-related health risks to the broader Australian and New Zealand populations. The overarching approach to the nutrition assessment has been to consider FSANZ's statutory objectives as stated in section 10 of the FSANZ Act, and to have regard to the Ministerial Policy Guideline 'Fortification of Food with Vitamins and Minerals' (the Policy Guideline).

The Policy Guideline permits the voluntary addition of vitamins and minerals to food *where there is a need for increasing the intake of a vitamin or mineral in one or more population groups demonstrated by actual clinical or sub-clinical evidence of deficiency or by data indicating low levels of intake*. For an assessment of the 'nutrition and health need' of the requested vitamin and mineral additions, the first step of the nutrition assessment has therefore been to determine nutritional need, by assessing the extent of existing inadequate vitamin and mineral intakes, or alternatively the extent of vitamin and mineral deficiencies within Australia and New Zealand. If a vitamin or mineral was identified as having an inadequate or deficient population intake, then an existing nutritional need had been demonstrated and did not require further assessment in the context of 'nutrition and health need'.

The Policy Guideline also states that voluntary fortification can be permitted where there is *generally accepted scientific evidence that the fortification can deliver a health benefit*. This potential for a 'health benefit' was investigated for those vitamins and minerals that do not have an existing level of inadequacy or deficiency, as a second step in the assessment of 'nutrition and health need'.

The process used to assess the nutrition and health need for a vitamin or mineral is illustrated in Figure 1 below. Figure 1 shows the results of this process for each of the 24 requested vitamins and minerals. The results in Figure 1 were based on the following criteria at each step:

Step 1:

- Inadequate intakes were defined as the situation where 3% or more of the whole population or two sub-population groups have an intake of a vitamin or mineral at a level below the Estimated Average Requirement (EAR)[38]. Six vitamins and minerals could not be assessed on the basis of inadequacy as they had no EAR (beta-carotene, biotin, pantothenic acid, chromium, manganese) or because dietary intake data was not available for this assessment (molybdenum).
- A level of deficiency was established for a vitamin or mineral if there was scientific evidence to show that clinical or sub-clinical deficiency states were prevalent in Australian and New Zealand populations.

Step 2:

- The potential for a 'health benefit' was determined by criteria established by FSANZ in relation to the levels of generally accepted scientific evidence.

[38] The EAR is a value representing the median requirement for a vitamin or mineral.

Figure 1: Assessment of Nutrition and Health Need

Vitamin / Mineral		Step 1 Nutritional Need	Step 2 Health Benefit	Existence of a Nutrition and Health Need
Group 1	Riboflavin Folate Vitamin B_6 Vitamin D Vitamin E Calcium Iodine Iron Magnesium Selenium Zinc	> 3% of population intakes were below the EAR, OR Evidence of deficiency existed	→	**Identified as having a nutrition and health need**
Group 2	Vitamin A (retinol) Thiamin Niacin Vitamin B_{12} Vitamin C Copper Phosphorus	< 3% of population had intakes below the EAR, AND No evidence of deficiency	Assessed for the potential to deliver a health benefit (none met FSANZ criteria for a 'health benefit')	→ **No nutrition and health need identified**
	Beta-carotene Chromium Biotin Pantothenic acid Manganese Molybdenum	Unable to assess for inadequacy, AND No evidence of deficiency		

Figure 1 shows that Group 1 met all criteria for demonstration of a nutrition and health need. Therefore, the vitamins and minerals with a nutrition and health need in support of their addition to FB are as follows:

Vitamins	Minerals
Riboflavin	Calcium
Folate	Iodine
Vitamin B_6	Iron
Vitamin D	Magnesium
Vitamin E	Selenium
	Zinc

As a final component of the nutrition assessment, FSANZ reviewed the energy and sugars content of FB and their potential impact on the overall diet. A potential risk was identified, that intakes of sugar-containing beverages (including those with a natural sugar content) would increase as a result of FB expanding the beverage sector of the market. There is evidence to show that consumption of standard sugar-containing beverages (e.g. soft-drinks) can significantly increase the overall intake of energy within the diet and thus contribute to weight gain. Therefore, a potentially higher beverage intake resulting from approval of Application A470 will likely increase the intake of sugars and energy in the Australian and New Zealand populations, and is potential health risk.

1. Introduction

The purpose of this assessment is to determine the nutritional and health need, and the health risk to Australian and New Zealand populations, associated with the addition of 24 vitamins and minerals to formulated beverages (FB) as requested by the Applicant.

FSANZ has conducted this nutrition assessment in accordance with its primary objectives as stated in the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act), which are also reflected in the high order principles of the Policy Guideline "Fortification of Food with Vitamins and Minerals" (the Policy Guideline):

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

Additional guidance has been obtained from the Policy Guideline, which contains five specific order policy principles for voluntary fortification that are of relevance to population nutrition. These principles state that:

- 'The voluntary fortification of vitamins and minerals to food should be permitted only:

  - Where there is a need for increasing the intake of a vitamin or mineral in one or more population subgroups demonstrated by actual clinical or subclinical evidence or by data indicating low levels of intake.
  - Where there is generally accepted scientific evidence that an increase in the intake of a vitamin and/or a mineral can deliver a health benefit.'

- 'The permitted fortification has the potential to address the deficit or deliver the benefit to a population group that consumes the fortified food according to its reasonable intended use'.
- 'Permission to fortify should not promote consumption patterns inconsistent with the nutrition policies and guidelines of Australia and New Zealand'.
- 'Permission to fortify should not promote increased consumption of foods high in salt, sugar or fat'.
- 'The fortification of a food, and the amounts of fortificant in the food, should not mislead the consumer as to the nutritional quality of the fortified food'.

Although guidance has been sought from the specific order principles of the Policy Guideline, the outcomes of this assessment are primarily driven by the information found within the available scientific literature, and results from the Dietary Intake Assessment (see Attachment 7).

2. Assessing the Nutrition and Health Need Associated with Proposed Vitamin and Mineral Additions

'Nutrition and health need' encompasses two concepts: i) nutritional need, referring to inadequate intakes or deficiency states; or ii) 'health benefits'. The follow sections detail the scientific assessments performed by FSANZ as a means of assessing these two concepts in the context of Application A470.

2.1 Nutritional Need – Inadequate Intakes Associated with the Requested Vitamins and Minerals

To determine the need for fortification, and its impact on population health, it is necessary to quantify the extent of inadequate population intakes of the relevant vitamin or mineral. To undertake this assessment three issues must be considered:

- the existence of a nutrient reference value[39] that can be used as a benchmark against intake data;
- how inadequate intakes are defined and measured against a nutrient reference value;
- the inadequate intakes of any specific population subgroup(s).

2.1.1 Benchmark Nutrient Reference Value – the Estimated Average Requirement

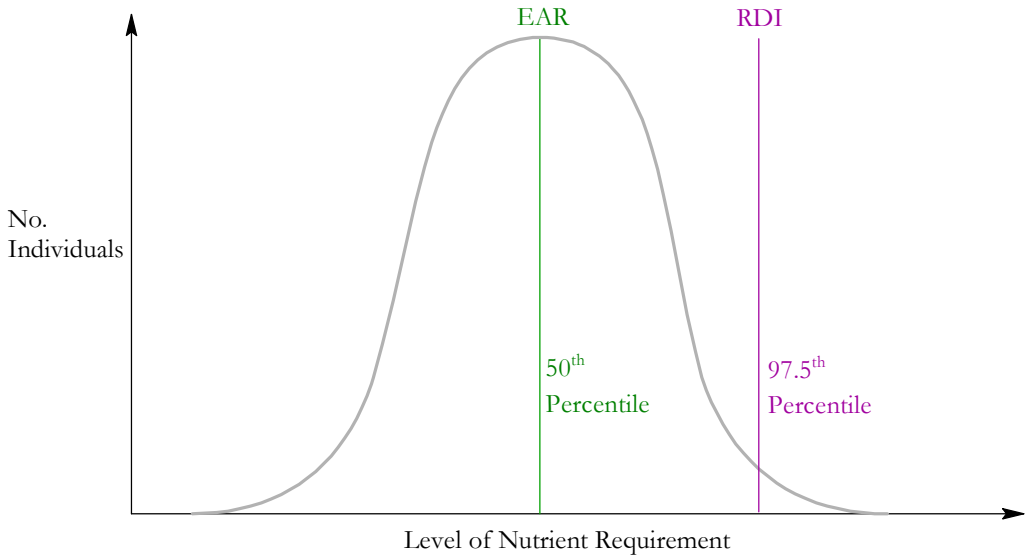
The estimated average requirement (EAR) is a value that represents the median requirement for the dietary intake of a particular nutrient in a given population group. EARs are commonly used by the United States (US), United Kingdom (UK) and Canada[40] to set other reference values. For example, the recommended dietary intake (RDI or its equivalent term) is set two standard deviations (97.5 percentile) above the EAR (United Kingdom Department of Health, 1993; United States Institute of Medicine, 2000a). Figure 1 below illustrates this relationship between the EAR and RDI.

An EAR can also be used as a public health benchmark for comparing and evaluating nutrient intakes, and is useful for this purpose because it is established directly from evidence of nutrient requirements and applies specifically to large populations. The EAR has been assessed as having a high statistical probability of being representative for this purpose (United States Institute of Medicine, 2000a).

[39] Nutrient reference values are figures set by official bodies (e.g. governments) for each nutrient that act as a measure of a population's nutritional status.

[40] Canada has adopted the nutrient reference values for the US.

Figure 2: Nutrient reference values across a distribution of nutrient requirements



EARs have not been formally established for the Australian or New Zealand populations, although a review of Australian and New Zealand nutrient reference values is due for completion in late 2005, where it is anticipated EARs will be established. Therefore, overseas EARs will primarily be used for Application A470; if an overseas EAR does not exist for a vitamin or mineral, then the EAR will be extrapolated from the RDI using the formula 0.7 x RDI, an approach that was used within the 1983 and 1985 Australian National Dietary Surveys (English *et al.*, 1987).

There are two sources of overseas EARs: the United States (US) Dietary Reference Intakes for vitamins and minerals (United States Institute of Medicine, 1997; 1998; 2000b; 2001) and the United Kingdom (UK) Dietary Reference Values (United Kingdom Department of Health, 1993). For a few vitamins and minerals the US EAR is equivalent to, or greater than the Australian and New Zealand RDIs. In this situation the US EAR loses its relativity to the RDI (as shown in Figure 1) when applied in the Australian and New Zealand context, and thus its suitability as a measure of the population's requirement for the relevant vitamin or mineral. Therefore, UK EARs are the preferred short-term benchmark for assessing nutritional inadequacy. US values have been used as an alternative if the UK has not set an EAR for a particular nutrient, and if no US value is available then the 0.7 x RDI formula has been used.

2.1.2 Criteria for Establishing an Inadequate Intake within the Population

The use of percentages below the EAR as a measure of an inadequate intakes is effective if the distribution of nutrient requirements is symmetrical around the EAR. For most vitamins and minerals this is the case, with the exception of iron; iron requirements are skewed due to higher requirements for women of childbearing age. Therefore, although this skewing is not expected to have a significant effect on assessments of iron, any outcomes for iron against the EAR have been treated with caution.

The United States Institute of Medicine has indicated that if any proportion of population intakes drop below the EAR, then the population can be said to have a level of inadequacy for the particular vitamin or mineral (United States Institute of Medicine, 2000a).

However, when applied to an actual assessment of intake data, a very small percentage of the population (i.e. 3% or less) with intakes below the EAR should be considered to represent an adequate population intake of the nutrient. This small percentage is a reflection of the inaccuracies that are inherent in population nutrient intake datasets. Therefore, only if more than 3% of the population has an intake below the EAR will the population as a whole be considered to have an inadequate intake of the relevant vitamin or mineral.

When assessing population intakes, two or more subgroups with greater than 3% of intakes below the EAR spread across a broad range of ages has been considered indicative of an inadequate population-wide intake of a vitamin or mineral. Particular attention has also been given to those age groups representative of the 20-39 year-old target consumer population for FB.

Population subgroups are based on those age groups allocated to the US or UK EARs, as the EARs have been established specifically for these age divisions. Some EARs may also differ across sex divisions for some nutrients, however FSANZ considers that sex groupings are too specific for a population-wide assessment of intakes.

2.1.3 Assessment of Individual Vitamins and Minerals Against the EAR.

Eighteen vitamins and minerals have been assessed against their respective UK or US EARs as shown in Tables 1 and 2 respectively below. Full details on the statistical process for assessing against EARs can be found at Attachment 7 – Dietary Modelling Methodologies for Nutrient Intake Assessments.

The food consumption data used for the intake assessment were from the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS. Both NNSs used a 24-hour food recall methodology. Approximately 10% percent of respondents from the Australian NNS and approximately 15% of people from the New Zealand NNS completed a second 24-hour recall. These second day data were used to adjust the majority of the vitamin and mineral intake estimates across two days, providing a better estimate of daily nutrient intakes across a longer period of time. For some vitamin and minerals, the second day adjustment could not to be calculated (see Attachment 7 for details on these vitamins and minerals).

The vitamin and mineral concentrations used for FB in the dietary intake assessments are those requested in the Application document. Vitamin and mineral concentrations for all other foods were those from the 1995 Australian, 1997 New Zealand NNS, or analytical survey data.

The nutrients have been assessed for inadequacy by estimating baseline intakes of nutrients and comparing these intakes to EARs. In order to determine whether consuming FB will address any inadequacy, estimated intakes of vitamins and minerals were calculated assuming that 5% of non-alcoholic beverages (excluding milks) will be replaced with FB. Vitamin and mineral intakes were then compared to the EAR.

Estimated intakes were calculated for various age groups, with age divisions allocated according to the particular type of EAR used for each vitamin and mineral. While the 1995 Australian NNS includes respondents aged 2 years and above, the 1997 New Zealand NNS only included respondents aged 15 years and above.

The results of the dietary intake assessment (Tables 1 and 2 below), demonstrate that Australian and New Zealand populations consume riboflavin, folate, vitamin B_6, vitamin E, calcium, iodine, iron, magnesium, selenium and zinc at an inadequate level according to FSANZ's criteria for inadequacy. In each case of inadequacy, the 20-39 year-old target population of FB also has an inadequate level of intake (19-50 year-old group in Table 1, 19-30 and 31-50 year-old groups in Table 2, and 19-54 year-old group in Table 3).

Table 1: Estimated Percentage of Respondents for Australian and New Zealand Population Groups With Vitamin and Mineral Intakes Below UK EARs (Results of 3% or more have been highlighted in bold text)

Nutrient	*Modelling*	*Sub-category*	*2-3 yrs*	*4-6 yrs*	*7-10 yrs*	*11-14 yrs*	*15-18 yrs*	*19-50 yrs*	*51+ yrs*	*2+ yrs#*
Thiamin	EAR (mg)	Males	0.4	0.5	0.6	0.7	0.8	0.8	0.8	-
		Females	0.4	0.5	0.5	0.6	0.6	0.6	0.6	-
	% below EAR	Aust	0	0	0	0	<1	<1	1	<1
		NZ	-	-	-	-	<1	<1	4	2
Riboflavin	EAR (mg)	Males	0.5	0.6	0.8	1.0	1.0	1.0	1.0	-
		Females	0.5	0.6	0.8	0.9	0.9	0.9	0.9	-
	% below EAR	Aust	0	0	0	0	**5**	**3**	**5**	**3**
		NZ	-	-	-	-	2	1	**3**	2
Niacin	EAR (mg)	Males	6.7	9.4	10.8	12.2	15.2	14.0	14.0	-
		Females	6.4	8.5	9.6	10.1	11.6	10.7	10.7	-
	% below EAR	Aust	0	0	0	0	0	0	<1	<1
		NZ	-	-	-	-	0	0	<1	<1
Folate	EAR (µg)	Males	50	75	110	150	150	150	150	-
		Females	50	75	110	150	150	150	150	-
	% below EAR	Aust	0	0	<1	**3**	**4**	**3**	2	2
		NZ	-	-	-	-	**4**	**3**	**8**	**5**
Vitamin B_{12}	EAR (µg)	Males	0.4	0.7	0.8	1.0	1.3	1.3	1.3	-
		Females	0.4	0.7	0.8	1.0	1.3	1.3	1.3	-
	% below EAR	Aust*	0	0	0	0	0	0	0	0
		NZ	-	-	-	-	0	0	0	0
Vitamin C	EAR (mg)	Males	20	20	20	22	25	25	25	-
		Females	20	20	20	22	25	25	25	-
	% below EAR	Aust	0	0	0	0	0	0	0	0
		NZ	-	-	-	-	0	0	0	0
Calcium	EAR (mg)	Males	275	350	425	750	750	525	525	-
		Females	275	350	425	625	625	525	525	-
	% below EAR	Aust	0	0	1	**25**	**30**	**15**	**25**	**20**
		NZ	-	-	-	-	**35**	**15**	**25**	**20**
Magnesium	EAR (mg)	Males	65	90	150	230	250	250	250	-
		Females	65	90	150	230	250	200	200	-
	% below EAR	Aust	0	0	**3**	**35**	**30**	**10**	**15**	**15**
		NZ	-	-	-	-	**20**	**5**	**20**	**10**
Phosphorus	EAR (mg)	Males	213	273	327	578	404	404	404	-
		Females	213	273	327	483	404	404	404	-
	% below EAR	Aust	0	0	0	<1	0	0	<1	<1
		NZ	-	-	-	-	0	0	0	0

* Vitamin B_{12} was not assessed in the 1995 Australian NNS. Therefore, vitamin B_{12} concentrations in foods from the 1997 New Zealand NNS were used in the assessment of vitamin B_{12} intakes for the Australian population (see Attachment 7 for more detail).

\# 15 years and above for New Zealand.

\- No intake data.

Table 2: Estimated Percentage of Respondents for Australian and New Zealand Population Groups With Vitamin and Mineral Intakes Below US EARs (Results of 3% or more have been highlighted in bold text)

Nutrient	*Modelling*	*Sub-category*	*2-3 yrs*	*4-8 yrs*	*9-13 yrs*	*14-18 yrs***	*19-30 yrs*	*31-50 yrs*	*51-70 yrs*	*71+ yrs*	*2+ yrs#*
Vitamin A	EAR (µg)	Males	210	275	445	630	625	625	625	625	-
		Females	210	275	420	485	500	500	500	500	-
	% below EAR	Aust	0	0	0	**3**	2	0	0	0	<1
		NZ				0	0	0	0	0	0
Vitamin B_6	EAR (mg)	Males	0.4	0.5	0.8	1.1	1.1	1.1	1.4	1.4	-
		Females	0.4	0.5	0.8	1.0	1.1	1.1	1.3	1.3	-
	% below EAR	Aust*	0	0	0	**10**	**15**	**25**	**45**	**60**	**25**
		NZ	-	-	-	0	0	**15**	**55**	**65**	**25**
Copper	EAR (µg)	Males	260	340	540	685	700	700	700	700	-
		Females	260	340	540	685	700	700	700	700	-
	% below EAR	Aust*	0	0	0	0	0	0	0	0	0
		NZ	-	-	-	<1	2	0	0	0	<1
Iron	EAR (mg)	Males	3.0	4.1	5.9	7.7	6.0	6.0	6.0	6.0	-
		Females	3.0	4.1	5.7	7.9	8.1	8.1	5.0	5.0	-
	% below EAR	Aust	0	0	2	**8**	**9**	**7**	<1	**3**	**5**
		NZ	-	-	-	**4**	**5**	1	<1	<1	2
Selenium	EAR (µg)	Males	17	23	35	45	45	45	45	45	-
		Females	17	23	35	45	45	45	45	45	-
	% below EAR	Aust*	**20**	**25**	**30**	**35**	**30**	**35**	**40**	**45**	**35**
		NZ	-	-	-	**50**	**45**	**15**	**60**	**75**	**40**
Zinc	EAR (mg)	Males	2.2	4.0	7.0	8.5	9.4	9.4	9.4	9.4	-
		Females	2.2	4.0	7.0	7.5	6.8	6.8	6.8	6.8	-
	% below EAR	Aust	0	0	**3**	**8**	**8**	**3**	**9**	**17**	**6**
		NZ	-	-	-	**5**	**4**	1	**13**	**18**	**7**

* Vitamin B_6, Copper, and Selenium intake data are available only for New Zealand (1997 NNS); the data for Australia has been adapted from the New Zealand NNS data for vitamin B_6 and copper, and derived from Australian survey data for selenium (see Attachment 7).

** 15-18 years for New Zealand.

\# 15 years and above for New Zealand.

\- no intake data

Table 3: Estimated Percentage of Respondents for Australian and New Zealand Population Groups With Vitamin and Mineral Intakes Below EAR (Derived by 0.7 x RDI) (Results of 3% or in bold text)

Nutrient	*Modelling*	*Sub-category*	*1-3 yrs*	*4-7 yrs*	*8-11 yrs*	*12-15 yrs***	*16-18 yrs*	*19-54 yrs*	*55-64 yrs*	*65+ yrs*	*2+ yrs#*
Vitamin E	EAR (mg α-tocopherol equivalents)	Males	3.5	4.2	5.6	7.4	7.7	7	7	7	-
		Females	3.5	4.2	5.6	6.3	5.6	4.9	4.9	4.9	-
	% below EAR	Aust	<1	**3**	2	**15**	**10**	**7**	**10**	**15**	**8**
		NZ	-	-	-	**4**	**9**	**3**	**3**	**3**	**3**

* Vitamin E was not assessed in the 1995 Australian NNS. Therefore vitamin E concentrations in foods from the 1997 New Zealand NNS were used in the assessment of vitamin E intakes for the Australian population.

** Only 15 year olds for New Zealand

\# 15 years and above for New Zealand.

\- no intake data

2.2. Nutritional Need – Evidence on Sub-clinical or Clinical Deficiencies

Nutritional need can also be determined outside of assessments on intake data, as inadequate population intakes can also express themselves through clinical indicators of deficiency.

A recent review of vitamin and mineral permissions in the *Australia New Zealand Food Standards Code* (the Code), Proposal P166 - Vitamins and Minerals in General Purpose Foods, identified vitamin D and iodine as having data showing an existing level of deficiency in Australia and New Zealand. The National Health and Medical Research Council (NHMRC) also identified vitamin D and iodine as the only two nutrients with an existing level of deficiency in Australia and New Zealand as part of its recent review of Nutrient Reference Values (NHMRC, 2005). Therefore, of the 24 vitamins and minerals proposed by the Applicant, FSANZ has focused its assessment on the prevalence of deficiency states in Australia and New Zealand to vitamin D and iodine.

2.2.1 Vitamin D

FSANZ commissioned an assessment (Nowson and Margerison, 2001) into the vitamin D status of Australians as part of Proposal P166 – Vitamins and Minerals. The vitamin D report gives a comprehensive assessment of the prevalence of vitamin D deficiencies in Australia. This report is still considered to be relevant today, and is also applicable to New Zealand given the similarities in climate, culture and food intakes.

The report by Nowson and Margerison (2001) details the following on vitamin D deficiency:

Elderly

For older persons living in the community the estimated prevalence of frank deficiency (FD) (serum 25-hydroxycholecalciferol <28 nmol/L) ranges from 17% to 22% of individuals (Inderjeeth *et al*., 2000; Pasco *et al*., 2001). FD for elderly persons in residential care has been measured at 22% of residents (Flicker *et al*., 2003), and at 45-67% for residents with limited mobility (Stein *et al*., 1996; Inderjeeth *et al.,* 2000; Flicker *et al.,* 2003).

The rates of marginal deficiency (MD) (serum 25-hydroxycholecalciferol = 28-100 nmol/L) are considerably higher in the elderly at 58% of individuals in the community (Pasco *et al.,* 2001), and 53-76% of elderly persons in residential care (Stein *et al.,* 1996; Flicker *et al.,* 2003).

Dark skinned pregnant women and their breast-fed infants

The majority of information on dark-skinned women and their infants in Australia is anecdotal. However, one published study (Grover and Morley, 2001), has indicated that 80% of pregnant dark-skinned, veiled women attending one antenatal clinic in a large teaching hospital had vitamin D levels <22 nmol/L (the lowest reference range value used within this study).

Adolescents

An estimate of MD prevalence in adolescents puts the rate at 68% (Jones, 2001), and FD has been estimated at 10% (Jones *et al.*, 1999).

General population

There is evidence that up to 8% of younger women (20-39 years) have FD at the end of winter and 33% have MD. The population group aged 20-80 years has also been estimated to have FD at 11% and MD at 43% during winter, and FD at 7% and MD at 30% for the whole year (Pasco *et al.,* 2001).

The information provided by Nowson and Margerison (2001) shows that there are several significant Australian population sub-groups that have vitamin D deficiency or are at risk of developing vitamin D deficiency.

2.2.2 Iodine

In the early 1990s it was reported that there was no evidence of iodine deficiency anywhere in Australia (Stanbury, 1996). In more recent years however, a downward trend in iodine status has been noted in both Australian and New Zealand populations (NHMRC, 2005).

Studies shown in Table 4 below indicate that iodine deficiency exists to various extents in both Australian and New Zealand population groups. In Australia, no national surveys have been undertaken to assess the iodine status of Australians, although national data collection in a National Iodine Nutrition Study is currently in progress. New Zealand has regularly monitored national iodine status because of the low iodine content of its soils. Monitoring of iodine status also occurs in Tasmania where iodised salt is now used in the majority of Tasmanian bread manufacture, however the data are currently unpublished.

Both the World Health Organization (WHO) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) suggest that no more than 20 percent of a population should have a urinary iodine level less than 50 μg/L, and that a median urinary iodine of 100μg/L or greater is indicative of iodine sufficiency (ICCIDD, 2001). Therefore, it is concluded from the studies of urinary iodine levels in Table 4 that a sizable proportion of the Australian and New Zealand populations are deficient in iodine to varying extents.

Table 4: Results from studies investigating iodine status of Australian and New Zealand populations

Author	Subjects	Urinary Iodine Concentration			
		No.	% < 50 μg/L	% <100 μg/L	Median Value (μg/L)
AUSTRALIA					
Gunton *et al.* (1999)	Pregnant women	81	19.8	49.6	
	Postpartum women	28	19.2	53.9	
	Patients with diabetes	135	34.1	71.9	
	Volunteers	19	26.3	73.7	
Guttikonda *et al.* (2003)	Children 5 -13 years	301	14	69	82
Li *et al.* (2001)	Children 6 -13 years	94	13.8		84
	Pregnant women from antenatal class	101	20.6		88
	Adult volunteers, medical staff	86	18		88
	Diabetes patients	85	23		69
McDonnell *et al.* (2003)	Children 11-18 years: Male	167	17	69	
	Children 11-18 years: Female	410	31	79	
	Total	577	27	76	
NEW ZEALAND					
Thomson *et al.* (1997)	Blood Donors	333	57	92	Male: 51 Female: 42
Skeaff *et al.* (2002)	Children 8 - 10 years	282	31.4	79.7	66
Thomson *et al.* (2001)	Men and women 18 - 49 years	233			59 ±33
Ministry of Health (2003)	Children 5 -14 years		28		All: 66 Male: 68 Female: 62

2.3 Vitamins and Minerals not Assessed on Nutritional Need

It is not possible to determine the nutritional need of Australian and New Zealand intakes for all of the vitamins and minerals requested by the Applicant. Biotin, pantothenic acid, β-carotene, chromium, and manganese do not have an overseas EAR that can be used to assess their adequacy (or an RDI that can be used for a proxy calculation), nor do they have any other evidence on clinical indicators that can be used to assess any possible deficiency state. Molybdenum has an EAR, however there are extremely limited, unassessed food composition data on this mineral that does not allow for a robust intake assessment against its EAR. Therefore, FSANZ has determined that an inadequate level of intake cannot be determined for to these vitamins and minerals, as there is no available evidence to demonstrate such an outcome.

Vitamin D does not have an overseas EAR that can be used, however there is evidence relating to vitamin D deficiency within Australia and New Zealand. This information has been reviewed in Section 2.2.1 above. Vitamin E also has no EAR, however a proxy derivation of the EAR from its RDI was undertaken as outlined in Section 2.1.1 above.

2.4 Assessing the Health Benefits from Increasing Individual Vitamin and Mineral Intakes

In addition to demonstrating a level of inadequacy or deficiency, the Policy Guideline also mentions that fortification can be permitted where there is generally accepted scientific evidence that an increase in the intake of a vitamin or mineral can deliver a health benefit.

As there is evidence that a number of vitamins and minerals are consumed at an inadequate or deficient level in Australia and New Zealand (see Sections 2.1 and 2.2 above), these vitamins and minerals can be considered eligible for addition to FB on the basis of a nutrition and health need. FSANZ has not assessed the potential to deliver a health benefit with an increased intake of these particular vitamins and minerals. Therefore, an assessment of health benefit has been undertaken on the balance (13) of the vitamins and minerals requested by the Applicant:

Vitamins	Minerals
vitamin A	chromium
beta-carotene	copper
thiamin	manganese
niacin	molybdenum
vitamin B_{12}	phosphorus
Vitamin C	
biotin	
pantothenic acid	

2.4.1 Health Benefit in the Context of Fortification with Vitamins and Minerals

There are two key elements to the concept of a 'health benefit' as stated in the Policy Guideline:

1 Generally accepted scientific evidence
2 An increase in the intake of a vitamin and/or mineral can deliver a health benefit

2.4.1.1 Generally Accepted Scientific Evidence

From scrutiny of the orthodox scientific nutritional and medical literature, generally accepted scientific evidence has been collected according to documented search strategies designed to draw in the totality of evidence. The data was assessed, and conclusions drawn as to an overall level of evidence.

An acceptable level of evidence that acknowledges a health benefit is where the weight of the totality of that evidence – mainly from well-designed and controlled observational and/or experimental studies in humans – is generally supportive of an association between a defined intake of vitamin and mineral and beneficial health outcome.

2.4.1.2 An Increase in the Intake of a Vitamin and/or Mineral can Deliver a Health Benefit

FSANZ considers the reference in the Policy Guideline to *'an increase in the intake'* is satisfied by a theoretical demonstration of changes in population intakes as they relate to possible new or amended permissions for voluntary addition of a vitamin or mineral to food.

It is accepted that increased intakes towards the RDI could deliver better nutrition for a population since the RDI, as a measure of nutritional adequacy, is a population recommendation that covers the nutritional needs of practically all healthy people. The potential delivery of nutritional benefits through voluntary fortification has been addressed through another component of the Policy Guideline, which refers to establishing nutritional need through assessment of dietary inadequacy or deficiency. Potentially increased intakes that traverse the EAR towards the RDI are anticipated to deliver better nutrition as a result of voluntary fortification. However, any nutritional benefits achieved through increases in intake from levels above the EAR towards the RDI are less certain and, as such, are not considered to constitute a separate 'health benefit' for the purposes of decision making on vitamin and mineral fortification.

Available evidence should therefore support a health benefit at intakes above the RDI but below an upper safe limit. By virtue of the definition of the RDI, such benefits are not likely to be nutritional in nature but related to other health benefits. Where an Australian/New Zealand RDI or similar value for nutritional adequacy has not yet been set, similar overseas values are used.

Health benefit is regarded as an increase in health status or reduction in chronic disease risk that is not nutritional in nature, however the term does not extend to pharmacological benefit or treatment of disease. Evidence of health benefit can be drawn from healthy populations as well as those at-risk or suffering diseases of public health significance. The selected list of diseases are those that contribute to more than 2% disability adjusted life years in the Australian and New Zealand burden of disease registers (Mathers *et al.*, 1999; Ministry of Health, 2001). These diseases include:

- Cardiovascular diseases;
- Cancer;
- Wound healing (injury);
- Bone disorders and bone maintenance;
- Diabetes;

- Gastrointestinal functioning / disorders;
- Chronic respiratory diseases; and
- Immune functioning / disorders.

Endpoints for health benefits are regarded as clinical endpoints as well as effects on physiological parameters (i.e. biomarkers of disease), but not biochemical changes or placebo effects.

In summary, the basis for determining the potential nutrition and health need for voluntary fortification of FB is based on either an assessment of nutritional need (with anticipated potential delivery of nutritional benefit) or evidence of other health benefit at intakes above the RDI for the populations and conditions described above. This is shown in the following figure where the vertical lines represent the two types of nutrient reference values.

Figure 3: Schematic representation of evidence required to meet nutrition and health needs

EAR	RDI	
Inadequate – nutritional need, anticipate nutritional benefit	Adequate	Other health benefit based on evidence at intakes > RDI

2.4.2 Criteria Used to Assess the Evidence Base of a Vitamin or Minerals 'Health Benefit'

The issues raised in Section 5.1 above have been applied to FSANZ's assessment of health benefit. However, to finalise an assessment of health benefit, FSANZ has categorised all identified, relevant material into six levels of evidence. A summary of the main characteristics for each level is shown in Table 5 below.

Table 5: Summary of the Categorisation of Evidence for a 'Health Benefit'

Level of Evidence	*Association with a health outcome*	*Contradictory evidence*	*Human studies necessary*	*Minimum type of evidence*	*Source of vitamin and mineral intakes*	*Support from chemical, cellular or animal models*
A	Insufficient evidence to establish an association					
0	Demonstrated lack of association					
1	Possible association with a high level of inconsistency in findings	Significant amount	No	Any		
2	Association with a moderate inconsistency in findings	Some	No	Any		

Level of Evidence	*Association with a health outcome*	*Contradictory evidence*	*Human studies necessary*	*Minimum type of evidence*	*Source of vitamin and mineral intakes*	*Support from chemical, cellular or animal models*
3	Association with little or no inconsistencies in findings	Little or none	Yes	Well-developed intervention or observational studies of suitable quality.	The identified health outcomes may occur with supplemental intake	
4	Causal relationship	Little or none	Yes	Well-developed intervention or observational studies of suitable quality.	The identified health outcomes must occur with intakes from food (i.e. not therapeutic doses)	Necessary

Level A Evidence

- The evidence base consists of a very limited number of studies, and therefore cannot be used to identify an association between the vitamin or mineral and a health outcome.

Level 0 Evidence

- Evidence exists that strongly confirms the absence of any health benefit associated with intakes of the vitamin or mineral above the RDI.
- The evidence base may also be a discontinued line of research.

Level 1 Evidence

- The evidence base suggests a possible relationship between the vitamin or mineral and a health outcome, but study results or outcomes may be inconsistent with each other or may reflect predominantly emerging evidence.
- There may be a significant number of contradictory findings within the evidence base.
- The evidence may be derived from any type of study: chemical, cellular or animal models; and/or experimental or observational studies.

Level 2 Evidence

- An association that is only moderately consistent between intakes of the vitamin or mineral beyond the RDI and the identified health outcomes. Alternatively, the evidence base may be insufficient to make a more definitive judgement, such as where available studies are of limited duration, have sample sizes of insufficient power, or have incomplete follow-up.
- There may be a proportion of studies with outcomes that contradict the association between the vitamin or mineral and the identified health outcomes.
- The evidence can be derived from any type of study: chemical, cellular or animal models; and/or experimental or observational studies.

Level 3 Evidence

- An association that is not fully consistent between intakes of the vitamin or mineral beyond the RDI and the identified health outcomes. Alternatively, the evidence base may be insufficient to make a more definite judgement, such as where available studies are of limited duration, have sample sizes of insufficient power, or have incomplete follow-up.
- There is little or no evidence contradicting the association.
- The evidence base must include human studies.
- At a minimum, the evidence base contains either well-designed experimental or observational studies (including cohort studies and/or case-control studies as a minimum).

Level 4 Evidence

- A consistent and causal relationship between intakes of the vitamin or mineral beyond the RDI and the identified health outcomes.
- There is little or no evidence contradicting the association.
- The evidence base must include human studies.
- The evidence base must show that vitamins and minerals provided in a food matrix can deliver the identified health outcomes (i.e. not just from supplemental intakes).
- At a minimum, the evidence base contains either well-designed experimental or observational studies (including cohort studies and/or case-control studies as a minimum).
- There must be chemical, cellular or animal model studies that support the findings of experimental and observational studies.

An increase in the intake of a vitamin or mineral is considered to have 'generally accepted scientific evidence' showing that it 'can deliver a health benefit' if the level of evidence is 3 or 4. The 3 and 4 levels are considered to demonstrate health benefit because these levels have little or no scientific material contradicting a positive health outcome.

The relevant scientific information on each of the 13 vitamins and minerals that require an assessment of their ability to deliver a health benefit has therefore been collated and categorised in accordance with the above measures.

2.4.3 Health Benefit Literature Searches

In acquiring scientific evidence on health benefits, the 'PubMed' and 'Nutrition Abstracts and Reviews' electronic databases were searched. The number of articles obtained through these literature searches is shown in Table 1 of the Appendix to this document.

If the search produced more than 130 results, then the original keywords were further refined to narrow the number of articles generated. The volume of material for beta-carotene and vitamin C was exceptionally large, and therefore PubMed was the only electronic database searched. In these cases, the draft NHMRC document "Nutrient Reference Values for Australia and New Zealand" (NHMRC, 2005) was cross-referenced for additional material.

When considering any literature that used supplemental doses of a vitamin or mineral, the study was excluded if it did not assess the intake of the vitamin/mineral alone; that is, the results from combination supplement doses (that contained the relevant vitamin/mineral) were not included in the assessment of health benefit.

2.4.4 Assessment of Health Benefits

The full results of FSANZ's assessments of health benefits can be found in Appendices 2-8 of this nutrition assessment report.

Of the vitamins and minerals that do not have an inadequate or deficient intake in Australia and New Zealand, none have been shown to have the potential to deliver a health benefit (evidence levels of 3 or 4). These vitamins and minerals have either an A, 0, 1 or 2 level of scientific evidence for their association with various health outcomes as shown in Table 6 below, a level that is too low to conclude that these vitamins and minerals have the potential to deliver a health benefit.

Table 6: Levels of Evidence on Health Benefits for the Proposed Vitamin and Mineral Additions

Level of Evidence	*Vitamins and Minerals Meeting the Evidence Level Category*
A	Thiamin, niacin, biotin, pantothenic acid, copper, manganese, and molybdenum.
0	Vitamin B_{12}
1	Vitamin C, β-carotene, phosphorus
2	Chromium
3	None
4	None

2.5 Summary of the Nutrition and Health Need Assessment

The Applicant has requested the addition of 24 vitamins and minerals to FB. Of these 24 vitamins and minerals the following assessments of nutrition and health need (inadequacy, deficiency and health benefit) have been made:

Table 7: Assessment of Nutrition and Health Need

Vitamin or Mineral	*Meets Inadequacy Criteria*	*Meets Deficiency Criteria*	*Meets Health Benefit Criteria*	*Assessed as Having a Nutrition and Health Need*
Vitamin A	No	No	No	
Beta-carotene	No	No	No	
Thiamin	No	No	No	
Riboflavin	✓			✓
Niacin	No	No	No	
Vitamin B_6	✓			✓
Folate	✓			✓
Vitamin B_{12}	No	No	No	
Biotin	No	No	No	
Pantothenic Acid	No	No	No	
Vitamin C	No	No	No	
Vitamin D	No	✓		✓
Vitamin E	✓			✓
Calcium	✓			✓

Vitamin or Mineral	*Meets Inadequacy Criteria*	*Meets Deficiency Criteria*	*Meets Health Benefit Criteria*	*Assessed as Having a Nutrition and Health Need*
Chromium	No	No	No	
Copper	No	No	No	
Iodine	N/A	✓		✓
Iron	✓			✓
Magnesium	✓			✓
Manganese	No	No	No	
Molybdenum	No	No	No	
Phosphorus	No	No	No	
Selenium	✓			✓
Zinc	✓			✓

N/A = not assessed.

3. The Potential for Formulated Beverage Fortification to Address Nutrition and Health Needs

The Policy Guideline mentions that in addition to demonstrating a nutrition and health need, a permitted fortification must have the *potential to address the deficit or deliver the benefit*.

As shown in Section 2 above, the ability to address a nutritional need is the only concern for FB, as there is no evidence to support a delivery of a health benefit from increases in the intakes of the vitamins and minerals proposed for addition to FB. Because any addressing of deficiency states requires monitoring of clinical indicators over time, the focus of this section has been on the ability to address inadequacy.

Therefore, to assess the ability to address an existing inadequacy, FSANZ has modelled the impact from FB fortification on the 9 vitamins and minerals identified in Section 2 as having an inadequate intake. If the percentage of respondents with intakes less than the EAR decreases, then the addition of that vitamin or mineral to FB can be said to have contributed to a correction in its inadequacy. Table 5 below summarises the results of this modelling process, showing the change in of respondents with intakes less than the EAR as a range across various age groups.

Table 8: The Change in Percentage of Respondents with Intakes Less Than the EAR Following Formulated Beverage Fortification

Nutrient	*Range of Change (% Respondents with Intakes < EAR)*	
	Maximum Negative Change	*Maximum Positive Change*
Riboflavin	-2	0
Vitamin B_6	0	5 (change in one subgroup only)
Folate	0	0
Vitamin E	0	6
Calcium	0	5
Iron	-3	0
Magnesium	0	10
Selenium	-5	5
Zinc	-5	0

Table 8 shows that the addition of vitamins and minerals to FB has an inconsistent impact on the intakes of these nutrients, with some age groups in the population experiencing an improvement in intakes (a positive change) while others either have no change or a drop in intakes. This information indicates that FB fortification has a variable impact across the population, and that it is difficult to conclusively determine whether the fortification has the potential to be effective or not. Given that the proposed vitamin and mineral additions to FB are voluntary and subject to implementation by industry, this uncertainty in the effectiveness of FB fortification is reinforced further.

Therefore, although FSANZ recognises the intention behind the specific order principle on effectiveness stated in the Policy Guideline, this principle cannot be employed successfully to FB and is therefore excluded from further consideration in this nutrition assessment.

4. Nutrition-Related Health Risks

The request to voluntarily fortify FB raises a number of nutritional issues that are broader than the assessment of nutrition and health needs. There are issues in this Application that represent potential health risks, namely whether the introduction of FB beverages into the Australian market will impact on wider dietary trends (in both Australia and New Zealand), and whether FB are an appropriate food vehicle for voluntary vitamin and mineral fortification.

The identification and prevention / mitigation of these health risks is reflected in both the Section 10 objectives of the FSANZ Act 1991 on the protection of public health and safety, and the prevention of misleading and deceptive conduct.

4.1 Nutritional Impact from the Macronutrient Profile of Formulated Beverages

4.1.1 Impact on Macronutrient Intakes from Beverage Substitution

One approach FSANZ has taken to determining the impact from the macronutrient profile of FB has been to examine the composition of FB currently available in Australia and New Zealand and the implications for beverage substitution.

The 2005 Australian and New Zealand stock-takes of beverages identified a total of 27 different FB, with 20 of the 27 FB on the Australian market and 10 of the 27 on the New Zealand market. This is in comparison to the eleven different FB identified in the 2003 Australia and New Zealand Food-Type Dietary Supplements Product Surveys (Food Technical Services, 2003; Food Concepts & Design Ltd, 2003). The ingredients of these products ranged from beverages with less than 2% fruit juice and no added sugars to beverages with greater than 5% fruit juice and added sugars.

The 2005 stock-take data shows that the energy and macronutrient composition per 100 ml varied between the beverages. The water-based beverages containing less than 2% fruit juice and 'no added sugar' had less than 2 kJ/100 ml and 0% sugars. The beverages containing 2-5% fruit juice and added sugar had approximately 38-94 kJ/100 ml and 2.2-5.4% sugars. Those beverages containing greater than 5% fruit juice and added sugar had approximately 171-196 kJ/100 ml and 9.7-11.3% sugars. The protein and fat contents of all FB surveyed were less than 1 g/100 ml.

The Applicant proposes that FB will replace some soft drink sales. For comparison, a standard lemonade soft drink contains 174 kJ and 10.8 g/100 ml of sugars, and thus has 1044 kJ and 64.8 g of sugars per 600 ml (the Applicant has requested a reference quantity of 600 ml for FB). These amounts are comparable to those found in FB made with greater than 5% fruit juice and added sugar.

4.1.2 Overall Dietary Impacts from the Macronutrient Profile of Formulated Beverages

FSANZ has also investigated the possible impact on the entire diet from the macronutrient profile of FB. Given that sugars are likely to be the only significant macronutrient in FB, the focus of this investigation has been on the impact for population intakes of energy and sugars.

There is evidence to show that consumption of standard sugar-containing beverages (including those with natural sources of sugar), whether FB or otherwise, can significantly increase the overall intake of energy within the diet and thus contribute to weight gain (Krebs-Smith, 2001; Ludwig *et al*., 2001; Somerset, 2003; Berkey *et al*., 2004; James *et al*., 2004). The majority of this evidence is based on epidemiological correlations between sugar-containing beverage consumption and weight gain. However, Krebs-Smith (2001) has also demonstrated that it is the contribution of additional sugar to the diet from sugar-containing beverages that is the contributor to increases in energy intakes.

Should FB increase the volume of sugar-based beverages consumed in the diet, either by substituting for other beverages with smaller serving sizes, or by expanding the overall consumption of these beverages as a whole, then an adverse impact on population health may result. This scenario is a real nutrition-related health risk, as the main driver for adding vitamins and minerals to FB is to increase the product's nutritional attractiveness and thus marketability, potentially above other existing beverage products. Although not all FB will contain high levels of sugars, products of this type are currently contained within the scope of the Applicant's request. It is therefore possible that an increased nutritional profile for FB will increase the intake of sugar-containing beverages across the population.

This nutrition assessment cannot fully determine the impact on energy or sugar intakes from FB permissions, as the impact would be dependent on the future in-roads that FB make into the Australian market, and the changes that an emerging Australian FB market may have on the current New Zealand FB market. However, the potential for an increase in energy intakes within Australian and New Zealand diets from proposed FB permissions (via increased sugar-containing beverage consumption) is still recognised as a potential health risk.

4.1.3 Conclusion

The substitution of other beverages by FB, as a process itself, will not have any significant adverse impacts on macronutrient intakes, as the macronutrient composition of these products is comparable to other non-fortified beverages. There is an additional concern, however, that the addition of vitamins and minerals to FB will provide additional motivation for consumers to purchase these beverages, and that this nutritional attractiveness will expand the beverage market, including the market for sugar-containing beverages. As such, there may be a health risk from the introduction of FB into the market, through increases in energy intakes resulting from increased sugar-containing beverage consumption.

4.2 Suitability of Formulated Beverages for Voluntary Fortification – The Influence on Bioavailability

Bioavailability refers to the biological availability of a nutrient to the human body. This property can be influenced by many factors, making it a highly variable attribute of vitamins and minerals. Because of this variability, a wide variety of research techniques have been applied to the measurement of bioavailability. These techniques include balance studies of the vitamin or mineral, changes in serum or urine vitamin/mineral concentrations (where intake is reflected by these changes), the use of isotopic tracers, the effect of the vitamin or mineral on target body systems, and *in vitro* assessments (Heaney, 2001).

4.2.1 Bioavailability Issues Specific to Various Vitamins and Minerals

Two of the most heavily researched nutrients in respect to bioavailability are iron and calcium, and are thus perhaps two of the best examples of mineral bioavailability. These two examples show that regardless of their source, minerals cannot be fully absorbed by the intestine even during ideal conditions (Turnlund, 1991). For example, balance and isotopic tracer studies have shown that maximum of 60% of ingested calcium can be absorbed during infancy, and this figure decreases with increasing age down to approximately 25% (excepting calcium uptake during pregnancy) (United States Institute of Medicine, 1997).

Additionally, any limitations in mineral bioavailability are unlikely to be due to the use of synthetic forms of these nutrients. In the case of iron, it is more often the quality of the overall diet that determines the bioavailability of consumed iron than the addition of iron salts to individual foods (Fairweather-Tait and Teucher, 2002). Recker *et al.* (1988) has also shown, through the use of isotopic tracers, that the use of a calcium salt in food (such as calcium carbonate) is as bioavailable as the form of calcium found in milk.

Compared to minerals, vitamins have fewer issues surrounding their bioavailability. Water-soluble vitamins are rarely affected by the food matrix, and are subject more to the physiological state of the consumer, or the presence of inhibitors and enhancers within a meal (Finglas, 2004). Fat-soluble vitamins are also affected little by the food matrix, although they do require the use of micelle carriers during digestion to be effectively available to the body. Thus, factors that can impact on the efficiency of micelle carriers (such as a low level of fat within a meal) may also have a negative effect on the bioavailability of fat-soluble vitamins (Fairweather-Tait and Southon, 2004).

4.2.2 The Variable Nature of Bioavailability

Current research has developed methods to account for the variable nature of vitamin and mineral bioavailability. However, a large degree of uncertainty still remains with any findings on vitamin and minerals bioavailability, as there are a wide variety of modifying factors that can confound results from scientific studies.

Confounding modifiers of bioavailability include the nutrient's release from the food matrix during digestion, physical interaction between other food components during digestion, and the form of the nutrient. There are also a number of host-related modifiers, including the host's nutritional status, developmental state, gastrointestinal secretions, mucosal cell regulation, and gut microflora (Fairweather-Tait and Southon, 2004).

A major influence on bioavailability is also the interaction between foods within a meal. Any assessment of vitamin and mineral bioavailability therefore must recognise that *in vitro* studies, and studies examining the fasting consumption of a single food, are unlikely to provide an accurate assessment of vitamin or mineral uptake and regulation within the body (Heaney 2001).

4.2.3 Conclusion

Due to the large number of modifiers influencing bioavailability, especially those that may confound scientific research into this area, FSANZ cannot fully assess the bioavailability of vitamin and mineral additions to FB.

FSANZ has reviewed the scientific literature on bioavailability for both vitamins and minerals (Section 4.2.1 above), however the uncertainty surrounding bioavailability studies means that a limited picture can only be formed. From this limited assessment, it can be determined that the addition of vitamins and minerals to FB is likely to be comparable to the bioavailability obtained from other food sources of these nutrients. For this reason, the Applicant's request to use vitamin and mineral chemical forms that are permitted for other generally consumed foods (i.e. the permitted forms listed in the Schedule of Standard 1.1.1 of the Code) is appropriate for the proposed addition of vitamins and minerals to FB.

5. Conclusion

There is no nutrition and health need for a number of the proposed vitamin and mineral additions to FB. The addition of the following vitamins and minerals to FB is not supported by the findings of this nutrition assessment:

Vitamins	Minerals
Vitamin A	Chromium
β-carotene	Copper
Thiamin	Manganese
Niacin	Molybdenum
Vitamin B_{12}	Phosphorus
Vitamin C	
Biotin	
Pantothenic Acid	

However, the following 11 vitamins and minerals do have a nutrition and health need in support of their addition to FB, by virtue of an existing inadequate intake or evidence of deficiency within the community:

Vitamins	Minerals
Riboflavin	Calcium
Folate	Iodine
Vitamin B_6	Iron
Vitamin D	Magnesium
Vitamin E	Selenium
	Zinc.

Although the above vitamins and minerals have a nutrition and health need supporting their addition to FB, this outcome does not mean that these additions are also safe. Safety considerations for vitamin and mineral additions have been assessed separately from nutritional need within the Draft Assessment Report for Application A470 (see Attachment 6).

Finally, in the context of the overall diet, there is the possibility that beverage intakes will increase as a result of FB expanding this sector of the market. A potential risk was identified, that intakes of sugar-containing beverages (including those with a natural sugar content) would increase as a result of FB expanding the beverage sector of the market. Therefore, a potentially higher beverage intake resulting from approval of Application A470 will likely increase the intake of sugars and energy in the Australian and New Zealand populations, and is potential health risk.

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Appendix 1

Electronic Literature Search on Health Benefits (number of articles identified)

Keywords	Vitamin A		β-carotene	Thiamin		Niacin		Vitamin B_{12}		Vitamin C
	PubMed	Nutrition Abstracts & Reviews	PubMed	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews	PubMed
[Vitamin/Mineral]	33604	3	6811	10751	1568	3136	837	9663	1510	29579
"[Vitamin/Mineral]" AND bone	1493	-	63	77	13	32	14	356	34	204
"[Vitamin/Mineral]" AND intake AND bone	73	-	-	-	-	-	-	13	-	40
"[Vitamin/Mineral]" AND cancer	8177	-	1952	259	32	127	38	506	74	1174
"[Vitamin/Mineral]" AND intake AND cancer	455	-	599	33		31	-	-	-	462
"[Vitamin/Mineral]" AND intake AND "cancer prevention"	132	-	81	-	-	-	-	-	-	40
"[Vitamin/Mineral]" AND intake AND "cancer risk"	121	-	128	-	-	-	-	-	-	125
"[Vitamin/Mineral]" AND chronic disease	233	-	73	98	2	8	2	103	7	130
"[Vitamin/Mineral]" AND intake AND chronic disease	34	-	-	-	-	-	-	-	-	-
"[Vitamin/Mineral]" AND cardiovascular disease	718	-	626	466	12	466	16	503	77	937
"[Vitamin/Mineral]" AND intake AND "cardiovascular disease"	71	-	71	38	-	21	-	59	-	80
"[Vitamin/Mineral]" AND intake AND "heart disease"	43	-	95	-	-	-	-	16	37	74
"[Vitamin/Mineral]" AND gastrointestinal	270	-	69	57	11	48	6	155	30	132
"[Vitamin/Mineral]" AND intake AND gastrointestinal	36	-	-	-	-	-	-	14	-	23
"[Vitamin/Mineral]" AND homocysteine	-	-	-	-	-	-	-	106	130	-
"[Vitamin/Mineral]" AND immune system	1941	-	338	173	3	55	2	416	8	524
"[Vitamin/Mineral]" AND intake AND immune system	64	-	49	7	-	-	-	14	-	63
"[Vitamin/Mineral]" AND osteoporosis	85	-	15	12	5	5	0	-	-	46
"[Vitamin/Mineral]" AND wound	498	-	82	83	1	15	0	47	1	170
"[Vitamin/Mineral]" AND intake AND wound	26	-	-	-	-	-	-	-	-	23
Total of shaded areas	685	3	726	405	79	215	78	417	400	644
Screening of article titles	201	0	141	37	15	18	2	50	61	141

Keywords	Biotin		Pantothenic Acid		Chromium		Copper	
	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews
[Vitamin/Mineral]	17914	424	2686	220	20328	940	51224	4345
"[Vitamin/Mineral]" AND bone	499	4	19	1	1430	19	862	125
"[Vitamin/Mineral]" AND intake AND bone	2	-	-	-	11	-	82	-
"[Vitamin/Mineral]" AND cancer	3283	13	41	1	799	25	1163	117
"[Vitamin/Mineral]" AND intake AND cancer	5	-	-	-	18	-	39	-
"[Vitamin/Mineral]" AND "chronic disease"	104	0	12	0	113	0	344	8
"[Vitamin/Mineral]" AND intake AND "chronic disease"	-	-	-	-	-	-	13	-
"[Vitamin/Mineral]" AND cardiovascular disease	486	2	57	2	29	0	111	39
"[Vitamin/Mineral]" AND intake AND "cardiovascular disease"	1	-	-	-	-	-	-	-
"[Vitamin/Mineral]" AND intake AND "heart disease"	-	-	-	-	66	0	-	-
"[Vitamin/Mineral]" AND diabetes	-	-	-	-	362	92	-	-
"[Vitamin/Mineral]" AND intake AND diabetes	-	-	-	-	31	-	-	-
"[Vitamin/Mineral]" AND gastrointestinal	116	3	33	1	36	0	295	61
"[Vitamin/Mineral]" AND intake AND gastrointestinal	-	-	-	-			21	-
"[Vitamin/Mineral]" AND immune system	1632	7	39	1	3918	6	1751	39
"[Vitamin/Mineral]" AND intake AND immune system	4	-	-	-	7	-	61	-
"[Vitamin/Mineral]" AND osteoporosis	3	0	1	0	36	0	85	27
"[Vitamin/Mineral]" AND intake AND osteoporosis	-	-	-	-			-	-
"[Vitamin/Mineral]" AND wound	128	0	59	1	461	0	230	10
"[Vitamin/Mineral]" AND intake AND wound	-	-			3	-	-	-
Total of shaded areas	363	29	261	6	252	142	406	300
Screening of article titles	0	0	4	5	20	29	46	35

Keywords	Manganese		Molybdenum		Phosphorus	
	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews	PubMed	Nutrition Abstracts & Reviews
[Vitamin/Mineral]	21916	1562	5896	306	53681	3231
"[Vitamin/Mineral]" AND bone	350	42	196	7	6030	486
"[Vitamin/Mineral]" AND intake AND bone	39	-	3	-	560	19
"[Vitamin/Mineral]" AND intake AND "bone health"	-	-	-	-	40	0
"[Vitamin/Mineral]" AND intake AND "bone status"	-	-	-	-	71	0
"[Vitamin/Mineral]" AND cancer	1140	25	237	10	3934	49
"[Vitamin/Mineral]" AND intake AND cancer	10	-	10	-	55	-
"[Vitamin/Mineral]" AND "chronic disease"	130	2	15	1	297	3
"[Vitamin/Mineral]" AND intake AND "chronic disease"	-	-	-	-	11	-
"[Vitamin/Mineral]" AND cardiovascular disease	451	0	51	3	1897	10
"[Vitamin/Mineral]" AND intake AND "cardiovascular disease"	12	-	-	-	63	-
"[Vitamin/Mineral]" AND intake AND "heart disease"	3	0	16	3	-	-
"[Vitamin/Mineral]" AND gastrointestinal	61	14	24	6	360	35
"[Vitamin/Mineral]" AND intake AND gastrointestinal			-	-	52	-
"[Vitamin/Mineral]" AND immune system	813	4	120	2	1669	5
"[Vitamin/Mineral]" AND intake AND immune system	9	-	-	-	8	-
"[Vitamin/Mineral]" AND osteoporosis	19	13	4	0	923	97
"[Vitamin/Mineral]" AND intake AND osteoporosis			-	-	115	-
"[Vitamin/Mineral]" AND wound	128	1	55	1	730	1
"[Vitamin/Mineral]" AND intake AND wound	2	-	-	-	28	-
Total of shaded areas	285	101	298	33	443	219
Screening of article titles	4	3	9	0	32	8

Appendix 2

Assessment of Health Benefit: Chromium

The searches conducted on the PubMed and Nutrition Abstract and Reviews databases yielded a total of 49 eligible studies on chromium. The abstracts of these articles were further reviewed to ensure that the subject matter, not just the title, was relevant to this assessment. In assessing the subject matter, articles were excluded if they used serum chromium as an indicator of chromium status. Serum chromium is very close to the detection limits of current analytical techniques, and cannot be accurately measured by these methods (United States Institute of Medicine, 2001). The available evidence was therefore reduced to 23 articles once duplicate material was eliminated. A detailed summary of these articles is provided in Tables A2-1 to A2-3 below. Of these 23 articles, 7 assessed both coronary heart disease (CHD) and diabetes endpoints.

Ten articles included an assessment of CHD endpoints following increased chromium intake, of which eight were intervention trials. There was no consistent set of findings across the evidence base on chromium intakes above the recommended level[41] and CHD, with two beneficial and four null studies identified. The other four studies report disparate results between various subgroups of their study populations, or between different CHD endpoints.

The greatest volume of scientific material on chromium related to diabetes related outcomes, with a total of 19 studies identified. The majority of these studies were intervention trials investigating the use of chromium supplements, with only one observation study that assessed chromium status via nail chromium concentrations. This evidence base predominantly indicated an inverse association between supplemental chromium use (at intakes above the recommended level), however the studies often varied in how this outcome was obtained. Three studies reported significant decreases in serum insulin levels with increased chromium intakes even though there was no concurrent change in serum glucose or HbA1c levels over time. Two other studies indicated that increased intakes of chromium well above the recommended level, rather than moderately increased above, were capable of producing significant benefits for diabetes/glucose metabolism. However, even with this variation in findings, there was also a moderate level of evidence (seven studies) showing no significant relationship between increased chromium intake and diabetes/glucose metabolism.

Five remaining articles, mostly observational studies, were identified that examined the relationship between cancer (3 studies) or weight management (2 studies). None of these studies indicated any definitive benefit with increased chromium intakes.

A strong evidence base exists indicating that increased chromium intakes have a beneficial influence on diabetes and blood glucose management, although the exact relationship has yet to be fully described within the current evidence base. Despite these strong positive findings, a moderately strong level of information also contradicts an association between chromium and improved diabetic/glucose management.

Chromium is Assigned an Evidence Level of 2

[41] The recommended intake for chromium used in the assessment of health benefits has been assigned the value of 35 μg/day, the AI for males as proposed by the NHMRC in their draft NRVs (NHMRC, 2005).

Table A2-1: Identified Studies on Chromium and Coronary Heart Disease

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Abraham *et al.* (1992)	Not reported	Biomarkers of CHD – cholesterol, HDL and triglyceride levels	Randomised controlled trial	7-16 months	Patients with athero-sclerosis aged 42-83 years	Chromium supplementation	38	250 mg chromium chloride	- Chromium supplementation significantly increased serum chromium levels ($p<0.05$). - There was no significant ($p>0.05$) difference in serum triglycerides and cholesterol levels between the two groups . - There was a significant increase ($p<0.005$) in serum HDL levels.
						Placebo treatment	38	-	
Anderson *et al.* (1997)	Double-blinded	Biomarkers of CHD – serum cholesterol, HDL and triglycerides	Randomised controlled trial	4 months	Persons with Type II diabetes aged 35-65 years.	High chromium supplementation	60	500 µg/day chromium picolinate	- 500 µg/day chromium supplementation significantly ($p<0.02$) decreased serum cholesterol levels compared to the placebo group. - There was no significant ($p>0.05$) impact of chromium supplementation on other measured study endpoints.
						Low chromium supplementation	60	100 µg/day chromium picolinate	
						Placebo	60	-	
Bahijiri *et al.* (2000)	Double-blinded	Biomarker of CHD – serum cholesterol, HDL and triglyceride levels.	Randomised controlled crossover trial	8 weeks for each treatment alternating with 8 week placebo washout	Persons with Type II diabetes aged 36-68 years.	Treatment 1 - chromium supplementation	78	200 µg/day chromium chloride	- Both chromium supplementations significantly ($p<0.001$) decreased serum triglyceride levels and significantly ($p<0.001$) increased serum HDL levels. - There was no significant ($p>0.05$) impact of chromium supplementation on serum cholesterol.
						Treatment 2 – Brewer's yeast	78	23.2 µg/day chromium	

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Offenbacher and Pi-Sunyer (1980)	Single-blinded	Biomarkers of CHD – serum cholesterol and triglyceride levels.	Randomised controlled trial	8 weeks	Persons (mean age 78 years)	Chromium supplementation via Brewer's yeast	12	11 µg/day chromium	Chromium supplementation significantly ($p>0.05$) decreased serum cholesterol and triglyceride levels compared to the placebo group.
						Placebo (Torula yeast)	12	-	
Offenbacher *et al.* (1985)	Single-blinded	Biomarkers of CHD – serum cholesterol and triglyceride levels.	Randomised controlled trial	10 weeks	Persons aged 63-86 years	Chromium supplementation	8	200 µg/day chromic chloride	There was no association between chromium supplementation and serum cholesterol and triglyceride levels.
						Chromium supplementation via Brewer's yeast	8	5 µg/day chromium	
						Placebo (Torula yeast)	7	-	
Pasman *et al.* (1997)	Double-blinded	Biomarkers of CHD – serum cholesterol, LDL, and HDL levels.	Randomised controlled trial	16 months	Females with BMI>30, mean age = 35 years	Diet + 50 g carbohydrate + chromium supplement	13	200 µg/day chromium picolinate	There was no significant ($p>0.05$) difference in serum lipid levels between the three groups over time.
						Diet + 50 g carbohydrate	11	-	
						Placebo (Diet only)	9	-	
Rabinovitz *et al.* (2004)	Single-blinded	Biomarkers of CHD – serum cholesterol, LDL, HDL and triglyceride levels.	Randomised controlled trial	21 days	Persons with Type II diabetes	Chromium supplementation	39	200 µg/day chromium picolinate	- There was a significant ($p<0.02$) inverse association between chromium supplementation and serum cholesterol levels. - However, there was no significant ($p>0.05$) association between chromium supplementation and HDL, LDL or serum triglyceride levels.
						Placebo	39	-	

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Tang *et al.* (2003)	n/a	Clinical – CHD with aged hypertension (compared to chromium status as measured by hair and fingernail concentrations)	Case-control	Single timepoint	Persons (mean age = 68 years)	Cases of CHD	99	n/a	Chromium concentrations of hair and fingernails were significantly ($p<0.05$) reduced in cases compared to controls.
						Controls	95	n/a	
Thomas and Gropper (1996)	Double-blinded	Biomarkers of CHD – serum cholesterol, LDL, HDL and triglyceride levels.	Crossover study	8 weeks for each treatment	Persons (mean age = 45 years)	Treatment 1 - chromium supplementation	8	200 µg/day niacin-bound chromium	There was no significant ($p>0.05$) association between chromium supplementation and serum cholesterol, HDL, LDL or triglyceride levels when compared to controls.
						Treatment 2 – placebo	5	-	
Uusitupa *et al.* (1992)	?	Biomarkers of CHD – serum cholesterol, HDL and triglyceride levels.	Randomised controlled trial	6 months	Persons with impaired glucose tolerance, aged 65-74 years	Supplementation with chromium-rich yeast	13	160 µg/day chromium	There was no (significant?) association between chromium supplementation and serum cholesterol, HDL or triglyceride levels when compared to the placebo treatment.
						Placebo	13	-	

Table A2-2: Identified Studies on the Chromium and Diabetes / Glucose Metabolism

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Abraham *et al.* (1992)	Not reported	Biomarkers of diabetes – serum glucose levels	Randomised controlled trial	7-16 months	Patients with athero-sclerosis aged 42-83 years	Chromium supplementation	38	250 mg chromium chloride	- Chromium supplementation significantly increased serum chromium levels ($p<0.05$). - There was no significant ($p>0.05$) difference in serum glucose levels between the two groups.
						Placebo treatment	38	-	
Anderson *et al.* (1997)	Double-blinded	Biomarkers of diabetes – fasting serum glucose and HbA1c levels	Randomised controlled trial	4 months	Persons with Type II diabetes aged 35-65 years.	High chromium supplementation	60	500 µg/day chromium picolinate	- 500 µg/day chromium supplementation significantly ($p<0.0001$) decreased serum glucose, insulin and HbA1c levels compared to the placebo group. - 100 µg/day chromium supplementation significantly ($p<0.0001$) decreased serum insulin levels, however had no significant ($p>0.05$) impact on serum glucose or HbA1c
						Low chromium supplementation	60	100 µg/day chromium picolinate	
						Placebo	60	-	
Anderson *et al.* (2001)	Double-blinded	Biomarkers of diabetes – fasting serum glucose, insulin and HbA1c levels	Randomised controlled trial	6 months	Persons with Type II diabetes aged <65 years.	Chromium supplementation	27	400 µg/day chromium pidolate	There was no significant ($p<0.05$) difference in serum glucose, insulin or HbA1c levels between the two study groups.
						Placebo	29	-	
Bahijiri *et al.* (2000)	Double-blinded	Biomarker of diabetes – fasting serum glucose and 2hr glucose.	Randomised controlled crossover trial	8 weeks for each treatment alternating with 8	Persons with Type II diabetes aged 36-68 years.	Treatment 1 - chromium supplementation	78	200 µg/day chromium chloride	Both chromium supplementations significantly decreased ($p<0.001$) decreased serum glucose levels.

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
				week placebo washout		Treatment 2 – Brewer's yeast	78	23.2 µg/day chromium	
Cefalu *et al.* (1999)	Double-blinded	Biomarkers of diabetes – serum glucose and insulin levels (measured over 2 and 24 hours following glucose tolerance test), and HbA1c.	Randomised controlled trial	8 months	Persons at risk of diabetes aged 42-53 years.	Chromium supplementation	15	1000 µg/day chromium picolinate	- Chromium supplementation significantly ($p<0.005$) decreased the insulin response to the glucose tolerance test compared to the placebo. - Chromium supplementation had no significant ($p>0.05$) effect on glucose or HbA1c levels.
						Placebo	14	-	
Cheng *et al.* (1999)	n/a	Biomarkers of diabetes – fasting and postprandial serum glucose levels	Single administration (follow-up to Anderson *et al.* 1997)	10 months	Persons with Type II diabetes aged 35-65 years.	Chromium supplementation	833	500 µg/day chromium picolinate	Chromium supplementation significantly ($p<0.05$) decreased serum glucose levels compared to the initial readings of the follow-up period.
Ghosh *et al.* (2002)	Double-blinded	Biomarkers of diabetes – fasting serum glucose, insulin and HbA1c levels.	Randomised controlled cross-over study	12 weeks for each treatment with a 4 week washout	Patients with Type II diabetes (mean age =53 years)	Treatment 1 - chromium supplementation	50	400 µg/day chromium picolinate	There was a significantly inverse association between chromium supplementation and fasting serum glucose ($p<0.001$), insulin ($p<0.05$) and HbA1c ($p<0.05$) levels.
						Treatment 2 – placebo	50	-	

Grant *et al.* (1997)	Double-blinded	Biomarkers of diabetes – fasting serum insulin levels (following a glucose tolerance test)	Randomised controlled trial	9 weeks	Obese females	Chromium supplementation	10	200 µg/day chromium picolinate	- There was no significant ($p>0.05$) difference between the study groups for serum glucose or HbA1c measurements. - There was a significant ($p<0.05$) inverse association between chromium supplementation and serum insulin levels.
						Chromium supplementation	10	200 µg/day niacin-bound chromium	
						Placebo	23	-	
Joseph *et al.* (1999)	Double-blinded	Biomarkers of diabetes – fasting serum glucose and insulin levels.	Randomised controlled trail	12 weeks	Persons with BMI >25 (mean age = 62 years)	Chromium supplementation	17	900 µg/day chromium picolinate	There was no significant ($p>0.05$) association between chromium supplementation and serum glucose and insulin levels.
						Placebo	15	-	
Jovanovic *et al.* (1999)	Double-blinded	Biomarkers of diabetes – fasting serum glucose, insulin and HbA1c levels.	Randomised controlled trial	8 weeks	Females with gestational diabetes (20-24 months pregnant) aged 25-43 years.	High chromium supplementation	10	8 µg/kg bw/day chromium picolinate	- Both chromium supplement groups had significantly ($p<0.05$) lower serum glucose and insulin levels compared to the placebo group. - Compared to the placebo group, HbA1c levels were significantly decreased ($p<0.05$) in the high chromium supplementation group only.
						Low chromium supplementation	10	4 µg/kg bw/day chromium picolinate	
						Placebo	10	-	
Offenbacher and Pi-Sunyer (1980)	Single-blinded	Biomarkers of diabetes – fasting serum glucose and insulin levels.	Randomised controlled trial	8 weeks	Persons (mean age 78 years)	Chromium supplementation via Brewer's yeast	12	11 µg/day chromium	Chromium supplementation significantly ($p<0.05$) decreased serum glucose and insulin levels compared to the placebo group.
						Placebo (Torula yeast)	12	-	

Offenbacher *et al.* (1985)	Not reported	Biomarkers of diabetes – fasting serum glucose and insulin levels.	Randomised controlled trial	10 weeks	Persons aged 63-93 years	Chromium supplementation	8	200 µg/day chromic chloride	There was no association between chromium supplementation and serum glucose or insulin levels.
						Chromium supplementation via Brewer's yeast	8	5 µg/day chromium	
						Placebo (Torula yeast)	7	-	
Pasman *et al.* (1997)	Double-blinded	Biomarkers of diabetes – fasting serum glucose and insulin levels.	Randomised controlled trial	16 months	Females with BMI>30, mean age = 35 years	Diet + 50 g carbohydrate + chromium supplement	13	200 µg/day chromium picolinate	Serum blood glucose and insulin levels did not significantly ($p>0.05$) differ between the three groups over time.
						Diet + 50 g carbohydrate	11	-	
						Placebo (Diet only)	9	-	
Rabinovitz *et al.* (2004)	Single-blinded	Biomarkers of diabetes – fasting serum glucose, insulin and HbA1c levels.	Randomised controlled trial	21 days	Persons with Type II diabetes	Chromium supplementation	39	200 µg/day chromium picolinate	- There was a significant ($p<0.01$) inverse association between chromium supplementation and serum glucose and HbA1c levels. - There was no significant ($p>0.05$) association between chromium supplementation and serum insulin levels.
						Placebo	39	-	

Rajpathak *et al.* (2004)	n/a	Clinical – incidence of diabetes (compared to chromium status as measured by toenail concentrations)	Case-control	7 years	Males aged 40-75 years	Cases of diabetes	688	n/a	- There was a significant ($p<0.01$) inverse association between chromium status and the incidence of diabetes in combination with CVD. - However, there was no significant ($p>0.05$) association between chromium status and diabetes incidence alone.
						Cases of diabetes and CVD	198	n/a	
						Age matched healthy controls	361	n/a	
Thomas and Gropper (1996)	Double-blinded	Biomarkers of diabetes – serum glucose and insulin levels as measured by a glucose tolerance test.	Crossover study	8 weeks for each treatment	Persons (mean age = 45 years)	Treatment 1 - chromium supplementation	8	200 µg/day niacin-bound chromium	There was no significant ($p>0.05$) association between chromium supplementation and serum glucose or insulin when compared to controls.
						Treatment 2 – placebo	5	-	
Trow *et al.* (2000)	Not blinded	Biomarkers of diabetes – serum glucose and insulin levels as measured by a glucose tolerance test.	Crossover study	4 weeks placebo then 8 weeks treatment	Persons with Type II diabetes	Habitual diet + chromium supplementation	12	100 µg/day chromium	There was no significant ($p>0.05$) association between chromium supplementation and serum glucose or insulin when compared to the non-treatment period.
						Habitual diet only	12	-	

Urberg and Zemel (1987)	Not reported	Biomarkers of diabetes – serum glucose levels as measured by a glucose tolerance test.	Randomised controlled trial	28 days	Persons	Chromium supplementation	5	200 µg/day chromium	- There was a significant ($p<0.05$) decrease in serum glucose over time with chromium + niacin supplementation. - There was no significant ($p>0.05$) change in glucose levels over time with chromium or niacin supplementation alone.
						Niacin supplementation	5	100 mg/day nicotinic acid	
						Chromium + niacin supplementation	6	200 µg/day chromium + 100 mg/day nicotinic acid	
Uusitupa *et al.* (1992)	Double-blinded	Biomarkers of diabetes – serum glucose and insulin levels (as measured by a glucose tolerance test), and HbA1c levels.	Randomised controlled trial	6 months	Persons with impaired glucose tolerance, aged 65-74 years	Supplementation with chromium-rich yeast	13	160 µg/day chromium	There was no association between chromium supplementation and serum glucose, insulin or HbA1c levels when compared to the placebo treatment.
						Placebo	13	-	

Table A2-3: Identified Studies on Cancer and Obesity Outcomes from Increased Chromium Intakes

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Crawford *et al.* (1999)	Double-blinded	Clinical – weight and fat mass (fat measured via bioimpedence)	Randomised controlled cross-over study	2 months on each treatment	Females with BMI>25	Treatment 1 – chromium supplementation	20	600 µg/day niacin-bound chromium	There was no significant ($p>0.05$) decrease in weight as a result of chromium supplementation, however there was a significant ($p<0.05$) loss of fat mass following supplementation.
						Treatment 2 – placebo	20	-	
Garland *et al.* (1996)	n/a	Clinical – breast cancer (compared to chromium status as measured by toenail concentrations)	Case-control (subset of the Nurses' Health Study Cohort)	4 years	Females aged 30-55 years	Cases of breast cancer	433	n/a	- There was no significant ($p>0.05$) association between chromium status and breast cancer risk amongst the total cohort. - There was, however a significant ($p<0.05$) inverse association between chromium status and breast cancer risk in pre-menopausal women. - The OR between the lowest (<0.52 µg/g) and highest (>2.37 µg/g) toenail concentrations of premenopasual women was 0.47.
						Matched controls	433	n/a	
Kilic *et al.* (2004)	n/a	Clinical – breast cancer (compared to chromium status as measured by hair concentrations)	Case-control	4 years	Females (mean age = 54 years)	Cases of breast cancer	26	n/a	There was a significant ($p<0.05$) positive association between chromium status and breast cancer incidence.
						Matched controls	27	n/a	

Pasman *et al.* (1997)	Double-blinded	Clinical – weight (BMI)	Randomised controlled trial	16 months	Females with BMI>30, mean age = 35 years	Diet + 50 g carbohydrate + chromium supplement	13	200 µg/day chromium picolinate	Chromium supplementation had no significant ($p>0.05$) impact on the weight of subjects.
						Diet + 50 g carbohydrate	11	-	
						Placebo (Diet only)	9	-	
Rogers *et al.* (1993)	n/a	Clinical – laryngeal, oesophageal, oral cancers (compared to chromium status as measured by toenail concentrations)	Case-control	4 years	Persons aged 20-74 years	Cases of cancer	507	n/a	There was no association between chromium status and cancer incidence.
						Controls	434	n/a	

Appendix 3

Assessment of Health Benefit: Vitamin A

A total of 201 articles were identified on the health benefits associated with vitamin A intake. A review of abstracts further refined the number of articles. The abstracts of these articles were further reviewed to ensure that the subject matter, not just the title, was relevant to this assessment.

When conducting the review of abstracts, it was noted that many of the articles referred to vitamin A and not retinol (β-carotene has been assessed separately in Section 5.5 below). Therefore, those articles' abstracts that made reference to retinol *per se* were only considered. As a check, four studies where the abstract made reference to vitamin A and had a strong study design (Feskanich *et al*., 2003; Cho *et al*., 2003; Lim *et al*., 2004; Steck-Scott *et al*., 2004) were selected and the full paper sourced. Of these four papers, three referred to retinol within the text (Feskanich *et al.,* 2003; Cho *et al.,* 2003; Lim *et al.,* 2004), one did not (Steck-Scott *et al.,* 2004).

The abstracts were also assessed to determine if serum retinol had been used as an indicator of vitamin A status of subjects. These articles were excluded, as serum retinol levels do not necessarily reflect retinol intake, and may be influenced by other dietary factors such as the intake of protein, energy or zinc (United States Institute of Medicine, 2001).

Following a review of abstracts, the available evidence was reduced to 16 articles once duplicate material was eliminated. The details of these articles are provided in Tables A3-1 to A3-3 below.

Twelve studies investigated retinol in relation to various cancers, showing that the relationship between retinol intake and cancer varies depending on the type of cancer. An inverse association between retinol intake and cancer risk was found several of the 12 studies. These inverse associations were based on linear trends comparing retinol intake with cancer, usually as ascertained by a semi quantitative food frequency questionnaire. Four cancer studies showed no statistically significant relationship between retinol intake and breast cancer. Two studies used biochemical indices to ascertain retinol status (breast tissue and plasma retinol), neither showing a relationship between retinol intake and a health outcome.

Two of the twelve cancer studies investigated melanoma endpoints, and showed an inverse relationship between retinol intake and incidence of melanoma. An inverse association between retinol intakes was observed for lung and colon cancer in one study. Of two studies investigating prostrate cancer, one showed an association between retinol intake and cancer incidence, the other did not. Single studies investigating ovarian and head/neck cancer did not show an association between retinol and cancer incidence.

The literature search revealed three studies investigating the relationship between vitamin A and bone health. One study investigated retinol intakes separate from total vitamin A intakes. This study investigated the relationship between retinol intake and bone mineral density and the relationship between retinol intake and fracture risk. Retinol intake was associated negatively with bone mineral density, and an increased intake was associated with increased risk of hip fracture. The remaining two studies investigated retinol as a component of vitamin A.

One showed an inverse relationship between retinol intake from food and supplements and hip fracture, and the other did not show any association between retinol and the risk of fracture.

There was only one other study outside of cancer and bone health investigations. This paper examined the effect of retinol intake on cataracts, and did not show a significant association.

The evidence base on vitamin A indicates that there may be a beneficial outcome for cancer risk, primarily melanomas. However there is also a strong level of evidence that supports the null hypothesis for cancer, as well as for other health-related endpoints.

Vitamin A is assigned an evidence level of 1

Table A3-1: Identified Studies on Vitamin A (Retinol) and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Bertone *et al.* (2001)	Clinical – ovarian cancer (Food frequency questionnaire to quantify typical consumption of retinol 5 years prior to diagnosis)	Retrospective population based case control	4 years	Women	Cases of ovarian cancer	327	Intake of retinol was unrelated to risk of ovarian cancer
					Controls	3129	
Bohlke *et al.* (1999)	Clinical – histologically confirmed breast cancer (compared to retinol intake as ascertained by food frequency questionnaire)	Case control study	Not reported	Women	Cases of breast cancer	820	In postmenopausal women there was no association between retinol intake and risk of breast cancer.
					Controls	1548	
Bosetti *et al.* (2004)	Clinical -Prostrate cancer (compared with retinol intake as ascertained by food frequency questionnaire)	Case control	9 years	Males <75 years of age	Cases of prostrate cancer	1294	- The risk of prostrate cancer was inversely associated with retinol intakes. - The odds ratio (OR) for highest vs. lowest quintiles of intake was 0.79.
					Controls	1451	
Cho *et al.* (2003)	Clinical – Breast Cancer (compared to retinol intake as ascertained by food frequency questionnaire)	Prospective cohort	8 years follow up	Women – 26-46 years at beginning of study (Nurses study)	Cases of breast cancer	714	- There was an inverse relationship between retinol intake and breast cancer, however this association was not statistically significant ($p>0.05$). - The relative risk (RR) between the highest quintile of intake compared to lowest was 0.80.
					Cohort	90 655	
Copper *et al.* (1999)	Clinical – measurement of plasma retinol in head and neck cancer patients	Case control	Not reported	Persons	Cases of head/neck cancer	25	There was no difference found in plasma retinol between cases and controls
					Controls	26	
Feskanich *et al.* (2003)	Clinical – melanoma (compared to dietary and supplemental retinol intake as measured by food frequency questionnaire).	Prospective cohort	4 years	Women in Nurses health study I and II	Cases of melanoma	414	- There was a significantly ($p<0.01$) inverse association between retinol intake from foods and supplements and melanoma incidence - The RR between the lowest (400 mg) and highest (>1800 mg) retinol intake was 0.39.
					Cohort	162000	

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Fontham *et al.* (1988)	Clinical – lung cancer (compared to retinol intake as ascertained by semi quantitative food frequency questionnaire)	Case-control	3 years	Persons	Cases of lung cancer	1253	- There was a significant ($p<0.05$) inverse association between retinol intake and adenocarcinoma risk. This risk was more pronounced amongst black subjects. - The OR for this association was 0.64.
					Controls without history of cancer	1274	
Ghadirian *et al.* (1997)	Clinical – colon carcinoma (compared to retinol intake as ascertained by food frequency questionnaire).	Case control	4 years	Persons	Cases of colon carcinoma	402	- There was a significant ($p<0.05$) inverse association between dietary retinol intake and colon cancer risk - The OR for this association was 0.069
					Controls	682	
Giovannucci *et al.* (1995)	Clinical - prostrate cancer (compared to retinol intake as ascertained by food frequency questionnaire)	Prospective cohort	6 years	Men	Cases of prostrate cancer	812	No consistent association was observed for dietary retinol and risk of prostrate cancer
					Cohort	47894	
Kushi *et al.* (1996a)	Clinical – breast cancer (compared to retinol intake as ascertained by food frequency questionnaire)	Prospective cohort	8 years	Postmenopausal women IOWA	Cases of breast cancer	879	There was no relation between retinol intakes and breast cancer incidence.
					Cohort	34387	
Naldi *et al.* (2004)	Clinical - Patients with histologically confirmed cutaneous malignant melanoma (compared with dietary vitamin A intake)	Case control	2 years	Men and women	Cases of melanoma	542	- There was a significant ($p<0.05$) inverse relationship between retinol intake and melanoma risk. - Adjusted OR for this association = 0.57.
					Controls	538	
Zhu *et al.* (1995)	Clinical – breast cancer (compared to vitamin A concentration in breast adipose tissue, and dietary vitamin A intake – method of analysis not reported).	Clinical case control	Not reported	Women	Cases of breast cancer	36	- Vitamin A concentration of breast adipose tissue was no different between the two groups. - Vitamin A intake was not statistically ($p>0.05$) different between cases and controls. - Vitamin A concentration of breast adipose tissue had a significant ($p<0.05$) correlation with dietary intake in breast cancer cases only.
					Controls with benign breast disease	45	

Table A3-2: Identified Studies on Vitamin A and Bone Health

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Feskanich *et al.* (2002)	Clinical – hip facture (compared with intake of retinol as estimated from diet records and food frequency questionnaire).	Prospective Cohort	18 year follow up	Women, nurses study	Cases of hip fracture	603	- There was a significant ($p<0.01$) positive association between total vitamin A intake and the incidence of hip fracture. This increased risk was attributable primarily to retinol. - The RR between the lowest (<500 µg/day) and highest (>2000 mg/day) quintiles of retinol intake was 1.89.
					Cohort	72 337	
Lim *et al.* (2004)	Clinical - bone mineral density and hip fracture (compared with intake of retinol as estimated from diet records and food frequency questionnaire).	Prospective Cohort	9.5 years	Post - menopausal women (IOWA women's health study)	Cases of hip fracture	6502	There was no significant ($p>0.05$) dose response relationship between retinol intake and hip fracture risk.
					Cohort	34 703	
Melhus *et al.* (1998)	Clinical - bone mineral density and hip fracture (compared with intake of retinol as estimated from diet records and food frequency questionnaire).	Cross sectional	5.5 years	Women	Women 28-74 years	175	Retinol intake was negatively associated with bone mineral density
		Nested case control	5.5 years	Women	Cases of hip fracture	247	- There was a significant ($p<0.01$) association between retinol intake and hip fracture risk. - For every 1 mg increase in retinol intake risk for hip fracture increased by 68%.
					Controls	873	

Table A3-3: Identified Studies on Other Health Outcomes Associated with Increased Vitamin A (Retinol) Intake

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Chasan-Taber *et al.* (1999)	Clinical – cases who had cataracts extracted (compared to food frequency questionnaire).	Prospective cohort	12 years	77466 female nurses aged 30-55 years	Cases of cataracts	1471	Retinol intake was not significantly ($p>0.05$) associated with cataract formation.

Appendix 4

Assessment of Health Benefit: β-carotene

A review of abstracts refined the 141 β-carotene articles identified from the PubMed and NHMRC sources. This process ensured that the subject matter was relevant to this assessment. In assessing the subject matter, articles that assessed changes in serum β-carotene against health outcomes were included, as there is evidence showing that serum β-carotene is reflective of a change in dietary β-carotene intake (United States Institute of Medicine, 2000b).

The available evidence used to assess β-carotene was reduced to 72 articles. A detailed summary of these articles is provided in Tables A4-2 to A4-3 below.

Eighteen articles were identified that examined the association between β-carotene intakes above the RDI (i.e. the vitamin A RDI expressed as retinol equivalents) and CHD. There was a clear division in the articles relating to CHD, with ten articles reporting a significant inverse association between CHD endpoints and β-carotene intakes, and eight articles that showed no significant association between CHD endpoints and β-carotene intakes.

The greatest number of articles (50) on β-carotene related to the association between its intake above the RDI and cancer. The majority of these articles (31) showed no significant association between cancer endpoints and β-carotene intakes. Nineteen articles showed a significant inverse relationship between cancer endpoints and β-carotene intakes. Six of the 50 cancer articles were intervention studies, of which only two showed an inverse relationship between increased β-carotene intakes and cancer risk.

There were four articles that reported on other health outcomes, including bone health, respiratory diseases, and the common cold. None of these articles indicated a significant beneficial health effect with β-carotene intakes above the RDI.

Although there is information to indicate that a beneficial association may exist between β-carotene intakes and CHD / cancer, the high volume of contradictory evidence shows that this association is most likely a weak one.

β-carotene is assigned an evidence level of 1

Table A4-1: Identified Studies on β-Carotene and Coronary Heart Disease (CHD)

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Asherio *et al.* (1999)	n/a	Clinical – ischaemic and haemorrhagic stroke (compared to β-carotene intake as measured by food frequency questionnaire).	Cohort	8 years	40-75 year males without CVD or diabetes	Total Stroke	328	n/a	There was no significant difference in the incidence of stroke ($p<0.05$) between highest and lowest quintiles of β-carotene intake.
						Ischaemic stroke	210	n/a	
						Haemorrhagic stroke	70	n/a	
Bolton-Smith *et al.* (1992)	n/a	Clinical – diagnosed and undiagnosed CHD (compared to β-carotene intake as measured by food frequency questionnaire).	Cross sectional study	10 years	Adult persons	Diagnosed CHD males	369	n/a	- CHD risk was significantly ($p<0.05$) lower between the highest and lowest quintiles of β-carotene intake for undiagnosed males. - There was no significant ($p>0.05$) difference in the risk of CHD between the highest and lowest quintiles of β-carotene intake for undiagnosed female or diagnosed CHD subjects.
						Diagnosed CHD females	235	n/a	
						Undiagnosed CHD males	659	n/a	
						Undiagnosed CHD females	795	n/a	
						Healthy male controls	3720	n/a	
						Healthy female controls	3749	n/a	
Daviglus *et al.* (1997)	n/a	Clinical – cases of stroke (compared to β-carotene intake)	Cohort	46 years	Middle-aged males	Cases of stroke	222	n/a	- There was no significant ($p>0.05$) association between β-carotene intakes and the risk of stroke. - Adjusted RR between the highest and lowest intake of β-carotene was 0.84.

de Lorgeril *et al.* (2001)	n/a	Biomarkers of congestive heart failure – peak exercise oxygen consumption, and left ventricular ejection function (compared to β-carotene intake)	Case-control	Not reported	Persons	Cases of congestive heart failure	21	n/a	- Serum β-carotene was inversely associated with the two biomarkers endpoints ($p<0.05$). - There was no significant ($p>0.05$) association between dietary β-carotene and the study endpoints.
						Age and gender matched controls	21	n/a	
Do *et al.* (2003)	n/a	Clinical – breast cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	2 years	Females aged 20-69 years	Cases if breast cancer	224	n/a	The intake of β-carotene was inversely, but not significantly ($p>0.05$) associated with breast cancer.
						Age matched controls	299	n/a	
Genkinger *et al.* (2004)	n/a	Clinical – mortality from cancer, CHD and all causes (compared to β-carotene intake as measured by a food frequency questionnaire)	Cohort	15 years	6151 persons	Cases of cancer	307	n/a	β-carotene intakes had no significant ($p>0.05$) impact on the mortality from CHD.
Hak *et al.* (2003)	Double - blinded	Clinical – MI incidence (compared to β-carotene intake as measured by food frequency questionnaire)	Randomised clinical trial	5 years	Male physicians aged 40-84	β-carotene supplement intake	531	50 mg/day	- There was no significant ($p>0.05$) difference in the incidence of Mi between the two study groups. - There was no significant ($p>0.05$) association between β-carotene intake and the risk of MI.
						Placebo intake	531	-	

Hak *et al.* (2004)	n/a	Clinical – stroke (compared to serum β-carotene levels)	Case-control	13 years	Male physicians aged 45-70 years	Cases of stroke	297	n/a	- There was a significant ($p>0.05$) inverse association between serum β-carotene levels and the risk of stroke. - The OR between the lowest and highest β-carotene intakes was 0.62.
						Age matched controls	297	n/a	
Hirvonen *et al.* (2000)	n/a	Clinical – stroke events (compared to β-carotene intake measured by a food frequency questionnaire)	Cohort	6.1 years	Male smokers	Cerebral infarction cases	736	n/a	- The risk of cerebral infarction was significantly ($p<0.001$) reduced with increasing dietary β-carotene intake. - The RR of cerebral infarction between 1st (0.81 mg/day) and 4th (3.69 mg/day) quintiles of dietary β-carotene intake was 0.74. - Dietary β-carotene intake was not significantly associated ($p>0.05$) with intracerebral haemorrhage or subarachinoid haemorrhage.
						Subarachinoid haemorrhage cases	83	n/a	
						Intracerebral haemorrhage cases	95	n/a	
Klipstein-Grobusch *et al.* (1999)	n/a	Clinical – myocardial infarction (MI) (compared to β-carotene intake measured by food frequency questionnaire)	Cohort	4 years	4802 persons aged ≥ 55 years	Cases of MI	173	n/a	- There was a significant ($p<0.02$) inverse association between β-carotene intake and the risk of MI. - The OR between the lowest (<1.13 mg/day) and highest (>1.57 mg/day) intakes of β-carotene was 0.55.
Kardinaal *et al.* (1995)	n/a	Clinical – acute MI (compared to serum β-carotene)	Case-control	2 years	Males aged < 70 years	Cases of acute MI	674	n/a	Tissue β-carotene levels were significantly ($p<0.05$) lower in cases compared to controls.
						Age matched controls	725	n/a	

Klipstein-Grobusch *et al.* (2001)	n/a	Clinical – peripheral arterial disease incidence (compared to dietary β-carotene intake measured by a food frequency questionnaire)	Cohort	4 years	4367 persons aged ≥ 55 years	Female cases of peripheral arterial disease	370	n/a	β-carotene intakes were not significantly ($p>0.05$) associated with the risk of peripheral arterial disease.
						Male cases of peripheral arterial disease	204	n/a	
Osganian *et al.* (2003b)	n/a	Clinical – coronary artery disease including fatal and non-fatal MI (compared to β-carotene intake measured by food frequency questionnaire)	Cohort	10 years	73286 females aged 30-55 years	Cases of coronary artery disease	998	n/a	- There was a significant ($p<0.05$) inverse association between β-carotene intake and the risk of coronary artery disease. - The OR between the lowest (1.72 mg/day) and highest (7.64 mg/day) intakes of β-carotene was 0.74.
Rapola *et al.* (1997)	Double-blinding	Clinical – non-fatal MI and fatal CHD	Randomised controlled trial	5.3 years	Male smokers	β-carotene supplement intake group	461	20 mg/day	There was no significant ($p<0.05$) difference in the incidence of non-fatal MI or fatal CHD between the two groups.
						Placebo intake group	438	-	
Singh *et al.* (1994)	n/a	Clinical – incident of coronary artery disease (compared to β-carotene intake as measured by a 7-day food recall)	Cross-sectional study	Not reported	Persons aged 26-65 years	Total population	152	n/a	β-carotene intakes were significantly ($p<0.01$) lower in individuals with coronary artery disease compared to those without CHD risk factors.
Singh *et al.* (1995)	n/a	Clinical – coronary artery disease (compared to β-carotene intake)	Cross-sectional study	Not reported	Persons aged 50-84 years	Total population	72	n/a	β-carotene intakes were significantly ($p>0.05$) lower in individuals with coronary artery disease compared to those without.

Tavani *et al.* (1997)	n/a	Clinical – non-fatal acute MI (compared to β-carotene intake)	Case-control	9 years	Females	Cases of non-fatal acute MI	433	n/a	- There was a significant ($p<0.01$) inverse association between β-carotene intake and the risk of acute MI. - The OR between the lowest and highest intakes of β-carotene was 0.5.
						Controls	869	n/a	
van Poppel *et al.* (1994)	Double - blinded	Biomarkers of CHD – total cholesterol, HDL, apolipoproteins A-I and B-100 and (a)	Randomised controlled trial	14 weeks	Male smokers	β-carotene supplement intake	25	20 mg/day	There was no significant ($p>0.05$) difference in the study parameters between the two study groups.
						Placebo intake	25	-	

Table A4-2: Identified Studies on β-Carotene and Cancer

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Adzersen *et al.* (2003)	n/a	Clinical – primary breast cancer (compared to β-carotene intake)	Case-control	2 years	Females	Cases of primary breast cancer	310	n/a	- There was no significant ($p>0.05$) association between β-carotene intake and breast cancer risk. - The OR between the lowest and highest β-carotene intakes was 0.46.
						Controls without dietary or endocrine conditions	353	n/a	
Albanes *et al.* (1996)	?	Clinical – lung cancer incidence	Randomised controlled trial	5-8 years	Male smokers aged 50-69 years	β-carotene supplement intake	?	20 mg/day	- There was a significant ($p<0.05$) increase in the incidence of lung cancer for the β-carotene supplement group compared to the placebo group. - The RR for β-carotene supplementation was 1.16.
						Placebo intake	?	-	
Albanes *et al.* (2000)	Double-blinded	Clinical – colorectal cancer incidence	Randomised controlled trial (sub-set of ATBC trial)	8 years	Male smokers aged 50-69 years	β-carotene supplement intake	7280	20 mg/day	β-carotene supplementation had no significant impact on the incidence between the two study groups ($p>0.05$).
						Placebo intake	7280	-	
ATBC Prevention Study Group (1994)	Double-blinded	Clinical – lung cancer and other cancers	Randomised controlled trial	8 years	Male smokers aged 50-69 years	Synthetic β-carotene supplement intake	7280	20 mg/day	- The β-carotene supplement group had a significantly ($p<0.01$) higher incidence of lung cancer compared to the placebo group. - Prostate cancer incidence was increased in the β-carotene supplement group, however the significance was not reported.
						Placebo intake	7280	-	

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Bertone *et al.* (2001)	n/a	Clinical – ovarian cancer (compared to dietary and supplemental β-carotene intake as measured by food frequency questionnaire)	Case-control	3 years	Females	Cases of ovarian cancer	327	n/a	There was no significant ($p<0.05$) difference in the risk of ovarian cancer between highest and lowest quintiles of β-carotene intake.
						Controls	3129	n/a	
Bohlke *et al.* (1999)	n/a	Clinical – breast cancer (compared to vitamin C intake measured by food frequency questionnaire)	Case-control	Not reported	Adult females	Breast cancer cases	820	n/a	- There was no association between β-carotene intake and breast cancer for post-menopausal women. - There was an inverse association between β-carotene intake and breast cancer for pre-menopausal women.
						Healthy controls	1548	n/a	
Candelora *et al.* (1992)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	3 years	Female non-smokers	Cases of lung cancer	124	n/a	- There was no significant ($p>0.05$) inverse association between β-carotene intake and lung cancer. - The OR between the lowest and highest β-carotene intakes was 0.4.
						Controls	263	n/a	
Ching *et al.* (2002)	n/a	Clinical – breast cancer (compared to serum β-carotene levels)	Case-control	2 years	Females aged 30-84 years	Cases of breast cancer	341	n/a	- There was a significant ($p<0.02$) inverse association between serum β-carotene levels and breast cancer. - The adjusted OR between the lowest ($\leq$0.4 μmol/L) and highest ($\geq$1.1 μmol/L) quartiles of serum β-carotene was 0.47.
						Age matched controls	151	n/a	

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Cramer *et al.* (2001)	n/a	Clinical – ovarian cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	5 years	Females	Cases of ovarian cancer	549	n/a	- There was a significant ($p<0.05$) inverse association between β-carotene intake and ovarian cancer. - The adjusted OR between the lowest (≤2.3 mg/day) and highest (>7.2 mg/day) quintiles of intake was 0.58
						Controls	516	n/a	
Daviglus *et al.* (1996)	n/a	Clinical – cases of prostate cancer (compared to β-carotene intake)	Cohort	30 years	Middle-aged males	Cases of prostate cancer	132	n/a	- No significant ($p>0.05$) association between the intake of β-carotene and the risk of prostate cancer. - Relative risks (RR) between the lowest and highest intake of β-carotene was 1.27.
Franceschi *et al.* (1999)	n/a	Clinical – colorectal cancer (compared to dietary β-carotene intake as measured by food frequency questionnaire)	Case-control	4 years	Persons with a median age of 62 years	Cases of colorectal cancer	1953	n/a	There was an inverse association between β-carotene intake and the risk of colorectal cancer.
						Controls	4154	n/a	
Genkinger *et al.* (2004)	n/a	Clinical – mortality from cancer, CHD and all causes (compared to β-carotene intake as measured by food frequency questionnaire)	Cohort	15 years	6151 persons	Cases of cancer	307	n/a	β-carotene intakes had no significant ($p>0.05$) impact on the mortality from cancer.
Giovannucci *et al.* (1995)	n/a	Clinical – prostate cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Cohort	6 years	47894 males	Cases of prostate cancer	812	n/a	There was no association between β-carotene intake and the risk of prostate cancer.

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Green *et al.* (1999)	Double-blinded	Clinical – skin cancer	Randomised clinical trial	4.5 years	Persons	β-carotene supplement intake	405	n/a	There was no significant ($p>0.05$) difference in the rate of skin cancer between the two study groups.
						Placebo intake	405	n/a	
Greenberg *et al.* (1990)	Double-blinded	Clinical – skin cancer	Randomised controlled trial	5 years	Persons with non-melanoma skin cancer	β-carotene supplement intake	903	50 mg/day	There was no significant ($p>0.05$) difference between the two groups in the incidence and prevalence of skin cancer.
						Placebo intake	902	-	
Greenberg *et al.* (1994)	Double-blinded	Clinical – incidence of new colon cancer polyps	Randomised controlled trial	4 years	Persons with history of colon cancer	β-carotene supplement intake	184	25 mg/day	There was no significant ($p>0.05$) difference in the incidence of colon cancer between the two study groups.
						Placebo intake	187	-	
Hansson *et al.* (1994)	n/a	Clinical – gastric cancer (compared to dietary and supplementary β-carotene intake)	Case-control	20 years	Persons	Cases of gastric cancer	338	n/a	- There was a significant ($p<0.01$) inverse association between β-carotene intake and the risk of gastric cancer. - The OR between the lowest (0.8 mg/day) and highest (4.3 mg/day) quartile of intake was 0.52.
						Controls	679	n/a	
Holmberg *et al.* (1994)	n/a	Clinical – breast cancer (compared to β-carotene intake)	Case-control	3 years	Females	Cases of breast cancer	265	n/a	- There was a significant ($p<0.05$) inverse association between β-carotene intake and the risk of breast cancer. - The OR between the lowest (2.7-3.9 mg/day) and highest (>5.3 mg/day) tertiles of intake was 0.6.
						Age matched controls	432	n/a	

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Jain *et al.* (2000)	n/a	Clinical – endometrial cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Cohort	5 years	56837 females	Cases of endometrial cancer	221	n/a	There was no significant ($p>0.05$) association between endometrial cancer and β-carotene intake.
Kaaks *et al.* (Kaaks *et al*., 1998)	n/a	Clinical – gastrointestinal cancers (compared to β-carotene intake as measured by a diet history)	Case-control	4 years	Persons aged 35-74 years	Cases of gastrointestinal cancer	201	n/a	- There was a significantly ($p<0.001$) inverse association between β-carotene intake and the risk of gastrointestinal cancer. - The OR between the lowest and highest quartile of intake was 0.5.
						Controls	2851	n/a	
Le Marchand *et al.* (1993)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by diet history)	Case-control	2 years	Persons	Cases of lung cancer	332	n/a	- There was a significant ($p<0.01$) inverse association between the intake of β-carotene and the risk of lung cancer. - The OR between the lowest and highest quartiles of intake was 0.5 and 0.3 for males and females respectively.
						Age matched controls	865	n/a	

McCann *et al.* (2001)	n/a	Clinical – ovarian cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	12 years	Females aged 20-87 years	Cases of ovarian cancer	496	n/a	- There was a significant ($p<0.05$) inverse association between the intake of β-carotene and the risk of ovarian cancer. - The OR between the lowest and highest intakes was 0.68.
						Controls	1425	n/a	
Männisto *et al.* (2004)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Pooled cohort	7-16 years	399765 Persons	Cases of lung cancer	3155	n/a	- When adjusted for age, β-carotene intake was inversely associated with the risk for lung cancer ($p<0.05$). - When controlling for other confounding variables, the inverse association was insignificant ($p>0.05$). - The OR between the lowest and highest intakes was 0.98.
Mayne *et al.* (1994)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by diet history)	Case-control	3 years	Persons	Cases of lung cancer	413	n/a	- There was a significant ($p<0.05$) inverse association between the intake of dietary β-carotene and the risk of lung cancer. - The OR between the lowest and highest β-carotene intakes was 0.7.
						Age and gender matched controls	413	n/a	
Michaud *et al.* (2000)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Control	10 years	51529 males aged 40-75 years	Cases of lung cancer	275	n/a	Adjusted β-carotene intakes had no significant ($p>0.05$) association with the risk of lung cancer in either males or females.
				14 years	121700 females aged 30-55 years	Cases of lung cancer	519	n/a	

Michaud *et al.* (2002)	n/a	Clinical – bladder cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Cohort	11 years	27111 male smokers aged 50-69 years	Cases of bladder cancer	344	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of bladder cancer.
Murtaugh *et al.* (2004)	n/a	Clinical – rectal cancer (compared to β-carotene intake as measured by food diet history)	Case-control	4 years	Persons aged 30-79 years	Cases of rectal cancer	952	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of rectal cancer.
						Age and gender matched controls	1205	n/a	
Negri *et al.* (1996)	n/a	Clinical – breast cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	3 years	Females	Cases of histologically confirmed breast cancer	2569	n/a	- There was an inverse association between the intake of dietary β-carotene and the risk of breast cancer. - The OR between the lowest and highest β-carotene intakes was 0.84.
						Controls with no history of cancer	2588	n/a	
Nkondjock and Ghadirian (2004)	n/a	Clinical – breast cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	4 years	Females aged 35-79 years	Cases of breast cancer	414	n/a	There was no significant ($p>0.05$) association between adjusted β-carotene intake and the risk of breast cancer.
						Age matched controls	668	n/a	
Norrish *et al.* (2000)	n/a	Clinical – prostate cancer (compared to β-carotene intake)	Case-control	2 years	Males	Cases of prostate cancer	317	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of prostate cancer.
						Controls	480	n/a	

Nyberg *et al.* (1998)	n/a	Clinical – lung cancer (compared to β-carotene intake)	Case-control	6 years	Persons aged > 30 years	Cases of lung cancer	124	n/a	- There was a significantly ($p<0.05$) inverse association between β-carotene intake and the risk of lung cancer. - The OR between the lowest and highest quintiles of intake was 0.47.
						Controls	235	n/a	
Ocke *et al.* (1997)	n/a	Clinical – lung cancer (compared to vitamin C intake as measured by diet history)	Cohort	19 years	561 males	Cases of lung cancer	54	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of lung cancer.
Ohno *et al.* (1988)	n/a	Clinical – prostate cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	3 years	Males	Cases of prostate cancer	100	n/a	- There was a significant ($p<0.01$) inverse association between the intake of dietary β-carotene and the risk of prostate cancer. - The RR between the lowest and highest β-carotene intakes was 0.48.
						Controls	100	n/a	
Rohan *et al.* (2002)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	5 years	Females	Cases of lung cancer	155	n/a	There was no significant ($p>0.05$) association between β-carotene intake and lung cancer.
						Controls	5361	n/a	
Schuurman *et al.* (2002)	n/a	Clinical – prostate cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Cohort	6.3 years	58279 males aged 55-69 years	Cases of prostate cancer	642	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of prostate cancer.

Shibata *et al.* (1992)	n/a	Clinical – cancer incidence (compared to β-carotene intake)	Cohort	8 years	11580 persons	Cases of cancer	1335	n/a	There was no significant ($p>0.05$) association between β-carotene intake and cancer incidence.
Slattery *et al.* (1990)	n/a	Clinical – cervical cancer (compared to β-carotene intake)	Case-control	3 years	Females	Cases of cervical cancer	266	n/a	There was no significant ($p>0.05$) association between the intake of dietary β-carotene and the risk of cervical cancer.
						Age matched controls	408	n/a	
Stefani *et al.* (1999)	n/a	Clinical – lung cancer (compared to β-carotene intake)	Case-control	4 years	Persons aged 30-89 years	Cases of lung cancer	541	n/a	- There was a significant ($p<0.001$) inverse association between the adjusted intake of dietary β-carotene and the risk of lung cancer. - The RR between the lowest (<1.94 mg/day) and highest (>5.86 mg/day) quartiles of β-carotene intake was 0.3.
						Controls	540	n/a	
Tavani *et al.* (1994)	n/a	Clinical – oesophageal cancer (compared to dietary β-carotene intake as measured by food frequency questionnaire)	Case-control	8 years	Persons	Histologically confirmed cases of oesophageal cancer)	316	n/a	- There was a significant ($p<0.05$) inverse association between the adjusted intake of β-carotene and the risk of oesophageal cancer. - The RR between cases and controls was 0.4.
						Controls	230	n/a	

Tavani *et al.* (1999)	n/a	Clinical – breast cancer (compared to dietary β-carotene intake as measured by food frequency questionnaire)	Case-control	11 years	Females	Cases of histologically confirmed breast cancer	579	n/a	- There was a significant ($p<0.01$) inverse association between the adjusted intake of β-carotene and the risk of breast cancer. - The RR between the lowest (32 IU/day) and highest (240 IU/day) quintiles of intake was 0.5.
						Controls	668	n/a	
Terry *et al.* (2002)	n/a	Clinical – colorectal cancer (compared to β-carotene intake as measured by food frequency questionnaire)	Case-control	3 years	Females	Cases of colorectal cancer	295	n/a	There was no significant ($p>0.05$) association between β-carotene intakes and the risk of colorectal cancer.
						Controls	5334	n/a	
Varis *et al.* (1998)	Double - blinded	Clinical – gastric cancer	Randomised controlled trail (subset of the ATBC trial)	5.1 years	Males aged 50-69 years with gastritis	β-carotene supplement intake	7282	20 mg/day	There was no significant ($p>0.05$) difference in the incidence of gastric cancer between the two study groups.
						Placebo intake	7287	-	
Verhoeven *et al.* (1997)	n/a	Clinical – breast cancer (compared to β-carotene intake)	Cohort	4.3 years	62573 females aged 55-69 years	Cases of breast cancer	650	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of breast cancer.
Voorrips *et al.* (2000)	n/a	Clinical – lung cancer (compared to dietary and supplemental β-carotene intake as measured by food frequency questionnaire)	Cohort	6.3 years	58279 males aged 55-69 years	Cases of lung cancer	939	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of lung cancer.

West *et al.* (1989)	n/a	Clinical – colon cancer (compared to dietary β-carotene intake as measured by food frequency questionnaire)	Case-control	4 years	Persons	Cases of colon cancer	231	n/a	- There was an inverse association between the adjusted intake of β-carotene and the risk of colon cancer. - The RR between the lowest and highest β-carotene intake was 0.5.
						Controls	391	n/a	
West *et al.* (1991)	n/a	Clinical – prostate cancer (compared to β-carotene intake as measured by a food frequency questionnaire)	Case-control	2 years	Males	Cases of prostate cancer	358	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of prostate cancer.
						Controls	679	n/a	
Wright *et al.* (2003)	n/a	Clinical – lung cancer (compared to β-carotene intake as measured by a food frequency questionnaire)	Case-control	3 years	Females	Cases of lung cancer	587	n/a	There was no significant ($p>0.05$) inverse association between the intake of β-carotene and the risk of lung cancer.
						Age matched controls	624	n/a	
Wu *et al.* (2004)	n/a	Clinical – prostate cancer (compared to dietary β-carotene intake as measured by a food frequency questionnaire)	Case-control	12 years	Males aged 40-75 years	Cases of prostate cancer	450	n/a	There was no significant ($p>0.05$) association between β-carotene intake and the risk of prostate cancer.
						Age matched controls	450	n/a	

Zhang *et al.* (1999)	n/a	Clinical – breast cancer (compared to dietary and supplemental β-carotene intake as measured by food frequency questionnaire)	Cohort	14 years	83234 females aged 30-55 years	Cases of breast cancer	2697	n/a	- Adjusted β-carotene intakes were inversely ($p<0.05$) associated with the risk of breast cancer in pre-menopausal women. - The RR between the lowest and highest β-carotene intakes of pre-menopausal women was 0.84. - There was an inverse, but non-significant ($p>0.05$) association between supplemental and dietary β-carotene intake and the risk of breast cancer in post-menopausal women.

Table A4-3: Identified Studies on β-Carotene and Other Health Outcomes

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Grievink *et al.* (2000)	n/a	Clinical – chronic respiratory symptoms (compared to serum β-carotene levels)	Case-control	1 year	Non-smoker Persons	Cases of chronic respiratory illness	491	n/a	There was no association between serum β-carotene levels and the symptoms of chronic respiratory illness.
						Controls	496	n/a	
Hemila *et al.* (2002)	n/a	Clinical – incidence of the common cold (compared to supplemental and dietary β-carotene intake)	Cohort	4 years	Male smokers	Total cohort	21796	n/a	Neither dietary nor supplemental β-carotene had an association with the incidence of the common cold.
Rautalahti *et al.* (1997)	n/a	Clinical – symptoms of chronic obstructive pulmonary disease	Randomised controlled trial	5.3 years	Male smokers	β-carotene supplement intake group	461	20 mg/day	There was no significant ($p<0.05$) difference in the symptoms of chronic obstructive pulmonary disease between the two study groups.
						Placebo intake group	438	-	
Wattanapenpaiboon *et al.* (2003)	n/a	Biomarker of bone metabolism – bone mineral content and BMD (compared to dietary β-carotene intake as measured by food frequency questionnaire)	Cross-population study	12 months	Persons aged ≥ 25 years	Males	69	n/a	There was no significant ($p>0.05$) association between β-carotene intake and bone mineral content or density.
						Pre-menopausal females	46	n/a	
						Post-menopausal females	90	n/a	

Appendix 5

Assessment of Health Benefit: Vitamin C

The 141 articles on vitamin C identified from the PubMed and NHMRC sources were further reviewed on the bases of their abstract summary to ensure that the subject matter was relevant to this assessment. In assessing the subject matter, articles were excluded if they used serum vitamin C levels as an indicator of vitamin C status. The body caps serum vitamin C concentrations at intakes above 80 mg/day; increases in dietary intakes beyond this level will not be detected by changes in serum vitamin C levels (United States Institute of Medicine, 2000b)

The available evidence was therefore reduced to 61 articles. A detailed summary of these articles is provided in Tables A5-1 to A5-5 below.

Of the 61 articles obtained, 24 were related to the association between vitamin C intake and CHD. Only one intervention study on CHD (Tofler *et al*., 2000) was found. This study showed an inverse relationship between supplemental vitamin C intake and total serum cholesterol, however there was no significant association with other CHD risk biomarkers.

There is little consistency in the results across the remaining 23 observational (case-control and cohort) CHD studies. Seven studies reported no significant association between vitamin C and CHD risk, and two even show an increased risk in CHD with increased vitamin C intakes. Fifteen studies (including a meta-analysis) report significant decreases in the risk of cardiovascular disease with increased vitamin C intake, however only six studies show this relationship throughout all of their study parameters. The other nine studies report disparate results between various subgroups of their study populations, of different CHD endpoints, or with supplemental versus dietary intakes of vitamin C. Of the eight studies that accommodate supplemental vitamin C intakes in their methodologies, there is support from the results for both an inverse association with CHD risk as well as the null hypothesis.

Twenty-five studies were obtained that assessed the impact of vitamin C intake on the risk of cancer. All of these studies were of either case-control or cohort design.

Unlike studies investigating CHD, the studies on cancer were more definitive in their results, with only three studies reporting differing outcomes amongst their study parameters. However, while a substantial number (13) of studies showed an inverse relationship between vitamin C intake and cancer risk, there was an equally strong level of support for the null hypothesis (9 studies). Five studies that included supplemental vitamin C intake in their analyses also showed conflicting results.

The effect of vitamin C intake on bone mineral density (BMD) was assessed in four studies. The results of these studies show a weak relationship between vitamin C intake and improvements in BMD. Two studies showed an increase in BMD in certain part of the body, but not consistently throughout, while one study reported an inverse relationship between vitamin C and BMD only where the calcium intake of subjects was less than 500 mg/day.

Five studies have investigated other health outcomes in respect to vitamin C intake, including cataract formation, the common cold and gastritis. The evidence showed some benefits from vitamin C intakes, however there were also a number that reported no significant association between vitamin C and a health outcome.

A significant proportion of the evidence base on vitamin C shows that increased intakes above the RDI have an association with improved health outcomes. However there is a high number of well-designed studies that do not support these findings. In many of the studies conducted on vitamin C, the results are not consistent throughout the study parameters, with health benefits occurring in certain circumstances or for certain groups, and not in others. Overall, there is a high degree of inconsistency in the evidence base on vitamin C.

Vitamin C is assigned an evidence level of 1

Table A5-1: Identified Studies on Vitamin C and Coronary Heart Disease

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Asherio *et al.* (1999)	n/a	Clinical – ischaemic and haemorrhagic stroke (compared to dietary and supplemental vitamin C intake measured by food frequency questionnaire).	Cohort	8 years	40-75 year males without CVD or diabetes	Total Stroke	328	n/a	There was no significant difference ($p<0.05$) between highest and lowest quintiles of vitamin C intake.
						Ischaemic stroke	210	n/a	
						Haemorrhagic stroke	70	n/a	
Bolton-Smith *et al.* (1992)	n/a	Clinical – diagnosed and undiagnosed CHD (compared to dietary vitamin C intake as measured by food frequency questionnaire).	Cross sectional study	10 years	Adult persons aged 40-59 years	Diagnosed CHD males	369	n/a	- CHD risk was significantly ($p<0.05$) lower between the highest and lowest quintiles of vitamin C intake for undiagnosed males. - There was no significant ($p>0.05$) difference in the risk of CHD between the highest and lowest quintiles of vitamin C intake for undiagnosed female or diagnosed CHD subjects.
						Diagnosed CHD females	235	n/a	
						Undiagnosed CHD males	659	n/a	
						Undiagnosed CHD females	795	n/a	
						Healthy male controls	3720	n/a	
						Healthy female controls	3749	n/a	
Daviglus *et al.* (1997)	n/a	Clinical – cases of stroke (compared to dietary vitamin C intake as measured by diet history)	Cohort	46 years	Males aged 40-55 years	Cases of stroke	222	n/a	- There was no significant ($p>0.05$) association between vitamin C intakes and the risk of stroke. - The RR between the highest and lowest vitamin C intake was 0.71.

de Lorgeril *et al.* (2001)	n/a	Biomarkers of congestive heart failure – peak exercise oxygen consumption, and left ventricular ejection function (compared to vitamin C intake)	Case-control	Not reported	Persons	Cases of congestive heart failure	21	n/a	There was no significant ($p>0.05$) association between dietary vitamin C intake and changes in study endpoints.
						Age and gender matched controls	21	n/a	
Enstrom *et al.* (1986)	n/a	Clinical – mortality from CVD and all causes (compared to dietary + supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	10 years	3119 persons aged >16 years	Death from all causes	276	n/a	There was no significant association ($p>0.05$) between vitamin C intake and mortality from CVD or all causes.
						Death from CVD	102	n/a	
Enstrom *et al.* (1992)	n/a	Clinical – mortality from CVD and all causes (compared to supplemental and dietary vitamin C intake as measured by food frequency questionnaire)	Cohort	10 years	Persons aged 25-74 years	Death from all causes	1809	n/a	- Vitamin C intake was associated with a significantly ($p<0.05$) decreased standard mortality ratio (SMR) for all causes. - Vitamin C intake was associated with a decreased SMR for CVD, however its statistical significance was not reported.
						Death from CVD	929	n/a	
Gale *et al.* (1995)	n/a	Clinical – mortality from stroke and CHD (compared to vitamin C intake measured by a 1-week food diary in years 1 and 2 of study)	Cohort	20 years	Elderly (65+ years) persons without a history of CVD	All subjects	730	n/a	- Adjusted RR between highest (45 mg/day) and lowest tertile (28 mg/day) of vitamin C was 0.5 ($p<0.003$). - Vitamin C was positively associated with an intake of other macro and micronutrients.
						Total deaths	643	n/a	
						Mortality from stroke	124	n/a	

Hirvonen *et al.* (2000)	n/a	Clinical – stroke events (compared to dietary vitamin C intake measured by a food frequency questionnaire)	Cohort (subset of the ATBC trial)	6.1 years	Male smokers aged 50-69 years	Cerebral infarction cases	736	n/a	- The RR of stroke as intracerebral haemorrhage between the 1st (52 mg/day) and 4th (141 mg/day) quintiles of dietary vitamin C intake was 0.39 ($p<0.05$). - Dietary vitamin C intake was not significantly associated ($p>0.05$) with cerebral infarction or subarachinoid haemorrhage.
						Subarachinoid haemorrhage cases	83	n/a	
						Intracerebral haemorrhage cases	95	n/a	
Klipstein-Grobusch *et al.* (1999)	n/a	Clinical – myocardial infarction (MI) (compared to dietary vitamin C intake measured by food frequency questionnaire)	Cohort	4 years	4802 persons aged ≥ 55 years	Cases of MI	173	n/a	There was no significant association between vitamin C intake and the risk of myocardial infarction.
Klipstein-Grobusch *et al.* (2001)	n/a	Clinical – peripheral arterial disease incidence (compared to dietary vitamin C intake measured by a food frequency questionnaire)	Cohort	4 years	4367 persons aged ≥ 55 years	Female cases of peripheral arterial disease	370	n/a	- There was a significant ($p<0.01$) inverse association between vitamin C intake and peripheral arterial disease in women. The RR between highest and lowest quartile of intake = 0.64. - There was no significant ($p>0.05$) association for males.
						Male cases of peripheral arterial disease	204	n/a	
Knekt *et al.* (1994)	n/a	Clinical – CHD mortality (compared to vitamin C intake as measured by 1yr diet history)	Cohort	6 years	5133 persons aged 30-69 years	Female CHD deaths	47	n/a	There was an association between vitamin C intakes and CHD mortality.
						Male CHD deaths	148	n/a	

Kritchevsky *et al.* (1995)	n/a	Biomarker of CHD – arterial wall thickness (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Cohort	11 years	11307 persons	Female CHD cases	210	n/a	There was no significant association between vitamin C intake and arterial wall thickness ($p>0.05$).
						Male CHD cases	416	n/a	
Kushi *et al.* (1996b)	n/a	Clinical – CHD mortality (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	6 years	34486 post-menopausal females	CHD deaths	242	n/a	- There was a positive association between increasing vitamin C intake and CHD mortality ($p<0.05$). - The RR between the lowest ($\leq$112 mg/day) and highest ($\geq$391 mg/day) vitamin C intakes was 1.08 and 1.49 for CHD mortality respectively.
Lee *et al.* (2004)	n/a	Clinical – CHD, coronary artery disease and stroke (compared to dietary and supplemental vitamin C intake measured by food frequency questionnaire)	Cohort	9 years	41836 post-menopausal women aged 55-69 years	1st quintile (vitamin C intake = 85 mg/day)	315	n/a	- There was a significant positive association between vitamin C intake and CHD ($p<0.01$), coronary artery disease ($p<0.01$) and stroke incidence ($p<0.05$). - The adjusted RR between highest and lowest quintile of intake was 1.84, 1.91 and 2.57 for CHD, coronary artery disease and stroke respectively.
						2nd quintile (vitamin C intake = 139 mg/day)	413	n/a	
						3rd quintile (vitamin C intake = 189 mg/day)	433	n/a	
						4th quintile (vitamin C intake = 279 mg/day)	413	n/a	
						5th quintile (vitamin C intake = 667 mg/day)	349	n/a	

Leng *et al.* (1994)	n/a	Clinical – peripheral arterial disease (compared to vitamin C intake as measured by food frequency questionnaire)	Cohort	Single time point	1592 persons aged 55-74 years	Cases of peripheral arterial disease	153	n/a	There was a significant difference in vitamin C intake between cases and controls ($p<0.05$).
						Healthy controls	122	n/a	
Mayer-Davis *et al.* (1997)	n/a	Biomarkers of CVD – serum HDL, LDL, and triglycerides (compared to diet and supplemental vitamin C intake as measured by food frequency questionnaire and diet history)	Cross-sectional (Study 1) and Cohort (study 2)	Study 1 = 1 year and Study 2 = 4 years	Type II Diabetics aged 40-69 years	Study 1	520	n/a	There was no significant association ($p>0.05$) in either study between vitamin C and serum levels of HDL, LDL or triglycerides.
						Study 2	422	n/a	
Nam *et al.* (2003)	n/a	Clinical – non-fatal ischaemic heart disease (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Retrospective case-control	1 year	Persons	Persons with MI or coronary artery disease	108	n/a	- Vitamin C intake was significantly ($p<0.05$) associated with non-fatal ischaemic heart disease incidence. - The OR between the lowest (<141.8 mg/day) and highest (≥220.2 mg/day) tertiles of vitamin C intake was 0.34.
						Aged-matched controls	142	n/a	
Okamoto (2002)	n/a	Biomarkers of CHD – serum lipids (compared with dietary vitamin C intake as measured by food frequency questionnaire)	Cross-sectional	2 months	Elderly persons (mean age of 65 years)	Total cohort	680	n/a	- Adjusted vitamin C intake had a significant ($p<0.01$) inverse association with serum LDL and apolipoprotein B. - Adjusted vitamin C intake had a significant positive association with serum HDL ($p<0.05$) and apolipoprotein A1 ($p<0.01$).

Osganian *et al.* (2003a)	n/a	Clinical – non-fatal MI and fatal CHD (compared to dietary and supplemental vitamin C intake as assessed by food frequency questionnaire)	Cohort	16 years	85118 females aged 30-55 years	CHD cases	1356	n/a	- Adjusted total vitamin C intake had a significant ($p<0.001$) inverse association with CHD risk. - The RR between the lowest (70 mg/day) and highest (704 mg/day) quintiles of vitamin C intake =0.7. - Vitamin C supplement use >400 mg/day or >2 years was associated with a reduced CHD risk compared to no use (RR = 0.72).
Rimm *et al.* (1993)	n/a	Clinical – fatal and non-fatal CHD events (compared to supplemental + dietary vitamin C intake as measured by food frequency questionnaire)	Cohort	4 years	39910 males aged 40-75 years	CHD cases	607	n/a	Neither dietary nor supplemental vitamin C intake was not significantly associated with CHD events ($p>0.05$).
Sahyoun *et al.* (1996)	n/a	Clinical – mortality from heart disease (compared to dietary and supplemental vitamin C intake as measured by a 3-day food record)	Case-control	12 years	747 persons aged 60-101 years	Mortality from heart disease	725	n/a	- Adjusted total vitamin C intake had an inverse association with mortality from heart disease, however this result was not significant ($p>0.05$). - The RR between the lowest and highest vitamin C intakes was 0.38.

Todd *et al.* (1995)	n/a	Clinical – CHD (compared to dietary vitamin C intake as measured by a food frequency questionnaire)	Cohort	2 years	10359 persons aged 40-59 years	Cases of diagnosed CHD	625	n/a	- Adjusted total vitamin C intake had a significantly ($p<0.01$) inverse association with CHD in males. - There was a significant ($p<0.01$) positive association between total vitamin C intake and CHD in females.
						Cases of undiagnosed CHD	1497	n/a	
						Age and gender matched controls	7618	n/a	
Tofler *et al.* (2000)	Double - blinded	Biomarkers of CHD – serum lipids, platelet adhesion, tissue plasminogen activator antigen, plasminogen activator inhibitor, fibrinogen, plasma viscosity, and non-Willebrand factor.	Randomised controlled crossover study	6 weeks for each intake with a placebo wash out period of 4 weeks	Healthy males aged 30-65 years	Vitamin C supplement intake	18	2 g/day	- There was a significant decrease in total cholesterol ($p<0.01$), and a significant increase in HDL ($p<0.05$) with vitamin C intake - There was no significant ($p>0.05$) association between vitamin C intake and the other biomarkers.
						Placebo intake	18	-	

Table A5-2: Identified Study on Vitamin C and CHD (Meta-Analysis)

Study	Blinding	Study Endpoint Type	Study Design		Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Knekt *et al.* (2004)	n/a	Clinical – incidence of all major CHD events and CHD mortality (compared to vitamin C intake as measured either by a food frequency questionnaire or by a diet history, and 4 studies also assessed supplemental vitamin C intake).	Meta-analysis of 9 cohort studies	Barefoot *et al.* (1995)	11 years	1824 persons	Female CHD cases	37	n/a	- Adjusted dietary vitamin C intake was not significantly ($p>0.05$) related to CHD incidence. The RR between lowest (45 mg/day) and highest (152 mg/day) quintiles of intake was 1.23. - Supplemental vitamin C intake up to 700mg/day significantly reduced CHD incidence compared to no intake (RR = 0.87, $p<0.02$). - There was no significant impact of vitamin C supplement intake on CHD mortality. - There was no significant ($p>0.05$) heterogeneity between the vitamin C results of the 9 cohorts.
							Male CHD cases	82	n/a	
				Knekt *et al.* (1994)	6 years	5133 persons aged 30-69 years	Female CHD deaths	47	n/a	
							Male CHD deaths	148	n/a	
				Kritchevsky *et al.* (1995)	11 years	11307 persons	Female CHD cases	210	n/a	
							Male CHD cases	416	n/a	
				Kushi *et al.* (1996a)	6 years	34486 post-menopausal females	CHD deaths	242	n/a	
				MONICA investigators (1988)	6 years	9364 persons	Female CHD cases	22	n/a	
							Male CHD cases	162	n/a	
				Pietnen *et al.* (1996)	8 years	4739 males	CHD cases	413	n/a	
				Rimm *et al.* (1993)	4 years	39910 males aged 40-75 years	CHD cases	607	n/a	
				Stampfer *et al.* (1993) part 1	6 years	48639 females	CHD cases	375	n/a	
				Stampfer *et al.* (1993) part 2	6 years	21450 females	CHD cases	412	n/a	

Table A5-3: Identified Studies on Vitamin C and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject Group Number	Dose	Results
Bandera *et al.* (1997)	Clinical – lung cancer (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	7 years	32689 males	Males with lung cancer	395	n/a	- There was a significant ($p<0.01$) inverse association and vitamin C intake and lung cancer in males. - Vitamin C intake had no association ($p>0.05$) with lung cancer incidence in females.
				25279 females	Females with lung cancer	130	n/a	
Bohlke *et al.* (1999)	Clinical – breast cancer (compared to dietary vitamin C intake measured by food frequency questionnaire)	Case-control	3 years	Females (mean age = 56 years)	Breast cancer cases	820	n/a	- There was no significant ($p>0.05$) association between vitamin C intake and breast cancer for post-menopausal women. - There was an inverse but non-significant ($p<0.05$) association between vitamin C intake and breast cancer for pre-menopausal women. - The OR between the lowest (<143 mg/day) and highest (>343 mg/day) intake of vitamin C by pre-menopausal women was 0.45.
					Healthy controls	1548	n/a	
Bueno de Mesquita *et al.* (1991)	Clinical – pancreatic cancer (compared to dietary vitamin C as measured by food frequency questionnaire)	Retrospective case-control	4 years	Persons aged 35-79 years	Cases of pancreatic cancer	164	n/a	- There was a significant ($p<0.05$) inverse association between adjusted vitamin C intake and pancreatic cancer incidence in women but not men. - The OR between the lowest and highest quintiles of vitamin C intake was 0.75
					Age and gender matched controls	480	n/a	

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject Group Number	Dose	Results
Daviglus *et al.* (1996)	Clinical – cases of prostate cancer (compared to dietary vitamin C intake as measured by diet history)	Cohort	30 years	2107 Males aged 40-55 years	Cases of prostate cancer	132	n/a	- There was no significant ($p>0.05$) association between vitamin C intake and the risk of prostate cancer. - Relative risk (RR) between the lowest ($\leq$74 mg/day) and highest (>121 mg/day) intake of vitamin C was 1.27.
Fontham *et al.* (1988)	Clinical – lung cancer (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Case-control	3 years	Persons	Cases of lung cancer	1253	n/a	- There was a significant ($p<0.001$) inverse association between adjusted vitamin C intake and lung cancer incidence. - The OR between lowest and highest tertile of vitamin C intake = 0.67.
					Controls without history of cancer	1274	n/a	
Freudenheim *et al.* (1990)	Clinical – rectal cancer (compared to dietary vitamin C intake as measured by diet history)	Case-control	8 years	Persons aged $\geq$ 40 years	Cases of rectal cancer	145	n/a	There was an inverse association between vitamin C intake and rectal cancer incidence, however this result was not significant ($p>0.05$).
					Aged and gender matched controls	277	n/a	
Ghadirian *et al.* (1991)	Clinical – pancreatic cancer (compared to vitamin C intake as measured by food frequency questionnaire)	Case-control	4 years	Persons	Cases of pancreatic cancer	179	n/a	There was an inverse association between vitamin C intake and pancreatic cancer, however this result was not significant.
					Age and gender matched controls	179	n/a	

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject Group Number	Dose	Results
Howe *et al.* (1990)	Clinical – breast cancer (compared to vitamin C intake as measured by food frequency questionnaire)	Pooled results of 12 case-control studies	1-5 years	Post-menopausal females	Cases of breast cancer	4427	n/a	There was a significant ($p<0.05$) inverse association between vitamin C intake and breast cancer for post-menopausal but not pre-menopausal women. The RR between the lowest (59 mg/day) and highest (305 mg./day) quintile of intake = 0.82.
					Controls	6095	n/a	
Howe *et al.* (1992)	Clinical – pancreatic cancer (compared to dietary vitamin C intake as measured by diet history)	Case-control (in five different international locations)	2 years	Persons aged 28-87 years	Cases of pancreatic cancer	802	n/a	- There was a significant ($p<0.001$) inverse association between vitamin C intake and pancreatic cancer. - The RR between lowest ($\leq$72 mg/day) and highest ($\geq$195 mg/day) quintile of intake = 0.41.
					Controls without a history of cancer	1669	n/a	
Knekt *et al.* (1991)	Clinical – lung cancer (compared to dietary vitamin C intake as measured by a diet history)	Cohort	20 years	4538 males aged 20-69 years	Cases of lung cancer	117	n/a	- There was a significant ($p<0.01$) inverse association between vitamin C intake and lung cancer. - The RR between highest and lowest tertile of intake = 0.3.

Kristal *et al.* (1999)	Clinical – prostate cancer (compared to vitamin C supplement use determined by a food frequency and supplement questionnaire)	Retrospective case-control	2 years prior to baseline	667 males – prostate cancer cases, aged 40-64 years	No supplement use	62.3% of cases	n/a	- There was an inverse but insignificant ($p>0.05$) association between vitamin C supplement intake and prostate cancer incidence. - The adjusted OR between highest and lowest categories of intake was 0.77.
					<1/ week	6.2% of cases	n/a	
					1-6/week	10.6% of cases	n/a	
					≥7/week	20.9% of cases	n/a	
				666 healthy male controls, aged 40-64 years	No supplement use	58.7 of cases	n/a	
					<1/ week	7.7 of cases	n/a	
					1-6/week	11.7 of cases	n/a	
					≥7/week	21.9 of cases	n/a	
Kushi *et al.* (1996a)	Clinical – breast cancer (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	6 years	34387 post-menopausal women aged 55-69 years	Case of breast cancer	879	n/a	There was no significant ($p>0.05$) inverse association between either dietary or supplemental vitamin C intake and breast cancer.
La Vecchia *et al.* (1997)	Clinical – histologically confirmed colorectal cancer (compared to dietary vitamin C as measured by food frequency questionnaire)	Case-control	4 years	Persons aged 23-74 years	Cases of colorectal cancer	1953	n/a	- There was a significant ($p<0.01$) inverse association between vitamin C intake and colorectal cancer. - The OR between highest and lowest quintile of intake = 0.73.
					Healthy controls (no history of cancer)	4154	n/a	

Levi *et al.* (2000)	Clinical – histologically confirmed colorectal cancer (compared to dietary vitamin C intake as measured by a food frequency questionnaire)	Case-control	5 years	Persons aged 27-74 years	Cases of colorectal cancer	223	n/a	- Vitamin C intake was inversely associated with the risk of colorectal cancer ($p<0.01$). - The OR between the lowest ($\leq$65 mg/day) and highest ($\geq$186 mg/day) tertile of intake was 0.45.
					Controls without diet-related illness	491	n/a	
Negri *et al.* (1996)	Clinical – breast cancer (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Case-control	3 years	Females aged 23-74 years	Cases of histologically confirmed breast cancer	2569	n/a	There was no significant ($p>0.05$) difference in vitamin C intake between cases and controls.
					Controls with no history of cancer	2588	n/a	
Ocke *et al.* (1997)	Clinical – lung cancer (compared to dietary and supplemental vitamin C intake as measured by diet history)	Cohort	19 years	561 males	Cases of lung cancer	54	n/a	There was no significant ($p>0.05$) association between vitamin C intake and the risk of lung cancer.
Satia-Abouta *et al.* (2003)	Clinical – colon cancer (compared to dietary and supplement vitamin C intake as measured by food frequency questionnaire)	Retrospective case-control	1 year	Persons aged 40-80 years	Cases of histologically confirmed colon cancer	613	n/a	- Adjusted total vitamin C intake (including supplements) had a significant ($p<0.05$) inverse association with the incidence of colon cancer. - The OR between the lowest (59 mg/day) and highest (644 mg/day) vitamin C intakes was 0.5.
					Aged matched controls	996	n/a	

Shibata *et al.* (1992)	Clinical – cancer incidence (compared to supplemental and dietary vitamin C intake as measured by food frequency questionnaire)	Cohort	8 years	11580 persons	Cases of cancer	1335	n/a	- Adjusted dietary vitamin C intake had no significant ($p<0.05$) association with the incidence of cancer. - There was a significant ($p<0.05$) inverse association between supplemental vitamin C intake and the risk of bladder cancer in men, and breast cancer in women.
Stefani *et al.* (1999)	Clinical – lung cancer (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Case-control	4 years	Persons aged 30-89 years	Cases of lung cancer	541	n/a	Adjusted total vitamin C intake had no significant ($p>0.05$) association with the risk of lung cancer.
					Controls	540	n/a	
Verhoeven *et al.* (1997)	Clinical – breast cancer (compared to supplemental and dietary vitamin C intake as measured by food frequency questionnaire)	Cohort	4.3 years	62573 females aged 55-69 years	Cases of breast cancer	650	n/a	There was no significant ($p>0.05$) association between vitamin C intakes and the risk of breast cancer.
Voorrips *et al.* (2000)	Clinical – lung cancer (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	6.3 years	58279 males aged 55-69 years	Cases of lung cancer	939	n/a	- Dietary vitamin C intake was inversely associated with the incidence of lung cancer ($p<0.05$). - The RR between the lowest (51 mg/day) and highest (138 mg/day) dietary vitamin C quintiles was 0.77. - Supplemental vitamin C intake was not significantly ($p>0.05$) associated with lung cancer incidence.

Wassertheil-Smoller *et al.* (1981)	Clinical – cervial cancer identified by pap smear (compared to supplemental and dietary vitamin C intake as measured by 3-day food recall)	Case-control	Single timepoint	Females aged 15-75 years	Cases of cervical cancer	87	n/a	Vitamin C intake had a significant ($p<0.05$) inverse association with the incidence of cervical cancer.
					Age matched controls	82	n/a	
Yong *et al.* (1997)	Clinical – lung cancer (compared to dietary and supplemental vitamin C intake as measured by a 24-hour recall)	Cohort	19 years	3968 males and 6100 females aged 25-74 years	Cases of lung cancer	248	n/a	- Dietary vitamin C intake was inversely associated with the incidence of lung cancer ($p<0.01$). - The RR between the lowest (<23 mg/day) and highest (>113 mg/day) dietary vitamin C quintiles was 0.66.
Zatonski *et al.* (1991)	Clinical – pancreatic cancer (compared to dietary vitamin C intake as measured by diet history)	Case-control	3 years	Persons (mean age = 60 years)	Cases of pancreatic cancer	110	n/a	- Vitamin C intake was inversely associated with the risk of pancreatic cancer ($p<0.01$). - The RR between the lowest ($\leq$83 mg/day) and highest ($\geq$135 mg/day) quartile of vitamin C intakes was 0.37.
					Age matched controls	195	n/a	
Zeegers *et al.* (2001)	Clinical – bladder cancer (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Case-control	6.3 years	120852 persons aged 55-69 years	Cases of bladder cancer	569	n/a	- Adjusted total vitamin C intake had an inverse association with the incidence of bladder cancer, however this result was not significant ($p>0.05$). - Supplemental vitamin C intake was not associated with bladder cancer, although the statistical significance of this result was not reported.
					Controls without history of cancer	3123	n/a	

Zhang *et al.* (1999)	Clinical – breast cancer (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	14 years	83234 females aged 30-55 years	Cases of breast cancer	2697	n/a	There was no significant ($p>0.05$) association between supplemental or dietary vitamin C intake and the risk of breast cancer.

Table A5-4: Identified Studies on Vitamin C and Bone and Osteoporosis

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Hall and Greendale (1998)	Biomarker of bone disorders – bone mineral density (BMD)	Cohort	1 year	45-64 post-menopausal females	Total cohort	775	- Each adjusted vitamin C intake of 100 mg/day increment = 0.017 g/cm^2 increase in neck and hip BMD ($p<0.005$). - The significant BMD increases were not observed with calcium intakes >500mg. - There was no significant association ($p>0.05$) between vitamin C intake and spine BMD.
Leville *et al.* (1997)	Biomarker of bone disorders – bone mineral density (BMD) (compared to supplemental and dietary vitamin C intake as measured by food frequency questionnaire)	Retrospective cross-sectional study	1 year	1892 females aged 55-80 years	Total study population		- There was no significant ($p>0.05$) association between vitamin C intake and BMD. - Women with supplement use $\geq$ 10 years had a significantly ($p<0.05$) higher BMD than those with use < 10 years.
Morton *et al.* (2001)	Biomarker of bone disorders – bone mineral density (BMD) (compared to supplemental vitamin C intake)	Cross-sectional	3 years	994 post-menopausal females	Daily users of vitamin C supplements	277	- Regular Vitamin C supplement users had significantly ($p<0.02$) higher neck and hip BMD compared to non-users. - Supplement use was not significantly associated with spine BMD ($p>0.05$). - There was a significant linear trend in vitamin C supplement use and ultradistal BMD ($p<0.04$), but not at other bone sites.
					Non-users of vitamin C supplements	717	

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Wang *et al.* (1997)	Biomarker of bone disorders – bone mineral density (BMD) (compared to supplemental and dietary vitamin C intake as measured by food frequency questionnaire)	Cross-sectional	1 year	Post-menopausal females aged 59-84 years	Total cohort	125	Vitamin C intake was positively associated with neck BMD ($p<0.05$), but not with spinal BMD.

Table A5-5: Identified Studies on Vitamin C and Other Health Outcomes

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Hankinson *et al.* (1992)	n/a	Clinical – incidence of cataract extraction (compared to dietary and supplemental vitamin C intake as measured by food frequency questionnaire)	Cohort	8 years	Females 45-67 years from 50828 cohort	Cases of cataract extraction	493	Supplement intake per day was not specified	- Dietary vitamin C was not associated with the risk of cataract extraction. - RR of cataracts was 0.5 for women using vitamin C supplements for more than 10 years ($p<0.05$), however this effect became insignificant ($p>0.05$) when the RR was adjusted for confounding factors.
Hemila *et al.* (2002)	n/a	Clinical – incidence of the common cold (compared to dietary vitamin C intake as measured by food frequency questionnaire)	Cohort (subset of the ATBC trial)	4 years	Male smokers aged 50-69 years	Placebo arm of study	4990	n/a	Dietary vitamin C had no association with incidence of the common cold.

Sasazuki *et al.* (2003)	Double-blinding	Biomarker of gastritis – serum pepsinogen and *H.pylori* (serum antibodies)	Pseudorandomised controlled trial	5 years	Males diagnosed with chronic gastritis	Supplement group 1	144	50 mg/day vitamin C	- In both groups, the *H.pylori* count significantly decreased over the study ($p<0.05$), however there was no difference between groups ($p>0.05$). - Serum pepsinogen status significantly decreased over the study period ($p<0.001$), however there was no significant difference between groups.
						Supplement group 2	161	500 mg/day vitamin C	

Appendix 6

Assessment of Health Benefit: Phosphorus

Forty articles on phosphorus were identified from the literature search of electronic databases, and their abstracts were further reviewed to ensure that the subject matter was relevant to this assessment. In assessing the subject matter, articles that assessed changes in serum phosphorus against health outcomes were included, as there is evidence showing that serum phosphorus is reflective of a change in dietary phosphorus intake (United States Institute of Medicine, 1997)

The available evidence was reduced to 16 articles. A detailed summary of these articles is provided in Tables A6-1 to A6-3 below.

Ten studies have looked into possible effects of high/supplemented phosphorus intakes (above the RDI) on bone health and/or osteoporosis. The majority (8) of these studies found no significant association between phosphorus intake and bone status, and some even reported a negative association between an increased phosphorus intake and bone mineral density (BMD). From this limited evidence, it would appear that increased phosphorus intakes either have no effect on bone health, or even may cause adverse health effects.

Four studies investigated phosphorus intakes in relation to cancer. Three of these studies indicated that increased phosphorus intakes were inversely associated with cancer risk. However, the small evidence base on cancer does not allow for the conclusive establishment of association between phosphorus and cancer. The results of these four studies also varied depending on the different types of cancers investigated.

Two studies, both conducted in the 1980s, investigated phosphorus intake and blood pressure. One study indicated an inverse association, while the other supported the null hypothesis.

Therefore, the evidence base on phosphorus provides only a tentative link to improved health outcomes. A large volume of contradictory evidence also exists, which confounds any association of phosphorus intake with improved health outcomes.

Phosphorus is Assigned an Evidence Level of 1

Table A6-1: Identified Studies on Phosphorus and Bone Metabolism

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dosage	Results
Bizik *et al.* (1996)	Clinical – parathyroid hormone levels, bone resorption markers (urinary deoxypyridinoline), urinary ammonia, urea and total N	Cohort	20 days	7 men aged 22-31 years old, average weight 70 kgs	Single group	7	Diet to day 10 with 800mg phosphorus, 1200mg calcium,, Days 10-20 with 1600mg/day dietary P.	High P intake was not found to promote bone resorption if the Ca:P ratio is <1:1.5
ChoonHie *et al.* (2004)	Clinical - Bone Mineral Density (BMD) as measured by dual energy x-ray absorptiometry.	Cross sectional	Single time point – collection of baseline data on bone health	Korean males of various age groups.	Elementary school children	80	n/a	Increased phosphorus intakes were positively related to BMD in all age groups.
					High school students	83	n/a	
					Adults 25 – 35 years old	87	n/a	
					Adults 60+ years old	98	n/a	
Goldsmith *et al.* (1976)	Clinical – bone density parameters.	Cross sectional	Not reported	Post-menopausal women with osteoporosis	Single group	7	Diet supplemented with phosphorus (inorganic phosphate)	- Bone forming surface decreased and bone resorbing surface increased in all patients. - Bone resorbing surface was highly correlated with total phosphorus intake.

Grimm *et al.* (2001)	Clinical – biochemical markers for bone status, bone-related hormones, markers of bone resorption and parameters of renal function (collectively: serum PTH, serum osteocalcin, creatine in urinary pyridinoline, creatine in pyridinoline deoxypyridinoline, urinary microalbumin) and digestive responses.	Crossover	14 weeks	Women aged 20-30 years old from a German university.	Control period Treatment period Control period	10	Diet with 1700mg P and 1500mg Ca/day (4 weeks) Diet with 3008mg P and 1995mg Ca/day (6 weeks) Diet – as for above (4 weeks	- There were no significant changes in bone-related hormones, markers of bone re-absorption or parameters of renal function. - Phosphorus supplementation caused intestinal distress, soft faeces or mild diarrhoea
Hoppe *et al.* (2000)	Clinical – whole body bone measurements	Cross-sectional	Single time point	10 year old healthy children from Denmark	Single group	105	n/a	- Bone area (size-adjusted) was negatively associated with phosphorus intakes. - Mean intake of phosphorus was 3.3g, which is above the RDI for this age group (1250mg/day).
Mendez *et al.* (2002)	Clinical – bone density measures.	Cross sectional	Single time point	Women aged 45 – 63 years old in northern Mexico.	Single group.	45	n/a	Dietary intake phosphorus had no significant ($p<0.05$) relation to bone density.
Metz *et al.* (1993)	Clinical – radial bone measurements	Cross-sectional	Not reported	24-28 year old Caucasian women	Single group	38	n/a	Phosphorus intake was negatively associated with radial bone measurements ($p<0.05$).
SeIn *et al.* (2003)	Clinical - osteoporosis	Case-control	Not reported	Korean premenopausal women	Case - osteoporotic Control – non-osteoporotic	78 78	n/a n/a	Serum levels of phosphorus and calcium showed significant ($p<0.001$) negative correlations with lumbar spine bone mineral density.

Whybro *et al.* (1998)	Biomarkers of bone metabolism – bone turnover and calcium homeostasis markers.	Study 1 - Randomised controlled cross-over trial.	1 week	Healthy volunteers 19-32 years old.	Single group, standard diet with 800mg P/day	10	Supplemented with 1000mg elemental P	There was no significant change in serum phosphate, osteocalcin or intact parathryin.
		Study 2 Randomised controlled trial.	1 week	Men aged 19-38 years	Diet only	12	-	There was no significant change in serum phosphate, intact parathyrin or urinary deoxypyridinoline.
					Diet+ low P	12	1000mg/day elemental P	
					Diet + moderate P	12	1500mg/day elemental P	
					Diet + high P	12	2000mg/day elemental P	

Table A6-2: Identified Studies on Phosphorus and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Chan *et al.* (2000)	Clinical – prostate cancer cases (compared to dietary phosphorus intake as measured by a food-use questionnaire)	Cohort (initially surveyed for another reason)	8 years	Finish male smokers, (originally recruited in a randomised trial study)	Cases – prostate cancer	184	There was an inverse association between phosphorus intakes and cancer risk independent of calcium intakes.
Launoy *et al.* (1998)	Clinical – squamous cell cancer of the oesophagus	Case-control	3 years	Males in 3 regions of France.	Cases	208	After adjustment of results for drinking and smoking, phosphorus intakes were found to have an independent protective factor against cancer incidence.
					Controls	399	
Negri *et al.* (2000)	Clinical – oral cancers	Case-control	5.5 years	Patients admitted to major teaching and general hospitals in Italy and Switzerland.	Histologically confirmed oral cancer cases	754	- There was an inverse association between phosphorus intake and pharyngeal cancer risk. The adjusted OR for this relationship was 0.88.
					Controls with no history of cancer	1775	

SooWon *et al.* (2003)	Clinical – stomach cancer	Case-control	Not reported	People in the Korean Republic	Case patients recently diagnosed with stomach cancer	102	- Phosphorus intake was significantly ($p>0.05$) higher amongst cases compared to controls.
					Controls people without gastrointestinal dieases	105	

Table A6-3: Identified Studies on Phosphorus and Cardiovascular Disease

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Gruchow *et al.* (1985)	Clinical - systolic blood pressure	Cross sectional – (subset of Health and Nutrition Examination Survey	n/a	Persons	n/a	n/a	Increased phosphorus intakes were positively associated with systolic blood pressure.
Joffres *et al.* (1987)	Clinical – blood pressure	Cross-sectional	n/a	Men with no history of cardiovascular disease or treated hypertension	Single group assessed by 24 hour recall	615	Phosphorus intakes were inversely associated with blood pressure.

Appendix 7

Assessment of Health Benefit: Vitamin B_{12}

From the 111 vitamin B_{12} articles identified, a review of their abstracts refined the final number of articles to 28. This process was used to ensure that the subject matter, not just the title, was relevant to this assessment. In assessing the subject matter of abstracts, articles that assessed changes in serum vitamin B_{12} against health outcomes were included, as there is evidence showing that serum vitamin B_{12} is reflective of a change in dietary vitamin B_{12} intake (United States Institute of Medicine, 1998). The details of the 28 articles are provided in Tables A7-1 to A7-3 below.

Of the 28 identified articles, 18 were related to coronary heart disease outcomes, either as clinical endpoints or as changes in serum homocysteine levels. The majority of the 18 articles (13) showed no significant association between CHD endpoints and vitamin B_{12} intakes beyond the RDI. There were only 2 articles in that showed a significant inverse association.

Seven articles were identified that examined the association between vitamin B_{12} intake above the RDI and cancer endpoints. The majority of these articles (5) also indicated no significant association between cancer endpoints and vitamin B_{12} intakes.

The three remaining articles assessed bone metabolism and gastrointestinal endpoints. The two studies on bone metabolism showed no significant association between vitamin B_{12} intakes above the RDI and bone disorders. The sole gastrointestinal article also showed no significant association between vitamin B_{12} intakes and gastrointestinal infections. With the small numbers of articles on bone metabolism and gastrointestinal functioning, these lines of research can be considered as new and emerging.

For CHD and cancer, the evidence base provides strong support for the null hypothesis. Therefore, on the basis of available evidence, increased intakes of vitamin B_{12} are considered to have no appreciative health benefit.

Vitamin B_{12} is assigned an evidence level of 0

Table A7-1: Identified Studies on Vitamin B_{12} and Coronary Heart Disease

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Appel *et al.* (2000)	Double-blinded	Biomarker of CHD – serum tHcy (compared to serum vitamin B_{12} levels)	Randomised controlled trial	3 week adaptation, 8 week study period	Persons aged $\geq$ 22 years	Control diet	39	n/a	An increase in vitamin B_{12} intake as a result of the intervention diets was not significantly ($p>0.05$) associated with tHcy.
						Diet = control with high intake of fruit and vegetables	41	n/a	
						Diet = low fat, high in fruit, vegetables and dairy	38	n/a	
de Bree *et al.* (2001)	n/a	Biomarker of CHD – serum homocysteine (tHcy) (compared to dietary and supplemental vitamin B_{12} intake as measured by food frequency questionnaire)	Cross-sectional	3 years	Persons aged 20-65 years	Males	1275	n/a	- There was a significant ($p<0.001$) inverse association between vitamin B_{12} intakes of both males and females and serum tHcy levels. - However, this result became statistically non-significant ($p>0.05$) when adjusted for confounding variables.
						Females	1160	n/a	
de Bree *et al.* (2003)	n/a	Clinical – CHD mortality (compared to serum vitamin B_{12} levels)	Case-control	10.3 years	Persons aged 20-59 years	Deaths from CHD	102	n/a	There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and the risk of CHD mortality.
						Controls	630	n/a	

He *et al.* (2004)	n/a	Clinical – incidence of ischaemic and haemorrhagic stroke (compared to dietary B_{12} intake as measured by food frequency questionnaire)	Cohort	14 years	43732 males aged 40-75 years	Cases of ischaemic stroke	455	n/a	- There was a significant (p=0.05) inverse association between vitamin B_{12} intakes and the risk of ischaemic stroke. - The RR between the lowest (5 µg/day) and highest (29 µg/day) intake of vitamin B_{12} was 0.73 for ischaemic stroke. - There was no significant (p>0.05) association between vitamin B_{12} intakes and the risk of haemorrhagic stroke.
						Cases of haemorrhagic stroke	125	n/a	
Huerta *et al.* (2004)	n/a	Biomarker of CHD – serum tHcy (compared to dietary vitamin B_{12} intake as measured by food frequency questionnaire)	Cross-sectional	Not reported	Elderly persons	Total cohort	140	n/a	There was no significant association between serum tHcy and vitamin B_{12} intake.
Hung *et al.* (2003)	n/a	Clinical – fatal CHD and CVD (compared to serum vitamin B_{12} levels)	Cohort	29 years	Persons aged 20-90 years	Male deaths from CHD or CVD	213	n/a	There was no significant (p>0.05) association between vitamin B_{12} levels and CHD/CVD mortality.
						Female deaths from CHD or CVD	159	n/a	
Jacques and Chylack, Jr. (1991)	n/a	Biomarker of CHD – serum tHcy (compared to dietary vitamin B_{12} intake as measured by food frequency questionnaire, and to serum vitamin B_{12} levels)	Cross-sectional	20 years	Persons aged 30-59 years	Total cohort	5135	n/a	- There was a significant (p<0.001) inverse association between adjusted plasma vitamin B_{12} and tHcy. - Adjusted dietary vitamin B_{12} intake was not significantly (p>0.05) associated with serum tHcy.
Kelly *et al.* (2003)	n/a	Clinical – incidence of stroke (compared to serum vitamin B_{12} levels).	Case-control	2 years	Persons (mean age = 68 years)	Cases of stroke	180	n/a	There was no significant (p>0.05) association between serum vitamin B_{12} levels and the risk of stroke.
						Age matched controls	147	n/a	

Leowattana *et al.* (2000)	n/a	Clinical – incidence of CAD (compared to serum vitamin B_{12} levels)	Cross-sectional	1 year	Persons (mean age = 58-60 years)	Cases of CAD	178	n/a	There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and CAD risk.
						Age matched healthy controls	178	n/a	
Medrano *et al.* (2000)	n/a	Clinical – mortality from CVD (compared to dietary vitamin B_{12} intake as measured by a 7-day food record)	Cohort	4 years	21155 persons	Cases of CVD deaths	Not reported	n/a	There was no significant ($p>0.05$) association between vitamin B_{12} intake and the risk of mortality from CVD.
Mennen *et al.* (2002)	n/a	Biomarker of CHD – serum tHcy (compared to dietary vitamin B_{12} intake as measured by 24-hour diet record, and serum vitamin B_{12} levels)	Cross-sectional	8 years	Persons aged 35-60 years	Total cohort	2070	n/a	- Adjusted serum vitamin B_{12} was not significantly ($p>0.05$) associated with tHcy. - Dietary vitamin B_{12} intake was not significantly ($p>0.05$) associated with tHcy.
Merchant *et al.* (2003)	n/a	Clinical – peripheral arterial disease (compared to dietary vitamin B_{12} intake as measured by food frequency questionnaire)	Cohort	12 years	46036 males aged 40-75 years	Cases of peripheral arterial disease	308	n/a	- There was no significant ($p>0.05$) association between vitamin B_{12} intake and the risk of peripheral arterial disease. - The RR of peripheral arterial disease from the lowest (5 μg/day) to the highest (22 μg/day) intake of vitamin B_{12} was 0.74.
Ortega *et al.* (2002)	n/a	Biomarker of CHD – serum tHcy (compared to compared to dietary vitamin B_{12} intake as measured by 7-day food record)	Cross-sectional	Not reported	Persons aged >65 years	Total cohort	130	n/a	There was no significant ($p<0.05$) difference in tHcy between subjects with lower than recommended vitamin B_{12} intakes and those with intakes above this levels.
Pancharuniti *et al.* (1994)	n/a	Clinical – early onset coronary artery disease (compared to serum vitamin B_{12} levels)	Case-control	3 years	Males aged 30-50 years	Cases of coronary artery disease	101	n/a	There was no significant ($p>0.05$) difference in the mean serum vitamin B_{12} levels between cases and controls.
						Age matched controls	108	n/a	

Shimakawa *et al.* (1997)	n/a	Biomarker of CHD – serum tHcy (compared to dietary and supplemental vitamin B_{12} intake as measured by food frequency questionnaire)	Case-control	3 years	Persons aged 45-64 years	Cases of carotid artery atherosclerosis	322	n/a	There was a significant ($p<0.01$) inverse association between vitamin B12 intake and serum tHcy.
						Controls without atherosclerosis	318	n/a	
Siri *et al.* (1998)	n/a	Clinical – coronary atherosclerosis (compared to serum vitamin B_{12} levels)	Case-control	2 years	Persons aged 25-65 years	Cases of atherosclerosis	131	n/a	There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and the risk of coronary atherosclerosis.
						Coronary referent controls	88	n/a	
Vrentzos *et al.* (2004)	n/a	Clinical – IHD (compared to dietary vitamin B_{12} intake as measured by a 3-day food record, and serum vitamin B_{12} levels)	Case-control	2 years	Persons aged 33-77 years	Cases of IHD	152	n/a	- Cases had significantly higher intakes of vitamin B_{12} ($p<0.05$), and significantly higher serum vitamin B_{12} levels ($p<0.01$) than controls. - There was, however, no significant ($p>0.05$) linear trend between vitamin B_{12} intakes, serum vitamin B_{12} levels, and the risk of IHD.
						Age and gender matched controls	152	n/a	
Waldmann *et al.* (2004)	n/a	Biomarker of CHD – serum tHcy (compared to serum vitamin B_{12} levels)	Cross-sectional	Not treported	Vegans aged 20-82 years	Total cohort	131	n/a	There was a significant ($p<0.001$) inverse association between serum vitamin B_{12} and tHcy levels when controlled for veganism.
Wasilewska *et al.* (2003)	n/a	Clinical – cardiac problems requiring surgery (compared to serum vitamin B_{12} levels)	Case-control	Not reported	Persons aged 24-80 years	Cases of cardiac surgery	55	n/a	There was no significant ($p>0.05$) difference in serum vitamin B_{12} levels between cases and controls
						Health controls	38	n/a	

Table A7-2: Identified Studies on Vitamin B_{12} and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject Group Number	Results
Alberg *et al.* (2000)	Clinical – cervical cancer (compared to serum vitamin B_{12} levels)	Case-control	15 years	Females aged >18 years	Cases of cervical cancer	39	There was no significant ($p>0.05$) association between vitamin B_{12} intake and the risk from cervical cancer.
					Age matched controls	39	
Goodman *et al.* (2000)	Biomarkers of cervical cancer – squamous intraepithelial lesions (SIL) and atypical squamous cells (compared to serum vitamin B_{12} levels)	Case-control	4 years	Females	Cases of SIL	185	There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and the risk of developing SIL or atypical squamous cell pap smear results.
					Cases of atypical squamous cels	147	
					Controls with normal pap smear	191	
Harnack *et al.* (2002)	Clinical – colorectal cancer (compared to vitamin B_{12} intake as measured by food frequency questionnaire)	Cohort	13 years	Females aged 55-69 years	Cases of colonic cancer	598	There was no significant ($p>0.05$) association between vitamin B_{12} intakes and the risk of colorectal cancer.
					Cases of rectal cancer	123	
Hartman *et al.* (2001)	Clinical – lung cancer (compared to serum vitamin B_{12} levels)	Case-control (subset of the ATBC trial)	8 years	Male smokers aged 50-69 years	Cases of lung cancer	300	- There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and the risk of lung cancer. - The OR between the lowest ($\leq$345 pg/mL) and highest (>580 pg/mL) serum vitamin B_{12} levels and lung cancer risk was 1.41
					Controls	300	
Hernandez *et al.* (2003)	Biomarkers of cervical cancer – premalignant cervical lesions (compared to dietary and supplemental vitamin B_{12} intake as measured by food frequency questionnaire)	Case-control	4 years	Females aged >18 years	Cases with premalignant lesions	214	- There was a significant ($p<0.05$) inverse association between supplemental vitamin B_{12} intake and the risk of developing premalignant lesions. - Dietary and total vitamin B_{12} intake was not significantly ($p>0.05$) associated with the risk of developing cervical cancer.
					Controls	271	

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject Group Number	Results
Vlajinac *et al.* (1997)	Clinical – prostate cancer (compared to dietary and supplemental vitamin B_{12} intake as measured by food frequency questionnaire)	Case-control	4 years	Males (mean age = 71 years)	Cases of histologically confirmed prostate cancer	101	- There was a significant ($p<0.05$) positive association between vitamin B_{12} intake and the risk of prostate cancer. - The OR between the lowest and highest intakes was 2.02.
					Age matched controls	202	
Zhang *et al.* (2003)	Clinical – breast cancer (compared to serum vitamin B_{12} levels)	Case-control	14 years	Females aged 30-55 years	Cases of breast cancer	735	There was no significant ($p>0.05$) association between serum vitamin B_{12} levels and the risk of breast cancer.
					Age matched controls	735	

Table A7-3: Identified Studies on Vitamin B_{12} and Other Health Outcomes

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Cagnacci *et al.* (2003)	Clinical – osteoporosis and osteopenia (compared to serum vitamin B_{12})	Case-control	1 year	Post-menopausal females (mean age = 53 years)	Cases of osteoporosis	28	There was no significant ($p>0.05$) difference in BMD between cases and controls when stratified on serum vitamin B_{12} levels.
					Cases of osteopenia	61	
					Healthy controls	72	
Shuval-Sudai *et al.* (2003)	Biomarker of gastrointestinal infection – *H.pylori* IgG antibodies (compared to serum vitamin B_{12} levels)	Cohort	Single timepoint	Persons	Subjects with seropositive result for *H.pylori* IgG antibodies	133	There was no significant ($p>0.05$) inverse association between serum vitamin B_{12} and *H.pylori* infection.

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Tucker *et al.* (2005)	Biomarker of bone disorders – BMD (compared to serum vitamin B_{12})	Cross-sectional	5 years	Persons aged 30-87 years	Total cohort	3532	- Hip BMD was significantly greater ($p<0.01$) with vitamin B_{12} levels >259 pM in males, and spine BMD at levels >185 pM in females. However, this significance was non-linear. - Spine BMD and hip BMD in males and females respectively were non-significantly associated with vitamin B_{12} levels ($p>0.05$).

Appendix 8

Assessment of Health Benefit: Thiamin, Niacin, Biotin, Pantothenic acid, Copper, Manganese, and Molybdenum

Following a review of the abstracts on for thiamin, niacin, biotin, pantothenic acid, copper, manganese, and molybdenum, the number of articles identified from the PubMed and NHMRC sources was reduced to a small number for each vitamin and mineral:

Thaimin: 7 articles
Niacin: 2 articles
Biotin: 0 articles
Pantothenic Acid: 0
Copper: 4 articles
Manganese: 1 article
Molybdenum: 1 article

The evidence on thiamin, niacin, biotin, pantothenic acid, copper, manganese, and molybdenum is contained in Tables A8-1 to A8-6.

For each of these vitamins and minerals, the evidence base is too small to conclusively establish a relationship between their increased intake and the delivery of a health benefit. It has therefore been determined that there is an absence of evidence on the potential for thiamin, niacin, biotin, pantothenic acid, copper, manganese, molybdenum and phosphorus to deliver a health benefit.

Thiamin, Niacin, Biotin, Pantothenic Acid, Copper, Manganese and Molybdenum are assigned an Evidence Level of "A"

Table A8-1: Identified Studies on the Thiamin and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
Bidoli *et al.* (2003)	Clinical - cancer of the larynx (compared to dietary thiamin intake as measured by food frequency questionnaire).	Case-control	8 years	Persons	Patients with incident cancer of larynx.	527	n/a	- Significant ($p<0.05$) inverse relations emerged between laryngeal cancer and thiamin intake - The OR between the lowest and highest thiamin intakes was 0.4.
					Patients with acute, non-neoplastic diseases	1297	n/a	
D'Avanzo *et al.* (1997)	Clinical – thyroid cancer	Case-control	6 years	Population of Northern Italy.	Histologically confirmed thyroid cancer cases.	399	n/a	There was no significant association between thiamin intake and the risk of thyroid cancer.
					Controls without cancer	617	n/a	
Hernandez *et al.* (2003)	Clinical – squamous intraepithelial lesions of the cervix (SIL) (compared to dietary and supplemental thiamin intake as measured by food intake survey).	Case-control	4 years	Multi-ethnic women identified from clinics in Oahu, Hawaii	High or low grade SIL	214	n/a	Thiamin from food displayed an inverse, dose-responsive association with high-grade SIL.
					Controls	271	n/a	
Marshall *et al.* (1992; HaengShi *et al*., 2001)	Clinical – oral cancer	Case-control	Not reported	Population of Western New York	Cases of oral cancer	290	n/a	Thiamin was associated with a decreased risk of oral cancer.
					Age and gender matched controls	290	n/a	

Negri *et al.* (1996)	Clinical – oral cancers (compared to dietary thiamin intake as measured by food frequency questionnaire).	Case-control	5.5 years	Patients admitted to major teaching and general hospitals in Italy and Switzerland.	Incident, histologically confirmed oral cancers	754	n/a	- There was an inverse association between the intake of dietary thiamin and the risk of oral cancer - The OR between the lowest and highest thiamin intakes was 0.82.
					Patients with no history of cancer admitted to hospitals with acute, non-neoplastic diseases.	1775	n/a	
Slattery *et al.* (1997)	Clinical – colon cancer (dietary thiamin intake as measured by an administered questionnaire).	Case-control	Not reported	Population of Northern California, Utah and the "Twin Cities" area of Minnesota.	Cases – colon cancer	1993	n/a	Thiamin intake was inversely associated with the risk of colon cancer.
					Controls	2410	n/a	

Table A8-2: Identified Studies on the Thiamin and Other Health Outcomes

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dose	Results
HaengShi *et al.* (2001)	Serum biomarkers of bone metabolism – fasting serum osteocalcin, calcium, phosphorous, estradiol, free testosterone (compared to thiamin intake as measured by a 24-hour recall over 3 days).	Cross-sectional	n/a	Postmenopausal women aged 50-77 years.	n/a	56	n/a	There was a statistically significant ($p>0.05$) association between serum calcium and high intakes of thiamin.

Table A8-3: Identified Studies on the Health Outcomes of Increased Niacin Intakes

Study		Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dosage	Results
Sasaki and Yanagibori (2001)	Biomarker of bone health – BMD (compared to – niacin intake as measured by diet history)	Cross-sectional	2 years	Japanese women 29-60 years	pre menopausal	243	n/a	- Increased niacin intakes were significantly ($p<0.05$) and positively associated with BMD in premenopausal women. - There was no significant ($p>0.05$) association between niacin intake and BMD for postmenopausal women.
					post menopausal	137	n/a	
Morris *et al.* (2004)	Clinical – incidence of Alzheimer's disease (compared to niacin intake as measured by food frequency questionnaire).	Cohort	Average 3.9 years	6158 persons > 65 years	Cases of Alzheimer's disease	815	n/a	- Adjusted total niacin intake, including intake from food and supplements, was significantly ($p<0.05$) and inversely associated with the incidence of Alzheimer's disease. - Dietary niacin intake alone also had a significantly ($p<0.01$) inverse association with Alzheimer's disease.

Table A8-4: Identified Studies on the Health Outcomes of Increased Copper Intakes

Study	Blinding	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Dosage	Results
Cashman *et al.* (2001)	Double-blind	Biomarkers of bone metabolism – serum osteocalcin, urinary creatinine, urinary pyridinoline.	Placebo-controlled, crossover	Treatment over 4 weeks, with a 3-week washout period.	Healthy females	High Cu supp.	16	6 mg copper sulphate	There was no significant difference ($p>0.05$) between study groups on biomarkers
						Low Cu supp.	16	3 mg copper sulphate	
						Placebo	16	-	

Cunzhi *et al.* (2003)	n/a	Study 1: Clinical – cervical cancer and uterine myoma (compared to tissue copper levels)	Paired Comparison	Single timepoint	Females aged 30-65 years with cervical or uterine cancer	Cancerous tissue samples from subjects	70	n/a	- Copper levels were significantly ($p<0.05$) higher in cervical cancer tissue samples than non-lesion tissue samples. - There was no significant ($p>0.05$) difference in copper levels between uterine and non-lesion tissues.
						Non-lesion tissue samples from subjects	70	n/a	
		Study 2: Clinical – cervical cancer and uterine myoma (compared to serum copper levels	Case-control	Single timepoint	Females aged 30-65 years.	Cases of cervical cancer	100	n/a	- The serum copper levels of cervical cancer subjects were significantly ($p<0.001$) higher than those of healthy subjects. - There was no significant ($p>0.05$) difference in the serum copper levels of uterine cases and controls.
						Cases of uterine cancer	100	n/a	
						Healthy controls	100	n/a	
Jones *et al.* (1997)	Not reported	Biomarkers of CHD – serum cholesterol, serum lipoprotein (a), VLDL lag time, and LDL oxidation.	Placebo-controlled, crossover	Treatment over 4 weeks	Adult males with elevated cholesterol	Copper supplement	20	2 mg/day of Cu	Cu supplementation had no significant impact ($p>0.05$) on any of the study's biomarker parameters.
						Placebo	20	-	
Sennese *et al.* (2004)	n/a	Clinical – colorectal cancer (comparison with dietary copper intake as measured by food frequency questionnaire)	Case-control	5 years	Persons aged 30-79 years	Colorectal cases	171	n/a	- There was a significant ($p<0.01$) inverse association between copper intakes and the risk of colorectal cancer. - The OR between the lowest and highest quartiles of copper intake was 2.4.
						Healthy controls	309	n/a	

Table A8-5: Identified Study on Manganese and Cancer

Study	Study Endpoint Type	Study Design	Length of Study	Subjects	Subject Grouping	Subject number	Results
Cunzhi *et al.* (2003)	Study 1: Clinical – cervical cancer and uterine myoma (compared to tissue manganese levels)	Paired Comparison	Single timepoint	Females aged 30-65 years with cervical or uterine cancer	Cancerous tissue samples from subjects	70	- Manganese levels were significantly ($p<0.05$) lower in cervical cancer tissue samples than non-lesion tissue samples. - There was no significant ($p>0.05$) difference in manganese levels between uterine and non-lesion tissues.
					Non-lesion tissue samples from subjects	70	
	Study 2: Clinical – cervical cancer and uterine myoma (compared to serum manganese levels	Case-control	Single timepoint	Females aged 30-65 years.	Cases of cervical cancer	100	The serum manganese levels of both case groups were significantly ($p<0.001$) higher than those of healthy subjects.
					Cases of uterine cancer	100	
					Healthy controls	100	

Table A8-6: Identified Study on Molybdenum and Cancer

Study	Study Endpoint Type	Study Design	Study Duration	Subjects	Subject Grouping	Subject number	Results
Nakadaira *et al.* (1995)	Clinical – cancer mortality (compared with levels of molybdenum in soils of 19 agricultural based areas in Japan).	Prospective cohort	10 years	Japanese residence of 19 areas within the Niigata province	Cancer mortality	Not reported	- There was a significant ($p<0.05$) inverse correlation between molybdenum levels and female mortality from rectal cancer. - There was also a significant ($p<0.01$) positive correlation between molybdenum soil levels and female mortality from pancreatic cancer.

Attachment 6

Risk Assessment - Micronutrients[42]
Application A470– Formulated Beverages

[42] For the purpose of this report, the term 'micronutrients' is used for vitamins and minerals.

Summary and Conclusions

Risk Assessment – Micronutrients

A risk assessment has been conducted in relation to the addition of certain vitamins and minerals to formulated beverages at a level of 25 % of the recommended dietary intake (RDI) per 600 ml serve. These include: vitamin A, β-carotene, thiamin, riboflavin, niacin, folate, vitamin B_6, B_{12}, D, E, biotin, pantothenic acid, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorus, selenium and zinc. The applicant has requested vitamin C to be added at 100% of the RDI per 600 ml serve.

The results of the risk assessment are provided below and are summarised in **Table 1**.

Micronutrients without risk for the general population
For the following micronutrients, it is concluded that addition to formulated beverages at a level of 25% of the RDI per 600 ml (100% of RDI per 600 ml for vitamin C) would raise no public health and safety concerns for any sector of the population: β-carotene, thiamin, riboflavin, niacin, folate, vitamin B_6, B_{12}, C, D, E, pantothenic acid, calcium, magnesium, phosphorus and selenium.

Micronutrients with some risk for sensitive subpopulations
For the following micronutrients, it is concluded that while the general population is without risk, there may be a risk for certain sectors of the population:

Copper: Individuals with Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis may respond adversely to copper in formulated beverages at a level of 0.75 mg per 600 ml.

Iodine: Individuals with thyroid disorders or a long history of iodine deficiency may respond adversely to iodine in formulated beverages at a level of 37.5 μg per 600 ml.

Iron: Individuals who are homozygous for hereditary haemochromatosis are susceptible to iron overload, even at normal dietary iron intakes, and are generally advised to avoid iron-supplements and highly iron fortified foods. As the majority of individuals with this condition are not diagnosed until sufficient iron has accumulated to produce adverse effects, the addition of iron to formulated beverages at a level of 3 mg per 600 ml serve may be a concern to these individuals.

Micronutrients with some risk for specific age groups
For the following micronutrients, there are potential risks for specific age groups if they were permitted to be added to formulated beverages:

Vitamin A: The dietary modelling results suggest that young children consuming formulated beverages may have excess intakes of retinol for several years and therefore be at risk of hepatoxicity. For all other age groups and life-stages, there is no appreciable risk posed by excess intake of retinol. There are potential safety concerns for children up to the age of 3 years, and maybe up to 6 years, with the addition of retinol to formulated beverages at a level of 187.5 μg in a 600 ml serve.

Manganese: An upper level of intake (UL) could not be established because of limitations with the human data and considerable uncertainty with the animal toxicity studies. The available data suggests that the margin between the intake level producing adverse effects in humans and animals and the estimated intake from food is very small. Based on the severity of the potential adverse effect (neurotoxicity), additional oral exposure to manganese beyond the levels normally present in food and beverages could pose a public health and safety risk. Therefore, there are potential safety concerns with the addition of manganese to formulated beverages at a level of 1.25 mg in a 600 ml serve.

Zinc: Dietary modelling indicated that children up to 8 years of age, who are consumers of a diet high in zinc, are predicted to exceed the UL for zinc. For adolescents up to the age of 18 years, who are consumers of a diet high in zinc, the intake is predicted to be 80% of the UL of zinc. Chronic zinc toxicity is associated with symptoms of copper deficiency. These adverse effects include anaemia, neutropaenia and impaired immune response. Furthermore, the potential contribution from other sources (e.g. dietary supplements) has not been taken into consideration in the dietary intake assessment. The intakes of zinc may therefore be underestimated for children and adolescents up to the age of 18 years and, for this group, formulated beverages at a level of 3 mg per 600 ml serve pose a public health and safety risk.

Micronutrients with insufficient data to assess risk
For the following micronutrients there was insufficient data to characterise the potential risk:

Biotin and Chromium: Due to insufficient data on potential adverse effects and only limited food composition data it was not possible to establish an UL for biotin and chromium or to undertake a complete dietary intake assessment. In the absence of sufficient information, it is currently not possible to evaluate the safety of the addition of biotin and chromium to formulated beverages.

Molybdenum: An UL has been established based on reproductive effects in rats. While some food composition data are available for molybdenum, it is insufficient to undertake a complete dietary intake assessment at this present time. In the absence of sufficient information, it is not currently possible to evaluate the safety of the addition of molybdenum to formulated beverages.

Assessment of permitted forms
For pantothenic acid, biotin, chromium, manganese, molybdenum and selenium, currently there are no forms permitted in Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions. The requested permitted forms for pantothenic acid, copper and selenium have been included in evaluations of the toxicity of the micronutrients assessed, and are considered to be acceptable as permitted forms.

Table 1: Risk Assessment of High Micronutrient intake

	UL (adults)	Intake from total diet / Suppl	Adverse effect which is the basis for an UL	Vulnerable groups identified	Dietary Intake Assessment	Risk Characterisation	Proposed to be added to formulated beverage
Vitamin A, retinol form, μg/day	3000	Total diet	Teratogenicity, hepatoxicity	young children	up to 3 years exceed UL	Potential safety concerns for children up to 8 years	No
β-Carotene, food	N/A	diet	no safety concerns with β-carotene from the diet	-		No safety concerns	**Yes**
β-Carotene, supplements	No UL established	Suppl	Insufficient data to set a UL			No safety concerns	
Thiamin	N/A	-	No indication of adverse effects	-	Not needed	No safety concerns	**Yes**
Riboflavin	N/A		No indication of adverse effects	-	Not needed	No safety concerns	**Yes**
Niacin, nicotinic acid, mg/day	10	Suppl	Flushing	-	Intake below UL in all age groups, except 2-8 years	adverse effects for nicotinic acid not relevant for children	**Yes**
Niacin, nicotinamide, mg/day	900	Total diet	No adverse effects at UL	-	Intake below UL in all age groups	No safety concerns with nicotinamide,	
Folate, (as folic acid), mg/day	1.0	Suppl	Progressing neurological symptoms in vitamin B_{12} deficient patients	-	Intake below UL in all age groups	No safety concerns	**Yes**
Vitamin B_6, mg/day	25	Total diet	Neuropathy	-	Intake below UL in all age groups	No safety concerns	**Yes**
Vitamin B_{12}	N/A	-	No indication of adverse effects	-	Not needed	No safety concerns	**Yes**

	UL (adults)	Intake from total diet / Suppl	Adverse effect which is the basis for an UL	Vulnerable groups identified	Dietary Intake Assessment	Risk Characterisation	Proposed to be added to formulated beverage
Vitamin C	no UL established	Total diet	Insufficient data to set a UL, low toxicity at high doses, guidance level of 1000 mg/day	-	Not needed	No safety concerns	**Yes**
Vitamin D, µg/day	50	Total diet	Serum calcium levels	-	Intake below UL in all age groups	No safety concerns	**Yes**
Vitamin E, mg/day	300	Total diet	Blood clotting related to vitamin K deficiency	-	Intake below UL in all age groups	No safety concerns	**Yes**
Biotin	No UL established	-	Insufficient data to set a UL	unknown	No data available	Not possible to perform risk characterisation	No
Pantothenic acid	N/A	-	No indication of adverse effects		Not needed	No safety concerns	**Yes**
Calcium, mg/day	2500	Total diet	No adverse effects at UL, at higher doses kidney stones, milk-alkali syndrome,	-	Intake below UL	No safety concerns	**Yes**
Chromium	No UL established		Insufficient data to set a UL	unknown	No data available	Not possible to perform risk characterisation	No
Copper, mg/day	10	Total diet	Hepatoxicity	Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis	Intake below or at UL in all age groups	No safety concerns	**Yes**

	UL (adults)	Intake from total diet / Suppl	Adverse effect which is the basis for an UL	Vulnerable groups identified	Dietary Intake Assessment	Risk Characterisation	Proposed to be added to formulated beverage
Iodine, µg/day	1100	Total diet	Elevated TSH levels	individuals with thyroid disorders or a long history of iodine deficiency	Intake below UL in all age groups (except 2-3 years old, no safety concern)	No safety concerns	**Yes,** but risk management to be considered
Iron, mg/day	No UL established	-	Insufficient data to set a UL, high iron stores in older adults	individuals who are homozygous for hereditary haemochromatosis	Intake in all age groups are below levels with potential adverse effects	No safety concerns	**Yes,** but risk managemen t to be considered
Magnesium, mg/day	350	Suppl	Osmotic diarrhoea		Intake below UL in all age groups (except 2-3 years old)	UL based on a mild reversible effect, and modelling assumes worst case scenario, therefore, not of concern for young children	**Yes,** but risk management to be considered
Manganese, mg/day	No UL established		Neurotoxicity, not possible to establish an UL for total intake, but risk of adverse effects above current intake	All individuals		Risks of adverse effects at levels currently in consumed in the diet	No
Molybdenum, µg/day	600	Total diet	Reproductive effects	Unknown	No data available	Not possible to perform risk characterisation	No
Phosphorus, mg/day	4000	Total diet	Serum inorganic phosphorus levels	-	Intake below UL in all age groups	No safety concerns	**Yes**

	UL (adults)	Intake from total diet / Suppl	Adverse effect which is the basis for an UL	Vulnerable groups identified	Dietary Intake Assessment	Risk Characterisation	Proposed to be added to formulated beverage
Selenium, mg/day	0.40	Total diet	Brittle nails and hair pathology, adverse effects nervous system	-	Intake below UL in all age groups	No safety concerns	**Yes**
Zinc, mg/day	40	Total diet	Reduced copper status	Children and adolescents	2-8 years exceed UL 9-18 years approx 80% UL	Potential safety concerns up to 18 years, because of other potential sources of intake	No

N/A = not applicable

Introduction

A risk assessment has been conducted to identify potential public health and safety risks associated with the addition of certain vitamins and minerals to formulated beverages at a level of 25 % of the recommended daily intake (RDI). These include: vitamin A, β-carotene, thiamin, riboflavin, niacin, folate, vitamin B_6, B_{12}, D, E, biotin, pantothenic acid, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorus, selenium and zinc. The applicant has requested vitamin C to be added at 100% of the RDI. In this Attachment, the hazard identification and characterisation, dietary intake assessment and the risk characterisation for each micronutrient are presented.

Hazard Identification and Characterisation

Upper Level of Intake (UL)

The Upper Level of Intake (UL) has been defined by the Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) as: *a quantitative level of total intake at which, or below, no harm is expected to occur assuming nutrient adequacy is met* (FAO/WHO, 2004).

ULs have been established for the general population for vitamins and minerals by a number of countries as well as by an expert FAO and WHO working group (FAO/WHO, 2002). Australia and New Zealand have currently no established upper limits for the general population for vitamins and minerals, however, the National Health and Medical Research Council (NHMRC) is currently in the process of developing Nutrient Reference Values for Australia and New Zealand, which include ULs (NHMRC, 2004).

The ULs established by the United Kingdom (UK Expert Group on Vitamins and Minerals, 2003), the United States (US Institute of Medicine, 2000a; US Institute of Medicine, 2000b; US Institute of Medicine, 2000c; US Institute of Medicine, 2001a; US Institute of Medicine, 2001b) the European Union (European Commission Health & Consumer Protection Directorate-General, 2000a) and FAO/WHO (FAO/WHO, 2002) were compared and considered for their thoroughness and appropriateness for Australian and New Zealand populations.

The UL is derived by dividing the no observed adverse effect level (NOAEL) by the uncertainty factor (UF). UFs are empirical values applied to take into account uncertainties in the data. For example, an UF may need to be applied when extrapolating from results in experimental animals to humans or when extrapolating results from selected individuals to another group. These factors allow for differences in sensitivity between individuals and between species that may result from differences in absorption, metabolism, or biological effect of the substance under consideration. UFs may also be applied to account for uncertainties due to data base deficiencies (e.g. absence of a NOAEL requiring extrapolation from a low observed adverse effect level (LOAEL)), a poor data base, studies with small numbers of subjects, or because of the nature of a particular adverse effect.

ULs are derived for different life-stage groups using relevant data. In the absence of data for a particular life-stage group, extrapolations are made from the UL for other groups on the basis of known difference in body size, physiology, metabolism, absorption and excretion of a nutrient.

When data are not available for children and adolescents, extrapolations are made on the basis of body weight using the reference weights from the draft Nutrient Reference Values for Australia and New Zealand (NHMRC, 2004), see table 2.

Table 2: Reference body weights[43]

Age	Reference weight, kg
1-3 years	13
4-8 years	22
9-13 years	40
14-18 years	61
Adult	69

For the safety assessment of vitamins and minerals, it has been assumed that the products could be used for a long-term period. Therefore, in the safety assessment, ULs are based preferentially on long-term effects.

As the vitamins and minerals are intended to be added to formulated beverages and would not be incorporated into a food matrix, it has been assumed that when ULs for certain micronutrients are set for supplement use only, these ULs are relevant for the risk assessment.

Permitted forms

For the following micronutrients, no permitted forms are specified in Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions: pantothenic acid, biotin, chromium, copper, manganese, molybdenum and selenium. Therefore, the Applicant requested the forms specified in table 3 for these micronutrients. An assessment of the permitted form was undertaken, when the risk characterisation did not indicate safety concerns with including the specified micronutrient in formulated beverages.

Table 3: Permitted forms requested by the Applicant

Micronutrient	Permitted form requested
Pantothenic acid	Calcium pantothenate Dexpanthenol
Biotin	d-Biotin
Chromium	Chromium sulphate Chromic chloride
Copper	Copper gluconate Cupric sulphate Cupric citrate Cupric carbonate
Manganese	Manganese chloride Manganese gluconate Manganese sulphate Manganese carbonate Manganese citrate
Molybdenum	Sodium molybdate VI dehydrate
Selenium	Seleno methionine Sodium selenate Sodium selenite

[43] The reference body weights used in this table for 14-18 years old and adults are the average of male and female body weights as specified by the NHMRC.

Dietary Intake Assessment

A dietary intake assessment was conducted to determine the impact of consuming FBs on nutrient intakes and to assess the potential risk to public health and safety. This Attachment focuses on the results of the dietary modelling relating to the safety assessments of the nutrients. However, further details on how the dietary intake assessments were conducted can be found at **Attachment 7 – Dietary modelling methodologies for nutrient intake assessments**, which details information on methodologies used for conducting the intake assessments for nutrients, including the data sources, assumptions made and limitations of the dietary modelling. The results for the intake assessment for inadequacy and health benefits can be found in **Attachment 5 – Nutrition Assessment**.

The food consumption data used for the intake assessment were individual dietary records from the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS. The 1995 NNS from Australia surveyed 13 858 people aged 2 years and above, and the 1997 New Zealand NNS surveyed 4 636 people aged 15 years and above. Both of the NNSs used a 24-hour food recall methodology. Approximately 10% percent of respondents to the Australian NNS and approximately 15% of people from the New Zealand NNS completed a second 24-hour recall. These second day data were used to adjust the majority of the nutrient intake estimates across two days, providing a better estimate of daily nutrient intakes across a longer period of time. See Attachment 7 for more details. For some nutrients, the second day adjustment was unable to be calculated for a number of reasons, including that the NNS data were not statistically robust enough to enable the adjustment to be done. Use of second day adjustments has been highlighted below in the dietary intake discussion for each of the nutrients, where relevant.

Mean nutrient intakes based on food consumption for day 1 only (from the 24-hour recall) will not differ much compared to mean intakes that are based on a longer period of time such as when second day adjustments are used using the second day 24-hour recall. However, estimated nutrient intakes based on day 1 food consumption only, will be overestimates at the 95^{th} percentile. Adjusting the nutrient intakes by using the second day food consumption data will bring in the tails of the intake distribution resulting in a lower, more realistic, 95^{th} percentile intake (Rutishauser I, 2000).

Nutrient concentrations for FBs used in the dietary intake assessments were derived from the application. Nutrient concentrations for all other foods were those from the relevant 1995 Australian or 1997 New Zealand NNSs. There were some nutrients which were included in the New Zealand NNS however were not included in the Australian NNS. For these nutrients (vitamin B_6, vitamin B_{12}, vitamin D, vitamin E, manganese and copper), the concentrations from the New Zealand NNS were used and matched to the most appropriate foods in the Australian NNS. For nutrients that weren't included in either of the NNSs (iodine and selenium), survey and analytical data were used. No intakes from dietary supplements were included in the assessments. However, for some nutrients, only the supplemental uses were relevant for the safety assessment based on how the ULs were established, therefore, only fortified foods were included in the intake assessment.

The nutrients have been assessed for safety at 'baseline' and for 'Scenario 2'. Baseline intakes are nutrient intakes based on 1995 food composition data and assuming FBs are not consumed. Scenario 2 assesses the impact on nutrient intakes assuming FBs are consumed containing the requested levels of nutrients.

Scenario 2 is a substitution scenario that assessed what will happen to nutrient intakes when people take specified beverages out of their diet, and replace them with formulated beverages. The food groups substituted were cordials (excluding those made up from powder), carbonated drinks, fruit juices, fruit juice drinks, sports drinks and bottled water. For Scenario 2 it is assumed that people drink the same amount of the FB as all of the beverages specified they replace, and do not follow any recommended serve size that may be specified on the label of FBs.

In order to determine if the level of intake of the nutrients is likely to be a public health and safety concern, the estimated dietary intakes were compared to a UL where one was set.

Various age groups were assessed, depending on the UL set for a particular nutrient. The 1997 New Zealand NNS only included respondents aged 15 years and above. The raw data from the 2002 New Zealand National Children's Nutrition Survey are not in DIAMOND to allow nutrient intakes to be calculated for Scenario 2. However, the publication from the children's survey summarising the results provided baseline nutrient intakes for age groups between 5 and 14 years (Ministry of Health, 2003). The results from this publication have been included for nutrients where available.

Estimated intakes of nutrients and the percentage of the relevant ULs for baseline and Scenario 2 are shown below.

Vitamins and Minerals

Vitamin A

Hazard identification and characterisation

Chemistry

The term *vitamin A* describes a group of lipid soluble compounds related metabolically to all-trans-retinol. In the diet vitamin A is found in products of animal origin, as retinyl esters. The retinol esters, together with their metabolites, and synthetic derivatives that exhibit the same properties, are called retinoids. Some carotenoids can be cleaved into retinol, via an enzymatic process, which occurs mainly in the small intestine, and is readily saturated. The toxicity of carotenoids differ from that of retinoids, and the risk of high intakes of carotenoids are not linked to the adverse effects of retinoids.

Function

Vitamin A is a micronutrient essential to most mammalian species. Vitamin A is essential to the processes of vision, reproduction, embryonic development, morphogenesis, growth and cellular differentiation. With the exception of the visual process, most processes are related to the control of gene expression, with vitamin A metabolites, such as retinoic acid, acting as nuclear receptor-ligands.

Sources of vitamin A

Foods rich in pre-formed vitamin A (retinol, retinyl esters) include dairy products, fortified margarine, liver and fish oils.

Absorption, distribution, metabolism and excretion

Approximately 80% of dietary pre-formed vitamin A is absorbed but this may be reduced if diets are low in fat or individuals are suffering from fat malabsorption syndrome. Aqueous dispersions and emulsions achieve higher plasma levels, at a faster rate, with lower faecal losses, than oily solutions. Dietary retinyl ester is released from food by proteolytic digestion and hydrolysed to retinol in the gut.

The retinol is taken up into enterocytes, undergoes re-esterification and is incorporated into chylomicra, which are released into the circulation via the lymph. Following the breakdown of chylomicra by serum lipases, the retinyl esters are released, taken up by hepatocytes and re-hydrolysed. The resulting retinol is transferred to the stellate (fat storing) cells and stored in the form of long-chain fatty esters. Approximately 90% of the body's vitamin A is stored in the liver this way. The availability of hepatic stores of vitamin A may be decreased if protein status is low.

Plasma retinol is usually maintained under tight homeostatic control and concentrations do not alter significantly unless hepatic stores are severely depleted. If hepatic storage capacity is exceeded, plasma levels of retinyl ester increase, but plasma levels of retinol itself do not. Mobilised retinol is transported in plasma bound to retinol-binding protein and transthyretin. Uptake into extra-hepatic tissues occurs via a receptor-mediated process. Once inside the cell, retinol undergoes a complex series of metabolic oxidations, isomerisations and conjugations, most of which are reversible. Several enzymes are involved in these reactions, including cytochromes P450. Cellular binding proteins direct the reactions. Other intracellular binding proteins facilitate transport of specific vitamin A metabolites, such as retinoic acid, into the nucleus of the cell, where they interact with the retinoid nuclear receptors (RARs and RXRs) and participate in the control of gene expression for differentiation and growth.

Oxidised products are excreted in the urine or conjugated with glucuronic acid and excreted in the urine or bile.

Toxicity

There are substantial data on the adverse effects of high vitamin A intakes. Acute toxicity is characterised by nausea, vomiting, headache, increased cerebrospinal fluid pressure, vertigo, blurred vision, muscular in-coordination, and bulging fontanel in infants. These are usually transient effects involving single or short-term large doses of greater than or equal to 150,000 μg retinol equivalents (RE)[44] in adults and proportionately less in children.

The clinical picture for chronic hypervitaminosis A is varied and non-specific and may include central nervous system effects, liver abnormalities, bone and skin changes, and other adverse effects. Chronic toxicity is usually associated with ingestion of large doses, greater than or equal to 30,000 μg RE/day for months or years. Both acute and chronic vitamin A toxicity are associated with increased plasma retinyl ester concentrations. For the purpose of deriving an upper limit, three primary adverse effects of chronic vitamin A intake were recognised: 1) reduced bone mineral density, 2) teratogenicity, and 3) hepatoxicity. High β-carotene intake has not been shown to cause hypervitaminosis A. Therefore, only adverse effects of preformed vitamin A or retinol were investigated.

[44] Vitamin A can be expressed on a weight basis as Retinol Equivalents (1 μg RE = 1 μg retinol). This takes into account the vitamin A potency of various esters.

Reduced bone mineral density
Chronic, excessive vitamin A intake has been shown to lead to bone mineral loss in animals, making such a consequence in humans biologically plausible. Most human case reports are not well described and epidemiological studies are inadequate in design. However, some studies provide interpretable evidence relating changes in bone mineral density and risk of hip fracture with variation in dietary intake of preformed vitamin A.

A report (Melhus *et al*., 1998) found that the risk for hip fracture in Swedish women is doubled for retinol intake greater than 1500 μg RE/day as compared to intakes less than 480 μg RE/day. Based on univariate analysis, the relative risk at intakes of 500-1000 μg/day, 1000-1500 μg/day and >1500 μg/day, compared with individuals with intakes 500 μg/day, were 0.93 (0.61-1.41), 1.27 (0.80-2.02) and 1.95 (1.15-2.11) respectively. The intake was from dietary sources and therefore it is possible that the effects detected may have arisen from unrecognised confounding; however the mechanistic data on the actions of retinoic acid on bone metabolism are consistent with the reported relationship. An intake of 1500 μg RE/day is close to the population reference intake (600 μg RE/day for women in Europe) and lower than the actual intakes for a substantial proportion of the population.

A similar dose response relationship was reported (Feskanich *et al*., 2002) in data from a large cohort of women in the US, studied over a period of 18 years. The cohort was divided into quintiles for total vitamin A intake (<1250, 1250-1699, 1700-2249. 2250-2999, >3000 μg RE daily) and also for retinol intake (<500, 500-849. 850-1299. 1300-1999, >2000). Significant trends were apparent between relative risk and the intakes from food and supplements of total vitamin A and also retinol. A significant increase in relative risk was reported using a multivariate analysis for the two highest quintiles of retinol intakes (1300-1999, >2000 μg RE/day) compared with the lowest quintile (<500 μg RE/day). The trend analyses for retinol from food and supplements ($P \leq 0.001$) compared with food only ($P=0.05$) indicates an important contribution from supplements and this would be less likely to be affected by dietary confounding than the data from the study of Melhus et al. (1998).

Both of these major epidemiology studies indicate an increased risk of bone fracture over an intake range similar to that normally consumed from food and supplements. The findings on bone density and the risk of fracture were reported at lower daily intakes than other adverse effects. However, the currently available data are not considered to provide sufficient evidence of causality, and are not appropriate for establishing an UL according the US and EU. Furthermore, these adverse effects would only be relevant to elderly people, which are not the target group for formulated beverages.

Teratogenicity
The teratogenic effects of retinoic acids, the active oxidised metabolites of vitamin A, have been known for a long time and documented both in animals and in humans. Children exposed *in utero* to isotretinoin (13CRA) exhibit a pattern of congenital malformations, known as 'the retinoic acid syndrome', which include defects of the craniofacies (small or absent external ears and auditory canals, cleft palate, micrognathia, low set ears, of the central nervous system (micro- or anopthalmia, cerebellar or cortical defects, microcephaly), of the thymus and of the cardiovascular system (transposition of the heart vessels, aortic arch hypoplasia, ventricular septal defects). The incidence of these defects was 25 times higher in the exposed children, and was greater when neuropsychological dysfunctions were assessed. Most of these anatomical defects appear to be associated with alterations in the migration of cells from the neural crest.

The gestational period at which exposure occurred is of critical importance in the generation of these effects. In humans the critical period seems to be between the second and the fifth week of pregnancy, although it is generally stated that caution should be taken from the very beginning and up to the 60th day of pregnancy. Some animal studies indicate that a high vitamin A dose would have a similar teratogenic potential whether there was adequate storage levels of vitamin A in the liver or whether there was vitamin A deficiency.

No association has been found in the majority of case-control studies between daily doses of vitamin A of 3000 μg retinoid equivalents (RE) or less and foetal malformation.

A prospective study (Rothman *et al*., 1995) was large enough to stratify the population according to the vitamin A intake. Moreover, the origin of the vitamin A intake (supplement or food) was available for all subjects. The authors found that for women taking more than 4500 μg RE of total vitamin A per day (from food and supplement) there was a 3.5 times higher prevalence of children born with cranial-neural-crest defects, compared to children of mothers ingesting less than 1500 μg RE/day.

When the analysis was restricted to the supplemental intake of vitamin A only, the prevalence of children with defects was 4.8 times higher for mothers ingesting more than 3000 μg RE/day than for those ingesting 1500 μg RE/day. The authors fitted a regression curve to their data, which indicated a rise in the ratio of prevalence of birth defects associated to the cranial-neural crest at doses greater than 3000 μg RE/day of vitamin A (food and supplement). The conclusions of the study remained the same when several potential confounding factors were considered.

An uncertainty factor is not considered necessary because this analysis is quite conservative and because the data from other studies indicated that the true threshold for an effect could be higher than this value. Based on these studies an upper level of 3000 μg RE/day was accepted by both the EU (European Commission Health & Consumer Protection Directorate-General, 2002c) and US (US Institute of Medicine, 2001b).

Hepatotoxicity

In humans, the available data clearly suggest that the occurrence of symptoms of hepatotoxicity depends both on the vitamin A dose taken on a regular bases, and on the duration of this intake. The most extensive report, included 41 cases, but reliable intake information was available on only 29 patients who had a mean daily intake of 28,770 μg RE (range, 6,000-120,000 μg RE). The duration on high intake averaged 7.17 ± 1.21 years (range 0.2-15 years). Interestingly, these authors reported that the most severely affected subjects, i.e. those with cirrhosis (n=13) had consumed significantly more vitamin A, both daily and in total, than the patients without cirrhosis. The lowest continuous daily consumption in patients with cirrhosis was 7500 μg RE/day taken over 6 years. A similar case (7500 μg RE/day for 6 years) has been reported more recently in which progressive liver failure led to death of the patient. Cases of hepatotoxicity have not been reported below 7500 μg RE/day, and it can be hypothesised that this value might be the upper threshold of the storage capabilities of the liver. It is not known if a dose lower than 7500 μg RE/day could induce hepatotoxicity if taken for more than 6 years, but such low intakes may not have been considered by physicians when they attempted to identify the cause of their patient's liver disease.

Differential sensitivity to vitamin A-induced hepatotoxicity has been considered by several authors. On a weight basis, it does not seem that children (more than one year old) are more sensitive than adults. In elderly people (64-88 years old) plasma retinyl esters and retinol values were correlated to their supplemental vitamin A intakes (up to 14,100 µg RE/day for 5 years), but not to liver function tests.

Evaluation

Vitamin A	UL in adults, µg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	3000	Total diet	teratology	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	1500	Total diet	Bone fracture and teratology	human
EU (European Commission Health & Consumer Protection Directorate-General, 2002c)	3000	Total diet	teratology and hepatotoxicity	human

* Guidance level; the UK did not derive an UL, because of uncertainty regarding the effects on incidence of bone fracture at low levels and the potential teratogenic effects, both of which may occur with the known dietary intakes of vitamin A.

Teratogenicity is considered a relevant end point, because of the severe and irreversible nature of this form of toxicity. Based on the available studies an UL of 3000 µg RE/day is considered appropriate. Although teratogenicity is only relevant to women of childbearing age, the UL of 3000 µg/day is appropriate for men, and for infants and children after correction for differences in body weight, because hepatoxicity was observed at 7500 µg/day. Using an uncertainty factor of 2.5 would result in an UL of 3000 µg/day. This UL does not apply for pro-vitamin A forms.

Based on the data from the US and EU evaluation, the ULs for **Vitamin A** for all age categories are:

1-3 years **600 µg RE/day**
4-8 years **900 µg RE/day**
9-13 years **1700 µg RE/day**
14-18 years **2800 µg RE/day**
Adult **3000 µg RE/day**

Dietary intake

Estimated intakes of vitamin A have been calculated for retinol (Table 4) and for beta-carotene (Table 5) at baseline and for Scenario 2.

The requested concentration of vitamin A in a 600 ml reference quantity is 187.5 µg of retinol equivalents.

Estimated intakes for retinol were able to be adjusted for the majority of the population groups assessed apart from teenagers 14-18 years for Australia and 19 years and above for both Australia and New Zealand.

Where second day adjustments could be made in DIAMOND, these were presented as the estimated intakes, as they provide a better indication of longer term nutrient intakes. Where second day adjustments could not be made, this was due to limited sample numbers in certain age groups and the distribution of intakes which meant the calculations could not be made. The estimated intakes for retinol for the population groups with unadjusted intakes will be higher than those for similar age groups that have adjusted intakes at the 95th percentile. The estimated intakes for younger children in New Zealand 5-14 years taken from the summary report are adjusted based on second day data (Ministry of Health, 2003).

Assuming FBs were consumed, intakes of retinol increased around 100 µg/day (around 10-20% of the UL) from baseline across all age groups assessed.

All estimated mean intakes of retinol were below the ULs at baseline and assuming retinol is consumed in FBs (Scenario 2). At the 95th percentile intake of retinol, only the estimated intakes for Australian children aged 2-3 years at baseline and from 2-8 years at scenario 2 exceeded the upper level.

Table 4: Estimated dietary intakes of retinol, before and after FBs are introduced into the diet, and percent of the upper level (UL)

	Mean intake µg/day (%UL)		95th percentile intake µg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	423 (70)	506 (85)	674 (110)	757 (130)
4-8 years, Aus	430 (50)	528 (60)	693 (75)	808 (90)
5-6 years, NZ	^286 (**)	NA	#433 (**)	NA
7-10 years, NZ	^326 (**)	NA	#443 (**)	NA
9-13 years, Aus	607 (35)	738 (45)	741 (45)	870 (50)
11-14 years, NZ	^368 (**)	NA	#509 (**)	NA
14-18 years, Aus†	611 (20)	777 (30)	1466 (50)	1766 (65)
15-18 years, NZ	446 (15)	562 (20)	578 (20)	716 (25)
≥19 years, Aus†	579 (20)	652 (20)	1142 (40)	1292 (45)
≥19 years, NZ†	522 (15)	569 (20)	940 (30)	1047 (35)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.
† Not adjusted for second day nutrient intakes.

Risk characterisation

The dietary modelling predicts that high consuming children aged 2-3 years will exceed their UL if retinol is added to formulated beverages at a level of 187.5 µg/600 ml serve (130% UL for 2-3 year olds). The adverse effect on which the UL for this age group was based was hepatoxicity. The LOAEL in adults for this adverse effect was 7500 µg/day for a period of 6 years. When this level is expressed on a body weight basis this would be approximately 1400 µg/day for 2-3 year olds. While the estimated intake is below this calculated LOAEL, uncertainty exists as to whether children might be more susceptible to hepatoxicity following high retinol intake.

Furthermore, as the LOAEL represents an actual level measured in adults, uncertainty exists as to whether, and if so at what level, hepatoxicity could occur at levels below this measured LOAEL. An uncertainty factor of 2.5 was therefore applied, since there are no adverse effects reported at this level. It is not clear whether an uncertainty factor of 2.5 is sufficient in the case of children who may be more susceptible to hepatotoxicity following high retinol intake.

It could be assumed that children above the age of 3 years could sustain these high intakes of retinol for up to 6 years which may put them at increased risk of hepatoxicity. This assumption is based on the 95th percentile for the 4-8 years age group which is estimated to be 90% of the UL when FBs are consumed, meaning 5% of this population group have higher intakes.

In conclusion, there are potential safety concerns for children up to the age of 3 years, and maybe up to 6 years, with the addition of retinol to formulated beverages at a level of 187.5 μg in a 600 ml serve. For all other age groups and life-stages, there is no appreciable risk posed by excess intake of retinol.

β-Carotene

Hazard identification and characterisation

Chemistry
β-carotene ($C_{40}H_{56}$) is a member of the carotenoids family of isoprenoid compounds, which are characterised by their polyunsaturated nature and antioxidant properties. The compound can exist in different geometrical forms (as cis- or trans- isomers); the majority of naturally occurring β-carotene, as well as virtually all of the compound prepared by chemical synthesis, is the all-trans isomer.

Function
Some dietary carotenoids serve as an important source of vitamin A, which is the major known function of carotenoids in humans. Its importance in any individual depends upon the level of preformed vitamin A in the diet.

Sources of carotenoids
β-carotene is synthesised in plants and microorganisms, but not in animals. The main food sources of β-carotene are yellow and green (leafy) vegetables and yellow fruits. Commercially available β-carotene is either synthetic or derived from palm oil, algae or fungi, and is widely used as a yellow colouring agent in foods and drinks.

Absorption, distribution, metabolism and excretion
Dietary fat and bile salts facilitate absorption in the upper small intestine, which occurs via incorporation into multilamellar lipid micelles. It has been estimated that, in humans, between 10 and 90% of the total β-carotene consumed in the diet is absorbed, with absorption decreasing as intake increases. Availability from food products is lower than that of a water-dispersed formulation, due to the need for disruption (by pepsin and proteolytic enzymes and by cooking), of the matrix of fibre, polysaccharide and protein. Bioavailability is reduced in very low fat diets.

A proportion of absorbed β-carotene is converted to retinol within intestinal mucosal cells. Unaltered β-carotene is transported via the lymph to the plasma where it is associated with lipoproteins.

Tissue uptake and distribution are not well characterised. In the case of regular high intake, long-term accumulation occurs preferentially in adipose tissues. Serum levels of β-carotene have been reported to be low in smokers, in individuals with a high alcohol intake, and in those with HIV infection. Low β-carotene status may be associated with conditions of impaired lipid absorption such as jaundice, liver cirrhosis and cystic fibrosis. β-Carotene is mainly converted to retinol (vitamin A) in the cytosol of intestinal mucosal cells. Experiments in rats have shown that the levels of β-carotene and of preformed vitamin A regulate the process. *In vitro* studies have shown that other β-carotene derivatives may also occur, but their biological activity, and whether they are synthesised *in vivo*, is unknown.

Carotenoid absorption and metabolism vary considerably between animal species. No single species provides a good model for studying all aspects of the biokinetics and metabolism of β-carotene in humans. The rat is particularly unsuitable, due to the high efficiency of conversion to vitamin A, such that significant levels of unaltered β-carotene are absorbed only when very high doses are given, for prolonged periods of time. The pre-ruminant calf, the ferret and the Mongolian gerbil are suggested to be more useful models, although it is apparent that there are many differences in carotenoids absorption, distribution and metabolism between these animals and humans.

Absorbed β-carotene is secreted into the bile and excreted in the faeces. It is also excreted in the sweat.

Toxicity

Animal studies

In animal studies, no adverse effects of high-dose oral β-carotene supplementation have been observed in several standard toxicological studies in various experimental animals (rat, mice, rabbits). These studies included acute studies up to 5000 mg/kg bw, chronic toxicity / carcinogenicity studies up to 1000 mg/kg bw/day for life in rats or mice, teratogenicity and reproductive toxicity studies. β-carotene shows no genotoxicity *in vitro* or at high doses *in vivo* and was not carcinogenic in experimental rodent studies.

However, β-carotene supplementation for 6 months (2.4 mg/kg bw/day, with or without exposure of the animals to cigarette smoke) was associated with the development of squamous cell metaplasia in the lungs of ferrets. The assessed histopathological endpoint, squamous metaplasia, may not be directly related to carcinogenesis, but this study did reveal interestingly related molecular/biochemical changes in the lungs of the animals tested.

Human studies

In humans, doses of 20-180 mg/day β-carotene have been used to treat patients with erythropoietic photoporphyria, with no evidence of toxicity and without the development of abnormally elevated blood vitamin A.

Hypercarotenaemia (high levels of β-carotene in the blood) is generally considered to be a benign condition. It is often related to unusually high intake of carotene-rich foods.

Hypercarotenodermia (yellowing of the skin, particularly the palms, soles of the feet, chin, behind the ears, over the knuckles and on the abdomen and buttocks) is a physical manifestation of β-carotene excess, which is caused by accumulation of the substance in fatty tissues, particularly subcutaneous fat. Although β-carotene is a precursor of vitamin A, excess intake has not been associated with vitamin A toxicity in humans, possibly because the conversion is tightly controlled.

The promise shown by β-carotene and other putative biological antioxidants as prospective agents for cancer prevention led to the instigation of numerous small scale supplementation studies and, of particular importance, a small number of large-scale, primary prevention trials in humans, involving supplementation with β-carotene, alone or in combination with other vitamins and/or minerals.

Some major prevention studies (Greenberg *et al*., 1990; McLarty, 1992; Blot *et al*., 1993; Li *et al*., 1993; Greenberg *et al*., 1994) did not show any adverse effects on increased tumours, but this might have been through their design.

The Alpha-Tocopherol/Beta-Carotene trial in Finland (ATBC study group, 1994) involved 29,133 male smokers (age 50-59) with a smoking history averaging one pack/day for 36 years. The 2x2 factorial design evaluated 20 mg β-carotene and/or 50 IU alpha-tocopherol (vitamin E) daily for 6.5 years. These doses represent a 10-fold and 5-fold excess over the median intake of β-carotene and α-tocopherol, respectively, in this population. After 2 years of treatment, median serum β-carotene levels had increased 17.5-fold in the β-carotene treatment groups. Participants receiving β-carotene alone or in combination, had significantly higher lung cancer incidence (Relative Risk (RR) 1.18; 95% Confidence interval (CI) 1.03-1.36) and higher mortality (RR 1.08; CI 1.01-1.16) than subjects receiving placebo. The excess lung cancer incidence was not apparent in the initial 18 months, but the incidence curves significantly diverged thereafter. Subsequent subgroup analysis (see (Albanes *et al*., 1996) revealed a higher risk in heavy smokers (20 or more cigarettes/day) (RR 1.25, CI 1.07-1.46) than in light smokers (5-19 cigarettes/day) (RR 0.97, CI 0.76-1.23). Associations with alcohol intake and with non-small-cell histology were also noted. The risk was confined to the heavier drinkers (more than 11 g ethanol per day).

Interestingly, in agreement with earlier observational studies, both dietary intake and serum β-carotene levels at baseline (before treatment) were found to be inversely related to risk of lung cancer during the trial (Albanes *et al.,* 1996).

The β-Carotene And Retinol Efficacy Trial (CARET) study ((Omenn *et al*., 1996b), see also (Omenn *et al*., 1996a; Omenn, 1998) successfully randomised 18,314 participants in the USA. 30 mg β-carotene and 25,000 IU vitamin A (retinyl palmitate) were administered daily to 14,254 smokers and former smokers (45% female) aged 50-59 at enrolment, and to 4,060 asbestos-exposed males (age 45-74). After five years of study the median serum β-carotene levels in the active treatment group was increased by 12-fold (170 ng/ml *versus* 2100 ng/ml). A total of 388 new cases of lung cancer were diagnosed during the 73,135 person-years of follow- up (mean 4.0 years). The active treatment group had a RR of lung cancer of 1.28 (CI 1.04-1.57), compared with the placebo group. The differences (significant from 24 months of treatment onwards) were greater as the intervention progressed. There were no statistically significant differences in the risks of other types of cancers. In the active group the RR of death from any cause was 1.17, of death from lung cancer, 1.46, and of death from cardiovascular disease, 1.26.

As in a further analysis from ATBC published in the same issue (Albanes *et al.,* 1996), there was an association (less clear trend than in ATBC study) of the excess lung cancer incidence between treatment groups with the highest quartile of alcohol intake, but no association with baseline serum β-carotene concentrations.

In the CARET study it is not possible to distinguish the β-carotene effects from those of the vitamin A, since the two compounds were administered in combination.

The Physicians Health Study was to test the effect of aspirin on cardiovascular disease incidence (Steering Committee of the Physicians' Health Study Research Group, 1989). β-carotene was added in a 2x2 design, using 50 mg β-carotene on alternate days. 22,071 male physicians were followed for a mean of 12.5 years. Those assigned to receive β-carotene had significantly higher serum concentrations than those given placebo (2240 nmol/l *vs.* 560 nmol/l) (4-fold). It has to be noted that this increase is lower compared with that obtained in the two previously considered trials, a situation that could be related to higher basal levels in the PHYS population and/or to a lower bioavailability of β-carotene compared with the other trials. In this healthy population, with 50% never-smokers and only 11% current smokers, 170 lung cancers were accumulated over the follow up period. The relative risks were 1.02 (CI 0.93-1.11) for overall mortality, 0.98 (CI 0.91-1.06) for all malignant neoplasms, and 0.93 for lung cancer.

In summary there was no effect of ß-carotene supplementation on total cancer, on total mortality, or on heart disease. Neither was an effect on lung cancer observed, but due to the lower number of cases, the power of the statistical analysis underlying this conclusion is rather weak.

Mechanisms
In light of the adverse findings in human intervention trials, in which β-carotene supplementation was associated with a promotional effect on lung tumourigenesis in smokers, studies in animals have been carried out to elucidate potential mechanisms by which these effects may have occurred. The EU has proposed three mechanisms in the evaluation, which are related to effects in the same target tissue, the lungs, where the adverse effects have been observed in humans. The first mechanism proposes that β-carotene has a co-carcinogenic effect through a P450 enzyme related activities. The second mechanism proposes altered retinoid signalling: a mechanism to enhance lung tumourigenesis after high doses of β-carotene supplementation in smokers. The last mechanism proposes a pro-oxidant activity of β-carotene at high levels.

Dose response assessment
No dose-response relationship for β-carotene effects is available from the intervention trials in humans, as single doses were used in each study, and the conditions were different across studies.

The study in ferrets also used a single daily dose. Further studies in ferrets using a range of different β-carotene doses and a wider range of selected parameters would be appropriate to assist in future toxicological evaluation.

It can be presumed that the effects of β-carotene are dependent on the specific source of exposure, and that differences will not be unexpected with different matrices or different formulations containing β-carotene, depending on the composition of accompanying antioxidants and of other components, and also depending on the relative proportion of isomers of β-carotene.

Evaluation

β-carotene	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000c)	no UL	suppl	Insufficient data	human
UK (UK Expert Group on Vitamins and Minerals, 2003)	7	suppl	Lung tumours in smokers	human
EU (European Commission Health & Consumer Protection Directorate-General, 2000b)	no UL	suppl	Insufficient data	human

β-Carotene is of low toxicity in both animals and man, and prior to the publication of a number of intervention studies was thought to be without adverse effect, other than a yellowing of the skin, which occurred after sustained high intake. However, supplementation of smokers and subjects previously exposed to asbestos has been associated with an increased risk of lung cancer.

The US and EU stated that the existing evidence from human trials indicated that supplemental β-carotene (20 mg/day or more) is contraindicated for use in current, heavy smokers. However, there is insufficient scientific basis to set a precise figure for an UL of isolated β-carotene, as no dose-response relationship for β-carotene effects is available either from the intervention trials in humans or from appropriate animal models. Moreover, it is not possible to be more specific in distinguishing different isomeric forms of β-carotene or specific formulations.

The UK has set an UL. There is no evidence that β-carotene supplementation has any effect on non-smokers. As a matter of prudence the UK has set an UL for supplementation based on the ATBC-study. The LOAEL from this study was 20 mg/day. Applying an uncertainty factor of 3, to extrapolate from a LOAEL to a NOAEL, results in a UL for supplementation of 7 mg/day. This UL applies to supplements only, as there is no evidence to suggest that current levels of β-carotene intake from food result in adverse effects.

Based on the data considered in the US, EU, and UK evaluation, there is **insufficient evidence to establish an UL for β-carotene for supplemental use.** However**, an UL for β-carotene from food or food additives does not need to be established**, based on no indication of adverse effects. Furthermore, 7 mg β-carotene per day is a conservative estimate for a guidance level for supplemental use.

Dietary intake

Dietary modelling has been conducted for all forms of β-carotene in food only, without making a distinction between natural β-carotene and β-carotene added to food as food additives or from food fortification. Dietary modelling results are shown in Table 5.

The concentration of β-carotene requested to be added to FBs by the Applicant was in the form of retinol equivalents (RE). For dietary modelling purposes, estimated intakes of β-carotene were expressed as micrograms per day (Table 5). Therefore, the requested concentrations of β-carotene in the FBs had to be converted to a concentration in micrograms for dietary modelling purposes.

The conversion was made using a factor of 12, (as per the Food Standards Code). Therefore, the requested concentration of vitamin A to be added to FBs was 187.5 µg RE/600 ml, or 31.3 µg/100g, resulting in a β-carotene concentration used in the dietary modelling of 376 µg/100g.

Estimated intakes for β-carotene were adjusted using second day data from the NNSs.

Estimated intakes of β-carotene increased with the consumption of FBs, between 30 and 100 µg/day from baseline intakes, depending on the population group assessed. There was no upper level for β-carotene to compare the estimated intakes.

Risk characterisation

The intake level from all food sources is much lower than the level at which increased lung tumours in smokers were observed in prevention studies when β-carotene supplementation was given.

In conclusion, the addition of β-carotene to formulated beverages at a level of 187.5 µg retinol equivalents per 600 ml serve poses no appreciable public health and safety risk.

Table 5: Estimated dietary intakes of beta carotene, before and after FBs are introduced into the diet

	Mean intake µg/day		95th percentile intake µg/day	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	1902	1934	4684	4725
4-8 years, Aus	2030	2077	5267	5282
5-6 years, NZ	^1488	NA	#2508	NA
7-10 years, NZ	^1848	NA	#3612	NA
9-13 years, Aus	2559	2627	4510	4689
11-14 years, NZ	^1992	NA	#3204	NA
14-18 years, Aus	3119	3211	5158	5338
15-18 years, NZ	2882	2982	4080	4345
≥19 years, Aus	3548	4432	6548	7821
≥19 years, NZ	3544	3591	6508	6562

***** Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
N/A = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Thiamin

Hazard identification and characterisation

Chemistry
Thiamin (vitamin B_1) is a relatively heat- and acid-stable, water-soluble compound, containing a pyrimidine and a thiazole nucleus linked by a methylene bridge. Derivatives of thiamin include the mono-, pyro- and triphosphate forms and the synthetic hydrochloride and slightly less water-soluble mononitrate salt. Synthetic non water-soluble derivatives of thiamin are available but these are not used in food supplements.

Function
Thiamin pyrophosphate (TPP) is a co-enzyme in several enzymatic reactions. TPP may also have a non-co-enzymic function during stimulation of neuronal cells and other excitable tissues, such as skeletal muscle.

Sources of thiamin
Foods providing rich sources of thiamin include unrefined grain products, meat products, vegetables, dairy products, legumes, fruits and eggs. In Australia, but not in New Zealand, there is mandatory fortification of flour used for making bread. Bread flour must contain no less than 6.4 mg/kg of thiamin (Standard 2.1.1 – Cereals and Cereal Products).

Absorption, distribution, metabolism and excretion
Thiamin present in food is efficiently absorbed. However, water-soluble supplements, such as thiamin hydrochloride and thiamin mononitrate, are poorly absorbed due to saturation of transport mechanisms. At physiological concentrations, intestinal uptake occurs mainly via a carrier-mediated transport mechanism. However, this process is saturable and at higher concentrations, uptake is predominately by slower passive diffusion.

In the blood and tissues, thiamin is present as the free form and mon-, di- (pyro) and triphosphorylated forms, which are interconvertible. Free and phosphorylated forms are transported within the erythrocytes, but plasma and cerebrospinal fluid contain only the free and monophosphorylated forms. Within the tissues most thiamin present is converted to the pyrophosphate form. Liver contains the highest concentration of thiamin. Catabolic metabolism amounts to approximately 1 mg/day, and most of this occurs in the liver.

Thiamin metabolites and thiamin in excess of requirements are excreted in the urine. The level of unchanged thiamin in the urine increases as intake increases.

Toxicity
In humans, orally ingested thiamin has a long history of use as an oral supplement for the treatment or prophylaxis of thiamin deficiencies without reported adverse effects. Due to its therapeutic action in some frequently observed clinical syndromes (such as chronic alcoholism), thiamin hydrochloride has been advised and used over a long period of time. There are no reports of adverse effects of oral thiamine, even at dosages of several hundred milligrams a day.

After parenteral administration, a small number of individuals may show an allergic response to lower doses, but reports of these lower dose-related events are rare.

The animal database is also very limited. The oral LD_{50} in mice is 3-15 mg/kg bw. A lethal dose of thiamin in rodents is preceded by CNS effects such as shock, muscle tremor, convulsions, respiratory disturbance and collapse, symptoms that are similar to acute thiamin toxicity in humans.

Due to the lack of oral dose-response studies, no LOAEL and NOAEL can be established in both human and animal studies.

Evaluation

Thiamin	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000b)	N/A	food	no adverse effects	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	100	supplemental	no specific effect	human
EU (European Commission Health & Consumer Protection Directorate-General, 2001c)	N/A	total diet	no adverse effect	human

N/A not applicable
* Guidance level, for water-soluble forms of thiamine only

Based on the data from the US and EU evaluations, it can be concluded that orally ingested thiamin has a very low toxicity. This may be because at intake levels higher than 5 mg absorption rapidly declines and, because absorbed thiamin is actively excreted in the urine.

Based on the data considered in the US and EU evaluation, **thiamin** has a very low oral toxicity, and therefore an **UL does not need to be established**.

Dietary Intake

No dietary intake estimates were calculated for thiamin, as it was determined to have very low oral toxicity, and no upper levels have been established, as outlined above.

Risk characterisation
No UL has been established for thiamin, based on the lack of adverse effects even at high doses. Therefore, no dietary modelling was required.

In conclusion, the addition of thiamin to formulated beverages at a level of 0.275 mg per 600 ml serve poses no appreciable public health and safety risk.

Riboflavin

Hazard identification and characterisation

Chemistry
Riboflavin is a water-soluble vitamin of the B group (vitamin B_2). It is stable to mineral acids in the dark at 27°C. Decomposition occurs in both acidic and alkaline solutions.

Function

Clinically, riboflavin promotes normal growth and assists in the synthesis of steroids, red blood cells, and glycogen. Flavin adenine dinucleotide (FAD) also play a role in oxidation-reduction reactions, interacting with a group of enzymes known as flavoproteins. Riboflavin helps to maintain the integrity of mucous membranes, skin, eyes and the nervous system. It supports the activity of antioxidants and is involved in the production of adrenaline by the adrenal glands. It is thought that riboflavin also aids the body in absorbing iron, since it is common for iron deficiency to accompany a deficiency in riboflavin.

Sources of riboflavin

Riboflavin is widely distributed in foodstuffs and all plant and animal cells contain it, but there are very few rich sources. Only yeast and liver contain more than 2 mg/100 g. Other good sources are milk, egg white, fish roe kidney and leafy vegetables.

Absorption, distribution, metabolism and excretion

Riboflavin is readily absorbed from the small intestine, primarily by a specialised transport mechanism involving phosphorylation of the vitamin to flavin mononucleotide (FMN). Passive diffusion plays only a minor role at levels ingested in the diet. Riboflavin has been shown to undergo active secretion into, and saturable reabsorption from, the kidney tubules in rat, dog and human.

Riboflavin is distributed to all tissues. It is present in red blood cells, and appears to bind to a subfraction of immunoglobulins in plasma. Very little riboflavin is stored. Free riboflavin is transformed in the liver to form flavin coenzymes, (FAD and FMN), which are utilised as electron transfer factors in enzymatic reductions.

When riboflavin is ingested in amounts approximately equivalent to the minimal daily requirement, only about 10-20% appears in the urine. As the intake is increased above minimal requirements, larger proportions are excreted unchanged. Riboflavin is also found in faeces, sometimes in quantities exceeding that ingested. This probably represents the riboflavin synthesised by intestinal microorganisms, which is not absorbed.

Toxicity

In animals oral riboflavin administration is of low toxicity, which can probably be explained by the limited capacity of the intestinal absorption mechanism.

Some evidence of adverse effects associated with the group of flavins is based on *in vitro* studies showing involvement in the formation of active oxygen species and in the axonal degeneration on intense exposure to ultraviolet and visible light.

The absorption of riboflavin reduces as the level of administration increases to high-level doses. Data on adverse effects from high oral riboflavin intake are insufficient to establish an UL. Given the lack of any demonstrated functional disorders or adverse structural effects in humans following excessive oral riboflavin intake and considering the reduced intestinal absorption following high dose exposure, the relevance of the mild effects shown in *in vitro* studies to human health is questionable.

Available data from 3-month human studies and from pharmacokinetics studies do not show adverse effects after oral administration. The minor gastrointestinal disorders, in some individuals are not clearly related to the riboflavin intake.

Evaluation

Riboflavin	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000b)	N/A	food	no adverse effects	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	40	Suppl	no specific effect	human
EU(European Commission Health & Consumer Protection Directorate-General, 2000g)	N/A	total diet	no adverse effects	human

N/A not applicable
* Guidance level,

Although limited, none of the available studies has reported significant adverse effects in humans following excess riboflavin consumption from food or supplements. Therefore, based on the present database it is not possible to derive an UL for riboflavin. The limited evidence available from clinical studies indicates that current levels of intake of riboflavin from all sources do not represent a risk to human health.

Based on the data considered in the US and EU evaluations, **riboflavin** has a very low toxicity and therefore **an UL does not need to be established**.

Dietary Intake

No dietary intake estimates were calculated for riboflavin, as it was determined to have very low toxicity, and no upper levels have been established, as outlined above.

Risk characterisation
No UL has been established for riboflavin, based on the lack of adverse effects even at high doses. Therefore, no dietary modelling was required.

In conclusion, the addition of riboflavin to formulated beverages at a level of 0.425 mg per 600 ml serve poses no appreciable public health and safety risk.

Niacin

Hazard identification and characterisation

Chemistry
Niacin (vitamin B_3) is the generic term for nicotinic acid (pyridine 3-carboxylic acid) and nicotinamide (nicotinic acid amide), and the coenzyme forms of the vitamin. Nicotinamide is the active form, which functions as a constituent of two coenzymes, namely, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). These coenzymes in their reduced states (NADH/NADPH) are the principal forms of niacin that exist in animal tissues.

Function
Niacin is not strictly speaking a vitamin because it is formed from the metabolism of tryptophan, and is not *per se* essential to the body, providing that there is an adequate supply of the essential amino acid tryptophan. In the form of the coenzymes NAD and NADP, niacin functions in many biological redox reactions.

Sources of niacin
Niacin is present in food largely as bound forms that require hydrolysis to release the free nicotinamide or nicotinic acid prior to absorption. In animal tissues niacin is present mainly as the coenzymes NAD and NADP.

Absorption, distribution, metabolism and excretion
In humans, niacin is rapidly absorbed from the stomach and intestine by a sodium carrier-mediated mechanism at low concentrations.

Niacin circulates in the plasma in the unbound form as both the acid and the amide. Each enters peripheral tissues by passive diffusion, followed by metabolic trapping by conversion to the pyridine dinucleotides, NAD(H) and NADP(H). Most is found as NAD(H) and the oxidised form NAD. The plasma half-life of nicotinic acid is relatively short, approximately one hour. Animal studies have shown that nicotinic acid rapidly disappears from the blood and is mainly concentrated in the liver, but also in adipose tissue and in the kidneys. The main metabolites in humans are N-methylnicotinamide, N-methyl-2-pyridone-5-carboxamide and N-methyl-4-pyridone-5-carboxamide.

The pattern of niacin products excreted after ingestion of the vitamin depends largely on the amount and form of niacin ingested and on the niacin status of the individual. However, the two major excretion products in humans are N-methylnicotinamide and N-methyl-2-pyridone-5-carboxamide, with minor amounts of the unchanged vitamin, nicotinamide-N-oxide and 6-hydroxynicotinamide also being excreted.

Toxicity
The principal identification of hazards associated with excessive intakes of niacin have arisen from studies in which high doses of nicotinic acid have been used for its therapeutic effects in lowering blood cholesterol and blood hyperlipidaemias. A number of hazards have been reported to be associated with high doses of nicotinic acid. In addition, nicotinamide has been investigated as a method for reducing the risk of development of diabetes.

The toxicity of nicotinic acid and nicotinamide are discussed separately.

Nicotinic acid
Vasodilation is commonly seen in patients given high doses of nicotinic acid for the treatment of hyperlipidaemias. Very large single doses cause hypotension, although tolerance develops to this effect after several days of continued high dose intake. In general, flushing is a mild and transient effect, although in many clinical trials it has resulted in patients withdrawing from treatment. The flushing activity appears to be related to the presence of a carboxyl group on the pyridine nucleus since compounds lacking this function, including nicotinamide, are not associated with facial flushing. Flushing is associated with periods of rapid rises in blood concentrations, and sustained-release formulations were developed for the use of nicotinic acid in the treatment of hypercholesterolaemia, in order to minimise this side-effect. Flushing is produced via prostaglandin D_2 release.

Theoretically if flushing occurred in the elderly, it could exacerbate mild postural hypotension, and could increase the risk of falls, which are a common cause of morbidity in the elderly. This risk relates to taking supplements containing nicotinic acid (not nicotinamide), especially if taken on an empty stomach.

At higher intakes of nicotinic acid over long periods of time, liver dysfunction has been reported. Symptoms such as elevated liver enzymes, elevated bilirubin levels and jaundice have been observed. Other adverse effects reported include hyperglycaemia and adverse ophthalmological effects such as blurred vision and cystoid macular oedema.

The more severe forms of toxicity of nicotinic acid occur principally at does of greater than 500 mg/day. The limiting adverse effect at lower dose is flushing, and this has been reported at much lower intakes than the other adverse effects. The most severe and potentially life-threatening adverse effects, such as hepatotoxicity, occur at doses one order of magnitude higher than have been reported for flushing. The dose of free nicotinic acid reported to produce flushing consistently in clinical studies is 50 mg/day. The available data indicated that flushing would be unlikely to occur repeatedly in subjects given less than 50 mg/day, but occasional flushing was reported at a dose of 30 mg of nicotinic acid daily.

Nicotinamide
Nicotinamide does not produce the flushing response that has been used as the basis for the upper level for nicotinic acid. There has been only one reported case of hepatoxicity in a patient receiving high-dose nicotinamide (however, nicotinamide has not been subject to extensive clinical trials (at 3 g per day or more) for use as a hypolipidaemic agent).

No significant adverse effects have been reported in trials on the possible benefits of nicotinamide in patients with or at risk of diabetes, where doses up to the equivalent of 3 g/day, for periods up to 3 years, have been used. The NOAEL from these studies is approximately 25 mg/kg bw/day. This value represents the lowest reported dose in a number of recent trials of high quality, many of which used sensitive biomarkers of hepatic function and glucose homeostasis, and included a range of age groups, with some subjects treated with up to 50 mg/kg bw/day.

Evaluation

Niacin	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000b)	35	Suppl	flushing	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	17 nicotinic acid 500 nicotinamide	Suppl. Suppl.	flushing no adverse effects	human
EU (European Commission Health & Consumer Protection Directorate-General, 2002e)	10 nicotinic acid 900 nicotinamide	Suppl Total	flushing no adverse effects	human

* Guidance level

Nicotinic acid
The US has set an UL for niacin based on flushing for all forms. The US did not add a separate UL for nicotinamide based on the fact that nicotinamide is not associated with flushing.

Both the UK and EU separated the effects for nicotinic acid and nicotinamide, because of the differences in adverse effects. The EU has established ULs, while the UK stated that there was insufficient data to establish a UL for both nicotinic acid and nicotinamide. FSANZ considers the EU approach to be the most appropriate.

The EU set a UL for nicotinic acid of 10 mg/day based on the available data indicating occasional flushing at 30 mg/day. An uncertainty factor of 3 was used to allow for the fact that a slight effect was reported, and that the study was performed in a small number of subjects, but taking into account the steep dose-response relationship. This results in an UL that is 300-fold below the dose frequently used clinically for the treatment of hypercholersterolemia (3 g/day) and which is associated with a high incidence of serious adverse reactions. The only reports of flushing associated with the ingestion of nicotinic acid with food have occurred following the addition of free nicotinic acid to food prior to consumption. Although flushing might be considered a minor health effect, it has been used as the basis for setting the UL for nicotinic acid, because of concerns about the possibility of a transient hypotensive episode, especially in the elderly, leading to an increased risk of falls.

The UL of 10 mg/day for free nicotinic acid is not applicable during pregnancy or lactation because of inadequate data relating to this critical life stage. The ULs for intake by children and adolescents have been derived on the basis of their body weights.

In summary, the ULs for **free nicotinic acid** for the various age groups are:

1-3 years	**2 mg/day**
4-8 years	**3 mg/day**
9-13 years	**6 mg/day**
14-18 years	**9 mg/day**
adults	**10 mg/day**

Nicotinamide
For nicotinamide a NOAEL of 1800 mg/day was established based on the absence of adverse effects in recent trials of high quality. An uncertainty factor of 2 has been used to allow for the fact that adults may eliminated nicotinamide more slowly than the study groups, many of which were children, and that data for children would not reflect the full extent of intersubject variability that could occur in an older population. The UL for nicotinamide is established at 900 mg/day for adults.

The UL of 900 for nicotinamide is not applicable during pregnancy or lactation because of inadequate data relating to this critical life stage. The ULs for intake by children and adolescents have been derived on the basis of their body weights

In summary, the ULs for **nicotinamide** for the various age groups are:

1-3 years	**150 mg/day**
4-8 years	**250 mg/day**
9-13 years	**500 mg/day**
14-18 years	**750 mg/day**
adults	**900 mg/day**

Dietary intake

Estimated dietary intakes of niacin were calculated for total dietary niacin from all foods in the diet, as well as for nicotinic acid from FBs only, both expressed as niacin equivalents (NE).

The concentration of nicotinic acid requested to be added to formulated beverages was 2.5 mg NE/600 ml reference quantity.

Estimated intakes of niacin from all foods in the diet were adjusted using second day NNS data.

Standard 1.3.2 – Vitamins and Minerals in the Code currently permits niacin to be added to a small range of foods, including some cereal based products, yeast extracts and legume based products. The concentrations of niacin in foods were those determined for the 1995 Australian and 1997 New Zealand NNSs expressed as NE. From the data it was not possible to distinguish between niacin present as nicotinic acid or nicotinamide. The food name descriptors used in the NNSs did not allow foods that may have been fortified with niacin to be identified.

Estimated intakes of niacin from all dietary sources increased by around 1 mg NE/day for all population groups assessed when FBs are consumed. Estimated intakes of niacin from all foods in the diet were not compared to a UL, as the UL is for free nicotinic acid added to foods.

Table 6: Estimated dietary intakes of total niacin from all foods (as NE), before and after FBs are introduced into the diet

	Mean intake mg NE/day		95th percentile intake mg NE/day	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	23.8	24.6	32.5	33.2
4-8 years, Aus	27.8	28.9	40.6	42.5
5-6 years, NZ	^23.9	NA	#30.3	NA
7-10 years, NZ	^28.0	NA	#38.5	NA
9-13 years, Aus	35.5	36.9	54.7	55.8
11-14 years, NZ	^32.8	NA	#43.2	NA
14-18 years, Aus	41.9	43.7	70.6	72.7
15-18 years, NZ	36.9	37.9	56.7	58.2
≥19 years, Aus	41.3	42.2	68.1	69.2
≥19 years, NZ	35.4	35.9	56.3	57.2

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Intakes of niacin as free nicotinic acid were estimated from added sources only in the diet. Baseline intakes could not be estimated, as the form of niacin in foods reported as consumed in the NNSs could not be determined. Therefore, it was assumed that no foods were fortified with nicotinic acid for the baseline estimate of intake.

For scenario 2 where FBs are consumed in place of other beverages in the diet, estimated intakes (adjusted using second day NNS data) did not exceed the UL for free nicotinic acid for any population group at the estimated mean intake, and only exceeded the UL at the 95th percentile intake for children aged 2 to 8 years.

Table 7: Estimated dietary intakes of nicotinic acid (as NE) from formulated beverages only, after FBs are introduced into the diet, and percent of the upper level (UL)

	Mean intake mg NE/day (%UL)	95th percentile intake mg NE/day (%UL)
Age group	**Scenario 2***	**Scenario 2***
2-3 years, Aus	1.00 (50)	2.86 (140)
4-8 years, Aus	1.31 (45)	3.17 (110)
5-6 years, NZ	NA	NA
7-10 years, NZ	NA	NA
9-13 years, Aus	1.63 (25)	3.70 (60)
11-14 years, NZ	NA	NA
14-18 years, Aus	1.90 (20)	5.08 (55)
15-18 years, NZ	1.35 (15)	3.62 (40)
≥19 years, Aus	0.97 (10)	3.19 (30)
≥19 years, NZ	0.65 (6)	2.30 (25)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

The hazard characterisation identified that it was appropriate to set different ULs for nicotinic acid and nicotinamide. Both forms are permitted forms for niacin in the Code (Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions). Therefore two different types of modelling were performed. In the first model, total niacin intake was calculated based on all foods in the diet at baseline and for Scenario 2, without making a distinction between nicotinic acid and nicotinamide. This modelling was performed because the UL for nicotinamide is based on total intake from all foods. The second model assumed at baseline that there are no foods on the market fortified with nicotinic acid since this form is currently not permitted to be added to beverages in the Code (Standard 1.3.2 – Vitamins and Minerals), and the UL for nicotinic acid relates only to the free form of nicotinic acid.

The dietary modelling for total intakes of niacin from the whole diet indicated that if nicotinamide were added as the permitted form to formulated beverages there are no safety concerns, since no adverse effects have been observed at much higher levels of intake (NOAEL was 1800 mg/day vs. intake levels of 30-70 mg/day for various age-groups).

The addition of nicotinamide to formulated beverages at a level of 2.5 mg in a 600 ml serve poses no appreciable risk to public health and safety.

For estimated intakes of niacin from added sources in FBs only, assuming that the permitted form would be nicotinic acid children at the 95th percentile intake, aged 2-8 years exceeded the UL for nicotinic acid (140% UL and 105% UL for age groups 2-3 and 4-8 years, respectively).

The UL for free nicotinic acid was derived from data on flushing, following administration of a single oral dose given in solution added to tomato juice and consumed with a meal. For children the level was based on a body weight basis. Flushing is not reported as being associated with the bound forms of nicotinic acid present in food. Very large single doses of nicotinic acid cause hypotension, although tolerance develops to this effect after several days of continued high dose intake. The adverse effects are considered mild and reversible (flushing) and have been based on the possibility that the flushing detected at higher doses in young subjects could result in transient hypotensive episodes later in life when elderly. Theoretically if flushing occurred in the elderly, it could exacerbate mild postural hypotension, and could increase the risk of falls, which are a common cause of morbidity in the elderly.

The relevance of flushing as an adverse effect in children is however questionable.

The addition of nicotinic acid to formulated beverages at a level of 2.5 mg in a 600 ml serve might pose a small risk for children, resulting in flushing. This particular adverse effect however is considered to be of minor significance for children.

In conclusion, the addition of niacin (all permitted forms) to formulated beverages at a level of 2.5 mg in a 600 ml serve poses no appreciable public health and safety risk.

Folate

Hazard identification and characterisation

Chemistry

Folate is a water-soluble vitamin. The term *folate* is used generically to refer to the various forms of the vitamin, both naturally-occurring and synthetic, and its active derivatives (Department of Health, 2000). Naturally-occurring folate generally contains more than one, typically five to seven, glutamate moieties attached to pteroic acid (polyglutamate). Folic acid (pteroylmonoglutamic acid) is the most common form of synthetic folate and contains a single glutamate moiety attached to pteroic acid. Folic acid is the most stable form of folate and is most often used in vitamin supplements and in fortified foods.

Function

Folate coenzymes within the cell are involved in one-carbon transfer reactions, including those involved in phases of amino acid metabolism, purine and pyrimidine synthesis, and the formation of the primary methylating agent, S-adenosylmethionine.

Sources of folate

Natural forms of folate are found in a wide variety of foods including green leafy vegetables, cereals, fruits, grains, legumes, yeast extract, and liver. Dietary forms are broken down to monoglutamates during storages processing and cooking. The synthetic pharmaceutical form used for food fortification and in supplements is folic acid, as this compound is more stable in comparison to other forms of the vitamin.

Absorption, distribution, metabolism and excretion

The majority of dietary folate is absorbed within the proximal region of the small intestine by active, carrier-dependent mechanisms, and also by passive diffusion. Polyglutamate forms are first hydrolysed to monoglutamates by conjugase enzymes within the enterocyte brush border. Ingested folic acid is enzymatically reduced and methylated within the intestinal lumen and enterocytes, although ingestion of high concentrations results in the direct appearance of the compound, unmodified, in the plasma.

Naturally-occurring food folate has been found to be only approximately 50% bioavailable. Folic acid supplements taken on an empty stomach have been shown to be 100% bioavailable, while folic acid added to food, or supplements taken with food are approximately 85% bioavailable.

Absorbed folate is excreted into the bile and undergoes entrohepatic circulation and reabsorption. The liver is also the main storage site, containing approximately half of the total body folate. The majority of plasma folate is present as 5-methyl-tetrahydrofolates (THF)-monoglutamate. Within cells, folate is retained in the cytoplasm by polyglutamation. 5-Methyl-THF is not a good substrate for polyglutamation, and must be first converted, via a vitamin B_{12}-dependent reaction, to THF. Alternatively, folic acid can be converted to polyglutamate (i.e. metabolically active) forms via a vitamin B_{12}-independent pathway.

Folate is excreted in the urine, either as the metabolically active form or as breakdown products, and in the faeces.

Toxicity

From the available data it can be concluded that (synthetic) folic acid used in supplements can cause adverse effects at high dose levels, whereas no adverse effects have been reported with the consumption of excess folate from foods.

Folic acid may lead to reversal of the haematological symptoms of vitamin B_{12} deficiency, potentially allowing the neuropathy associated with vitamin B_{12} deficiency to develop untreated. Vitamin B_{12} deficiency is most prevalent in older people. A serious adverse effect known in humans is the potential of progression of the neurological symptoms associated with vitamin B_{12} deficiency. Masking of the vitamin B_{12} deficiency in PA patients occurs with high frequencies and consistently with daily intakes of 5 mg; however, insufficient data are available for evaluation of dose levels between 1-5 mg. Both the US and EU considered the level of 5 mg per day as the LOEL.

Folic acid is generally considered safe when used therapeutically. Adverse effects may, potentially occur in specific groups, such as individuals being treated with drugs that interact with folic acid metabolism. Women who take folate supplements at up to 4 mg/day in order to reduce the risk of neural tube defect in the foetus do not report adverse effects.

Evaluation

Folate	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000b)	1.0 (as folic acid)	Suppl	progressing neurological symptoms in vitamin B_{12} deficient patients	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	1.0 (as folic acid)	Suppl	masking vitamin B_{12} deficiency	human
EU (European Commission Health & Consumer Protection Directorate-General, 2000c)	1.0 (as folic acid)	Suppl	progressing neurological symptoms in vitamin B_{12} deficient patients	human

* Guidance level

Both the US and EU concluded that the progression of the neurological symptoms due to folic acid supplementation should be considered as the most serious adverse effect. Masking of the haematological signs in pernicious anaemia patients was considered a diagnostic problem that could be circumvented by using more specific tests to identify cases of undiagnosed B_{12} deficiency. Both the US and EU set a LOAEL of 5 mg folic acid and used an uncertainty factor of 5 because no NOAEL could be derived resulting in an UL of 1 mg of folic acid. No data are available to suggest that other life-stage groups have increased susceptibility to adverse effects of high folic acid intake. Therefore, the UL is also applicable for pregnant or lactating women. The UL of 1000 µg/day for adults was adjusted for children and adolescents on the basis of relative body weight and values have been rounded down.

Based on the data considered in the US and EU evaluations, the ULs for **folic acid from fortified foods or supplements** for the various age groups are as follows:

1-3 years: 300 µg/day
4-8 years: 400 µg/day
9-13 years 600 µg/day
14-18 years 800 µg/day
19 and older 1000 µg/day

Dietary intake

Dietary modelling has been performed for folic acid only for the risk assessment, where for the baseline situation, it has been assumed that only breakfast cereals are fortified with folic acid.

Food composition data in the NNS were for total dietary folate for each food, not from added sources only so could not be used in this risk assessment. Therefore, a dataset was constructed assigning folic acid concentrations to breakfast cereals to enable an intake of folic acid from added sources to be estimated for the baseline and with FBs included in Scenario 2. The requested concentration of folic acid to be added to FBs was 50 µg/600 ml reference quantity.

Estimated intakes for folic acid increase around 30 µg/day with the consumption of FBs. Estimated intakes do not exceed the UL for any population group assessed.

Table 8: Estimated dietary intakes of folic acid from fortified foods only, before and after FBs are introduced into the diet, and percent of the upper level (UL)

	Mean intake µg/day (%UL)		95th percentile intake µg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	43.7 (15)	64.8 (20)	94.0 (30)	125.9 (40)
4-8 years, Aus	52.8 (15)	79.7 (20)	133.6 (35)	167.5 (40)
5-6 years, NZ	NA	NA	NA	NA
9-13 years, Aus	69.1 (10)	102.9 (15)	208.1 (35)	246.3 (40)
7-10 years, NZ	NA	NA	NA	NA
11-14 years, NZ	NA	NA	NA	NA
14-18 years, Aus	66.5 (8)	106.8 (15)	228.1 (30)	272.0 (35)
15-18 years, NZ	37.1 (5)	65.4 (8)	146.7 (20)	173.4 (20)
≥19 years, Aus	44.8 (4)	64.9 (6)	156.6 (15)	187.9 (20)
≥19 years, NZ	35.4 (4)	48.8 (5)	146.7 (15)	148.0 (15)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
NA = not assessed, because the New Zealand 2002 CNS did not include folic acid in isolation of folate.

Risk characterisation

Folate supplementation is recommended at a dose of 400 µg per day for women of childbearing age, and this needs to be taken into consideration when assessing the risk of high intake of folic acid.

For the adult population the 95th percentile intake was approximately 150 µg/day of folic acid for both Australia and New Zealand populations from fortified foods, including formulated beverages. In children, consumption of fortified foods would result in 95th percentile intakes there were 35-40% of the UL for the various age groups.

If it is assumed that all women of childbearing age took folic acid supplementation at the recommended dose of 400 µg per day, this would still not result in the UL for folic acid being exceeded. For children, folic acid supplementation is not considered to be relevant, since they are not a target group.

Therefore, the addition of folic acid to formulated beverages at a level of 50 µg in a 600 ml serve poses no public health and safety risk assuming only breakfast cereals are fortified.

Vitamin B_6 (pyridoxine)

Hazard identification and characterisation

Chemistry

Vitamin B_6 comprises a group of six related compounds, pyridoxal, pyridoxine, pyridoxamine and their respective 5'-phosphates. Pyridoxal 5'-phosphate is a coenzyme for more than 100 enzymes involved in amino acid metabolism, including aminotransferases, decarboxylases, racemases, and dehydratases.

Function

The cofactor forms of pyridoxine are pyridoxal-5'-phosphate and pyridoxamine-5'-phosphate. Pyridoxal phosphate is involved as a cofactor particularly in the metabolic transformation of amino acids, including decarboxylation, transamination and racemisation. Vitamin B_6 is a cofactor in the conversion of tryptophan to 5-hydroxytryptamine and of methionine to cysteine. Pyridoxine can modify the action of steroid hormones in vivo by interacting with steroidreceptor complexes. Pyridoxine is essential for the manufacture of prostaglandins and for the formation of red blood cells.

Pyridoxine is involved in cellular replication and antibody production. An adequate supply of pyridoxine is necessary for the function of the nervous system. The vitamin is involved in the biosynthesis of several neurotransmitters, including serotonin, gamma amino-butyric acid (GABA), dopamine and noradrenaline and so has a role in the regulation of mental processes and mood. It is also involved in sodium-potassium balance, histamine metabolism, the conversion of tryptophan to niacin, absorption of vitamin B_{12} and the production of hydrochloric acid in the gastrointestinal tract.

Clinical signs of deficiencies include retarded growth, acrodynia, alopecia, skeletal changes and anaemia, while changes in neurotransmitters such as dopamine, serotonin, noradrenalin, tryptamine, tyramine, histamine, GABA and taurine, affect brain function and can lead to seizures and convulsions.

Sources of vitamin B_6

Pyridoxine is found in chicken (4.2 mg/kg), fish, liver, kidney, pork, eggs (1.1 mg/kg), milk, wheat germ (11.5 mg/kg) and brewer's yeast (25 mg/kg). Other sources include brown rice (5.5 mg/kg), soybeans (6.3 mg/kg), oats, whole-wheat grains, peanuts and walnuts (7.3 mg/kg). Long-term storage, canning, roasting or stewing of meat and food processing techniques can destroy pyridoxine. Boiling reduces the pyridoxine content of food because of losses into the water. In Australia and New Zealand various foods can be voluntary fortified with vitamin B_6 at levels of 0.11-0.5 mg per reference dose (Standard 1.3.2 – Vitamins and minerals).

Absorption, distribution, metabolism and excretion

The phosphate forms of vitamin B_6 in food are dephosphorylated in the intestinal lumen, and pyridoxine, pyridoxal and pyridoxamine are taken up from the small intestine by an energy dependent process. All three are converted to pyridoxal phosphate in the tissues.

A proportion of the vitamin B_6 present in plant-based foods is biologically unavailable because it is present as pyridoxine glycosides that are not hydrolysed by intestinal enzymes. These glycosides may be absorbed, but do not act as a coenzyme in the body and are excreted unchanged in the urine.

All three forms of vitamin B_6 (pyridoxine, pyridoxal and pyridoxamine) are readily absorbed in the small intestine. The extent of absorption is decreased following gastric resection or in patients with malabsorption syndrome. Excess pyridoxine is excreted in the urine, and an adequate daily intake is therefore essential.

Pyridoxine in food is converted to active forms in the liver, a process which requires zinc and riboflavin. Vitamin B_6 is stored in the liver, with about 50% also being present in muscle, bound to glycogen phosphorylase. Pyridoxine is also stored in the brain.

The total body storage for adults is between 6 and 27 mg. Pyridoxine in the form of pyridoxal crosses the placenta, with foetal plasma concentrations being five times the level found in maternal plasma. The three forms of vitamin B_6 are present in body tissues, mainly as 5-phosphorylated derivatives of pyridoxal and pyridoxamine. The half-life of pyridoxine is 15-20 days, and it is not significantly bound to plasma proteins.

Pyridoxine, pyridoxal and pyridoxamine are all largely metabolised in the liver through phosphorylation by pyridoxal kinase. Pyridoxine phosphate is oxidised to the active coenzyme form, pyridoxal-5-phosphate, by an enzyme found mainly in liver. Pyridoxal-5-phosphate interconverts with pyridoxamine-5-phosphate through enzymatic transamination. The phosphorylated forms are hydrolysed by phosphatases. Pyridoxal is oxidised in the liver to pyridoxic acid.

Pyridoxic acid, the main excretory metabolite, is eliminated via the urine.

Toxicity

High doses of vitamin B_6 have been used for the treatment of premenstrual syndrome, depression, Down's syndrome, hyperkinesis, autism, neurosis, Hodgkin's disease and Parkinson's disease.

The principal toxicity of concern associated with excessive intakes of vitamin B_6 is neuronal damage, and sensory and motor effects. The initial observations were from studies in experimental animals, but more recent studies using human volunteers and patients, as well as case reports, have shown that the effects can also be produced also in humans. The effect occurs after consumption of high doses and/or long duration. Generally the symptoms are reversible once the exposure is stopped but in some cases involving high doses, the effects are irreversible. Progressive sensory ataxia occurs, presenting initially as unstable gait and numb feet, then numbness in the hands, followed by profound impairment of position sense and vibration sense in the distal limbs. The senses of touch, temperature and pain are less affected.

The available dose-response data in humans are difficult to analyse because many of the publications relate to case reports and true incidence data are not available. It is generally accepted that 500 mg of pyridoxine daily represents a potentially toxic dose for adults. The data for doses between 100 mg/day and 500 mg/day are less clear, largely because they relate to case reports or observations in groups of patients, that were not subject to a proper double-blind, placebo-controlled evaluation. The various studies show clear effects at 500 mg/day or more, a low incidence of effects at 200 mg/day in one study (if taken for up to 2 years) and the possibility of effects at about 100 mg/day (if consumed for about 3 years). In consequence a clear NOAEL has not been established and an intake of 100 mg/day cannot be excluded as a possible effect level for long-term intake.

Evaluation

Vitamin B_6	**UL in adults, mg/day**	**Total diet / Suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000b)	100	Total diet	neuropathy	human
UK (UK Expert Group on Vitamins and Minerals, 2003)	10	Suppl	histological changes in nerves	dogs
EU (European Commission Health & Consumer Protection Directorate-General, 2000h)	25	Total diet	neurological effects	human

The US has set the UL for vitamin B_6 at 100 mg/day, based on neuropathy in human studies. A NOAEL of 200 mg/day could be identified by the critical evaluation of two studies, one where 70 patients with diabetic neuropathy or carpal tunnel syndrome were treated with 100 to 150 mg/day of pyridoxine- some for up to 5 years. In this study no sensory neuropathy was detected. In the second study 24 patients were treated for carpal tunnel syndrome with pyridoxine at doses of 100 to 300 mg/day for 4 months. A NOAEL of 200 mg/day represents the average of 100 and 300 mg/day. Other studies supported a NOAEL of 200 mg/day. An uncertainty factor of 2 was selected based on the limitations of the data, and therefore the UL in the US is set at 100 mg/day.

The UK stated that the human data are inadequate to establish an UL, since the effect levels are unclear and the studies at low levels of intake are of limited quality. Therefore the safe upper level is based on animal data, in which histological changes were apparent in the nerves of dogs treated with 50 mg/kg bw/day for 100-112 days. Clinical signs of toxicity were not apparent in this group but were observed in the high dose group, which received 200 mg/kg bw/day. Using uncertainty factors of 300 (consisting of 3 for LOAEL to NOAEL extrapolation of a histopathological change, 10 for inter-species and 10 for inter-individual variation) a safe UL of 0.17 mg/kg bw/day can be derived. This relates to supplemental pyridoxine because the basal pyridoxine content of the diet in the key study is unknown. This UL is equivalent to 10 mg/day in a 60 kg adult.

The EU derived the UL from a study where vitamin B_6 intake and clinical signs were monitored in women attending a private clinic specialising in the treatment of premenstrual tension. Based on the apparent inverse relationship between dosage and duration of intake, a significant difference in duration of intake (average 2.9 years), but not dosage in women with 'neurological effects' while taking low doses is exactly the relationship that would be predicted. An upper level has been calculated by dividing the average intakes in this study of approximately 100 mg per day (the mean intake was 117 mg/day and the median was <100 mg/day) by a factor of 2, because the intake corresponds to a possible effect level for long-term intake, and by a second factor of 2 to allow for deficiencies in the database. A larger uncertainty factor was not considered necessary, because the data were for a sub-group with high plasma concentrations, and because the resulting UL of 25 mg per day has not been associated with adverse effects in any of the large number of published studies. Therefore the upper limit in the EU is 25 mg/day.

As the UL of both the EU and US were based on human data, using total dietary intake, they are considered more relevant than the UL derived by the UK. The UL from the EU report is considered the most relevant, because it was derived from longer-term studies in humans as compared to the US UL, and the apparent inverse relationship between dose and time of treatment.

Based on the data from the EU evaluation, the ULs for **vitamin B_6** for all age categories are:

1-3 years	**7 mg/day**
4-8 years	**10 mg/day**
9-13 years	**15 mg/day**
14-18 years	**20 mg/day**
Adult	**25 mg/day**

Dietary intake

Estimated dietary intakes were calculated for vitamin B_6 from all foods in the diet, and have been adjusted using second day intakes from the NNSs. Estimated intakes at baseline and for Scenario 2 are shown in Table 9.

Vitamin B_6 was not included in the 1995 Australian NNS. Therefore, in order to estimate intakes for the Australian population, the concentration data from the New Zealand NNS were matched to the most appropriate Australian food code, and these values were used to estimate dietary intakes for the Australian population groups.

The concentration of vitamin B_6 requested to be added to formulated beverages was 0.4 mg pyridoxine/600 ml reference quantity.

Estimated intakes of vitamin B_6 increased by around 0.5 mg/day or less when FBs are consumed, across all population groups assessed. Estimated mean intakes are lower for Scenario 2 when it is assumed FBs are consumed, compared to baseline for 15-18 year olds from New Zealand. This would be due to consumers substituting an FB for a beverage or beverages that were higher in vitamin B_6 content than the FB.

Estimated intakes do not exceed the UL for any population group assessed.

Table 9: Estimated dietary intakes of Vitamin B_6, before and after FBs are introduced into the diet, and per cent of the upper level (UL)

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	1.2 (15)	1.3 (20)	1.7 (25)	1.9 (30)
4-8 years, Aus	1.2 (10)	1.4 (15)	1.9 (20)	2.2 (20)
5-6 years, NZ	^1.2 (**)	NA	#1.6 (**)	NA
7-10 years, NZ	^1.3 (**)	NA	#1.8 (**)	NA
9-13 years, Aus	1.6 (10)	1.8 (10)	2.4 (15)	2.7 (20)
11-14 years, NZ	^1.5 (**)	NA	#2.1 (**)	NA
14-18 years, Aus	1.7 (9)	2.1 (10)	3.2 (15)	3.7 (20)
15-18 years, NZ	1.6 (8)	1.5 (7)	2.1 (10)	2.3 (10)
≥19 years, Aus	1.6 (6)	1.7 (7)	2.8 (10)	3.0 (10)
≥19 years, NZ	1.5 (6)	1.4 (6)	2.3 (9)	2.3 (9)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Toxicological evaluation and dietary intake data indicate that no age-groups are likely to approach the UL -set for vitamin B_6, either at the mean level of intake or at the high level of intake when included in formulated beverages (7%UL and 10%UL for Australia and 6%UL and 10%UL for New Zealand, for mean and high consumer adults respectively). The group exposed to the highest level as a percentage of the UL were children aged 2-3 years. High consumers in this age group were still only estimated to have an intake of vitamin B_6 equivalent to 30% of the UL.

It is concluded that addition of vitamin B_6 to formulated beverages at a level of 0.4 mg pyridoxine in a 600 ml serve poses no appreciable public health and safety risk.

Vitamin B_{12}

Hazard identification and characterisation

Chemistry
Vitamin B12 (cobalamin, Cbl) is a water-soluble vitamin and a member of a family of related molecules known as corrinoids which contain a corrin nucleus made up of a tetrapyrrolic ring structure. The centre of the tetrapyrrolic ring nucleus contains a cobalt ion that can be attached to methyl, deoxyadenosyl-, hydroxo- or cyano- groups.

Function
Vitamin B_{12} plays a specific role in amino acid metabolism, i.e. in methylation reactions together with folate, in the methionine synthase reaction, and in the rearrangement of methylmalonyl CoA in succinyl CoA.

Sources of Vitamin B_{12}

Major dietary sources of vitamin B12, mainly in the forms of methyl, deoxyadenosyl- and hydroxocobalamin, include meat, particularly liver and fish. Hydroxocobalamin and, in particular, cyanocobalamin are synthetic forms used in the fortification of food.

Absorption, distribution, metabolism and excretion

Vitamin B_{12} requires intrinsic factor (IF), secreted mainly from the gastric parietal cells, to ensure adequate absorption at normal dietary intake levels. Thus the absorption of physiological doses of vitamin B_{12} is limited to approximately 0.0015 – 0.002 mg/dose or meal, due to saturation of the uptake system. Regardless of dose, approximately 1.2% of vitamin B12 is absorbed by passive diffusion and consequently this process becomes quantitatively important at pharmacological levels of exposure. Protein binding in certain foods may reduce the bioavailability of the vitamin, particularly in individuals with impaired gastric acid and/or digestive enzyme secretion. The different forms of crystalline cobalamin appear to be absorbed or retained to different extents, depending on the dose. Differences are most apparent at low doses.

Ingested vitamin B_{12} is released from the food matrix by the action of digestive enzymes and gastric acid and becomes bound to salivary haptocorrin-binding proteins. As the pH rises further along the gut, and under the influence of pancreatic enzymes, vitamin B_{12} is released from the salivary haptocorrin and becomes complexed with intrinsic factor (IF). The cobalamin-IF complex binds to a specific cell wall receptor of the ileal enterocyte and is internalised by endocytosis. Once inside the cell, the IF is degraded and the liberated vitamin is converted to the methyl or the deoxyadenosyl form, is bound to transcobalamin II (TC II) binding protein and then exported into the portal blood. In the general circulation, most cobalamin is bound to transcobalamin I (TC I) but the majority of cobalamin available for uptake into the tissues is that bound to TC II.

Vitamin B_{12} is distributed into the liver, bone marrow and virtually all other tissues, including the placenta and breast milk of nursing mothers. The liver is the predominant storage site for vitamin B_{12}. Uptake into cells occurs through receptor mediated endocytosis involving specific TC II cell wall receptors. Once inside the tissues/cells, the complex is degraded by the lysosomes, and the released cobalamin is metabolised either to methyl-cobalamin in the cytosol, where it binds to methionine synthase, or to deoxyadenosyl-cobalamin in the mitochondria, where it binds to methylmalonyl CoA mutase.

Excretion occurs mainly via the faeces and urine, but also through the shedding of skin cells. Excretion is very slow, with significant enterohepatic cycling.

Toxicity

No adverse effects have been associated with excess vitamin B_{12} intake from food or supplements in healthy individuals. Vitamin B_{12} has a history of safe long-term use as a therapeutic agent given in high dosage per os, or via intramuscular injections, for treatment of disorders associated with impaired vitamin B_{12} absorption, such as in gastrectomy and malabsorption.

No systematic toxicological studies have been reported for vitamin B12. There are no reports attributing carcinogenic, mutagenic or teratogenic potential to cyanocobalamin. In one study a tumour promoting effect was reported in a rat model, but this study is not considered relevant for safety assessment in humans.

There are also no adverse effects known for vitamin B_{12} from foods, or from supplements in amounts far in excess of needs. Some studies suggested acne formation after high parenteral doses of hydroxocobalamin, but not with cyanocobalamin, or after a combination of vitamins A, B_6 and B_{12} given orally.

Oral and parenteral supplementation with dosages between 1-5 mg every fortnight or month have been given for long periods, up to at least 5 years, to patients with compromised vitamin B_{12} absorption, without any identified adverse effects. It should be noted, however, that these studies were not designed to identify adverse effects.

Evaluation

Vitamin B_{12}	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000b)	N/A		No adverse effects	
UK (UK Expert Group on Vitamins and Minerals, 2003)*	2.0	Suppl	No adverse effects	Humans
EU (European Commission Health & Consumer Protection Directorate-General, 2000f)	N/A		No adverse effects	

N/A not applicable
* Guidance level

There are no clearly defined adverse effects produced by vitamin B_{12} that can be used to define a LOAEL or NOAEL, and which can be used as a basis for deriving an UL.

When high doses are given orally only a small percentage of vitamin B_{12} can be absorbed from the gastrointestinal tract, which may explain the apparent low toxicity.

Based on the data considered in the US and EU evaluation, **vitamin B_{12}** has a very low oral toxicity, and therefore an **UL does not need to be established**.

Dietary intake

No dietary intake estimates were calculated for thiamin, as it was determined to have very low oral toxicity, and no upper levels have been established, as outlined above.

Risk characterisation
No UL has been established for vitamin B_{12}, based on the lack of adverse effects even at high doses. Therefore, no dietary modelling was required.

In conclusion, the addition of vitamin B_{12} to formulated beverages at a level of 0.5 µg per 600 ml serve poses no appreciable public health and safety risk.
Vitamin C

Hazard identification and characterisation

Chemistry
Vitamin C is a six-carbon compound structurally related to glucose, consisting of two inter-convertible compounds: L-ascorbic acid, which is a strong reducing agent, and its oxidised derivative L-dehydroascorbic acid.

Function
Vitamin C is a strong reducing agent and as an antioxidant is involved in prevention of the damaging effects of free radicals. Vitamin C is involved in the synthesis of collagen, neurotransmitters and carnitine; it is an enzyme co-factor and also increases the gastrointestinal absorption of non-haem iron.

Sources of vitamin C
Food of plant origin, particularly citrus and soft fruits and leafy green vegetables, are major sources of vitamin C. Kidney and liver are good animal-derived sources of vitamin C.

Absorption, distribution, metabolism and excretion
Gastrointestinal absorption of vitamin C is efficient and occurs in the small intestine via a saturable active transport mechanism. Absorption efficiency of low oral doses of vitamin C (4-64 mg) may be as high as 98%, but decreases with increasing doses of the vitamin.

Ascorbic acid is widely distributed in all tissues of the body, with higher levels found in the adrenal glands, pituitary and retina, and lower levels in kidney and muscle tissue. Vitamin C is oxidised to dehydroascorbic acid, which is hydrolysed to diketogulonic acid and then oxidised to oxalic and threonic acid. Some oxidation to carbon dioxide occurs at high doses.

Unmetabolised vitamin C and vitamin C metabolites, such as oxalate, are largely excreted in urine. Approximately 3% of a 60 mg oral dose is excreted in the faeces. More of the vitamin is excreted unchanged at higher levels of vitamin C intake.

Toxicity
The vitamin is of low acute toxicity as indicated by the limited data available from studies in animals and humans. Despite the extensive use of high doses of vitamin C in some vitamin supplements, there have been few controlled studies that specifically investigated adverse effects. Overall, acute gastrointestinal intolerance (e.g., abdominal distension, flatulence, diarrhoea, transient colic) is the most clearly defined adverse effect at high intakes, but there are limited data on the dose-response relationship for adults or for groups such as children or the elderly.

The US evaluation considered a 3 g/day intake as the LOAEL, based on human data which suggest that an intake of vitamin C greater than 3 g/day is likely to cause osmotic diarrhoea in many individuals, although some reports involving a few individuals suggest this may occur at 3 g/day.

While there is uncertainty whether high intakes of vitamin C increase renal excretion of oxalate which could increase the risk of renal stones, an increased risk of kidney stones was not found in individuals with habitual intakes of 1.5 g/day.

Evaluation

Vitamin C	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000c)	2000	Suppl	osmotic diarrhoea and gastrointestinal	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	1000	Suppl.	gastrointestinal	human
EU (The Scientific Panel on Dietetic Products, 2004)	-		insufficient data	
WHO/FAO (FAO/WHO, 2002)	1000*	total	gastrointestinal	human

* Guidance level

Available human data suggest that supplemental daily doses of vitamin C up to about 1 g in addition to normal dietary intakes are not associated with adverse gastrointestinal effects, but that acute gastrointestinal effects may occur at higher intakes (3-4 g/day). While there is uncertainty whether high intakes of vitamin C increase renal excretion of oxalate, which could increase the risk of renal stones, an increased risk of kidney stones was not found in individuals with habitual intakes of 1.5 g/day. The absorption of vitamin C is saturated at high doses, and therefore intakes above 1 g/day would be associated with negligible increased uptake and tissue levels, but an increased risk of adverse gastrointestinal effects. There are no data on the gastrointestinal absorption or tolerability of esterified forms of vitamin C, such as ascorbyl palmitate, but such esters might be expected to show similar properties, and therefore this conclusion applies to these forms as well as ascorbic acid and its salts.

The US set a UL for vitamin C based on osmotic diarrhoea. The US used an uncertainty factor of 1.5 to extrapolate from LOAEL to NOAEL. Thus the 3 g/day intake is considered a LOAEL, and a NOAEL of 2 g/day is estimated for adult humans. Because the database has no other significant sources of uncertainty and because of the mild, reversible nature of osmotic diarrhoea caused by high vitamin C intakes, no further uncertainty factors were considered necessary.

The evaluation from the FAO/WHO was very limited and based on osmotic diarrhoea.

Gastrointestinal effects are the most common adverse effects but these are associated with acute, high doses of vitamin C given over a short period of time.

Based on the data considered in the US, UK and EU evaluation, **vitamin C** has a very low oral toxicity, and therefore an **UL does not need to be established**. For guidance purposes, a dose of 1000 mg/day, in addition to normal dietary intakes, would not be expected to have any significant adverse effects.

Dietary intake

Intakes of vitamin C were estimated at baseline and for scenario 2 assuming FBs are consumed. Results are shown in Table 11. The estimated intakes have been adjusted based on second day nutrient intakes from the NNSs.

The concentration of vitamin C requested to be added to formulated beverages was 40 mg/600 ml reference quantity.

Intakes of vitamin C increased by around 10 to 15 mg/day when FBs are consumed, depending on the population group assessed. Estimated intakes were not compared to ULs as none were established for vitamin C.

Table 11: Estimated dietary intakes of Vitamin C, before and after FBs are introduced into the diet

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	105	113	215	197
4-6 years, Aus	106	115	216	195
5-6 years, NZ	^104	NA	#156	NA
7-10 years, Aus	108	124	245	246
7-10 years, NZ	^113	NA	#159	NA
11-14 years, Aus	114	133	235	253
11-14 years, NZ	^117	NA	#193	NA
15-18 years, Aus	131	156	273	315
15-18 years, NZ	123	142	225	252
≥19 years, Aus	124	138	251	269
≥19 years, NZ	111	119	213	224

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation
Dietary intake of vitamin C for high consumers at baseline was estimated to be 210-250 mg per day for adults, and at 220-270 mg per day for adults when FBs are consumed. These intake of vitamin C are significantly lower than the guidance level of 1000 mg/day.

In conclusion, the addition of vitamin C to formulated beverages at a level of 40 mg per 600 ml serve poses no appreciable public health and safety risk.

Vitamin D

Hazard identification and characterisation

Chemistry
Vitamin D refers to a group of fat-soluble seco-steroid compounds. Two nutritionally significant compounds are vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Both vitamins are metabolised in the liver and kidney to an active steroid hormone.

Function
The principal function of vitamin D ($1,25(OH)_2D$) in the body is to maintain intracellular and extracellular calcium concentrations within a physiologically acceptable range. The vitamin accomplishes this goal through the action of $1,25(OH)_2D$ on regulating calcium and phosphorus metabolism in the kidney, small intestine and bone.

In the kidney, $1,25(OH)_2D$ regulates calcium transport in the proximal tubule; in the small intestine, it regulates calcium and phosphate uptake from the gut. $1,25(OH)_2D$ is also involved in the maintenance of plasma calcium levels via bone resorption and formation. $1,25(OH)_2D$ regulates the synthesis of parathyroid hormone (PTH) by a negative feedback mechanism.

Sources of vitamin D

Throughout the world, the major source of vitamin D for humans is the exposure of the skin to sunlight. During sun exposure, the ultraviolet B photons with energies between 290 and 315 nm are absorbed by cutaneous 7-dehydrocholesterol to form the split (seco) sterol previtamin D_3. Upon prolonged UV exposure a regulation mechanism is operating in that both previtamin D_3 and vitamin D_3 can be photolysed to inert compounds. Hence, sunlight alone apparently cannot cause overt toxicity due to overproduction of vitamin D. Some studies indicate that the degree of pigmentation of the skin also has an impact on the amount of vitamin D synthesised as melanin absorbs UV B photons: the darker the skin, the less is produced. Skin thickness decreases linearly with age from the age of 20 years and there is a marked decrease in the precursor 7-dehydrocholesterol in the skin and less vitamin D production.

Vitamin D is found in only a few foodstuffs, with fatty fish and fish oils, liver, milk and eggs being the main natural sources. In Australia and New Zealand various products can be fortified with vitamin D (10 to 25% of the recommended daily intake) according to Standard 1.3.2 – Vitamins and Minerals.

Furthermore, in Standard 2.4.2 – Edible oil spreads, table edible oil spreads and table margarine, must contain no less than 55 μg/kg of vitamin D. However this subclause does not apply to table edible oil spreads and table margarine produced in, or imported into, New Zealand.

Absorption, Distribution, Metabolism and Excretion

Vitamin D is absorbed from the small intestine as bile salt-dependent micelles and circulated in the body via the lymph. Absorption of polar derivatives, such as 25(OH)D, is more efficient and less dependent on bile salts. These polar derivatives are generally not present in any significant amount in food or food supplements, although small amounts of 25(OH)D are found in meat and breast milk.

The importance of the chemical form of vitamin D, i.e. vitamin D_2 or D_3 with a lower biological efficiency of vitamin D_2, should be noted. In addition the vehicle used (fat or emulsion) could influence bioavailability. Vitamin D from cod liver oil emulsified in milk is about three times as potent as vitamin D given in cod liver oil or propylene glycol.

There is substantial storage of vitamin D in adipose tissue. Vitamin D is metabolised to the steroid hormone 1,25-dihydroxyvitamin D ($1,25(OH)_2D$), a process which is promoted by parathyroid hormone (PTH). The first step of activation takes place by hydroxylation at position C-25, mainly in the liver. The product, 25-hydroxyvitamin D (25(OH)D), is transported to the kidneys, where 1α-hydroxylation takes place and the active form of vitamin D is formed. This reaction is regulated by parathyroid hormone (PTH), which is secreted in response to low plasma calcium levels.

The 25-hydroxylation of vitamin D is poorly regulated, i.e. the capacity of the 25-hydroxylase in the liver is high. The levels of 25(OH)D increase in proportion to vitamin D intake, and for this reason, plasma 25(OH)D levels are commonly used as indicator of vitamin D status.

There is a consensus that serum 25(OH)D concentration is a correct functional indicator of vitamin D status. A level of 25(OH)D below 27.5 nmol/L is considered to be consistent with vitamin D deficiency in infants, neonates and young children. Little information is available about the level of 25(OH)D needed to maintain normal calcium metabolism and peak bone mass in adolescents and middle aged adults. For elderly there is increasing evidence of a greater requirement of vitamin D to maximise bone mineralization. Less certain and more controversial is the optimal serum concentration of 25(OH)D.

Vitamin D is principally excreted in the bile. It is also metabolised to water-soluble metabolites, such as calcitroic acid, and excreted in the urine.

Toxicity

The principal critical effect of hypervitaminosis D/vitamin D toxicity is hypercalcaemia. It has, however, been reported that patients with hypervitaminosis D (increased level of 25(OH)D >130 nmol/L), hypercalciuria and a depressed PTH status can be normo-calcaemic. Thus, hypercalciuria apparently is an earlier phenomenon than hypercalcaemia that could predispose to kidney stone formation.

There is limited evidence that suggests that direct effects of high concentrations of vitamin D may be expressed in various organ systems, including kidney, bone, central nervous system, and cardiovascular system.

The most frequently noted clinical manifestations of hypervitaminosis D are anorexia, weight loss, weakness, fatigue, disorientation, vomiting and constipation. Hypercalcaemia may also lead to growth retardation in children, irritability, asthenia, persisting fever, polyuria and polydipsia, dehydration, hypertension and functional renal insufficiency. Long-term toxicity with persistent hypercalcaemia may cause excess calcium precipitates as extra-skeletal calcium in soft tissues, particularly in the renal parenchyma, urinary tracts, vascular walls, muscles and tendons.

The vitamin D intake associated with exceeding the upper reference value of 25(OH)D in serum would vary greatly in the population. It is, for instance, dependent on the exposure to sunlight and sensitivity to vitamin D. The importance of the chemical form of vitamin D, i.e. vitamin D_2 or D_3 with a lower biological efficiency of vitamin D_2, should be noted. In addition the vehicle used (fat or emulsion) could influence bioavailability. Vitamin D from cod liver oil emulsified in milk is about three times as potent as vitamin D given in cod liver oil or propylene glycol. For some individuals an intake of 250 µg vitamin D would not exceed of this value while in others this could occur. Data indicate that the upper reference value of serum 25(OH)D at 150 nmol/L or 200 nmol/L is exceeded by 5% of the population at an approximate vitamin D intakes of about 80 or 100 µg/day, respectively. These levels of 25(OH)D in serum can be considered NOAELs with respect to increased risks of hypercalciuria and hypercalcaemia, respectively. On the other hand, two studies reported that the upper reference serum concentration of 25(OH)D was not exceeded upon supplementation with 100 µg cholecalciferol (vitamin D_3)/day.

Taking into account all the information the risk of hypercalciuria/hypercalcaemia probably starts to increase in some parts of the population at an intake above 100 μg vitamin D/day. The risk of exceeding the upper reference concentration of 25(OH)D in serum will also increase. A dose of 100 μg vitamin D/day and a serum level of 200 nmol 25(OH)D/L are considered a NOAEL.

Children
In infants the regulation of 1α-hydroxylase and the normal feedback suppression by $1,25(OH)_2D$ on the kidney enzyme seem to work less well compared to adults.

The upper reference level for 25(OH)D for infants is similar to that of adults and the approach used for adults by setting the UL at an oral dose of vitamin D not associated with exceeding the upper reference level (i.e. 130-150 nmol/L) could in theory be done. A problem is that there are very few data on doses of vitamin D above the recommended intake and corresponding concentrations of 25(OH) in serum.

A small and old study considering hypercalcaemia indicated a NOAEL of 45 μg vitamin D/day for infants. However, in two more recent and larger well-controlled studies in infants receiving 25 μg vitamin D_2/day in addition to breast milk or 32 μg vitamin D_2/day, hypercalcaemia was not observed. Based on these data, a NOAEL of 25 μg/day can be derived.

Vulnerable groups
The feedback mechanism of $1,25(OH)_2D$ synthesis seems to operate poorly, if at all, in tissues other than that of the renal tubule. In patients with sarcoidosis, $1,25(OH)_2D$ is believed to be synthesised in macrophages, which in these patients have an increased enzyme capacity, or other cells in the granulomas. Also the clearance of $1,25(OH)_2D$ may be decreased. Contrary to normal in these patients there is a positive correlation between 25(OH)D within reference levels and 1,25(OH)2D in serum. Even normocalcaemic patients with sarcoidosis have unregulated production of $1,25(OH)_2D$ in response to vitamin D. Also exposure to sunlight may increase the level of active metabolite.

In some lymphomas, typically B-cell lymphomas, there is an increased blood level of $1,25(OH)_2D$, which is probably synthesised by lymphocytes.

Excessive endogenous synthesis of $1,25(OH)_2D$ occurs in children with subcutaneous fat necrosis.

Vitamin D deficiency can mask primary hyperparathyroidism and this could account for the occasional cases of hypercalcaemia observed when large groups of elderly people are given vitamin D supplements.

Evaluation

Vitamin D	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000a)	0.050	total diet	serum calcium levels	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	0.025	suppl	serum calcium levels	human
EU (European Commission Health & Consumer Protection Directorate-General, 2002d)	0.050	total diet	serum calcium levels	human

* Guidance level

The EU evaluation was the most extensive evaluation available for vitamin D. The following paragraphs are from the EU evaluation.

The EU established a NOAEL of 100 µg/day for the adult population. An uncertainty factor of 2 is considered adequate to account for the inter-individual variation. An UL of 50 µg vitamin D/day is considered to offer adequate protection against the risk of hypercalciuria and hypercalcaemia.

The EU indicated that no data was available to suggest that other life-stage groups have increased susceptibility to adverse effects of high vitamin D intake. Given the minor impact of circulating vitamin D on calcium levels *in utero* and in breast-fed infants with maternal supplements of 25 and 50 µg vitamin D/day there does not seem to be an increased sensitivity during this period. Therefore the UL of 50 µg/day should be considered to apply also to pregnant and lactating women.

For infants, the lower values from studies with infants taking into account the higher biological activity and toxicity of vitamin D_3 and the other information provided above an UL of 25 µg vitamin D/day for infants 0-24 months of age is derived. It seems that susceptibility towards vitamin D changes with age. Using a cautious approach taking into consideration a lower weight in children up to 10 years the following upper limits are set: UL of 25 µg vitamin D/day for children from 2 up to and including 10 years of age and an UL of 50 µg/day for adolescents 11-17 years of age.

It should be noted that the intake of vitamin D via food would add to synthesis caused by exposure to sunlight. Depending on the amount of sunlight the risk of adverse effects at an intake at the UL would increase.

Based on the data considered in the EU evaluation, the UL for **vitamin D** for the various age groups are:

1-10 years 25 µg/day
11 and over 50 µg/day

Dietary intake

Intakes for vitamin D were estimated at baseline and for Scenario 2 assuming FBs were consumed.

The concentration of vitamin D requested to be added to formulated beverages was 2.5 µg/600 ml reference quantity.

Vitamin D was not included in the 1995 Australian NNS, therefore, there were no concentration data available in DIAMOND for Vitamin D for Australia. Vitamin D was included in the New Zealand 1997 NNS, however, was not included in the New Zealand 2002 CNS. The concentrations of Vitamin D in food from the 1997 New Zealand NNS were matched to the most appropriate foods in the 1995 Australian NNS to enable an estimated intake to be calculated for Australia.

Estimated intakes for vitamin D were able to be adjusted for the majority of the population groups assessed apart from respondents aged 4-18 years for Australia. Where second day adjustments could be made, these were presented as the estimated intakes, as they provide a better indication of longer term nutrient intakes. Where second day adjustments could not be made, this was due to limited sample numbers in certain age groups and the distribution of intakes which meant the calculations could not be made. The estimated intakes for vitamin D for the population groups with unadjusted intakes will be higher at the 95th percentile than those for similar age groups that have adjusted intakes. The estimated intakes for younger children in New Zealand 5-14 years were not included in the 2002 New Zealand children's nutrition survey and therefore could not be include here (Ministry of Health, 2003).

Estimated intakes of vitamin D increased by around one to two micrograms per day with the consumption of FBs. Estimated intakes did not exceed the UL for any population group assessed.

Table 12: Estimated dietary intakes of Vitamin D, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake µg/day (%UL)		95th percentile intake µg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	1.3 (5)	2.2 (9)	2.1 (8)	4.2 (15)
4-8 years, Aus^	1.5 (6)	2.8 (10)	3.6 (15)	6.7 (25)
5-6 years, NZ	NA	NA	NA	NA
7-10 years, NZ	NA	NA	NA	NA
9-13 years, Aus^	2.0 (4)	3.7 (7)	5.2 (10)	8.6 (15)
11-14 years, NZ	NA	NA	NA	NA
14-18 years, Aus^	2.1 (4)	4.3 (9)	5.4 (10)	10.9 (20)
15-18 years, NZ	2.3 (5)	2.3 (5)	4.1 (8)	4.1 (8)
≥19 years, Aus	2.0 (4)	3.0 (6)	3.8 (8)	6.1 (10)
≥19 years, NZ	2.4 (5)	2.4 (5)	3.9 (8)	4.0 (8)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
NA = not assessed, because Vitamin D was not included in the New Zealand 2002 CNS.
^ Not adjusted for second day intakes.

Risk characterisation

Toxicological evaluation and dietary intake data indicate that both children and adult Australian and New Zealand consumers are unlikely to approach the UL set for vitamin D, at the high level of intake either at baseline or when included in formulated beverages (10% UL and 8% UL for adults from Australia and New Zealand, respectively).

The group with the highest level of intake as a percentage of the UL were children aged 4-8 years (25% UL), at a level of intake still well below the UL.

Therefore, dietary intake of vitamin D for all consumers is considered to be within the safe range of intake for both mean and high consumers.

In conclusion, the addition of vitamin D to formulated beverages at a level of 2.5 μg in a 600 ml serve poses no appreciable public health and safety risk.

Vitamin E

Hazard identification and characterisation

Chemistry
Vitamin E is the term used to describe a group of related fat-soluble tocochromanols, including eight naturally occurring components, which exhibit antioxidant activity and are nutritionally essential. The two major homologous series of tocochromanols, the tocopherols and tocotrienols, both have vitamin E activity in humans and animals and are synthesised by higher plants and cyanobacteria.

In all homologues, the basic structural unit is a chroman ring system (2-methyl-6-hydroxychroman) with an isoprenoid side chain of 16 C atoms. The compounds, including α-, β-, γ-, and δ-homologues, differ in number and position of the methyl substituents in the chroman ring. Tocopherols differ from their corresponding tocotrienols in having a saturated side chain. The presence of the phenolic hydroxyl group in the tocochromanols is important for their activity as antioxidants. At least one methyl group in the benzene ring is of primary importance. α-Tocopherol with three methyl groups is the most active of all homologues, followed by β-, γ-, and δ-tocopherol. The only forms retained in human plasma are the RRR-α-tocopherol and the 2R-stereoisomers, RSR-, RRS- and RSS-α-tocopherol; the various 2S-stereoisomers (SRR-, SSR-, SRS- and SSS-α-tocopherol) which form part of synthetic *all rac-α*-tocopherol are not maintained in plasma. The vitamin E activity is expressed as *RRR*-α-tocopherol equivalents, which accounts for about 90% of the activity in human tissue; the relative potency of α-, β-, γ-, and δ-tocopherol is reported to be approximately 100:50:25:1. The commercially available synthetic form is all rac-α-tocopheryl acetate with the activity of 0.67 x *RRR*-α-tocopherol. For practical purposes, 1 International Unit (I.U.) of vitamin E is referred to as 1 mg of all rac-α-tocopheryl acetate.

In this assessment the term vitamin E is related to α-tocopherol equivalents.

Function
The basic mode of action of tocopherols in human tissue is to prevent the oxidation of polyunsaturated fatty acids (PUFA) by trapping free radicals and donating hydrogen. It is effective in protecting the integrity of lipid and phospholipid in membranes and thus the requirement for vitamin E and the recommended intake is determined to a large extent by the intake of PUFAs. It has been shown that increasing the PUFA content of a diet low in α-tocopherol equivalents has adverse effects on tocopherol status.

Sources of vitamin E
The major food sources of vitamin E are vegetable oils, unprocessed cereal grains, and nuts with smaller amounts in fruits and vegetables and meats (mainly the fatty portion).

Absorption, distribution, metabolism and excretion

The bioavailability of vitamin E is related to the efficiency of absorption. Intestinal absorption of lipids and fat-soluble vitamins depends on pancreatic function, biliary secretion to form micelles with the hydrolysed fat, and transfer across intestinal membranes. Nearly all of the vitamin E absorbed across the intestinal mucosa is free tocopherol. *In vivo* and *in vitro* studies suggest that the rate of uptake of vitamin E is controlled by passive diffusion. Absorption of tocopherols is incomplete; the extent of absorption is dependent on intake and varies between 20-80%. The proportion absorbed decreases with increasing amount added to experimental diets; the average absorption is about 40-60% while pharmacological doses of 200 mg and more are absorbed to the extent of <10%. Cannulation studies indicate that there is no difference in absorption between α-tocopherol and α-tocopheryl acetate at physiological doses. At high levels of intake, (>400 IU/day) a higher degree of absorption was obtained with free tocopherol than tocopheryl esters.

About 90% of the free α-tocopherol is transported via the lymphatic system into the bloodstream, where it is distributed into lipoproteins on passage into the liver. The main systemic transport system of tocopherols is the LDL-fraction (55-65%) followed by the HDL (24-27%) and VLDL (8-18%). There is very close correlation (r=0.925) between the total serum α-tocopherol and that portion carried by LDL.

In human metabolism, vitamin E is known to interact with other nutrients which are also involved in the pathways of oxidation processes. Vitamin C, selenium and zinc interact synergistically with vitamin E. Conversely, an iron overload is associated with a lowering of serum vitamin E levels.

At normal intake levels, vitamin E is conjugated with glucuronic acid and this conjugate is excreted (via bile) in the faeces. Up to 30-70% of vitamin E is excreted via this route with less than 1% being excreted in the urine. Some vitamin E may be eliminated via the skin.

Toxicity

Animal studies

Vitamin E has a very low acute oral toxicity.

Two long-term studies of up to 16 months and 2 years duration respectively have been conducted in rats (Yang and Desai, 1977; Wheldon *et al*., 1983). A LOAEL of 500 mg/kg body weight/day can be identified based on a critical evaluation by Wheldon et al (Wheldon *et al.,* 1983). They fed rac-α-tocopheryl acetate to Charles River CD strain rats at levels of 500, 1000, or 2000 mg/kg body weight/day for 104 weeks. Haemorrhages from the gut, the urinary tract, the orbit and meninges, and the claws were observed in male rats only by week 15 in the highest-dose group, by week 16 in the intermediate-dose group, and by week 18 in the low-dose group. Additional vitamin K supplementation (10 mg vitamin K_3/day) was initiated at week 24 and prothrombin times returned to normal by week 26. Although this was a chronic study, the correction of vitamin K levels at week 24 means that the combined vitamin E-vitamin K effect was evaluated only on a sub-chronic basis. The only other treatment-related effect of significance was the presence of vacuolated lipid staining macrophages in the liver.

Human studies
Vitamin E has low toxicity. At very high doses, however, vitamin E can produce signs indicative of antagonism with the function of other fat-soluble vitamins (vitamins A, D, K). Isolated reports of adverse effects in humans consuming up to 1000 IU of vitamin E per day include headache, fatigue, nausea, double vision, muscle weakness, mild creatinuria and gastrointestinal distress. A number of human supplementation studies on vitamin E are available.

The principal negative effect observed was on prothrombin time or other factors related to blood clotting. In several studies no effects were reported but in others there were effects on blood clotting and it was claimed that high doses of vitamin E only influenced blood clotting in cases of low vitamin K status. One of the reported adverse effects concerns decreased blood coagulation. Studies with healthy humans with vitamin E supplementation have shown that there are no changes in platelet aggregation or adhesion with daily vitamin E intake up to 800 mg α-tocopherol equivalents (1,200 IU). The question of bleeding time was studied by Meydani et all (Meydani *et al*., 1998) who found no adverse effects, including the bleeding time, after a 4-month daily supplementation with 60, 200 or 800 IU (40, 134 or 537 mg α-tocopherol equivalents) vitamin E (88 healthy volunteers, aged >65 years divided between control and three dose groups, extensive measurements of parameters). The published reports concluded that vitamin E at high dietary intakes affects blood coagulation if vitamin K status is inadequate. High doses of α-tocopherol affected the vitamin K metabolism by reducing the cyclooxygenase pathway and therefore thromboxane synthesis, thus impairing the thromboxane-dependent blood coagulation and also decreasing the coagulation factor II and VII. It was suggested that high doses (800-1200 α-tocopherol equivalents) should be avoided for two weeks prior to and following surgery. In a critical comment on the high upper level for vitamin E of 1000 mg/day derived by the US Food and Nutrition Board attention was drawn to the observation that the tendency to haemorrhage in aspirin users is increased by vitamin E (Liede *et al*., 1998).

The effects on blood clotting are not, however, the only adverse effects requiring consideration. Side effects reported in therapeutic use of vitamin E supplements include severe muscular weakness and fatigue induced in adults receiving daily doses of 720 mg α-tocopherol. These side effects were confirmed in a double-blind study on two healthy male subjects given the same dose of α-tocopherol and the symptoms were associated with a large increase in 24 hr urinary creatinine and elevated serum creatine phosphokinase.

When patients with porphyria cutanea tarda were given daily doses of 1.0 g α-tocopherol for 3 months there was a marked increase in 24 hour urinary androgens (androsterone, etiocholanolone plus dehydroepiandrosterone) from 3.5 to 4.6 mg/day while mean 24 hour pregnanediol fell from 2.2 to 0.5 mg/day. The authors concluded that the significance of these endocrine changes was uncertain but could be important for patients with endocrine sensitive tumours.

A group of 52 elderly patients (average age 72 years) showed an average increase in serum cholesterol of 74 mg/dL when given repeated daily doses of 300 mg α-tocopherol. Conversely, no such increase was seen in a small group of healthy men taking 588 mg α-tocopherol (800 I.U.) daily.

There are limited data relating to the effects of vitamin E on morbidity and mortality from chronic diseases. In the ATBC study (ATBC study group 1994) an increase was observed in the numbers of deaths from haemorrhagic stroke among male smokers. Although the number of haemorrhagic stroke cases with 50 mg α-tocopherol was 66 compared to 44 in the control group (total n = 29,133) no statistical significance was published. A more recent analysis of this study indicated that there was an increased risk of subarachnoidal haemorrhage in hypertensive men (RR 2.45; CI 1.08-5.55) and a significantly higher mortality. Gingival bleeding occurred more frequently in subjects who were also taking aspirin. In two other studies, the Secondary Prevention with Antioxidants of Cardiovascular Disease in endstage renal disease (SPACE) and the Primary Prevention Project Collaborative Group of the Primary Prevention Project, (Boaz *et al*., 2000; de Gaetano, 2001) there was a non-statistically significant increase in fatal haemorrhages.

Evaluation

Vitamin E	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000c)	1000	Suppl	haemorrhagic toxicity	animals
UK (UK Expert Group on Vitamins and Minerals, 2003)	540	Suppl	blood clotting	human
EU (European Commission Health & Consumer Protection Directorate-General, 2003d)	300	Total	blood clotting	human

US (2000)
Based on considerations of causality, relevance, and the quality and completeness of the database, the US selected haemorrhagic effects as the critical endpoint on which to base the UL for vitamin E. The human data fail to demonstrate consistently a causal association between excess α-tocopherol intake in normal, apparently healthy individuals and any adverse health outcome. The human data demonstrating the safety of supplemental α-tocopherol have been accumulated primarily in small groups of individuals receiving supplemental doses of 3,200 mg/day of α-tocopherol or less (usually less than 2,000 mg/day) for relatively short periods of time (weeks to a few months). Thus, some caution must be exercised in judgments regarding the safety of supplemental doses of α-tocopherol over multiyear periods.

The haemorrhagic effects seen in experimental animals are encountered only with very high doses of α-tocopherol and can be corrected by administration of supplemental vitamin K. A LOAEL of 500 mg/kg body weight/day was derived from a rat study (Wheldon *et al.,* 1983). Although this was a chronic study, the correction of vitamin K levels at week 24 means that the combined vitamin E-vitamin K effect was evaluated only on a subchronic basis. An uncertainty factor of 36 was used (2 LOAEL-NOAEL; 2 subchronic-chronic; 3 interspecies; 3 intraspecies). With this uncertainty factor the US established a UL of 1,000 mg/day.

EU (2003)
The establishment of a NOAEL depends on the interpretation of asymptomatic effects on clinical biochemical parameters reported in some human studies and supported by similar effects in experimental animals.

No NOAEL could be established from the chronic toxicity studies in the rat with respect to blood clotting and liver histology. The Committee decided that the critical effect is on blood clotting and that the study by Meydani et al (Meydani *et al.,* 1998) provided the best basis for an evaluation of the UL. The NOAEL established in this study was 540 mg/day. The Committee concluded that an uncertainty factor of 2 would adequately cover inter-individual differences in sensitivity. Therefore, EU established a UL for vitamin E of 270 mg/day for adults, rounded to 300 mg/day.

UK (2003)
In the trials by Gillilan *et al.* (Gillilan *et al*., 1977) and Meydani *et al.* (Meydani *et al.,* 1998) the biochemical and physiological effects of vitamin E were investigated in some detail and the findings indicate that supplemental doses of 800 to 1600 IU/day are without apparent adverse effect. The results were derived from small groups that may not be representative, thus an additional uncertainty factor could be applied to account for interindividual variation. However, the results of the larger CHAOS trial (2002 patients with atherosclerosis, 3-981 days of treatment with 800 IU/day for first 546 patients and 400 IU for remainder; (Stephens *et al*., 1996) support the view that 800 IU/day supplemental vitamin E would not result in any adverse effects and, taking the three studies together, no further uncertainty factors are necessary.

UK recommended a Safe Upper Level of 800 IU/day (540 mg *d*-α-tocopherol equivalents/day) supplemental vitamin E . This is equivalent to 9.0 mg/kg bw/day for a 60 kg adult. Assuming an intake of 18 mg/day from food, a total intake of 560 mg *d*-α-tocopherol equivalents/day would not be expected to result in any adverse effect. This is equivalent to 12.4 mg/kg bw/day.

Evaluation by FSANZ
The US evaluation is now somewhat dated since there are now additional clinical studies with larger patient groups and for longer duration available. Without going back to the original studies, it is not possible to comment on the reasons for establishing an uncertainty factor of 36.

The evaluation of both EU and UK are based on human studies. Both EU and UK decided that the Meydani study (Meydani *et al.,* 1998)was the most relevant clinical study, because it looked at an extensive range of relevant safety parameters. The NOAEL in this study is 540 mg/day. The disadvantage of this study is that the number of subjects was low (17-19 subjects/group) and the duration was only 4 months.

The EU in their evaluation has chosen a UF of two because they considered it would adequately cover inter-individual differences in sensitivity. A larger uncertainty factor was not considered necessary because data from a number of other, albeit older and less well-controlled studies showed no adverse effects at considerably higher intakes.

The UK did not consider a UF necessary because the CHAOS trial supports the view that 800 IU/day would not result in any adverse effect. This was slightly unusual since the UK report itself indicated that the CHAOS trial was limited in its capacity to detect adverse effects.

FSANZ is of the opinion that a UF of 2 is warranted because, on the basis of the available data, there is still some uncertainty associated with the level of 540 mg/day being safe for the whole population.

The epidemiological studies indicated that severe adverse effects would not occur at the doses as administrated, but the studies were not designed specifically for assessing the safety assessment of vitamin E and thus more subtle effects would not be identified. The critical adverse effect indicated by the US, UK and EU reports is blood coagulation - this would not be assessed adequately in the prevention studies examined.

In conclusion, on the basis of the available data, FSANZ has established an UL of 300 mg/day for vitamin E, similar to the EU. There are no data specifically relating to children and adolescents. The UL for children and adolescents is derived by scaling the adult upper limit on the basis of body weight.

In summary, the UL for **vitamin E (as α-tocopherol equivalents)** for the various age groups are:

1-3 years	**70 mg/day**
4-8 years	**100 mg/day**
9-13 years	**180 mg/day**
14-18 years	**250 mg/day**
adult	**300 mg/day**

Dietary intake

Intakes of vitamin E were calculated at baseline, and assuming FBs were consumed in Scenario 2. Estimated intakes were adjusted based on second day intake data from the NNSs.

The concentration of vitamin E requested to be added to formulated beverages was 2.5 mg/600 ml reference quantity.

Concentrations of vitamin E for Australia were not available in the 1995 NNS, therefore, concentrations from the 1997 New Zealand NNS were matched to the most relevant food in the Australian NNS to allow dietary modelling to be conducted.

Estimated intakes for vitamin E increased from baseline by between 1 and 3 mg/day, depending on the population group assessed. Estimated mean intakes are lower for Scenario 2 when it is assumed FBs are consumed, compared to baseline for New Zealanders aged 19 years and over. This would be due to consumers substituting a FB for a beverage or beverages that were higher in vitamin E content than the FB. Estimated intakes of vitamin E did not exceed the UL for any population group assessed.

Table 13: Estimated dietary intakes of Vitamin E, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	6.0 (9)	6.9 (10)	9.2 (15)	10.7 (15)
4-8 years, Aus	7.0 (7)	8.3 (8)	10.8 (10)	12.6 (15)
5-6 years, NZ	^6.6 (**)	NA	#6.3 (**)	NA
7-10 years, NZ	^7.5 (**)	NA	#7.3 (**)	NA
9-13 years, Aus	9.1 (5)	10.8 (6)	13.8 (8)	16.1 (9)
11-14 years, NZ	^9.4 (**)	NA	#8.9 (**)	NA
14-18 years, Aus	9.5 (4)	11.5 (5)	15.4 (6)	18.7 (7)
15-18 years, NZ	10.2 (4)	9.9 (4)	15.6 (6)	15.3 (6)
≥19 years, Aus	9.6 (3)	10.6 (4)	16.1 (5)	17.6 (6)
≥19 years, NZ	10.0 (3)	9.5 (3)	15.9 (5)	15.5 (5)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Toxicological evaluation and dietary intake data indicate that both children and adult Australian and New Zealand consumers, are unlikely to approach the UL for vitamin E, at the high level of dietary intake, either at baseline or when included in formulated beverages (15% UL for children 2-3 years and 6% UL and 5% UL for adults from Australia and New Zealand, respectively). Therefore, dietary intake of vitamin E for all consumers is considered to be within the safe range of intake for both mean and high consumers.

In conclusion, the addition of vitamin E to formulated beverages at a level of 2.5 mg alpha-tocopherol equivalents in a 600 ml serve poses no appreciable public health and safety risk.

Biotin

Hazard identification and characterisation

Chemistry

D-Biotin (biotin, coenzyme R, vitamin H) is a water-soluble vitamin. It has a bicyclic ring structure. One ring contains an ureido group and the other contains a heterocyclic sulphur atom and a valeric acid side-group.

Function

Biotin acts as an essential cofactor for the acetyl-CoA, propionyl-CoA, ß-methylcrotonyl-CoA and pyruvate carboxylase enzymes, which are important in the synthesis of fatty acids, the catabolism of branched-chain amino acids and the gluconeogenic pathway. Biotin may also have a role in the regulation of gene expression arising from its interaction with nuclear histone proteins.

Sources of biotin

Biotin is widely distributed in natural foodstuffs but at very low levels compared to other water-soluble vitamins. Foods relatively rich in biotin include egg yolk, liver, kidney, muscle and organ meats, and some vegetables.

Absorption, distribution, metabolism and excretion

Biotin uptake from the small intestine occurs by a carrier-mediated process that operates with a high carrier affinity and also by slow passive diffusion. The carrier is driven by an electron-neutral sodium (Na+) gradient, has a high structural specificity and is regulated by the availability of biotin, with upregulation of the number of transporter molecules when biotin is deficient. The colon is also capable of absorbing biotin via a similar transport mechanism. Approximately 80% of biotin in plasma is in the free form and the remainder is either reversibly or covalently bound to plasma proteins. The existence of a specific biotin carrier protein in plasma is a subject of debate. Factors determining the bioavailability of biotin present in the diet are uncertain.

There are few data concerning the bioavailability of crystalline biotin supplements, but a recent study has suggested that doses as high as 22 mg may be completely absorbed. The nutritional significance of biotin synthesis by bacteria present in the lower gut is a subject of controversy.

Uptake into tissues occurs by specific transport mechanisms dependent upon Na+ gradients. Transplacental transport is thought to involve the active accumulation of biotin within the placenta followed by its passive release into the foetal compartment. Biotin is metabolically trapped within the tissues by its incorporation into carboxylase enzymes. In the normal turnover of cellular proteins, carboxylase enzymes are broken down to biocytin or oligopeptides containing lysyl-linked biotin. Biotin may be released for recycling by the hydrolytic action of biotinidase. Liberated biotin may be reclaimed in the kidney against a concentration gradient. Biotin not incorporated into carboxylase enzymes may be metabolised oxidatively at the sulphur present in the heterocyclic ring and/or at the valeric acid side chain.

Biotin metabolites are not active as vitamins and are excreted in the urine. Very little biotin is thought to undergo biliary excretion and the substantial amounts of biotin that appear in the faeces are derived from colonic bacteria.

Toxicity

The US considered the data on adverse effects from high biotin intake not sufficient for a quantitative risk assessment and a UL could not be derived. Several studies involving high biotin intakes reported no adverse effects. No adverse effects have been reported after intravenous administration of 50 mg of biotin to haemodialysis patients. Also no adverse effects have been reported in mother and infant after administration of 120 mg/day of biotin during the ninth month of pregnancy. Some case studies with 10 mg/day of biotin also did not report any adverse effects.

The animal toxicity database for biotin is very limited, especially when given by the oral route.

Evaluation

Biotin	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000b)	No UL		Insufficient data	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	0.9	Suppl	Insufficient data	human
EU (European Commission Health & Consumer Protection Directorate-General, 2001a)	No UL		Insufficient data	human

* Guidance level

No upper daily limit for biotin is set in either the EU (European Commission Health & Consumer Protection Directorate-General, 2001a) or the US (US Institute of Medicine, 2000b), based on the lack of data and no reported adverse effects in humans and animals. .

The EU characterised the risk of human toxicity from the usual dietary intake of biotin and from biotin supplements to be low according to available data. There are insufficient data to draw any conclusions concerning the safety of very high-level supplements.

Although no numerical UL can be established, existing evidence from observational studies indicates that current levels of intake from biotin in the EU from all sources do not represent a health risk for the general population

Based on the data considered in the US and EU evaluation, the available data on **biotin is too limited to set an UL.**

Dietary intake

There were no food composition data available to enable a comprehensive dietary intake assessment to be conducted for biotin. Whilst there are small amounts of data available, these data were either not from Australian or New Zealand sources, were not extensive enough across the whole diet, or were not in the correct format or had not been assessed for accuracy.

Risk characterisation

Due to insufficient data it was not possible to establish an UL for biotin. However this does not mean that there are hazards associated with high intakes of biotin. For biotin only limited food composition data are available therefore it is not currently possible to undertake a complete dietary intake assessment for biotin.

In the absence of sufficient information on potential adverse effects and food composition data it is currently not possible to evaluate the safety of the addition of biotin to formulated beverages.

Pantothenic acid

Hazard identification and characterisation

Chemistry
Pantothenic acid consists of a pantoic acid moiety amide-linked to a ß-alanine subunit. Pantetheine consists of pantothenic acid linked to a ß-mercaptoethylamine group. In living systems, the compound is a component of coenzyme A (CoA), which is composed of 4'-phosphopantetheine linked to adenosine 5'-monophosphate, modified by a 3'-hydroxyl phosphate. 4'-Phosphopantetheine is also found covalently linked to various proteins, particularly those involved in fatty acid metabolism.

Function
Pantothenate, usually in the form of CoA-containing species (e.g. acetyl CoA, succinyl CoA), fulfils multiple roles in cellular metabolism and in the synthesis of many essential molecules.

Sources of pantothenic acid
Pantothenic acid is widely distributed among foods, especially high concentrations are found in yeast and organ meat (liver, kidney), eggs, milk, whole grain cereals and vegetables. In most foods it is present in bound form (as CoA), requiring enzymatic treatment for analysis of total contents.

Absorption, distribution, metabolism and excretion
Pantothenic acid is readily absorbed throughout the gastrointestinal tract. Ingested CoA is hydrolysed within the intestinal lumen, via the formation of dephospho-CoA, phosphopantetheine and pantetheine, to pantothenic acid. Uptake of these latter two compounds into intestinal tissues has been demonstrated, and subsequently the enzyme, pantetheinase, can hydrolyse pantetheine to pantothenic acid. Uptake into intestinal cells occurs both by a sodium-dependent active transport mechanism and by passive diffusion. Limited data are available regarding the bioavailability of dietary pantothenic acid. One study found that pantothenic acid in natural foods was approximately 50% bioavailable compared with calcium pantothenate given in a formula diet, as assessed by subsequent urinary excretion of the vitamin.

Absorbed pantothenic acid is transported to body tissues via the blood, primarily as bound forms within erythrocytes. Plasma levels do not correlate well with dietary intake. The majority of tissues import pantothenic acid via an active sodium co-transport mechanism. Analysis of rat tissues has shown high concentrations of pantothenic acid in the heart and kidneys. CoA is synthesised from pantothenic acid within cells, with the first, and apparently rate-limiting, step catalysed by pantothenate kinase.

Catabolism of CoA leads to the formation of pantothenate, which is excreted in the urine. Excretion levels correlate well with dietary intake.

Toxicity
The available toxicological data on pantothenic acid are limited. However, case reports and some earlier, uncontrolled human studies suggested a lack of acute or chronic toxic effects of pantothenic acid compounds (calcium or sodium pantothenate, panthenol) at very high doses (approximately 10,000 mg/day, in some cases for a number of years). However, doses at such levels have been associated with diarrhoea and gastrointestinal disturbances.

In more recent, controlled studies, no side effects have been reported with pantothenic acid supplementation at levels up to approximately 2000 mg/day, for periods varying from several days to several weeks. These studies were generally designed to assess the potential benefits of pantothenic acid supplementation in specific subgroups, for example patients suffering joint disease.

Data regarding the toxicity of pantothenic acid and its commonly used pharmaceutical forms in experimental animals are also limited. However, doses of 500 and 2000 mg/kg bw/day in rats and 200-250 mg/kg bw/day in dogs and monkeys, given in the diet for periods of six months, were not associated with adverse effects.

Evaluation

Pantothenic acid	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000b)	N/A		Insufficient data, no adverse effects	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	200	Suppl	Insufficient data-	human
EU (European Commission Health & Consumer Protection Directorate-General, 2002b)	N/A		Insufficient data, no adverse effects	human

N/A not applicable
* Guidance level

No UL for pantothenic acid is set in either the EU (Scientific Committee on Food, 2003) or the US (United States Institute of Medicine, 2000a), based on the lack of data and no reported adverse effects in humans and animals.

Based on the data considered in the US and EU evaluation, **pantothenic acid** has a very low oral toxicity, and therefore an **UL does not need to be established**.

Permitted forms

The Applicant requested the following forms to be permitted for pantothenic acid: calcium pantothenate and dexpanthenol. Both forms are already permitted in Standard 2.9.1 – Infant Formula Products.

Within the assessment of pantothenic acid toxicity by the EU the following was stated on the various forms of pantothenic acid. *Pantothenic acid (MW 219.23) is the only occurring natural form. Free pantothenic acid and its sodium salt are chemically unstable, and therefore the usual pharmacological preparation is the calcium salt (calcium pantothenate). The alcohol, panthenol, is a synthetic form which can be oxidised in vivo to pantothenic acid*.

Dexpanthenol is a synonym of panthenol (The Merck Index, 2001).

In conclusion, the available evidence indicates that both calcium pantothenate and dexpanthenol are appropriate as permitted forms for pantothenic acid.

Dietary intake

No dietary intake estimates were calculated for pantothenic acid, as it was determined to have very low oral toxicity, and no upper levels have been established, as outlined above.

Risk characterisation
No UL is established for pantothenic acid, based on the lack of adverse effects even at high doses. Therefore, no dietary modelling was required.

In conclusion, the addition of pantothenic acid to formulated beverages at a level of 1.25 mg per 600 ml serve poses no appreciable public health and safety risk.

Calcium

Hazard identification and characterisation

Chemistry
Calcium is an alkaline earth metal belonging to Group II of the periodic table. It is a divalent cation with an atomic weight of 40. Calcium shows a single oxidation state of +2. It is the fifth most abundant element in the human body.

Function
In the vertebrate skeleton, calcium provides rigidity in the form of calcium phosphate, embedded in collagen fibrils. Calcium is also a key component in the maintenance of cell structure. Membrane rigidity, viscosity and permeability are partly dependent on local calcium concentrations. Calcium fulfils important physiological roles as a cofactor for many enzymes, as an important component of the blood clotting mechanism and through an active role as an intracellular signal. This signalling controls events such as cell aggregation, muscle contraction and cell movement, secretion, transformation and cell division, as well as muscle protein degradation.

Sources of calcium
Calcium must be ingested with the diet in sufficient amounts to allow for calcium deposition during bone growth and modelling and to compensate for obligatory intestinal, daecal and dermal losses during the life-time.

Foods vary widely in calcium content. The best sources are milk and milk products, from which about 32% is absorbable. Some plants are good sources of well-absorbable calcium, e.g. brassica, almonds, dried apricots. However, some vegetables contain considerable amounts of calcium, which is poorly absorbed because of a high content in oxalate (rhubarb, spinach) and which forms sparingly soluble calcium oxalate. Drinking water and mineral waters can also be good sources of absorbable calcium.

Within populations and population groups dietary calcium intakes show a great variability related to varying dietary habits.

In Australia and New Zealand various products can be voluntary fortified with calcium, such as breakfast cereals, certain milk products and analogues for milk products at 25 to 50% pf the recommended daily intake according to Standard 1.3.2 – Vitamins and Minerals.

Furthermore, FSANZ is currently assessing the extension of voluntary fortification of certain food groups with calcium in Application A424 – Fortification of Foods with Calcium and A500 – Addition of Calcium to Cereal Based Beverages.

Absorption, distribution, metabolism and excretion

About 25 - 50% of dietary calcium is absorbed and delivered to the exchangeable calcium pool. Most of the calcium in food is in the form of complexes with other dietary constituents, which must be broken down and the calcium released in a soluble and ionised form before it can be absorbed.

Calcium crosses the intestinal mucosa by both active and passive transport mechanisms. The active transport mechanism is a saturable, transcellular process which involves the calcium-binding protein, calbindin. Calbindin is regulated by the hormonal form of vitamin D (1,25-$(OH)_2D_3$). The passive transport mechanism is a nonsaturable, paracellular process which is not affected by calcium status or parathyroid hormone. The efficiency of calcium absorption increases when calcium intakes are low and decreases when calcium intakes are high.
Two major factors affect the efficiency of calcium absorption. Firstly, interactions with other dietary constituents can affect calcium absorption. Secondly, absorption is regulated by physiological factors, including hormones. Compounds enhancing calcium absorption include fibre, lactose, vitamin D. Dietary factors antagonising calcium absorption include vitamin D deficiency, calcium-phosphorus imbalance, phytic acid, oxalic acid, dietary fibre and excessive fat.

Fractional calcium absorption is highest (about 60%) in breastfed infants. Net calcium absorption, defined as intake minus faecal excretion in percent of intake, is lower in infants fed cows' milk formula, decreases in young childhood, shows a rise in puberty, decreases to 15 to 20% in young adults and declines gradually thereafter. Calcium absorption is increased in pregnant and lactating women compared to non-pregnant women.

The calcium content of the human body is 25 to 30 g at birth (0.8% of the body weight) and between 900 and 1300 g in adult men (up to 1.7% of body weight). Of this, 1% is located in the serum, lymph and other fluids and the remaining 99% is located in the bone (as hydroxyapatite) and teeth. The cellular regulation of calcium concentration is also important. The concentration of ionised calcium in serum is closely regulated to within 10% of approximately 2.5 mmol/l.. Calcium is present in blood in three different forms: as free Ca^{2+} ions, bound to protein (about 45%), and complexed to citrate, phosphate, sulphate and carbonate (about 10%).

Distribution of the free ionised calcium is dependent upon interactions between three major hormones, PTH, calcitonin and vitamin D. Additionally, other hormones affect calcium metabolism including oestrogen, testosterone, glucocorticoids, thyroid hormones, growth hormone and insulin.

The majority of absorbed calcium is stored in the skeleton. Excess absorbed calcium is excreted in urine, faeces, and to a lesser extent, sweat. Calcium balance is positive in healthy children, adolescents and young adults before bone growth and modelling cease, provided that they have an adequate calcium intake.

Renal calcium excretion is the result of glomerular filtration (about 8 to 10 g calcium per day in adults) and tubular reabsorption (normal over 98% of the filtered load), which is primarily passive in the proximal tubules and for 20% active in the distal part of the convoluted tubules and connecting tubules. Active transport is under the control of parathyroid hormone, calcitonin and $1,25(OH)_2D$. Renal excretion is not strongly related to dietary calcium intake in healthy persons.

Toxicity

This section of the assessment is mainly based on the EU assessment report (European Commission Health & Consumer Protection Directorate-General, 2003a).

Acute hypercalcaemia can impair renal function by causing vasoconstriction with consequent decreases in both the renal blood flow and glomerular filtration rate. Hypercalcaemia increases absorption of bicarbonate in the proximal tubule, thus predisposing the patient to metabolic alkalosis. Chronic hypercalcaemia, hyperphosphataemia and metabolic alkalosis promote irreversible renal calcification.

Calcium levels in the body are under control of genetic and hormonal factors. Therefore an excessive accumulation of calcium in blood or tissue solely through excessive calcium consumption should not occur in the absence of diseases such as bone cancer, hyperthyroidism, and hyperparathyroidism or in the absence of excessive vitamin D intake. Adverse effects which have been reported due to high calcium intakes include the so-called milk-alkali syndrome, the formation of kidney stones in persons with a propensity for nephrolithiasis, hypercalciuria and for hyperabsorption of calcium, and interference with the absorption of other minerals

Kidney function

Some peri-menopausal women with total calcium intakes between 2 and 3 g/day may show a tendency for compromised glomerular function as indicated by increases in serum creatinine. No such effect was observed in another study with women receiving comparable calcium amounts. This finding should be investigated systematically before it is attributed to calcium.

Milk-alkali syndrome

Manifestation of the milk-alkali syndrome through the combined intake of calcium both from food and especially from supplements and of absorbable alkalinising substances is facilitated by renal insufficiency, alkalosis and dehydration due to vomiting and anorexia and/or the use of thiazide diuretics, which increase renal tubular calcium reabsorption. All reported cases of milk-alkali syndrome in association with the prolonged or acute ingestion of calcium supplements used calcium carbonate as the nutrient source. In these reports the supplemental calcium intakes were reported as between 1.0 and 23 g/day. Their dietary calcium intakes are often not known. The US (1997) has taken the approximate median of 4.8 g of reported calcium supplements as the LOAEL for total calcium intake, applied an uncertainty factor of 2 and defined an upper level of 2.5 g calcium/day. The EU considered this LOAEL inappropriate. Seven low-supplement users are reported not to have an additional high dietary calcium intake (>0.9 g/day). It is questionable if it is justified to derive a LOAEL for the total dietary calcium intake from data on effects of alkalinising substances plus calcium.

The use of calcium carbonate supplements in doses up to 2000 mg/day, and thereby achieving total daily calcium intakes up to more than 3000 mg/day, for preventive purposes in presumably healthy subjects, has not provoked the development of the milk-alkali syndrome, whereas the administration of large amounts (11.2 g calcium/day) of calcium carbonate in addition to large amounts of milk (1.8 g calcium/day) over 7 days to 20 gastric/duodenal ulcer patients resulted in reversible hypercalcaemia (2.8 mmol/L) in nine patients and renal insufficiency in all. The control group of 20 patients with gastric/duodenal ulcers who received aluminium hydroxide and milk for the same duration did not develop these abnormalities.

Cases of milk-alkali syndrome have been reported with long-standing calcium intakes in the range of 2 to 2.5 g/day with chronic high intakes of antacids and of low supplemental calcium intakes (1g/day) in addition to unknown dietary intakes plus sodium bicarbonate. These observations seem to indicate that the harmful calcium dose can be lower than 3 g/day if taken together with alkali.

The EU concluded that on the basis of the available evidence, a calcium dose, which by itself might cause milk-alkali syndrome, could not be identified.

Kidney stones
The quantitative relationship between calcium intake, both from the diet and from supplements, and hypercalciuria as a risk factor for nephrolithiasis is far from clear. Also, it is dependent on other dietary factors, especially sodium intake. From epidemiologic studies it appears that dietary calcium intakes in the range of recent recommendations have a favourable effect in the prevention of kidney stone formation and that lower intakes increase the risk. From the available data no conclusion is possible on a detrimental calcium dose in individuals with idiopathic hypercalciuria (up to 6% of the population). From the study in patients with kidney stones and idiopathic hypercalciuria it can be deduced that a sodium restricted diet with a normal recommended calcium content of 1200 mg/day does not raise urinary calcium excretion but reduces it.

In conclusion, both observational studies on the relationship between total calcium intake and kidney stone incidence and interventional studies with calcium supplements do not allow definition of a calcium intake on a population basis which promotes kidney stone formation.

Interaction with minerals
The studies of acute effects of single calcium supplements at various doses and from various sources on iron and zinc absorption cannot be converted into general statements on a dose dependent negative effect of total daily dietary calcium intake, because the timing of the supplement and other interfering factors of the diet have to be taken into account.

The EU concluded that single-dose experiments demonstrate interference of both dietary and supplemental calcium with the absorption of other minerals. This effect is not demonstrable in long-term observational and interventional studies at dietary calcium intakes in the range of recommended intakes and at supplemental calcium of up to 2000 mg/day in adults and up to 1200 mg/day in one study with infants.

Vulnerable groups

Persons at risk from developing milk-alkali syndrome include those using drugs such as thiazide and those with renal failure. These groups should be identified and monitored for alkalosis and hypercalcaemia when using calcium supplements. This would be particularly important for patients with renal failure who already receive calcium carbonate therapy to control serum phosphorous levels.

Patients with absorptive or renal hypercalcuria, primary hyperparathyroidism and sarcoidosis may have a higher risk of renal stone formation following calcium supplementation.

It has been proposed that there may be an individual hypersensitivity to developing hypercalcaemia. This is because only a limited number of individuals develop the metabolic complications involved in MAS, and excessive calcium intake alone is not enough to induce hypercalcaemia.

Evaluation

Calcium	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000a)	2,500	Total	Milk-Alkali syndrome	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	1,500	Suppl	gastrointestinal	human
EU (European Commission Health & Consumer Protection Directorate-General, 2003a)	2,500	Total	evidence from different interventional studies	human

* Guidance level

FSANZ considers the EU assessment as the most comprehensive and complete and therefore the ULs are based on the EU assessment.

Adults

The UL for calcium is derived from different interventional studies of long duration in adults, some of which were placebo-controlled in which total daily calcium intakes of 2500 mg from both diet and supplements were tolerated without adverse effects. Because of the abundance of data the application of an uncertainty factor was considered unnecessary. An UL of 2500 mg of calcium per day for calcium intake from all sources is proposed. There are no data to suggest an increased susceptibility for pregnant and lactating women.

Children and adolescents

No adverse effects of calcium citrate-malate supplements (500 to 1000 mg calcium over 1.5 to 3 years) and of extra dairy foods or foods fortified with milk extracts (700 to 820 mg calcium extra over one year) were reported in 217 children between 6 and 14 and 6.6 and 11 years, respectively in comparison to unsupplemented controls.

These data are considered insufficient to derive an UL for children and adolescents. The EU decided that it was inappropriate to base the UL for calcium for this age group on the UL for adults of 2500 mg calcium/day, with correction for differences in basal metabolic rate using scaling according to body surface area (body weight$^{0.75}$).

For calcium deposition in bone during the growth period proportionality to lean body mass cannot be assumed. Therefore, age-dependent ULs for children and adolescents cannot be proposed.

The EU concluded in their risk characterisation that, although there are no data to set a numerical UL for children and adolescents no appreciable risk has been identified even with current extreme levels of calcium intake in this age group.

In summary, the UL for **calcium** for the various age groups are:
1-18 years not necessary to set UL, no risks identified in children
adults 2500 mg/day

Dietary intake

Intakes of calcium were estimated at baseline and when formulated beverages are consumed. Results are in Table 14. Estimated intakes were adjusted based on second day intake data from the NNSs.

The concentration of calcium requested to be added to formulated beverages was 200 mg/600 ml reference quantity.

Estimated intakes increased from baseline by around 100 mg/per day when FBs were consumed across the population groups assessed. The UL was not exceeded for adults in Australia or New Zealand.

Risk characterisation
Toxicological evaluation and dietary intake data indicate that adult Australian and New Zealand consumers are unlikely to approach the UL for calcium, either at the mean or high level of dietary intake, at baseline or including formulated beverages (40% UL and 70% UL for Australia and 35% UL and 60% UL for New Zealand, respectively). Therefore, the estimated dietary intake of calcium for adults is considered to be within the safe range of intake for both mean and high consumers.

If intakes for children and adolescents are compared to ULs for adults, 95th percentile consumers in the highest intake group (15-18 year old Australians, 2157 mg/day) have an intake below the UL. High intake of calcium in adolescents would most likely be beneficial for bone health.

In conclusion, the addition of calcium to formulated beverages at a level of 200 mg in a 600 ml serve poses no appreciable public health and safety risk, assuming baseline levels of fortification in other foods and not taking supplement use into account.

Table 14: Estimated dietary intakes of calcium, before and after FBs are introduced into the diet, and percent of upper level (UL) for adults

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	806	886	1257	1328
4-6 years, Aus	769	866	1253	1359
5-6 years, NZ	^675	NA	#960	NA
7-10 years, Aus	867	992	1440	1533
7-10 years, NZ	^730	NA	#1005	NA
11-14 years, Aus	927	1058	1633	1698
11-14 years, NZ	^839	NA	#1166	NA
15-18 years, Aus	963	1131	1928	2157
15-18 years, NZ	865	968	1604	1703
≥19 years, Aus	831 (35)	913 (35)	1555 (60)	1681 (65)
≥19 years, NZ	793 (30)	841 (35)	1397 (55)	1466 (60)

***** Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Chromium

Hazard identification and characterisation

Chemistry
Chromium is a metallic element that can exist in a variety of oxidation states; oxidation states other than 0, +2, +3 and +6 are uncommon. Biologically, trivalent (III) and hexavalent (VI) chromium are most important. Chromium in foods or supplements are in the trivalent form.

Function
Trivalent chromium has been shown to potentiate insulin action and thereby influences carbohydrate, lipid and protein metabolism.

Sources of chromium
Chromium in foods or supplements is in the trivalent form. Processed meats, whole grain products, pulses and spices are the better sources of chromium, but chromium levels are low in staple foods.

Absorption, distribution, metabolism and excretion
Intestinal absorption of trivalent chromium is low (0.5-2.0%). The mechanism of absorption has not been clearly defined, but it appears to involve processes other than passive diffusion.

Absorbed trivalent chromium does not enter blood cells, but binds to plasma proteins such as transferrin and is transported to the liver. In contrast, hexavalent chromium does penetrate red blood cells, where it is reduced by glutathione to trivalent chromium, which binds to haemoglobin. Excess hexavalent chromium is taken up into the kidneys, spleen, liver, lungs and bone.

Ingested trivalent chromium remains largely unabsorbed and is excreted via the faeces. Absorbed chromium is mainly excreted via urine, with only small amounts being eliminated in perspiration and bile.

Toxicity

The data on oral chromium toxicity are limited. However, it is apparent that the toxicity of chromium varies depending on the valency state, with hexavalent (VI) chromium, being generally more toxic than trivalent (III) chromium. This assessment concentrates on the evaluation of trivalent chromium, as this is the form found in food and dietary supplements. Ingested trivalent chromium has a low level of toxicity, due partly to its poor absorption. Chromic acid at chronic doses of up to 750 mg chromium/kg bw/day given in food to adult animals for periods of up to 24 weeks was not associated with adverse effects. Absorption was not demonstrated in this study.

Chromium picolinate and chromium chloride were not associated with adverse effects at doses of 15 mg chromium/kg bw/day. Increased levels of tissue chromium indicated that absorption had occurred. Higher doses of chromium (approximately 100 mg/kg bw/day) are associated with reproductive and developmental effects, although these may be secondary to parental toxicity. In general, hexavalent chromium has given positive results in *in vitro* mutagenicity tests, whereas trivalent chromium compounds have been negative.

Limited data from human supplementation studies have indicated that doses up to 1 mg/day of trivalent chromium compounds in general were not associated with adverse effects, although it is unclear what adverse effects were evaluated. The human studies were conducted in a variety of small groups and investigated a range of different endpoints, so limited conclusions may be drawn from these.

Evaluation

Chromium	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2001b)	no UL	total diet	insufficient data	human
UK(UK Expert Group on Vitamins and Minerals, 2003)*	10	total diet	no adverse effects	animal
EU (European Commission Health & Consumer Protection Directorate-General, 2003c)#	no UL	total diet	insufficient data	human
WHO (WHO, 1996)	0.25	supplementation	no adverse effect	human

* Guidance level, applies for trivalent chromium only. Chromium picolinate is excluded from this guidance level.

not applicable for chromium picolinate.

Both the EU and US concluded that the data were too limited to derive an UL.

Adequate human data on trivalent chromium is limited. No adverse side effects were reported in a number of supplementation trials, in which subjects received up to 1 mg chromium/day, mostly as picolinate for several months. These trials, however, were mainly studies of efficacy and not designed to find potential toxic effects.

The limited data from studies on subchronic, chronic, and reproductive toxicity on soluble trivalent chromium salts and the available human data do not give clear information on the dose response relationship. Therefore, an UL can not be derived.

The UK also concluded that overall there are insufficient data from human and animals studies to derive a safe upper level for chromium. However, in their opinion a total daily intake of about 0.15 mg trivalent chromium per kg body weight and day (or 10 mg/person) would be expected to be without adverse health effects. This value was based (using a 100-fold margin of safety) on a 24-week rat study, which indicated that 15 mg trivalent chromium/kg bw/day is not associated with adverse effects.

Based on the data considered in the US and EU evaluation, there are **insufficient data to establish a UL** for **soluble chromium III salts**.

Dietary intake

There were no food composition data available to enable a comprehensive intake assessment to be conducted for chromium. Whilst there are small amounts of data available, these data were either not from Australian or New Zealand sources, were not extensive enough across the whole diet, were not in the correct format or had not been assessed for accuracy.

Risk characterisation
Due to insufficient data it is not possible to establish an UL for chromium, however this does not mean there are no hazards associated with high intakes of chromium. For chromium, limited food composition data are available therefore it is not possible to undertake a complete dietary intake assessment for chromium at the present time.

In the absence of sufficient information on potential adverse effects and food composition data it is currently not possible to evaluate the safety of the addition of chromium to formulated beverages.

Copper

Hazard identification and characterisation

Chemistry
Copper has two valency states, cuprous (copper I) and cupric (copper II). It occurs in nature mainly in the form of its oxide, Cu_2O and sometimes as the chloride, $CuCl_2$ which, in the presence of humidity and oxygen, is oxidised to the basic copper (II) chloride, Cu(OH)Cl. The most important copper compounds in the aquatic environment are cupric chloride, cuprous nitrate and cupric sulphate.

Function
Copper is an essential micronutrient normally subject to effective homeostatic control. It is involved in the function of several enzymes, including cytochrome c oxidase, amino acid oxidase, superoxide dismutase and monoamine oxidase. Copper is thought to be required for infant growth, host defence mechanisms, bone strength, red and white cell maturation, iron transport, cholesterol and glucose metabolism, myocardial contractility and brain development.

Sources of copper

The main dietary sources of copper are shellfish, fish, liver, meats, nuts and chocolate. A lower concentration is found in legumes, grains, human milks, and especially cows milk. In drinking water in both New Zealand and Australia the guidance level, based on aesthetic considerations is 1 mg/L, with typical concentrations of about 0.05 mg/L (Ministry of Health, 2000; NHMRC and NRMMC, 2004).

Administration, distribution, metabolism and excretion

In mammals, absorption of copper occurs primarily in the small intestine. The efficiency of absorption of the metal ion is high; values for apparent absorption by adult humans average between 55% and 75% and do not drop appreciably with age. Actual absorption rates for rats are lower at 30–50%. Data from animal studies as well as from human studies indicate that the actual proportion of ingested copper that is absorbed will increase if copper intake is low, and vice versa. Studies with rats have confirmed that this also holds true with extreme intakes of copper where copper intake ten times normal will result in a copper absorption as low as 10%. This data is indicative that copper levels in the body are under homeostatic control.

Copper is absorbed across the brush border in the cells of the intestinal mucosa and is then subsequently transferred across the basolateral membrane into the interstitial fluid and blood. The basolateral membrane is the site where competition for absorption between copper and other transition metal ions takes place. Abnormally high concentrations of zinc, and possibly also iron, directly or indirectly inhibit uptake and transfer of copper from the diet to the blood.

On entering the interstitial fluid and blood plasma from the intestinal cells, copper initially becomes bound to two proteins, albumin and transcuprein, in the portal blood and general circulation. These two proteins appear to be the primary components of the exchangeable plasma copper pool. Albumin is responsible for binding about 18% of the ionic copper in human plasma. The rest of the copper is bound to ceruloplasmin (~65%), transcuprein (~12%) and components of low molecular weight. Ceruloplasmin copper is not part of the exchangeable copper pool; copper is added during the synthesis of ceruloplasmin by the liver.

Most of the bound copper is then rapidly deposited in liver hepatocytes, with lesser amounts entering the kidney. Appreciable copper uptake by other tissues is only seen once ceruloplasmin, bearing newly absorbed copper, is secreted into the plasma.

Therefore, there appears to be two phases of copper distribution. The first phase, mediated primarily by transcuprein involves transport into the liver (and kidney) and the second phase, mediated by ceruloplasmin involves distribution of copper to the other tissues.

On entering the cells, copper normally finds its way readily to the sites where it is needed. Most of the copper appears to be active or in transit with little or no excess copper stored. In most mammals, copper is excreted easily. The rate of excretion appears to be the main process for maintaining copper homeostasis.

Of the net copper that is absorbed and lost daily by human adults, only a tiny fraction enters the urine. The major excretory route appears to be the bile. Bile has the highest copper concentration of the body fluids and it has been estimated that about 2.5 mg of copper per day is secreted into the gastrointestinal tract. However, other fluids secreted in the gastrointestinal tract also contain copper, and together these contribute about another 2mg per day. All but 0.5–1.0 mg of the total copper must be reabsorbed every day to maintain the status quo.

Evidence indicates that most of the non–reabsorbed copper comes from bile and, therefore, it seems likely that it is the main route of net copper excretion. The biliary route may also be a more prominent route of copper excretion when large doses of copper enter the body acutely.

Toxicity

FSANZ[45] reviewed copper toxicity in 1999 as part of Proposal P157 – Metal Contaminants (ANZFA, 1999). Since then new evaluations have become available and therefore the safety of copper has been revisited.

The compartmentalisation and metabolism of copper is highly regulated through homeostatic mechanisms. Toxicity is likely to occur only when such homeostatic control within any particular compartment is overwhelmed and/or basic cellular defence or repair mechanisms are impaired. The essentiality and potential toxicity of copper in biological systems results from the chemical properties of the copper ion. Copper is fairly reactive and able to bind strongly to many types of electron rich structures. In excess, this property can cause a number of adverse reactions such as cellular injury due to the production of oxygen radicals, structural impairment of essential metal binding sites by the displacement of metal in receptors and transporter proteins, and functional impairment of DNA and other macromolecules through direct binding of copper.

Reviews of the toxicity studies in experimental animals indicate that these studies are not useful for setting an upper limit for humans. Very few of these studies used chronic exposure, only one or two doses were used, and the reporting of experimental details and results was incomplete. In addition, some studies used routs of exposure that are not relevant to human intake. Finally, animal species vary markedly in their sensitivity to copper; thus it is difficult to determine the most appropriate model in which to assess human toxicity to copper.

Acute copper toxicity is infrequent in humans, and is usually a consequence of ingesting contaminated foodstuff and beverages or from accidental or intentional ingestion of high quantities of copper salts. Case reports of single oral exposures to high levels of copper have been reported. Such exposures, including suicide attempts with $CuSO_4$, have occurred in youths and adults at doses ranging from 0.4 to 100g Cu.

Symptoms include vomiting, lethargy, acute haemolytic anaemia, renal and liver damage, neurotoxicity, increased blood pressure and respiratory rates. In some cases, coma and death followed.

For the general population, the majority of reports of chronic copper toxicity relate to exposure through contaminated drinking water and these are usually confounded by lack of characterisation of the microbiological quality of the water supplies and limitations in reporting.

One study reported that recurrent episodes of gastrointestinal illness in certain members of a family could be attributed to a copper main. The median level in the incoming water was 3.07mg/L; a single maximum level taken was 7.8mg/L. No estimated dose was provided or able to be inferred from this data. No symptoms were observed in two other families of similar age and sex distribution exposed to lower levels (medians, 1.58 and 0.02mg/L). Symptoms ceased with a change in the water source.

[45] as the Australia New Zealand Food Standards Authority (ANZFA)

Another study described a case of micronodular cirrhosis and acute liver failure in a 26 year old male who consumed copper tablets at 30mg/day for two years followed by 60mg/day for an unspecified period before presenting with symptoms of liver failure. Laboratory investigations revealed normal serum copper levels (22.6mmol/L) and serum ceruloplasmin (0.27mmol/L) but very high urinary excretion of copper (207mmol/24 hour) compared to normal (<1.2µmol/24 hour). Mean copper content of the liver was 3230µg/g (normal range 20–50µg/g). Histology of the liver resembled that of ICC and Wilson disease. This case gives some indication of a level of chronic copper consumption in humans that may lead to toxicity, assuming that the individual concerned did not have a predisposition to copper toxicity.

Very little information is available on the reproductive and developmental toxicity of copper to humans. An epidemiological study of a population of Massachusetts's women found no association (after adjusting for confounding variables) between the occurrence of spontaneous abortion and exposure to copper in drinking water (>1mg/litre) during 1976–1978. In a small trace element status study, a significant positive relationship between placental copper and birthweight and a negative correlation between the copper/zinc ratio and birthweight were found. This data is inadequate to assess the reproductive or developmental effects of copper in humans.

A number of epidemiological studies on cancer in the general population have been done. These studies have generally relied on serum copper concentrations as an indicator of an individuals copper status. It is questionable whether serum copper concentrations accurately reflect copper intake as it has been reported that in cases of chronic copper overload plasma copper concentrations are not elevated, and in one of the studies reported no significant correlation could be found between copper intake and copper blood level. These studies are therefore uninformative with respect to the possible aetiological role of copper in the disease.

Vulnerable groups

As copper is an essential metal, there are homeostatic mechanisms to maintain copper levels within defined limits. However, a number of disorders in homeostatic mechanisms can result in toxicity from exposure to copper at levels which are tolerated by the general population.

This form of copper toxicity is observed principally in patients with Wilson's disease and from the occurrence of infantile cirrhosis in areas of India (ICC, Indian Childhood Cirrhosis), and isolated clusters of cases in Germany, Austria and other countries (ICT, Idiopathic Copper Toxicosis) that have also been related to excess copper intake. Wilson's disease is a condition with a well-defined genetic basis with patients exhibiting impaired biliary excretion of copper, which is believed to be the fundamental cause of copper overload. Wilson disease patients typically present with hepatic and/or neurologic dysfunction. The worldwide incidence of Wilson's disease is 1 in 30,000 and the corresponding prevalence of the heterozygous and asymptomatic carrier of a mutated ATPase gene is 1 in 90 (European Commission Health & Consumer Protection Directorate-General, 2003b).
ICC and ICT are conditions related to copper excess which may be associated with genetically–based copper sensitivity although this has not been demonstrated unequivocally.

Evaluation

Copper	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	10	Total	hepatotoxicity	human
UK (UK Expert Group on Vitamins and Minerals, 2003)	10	Total	forestomach, kidney and liver damage	animal
EU (European Commission Health & Consumer Protection Directorate-General, 2003b)	5	Total	hepatotoxicity	human
WHO/FAO (WHO, 1996)	10 (f), 12 (m)	Total	hepatotoxicity	human
ANZFA (ANZFA, 1999)*	13	Total	hepatoxicity	human

* Provisional maximum tolerable daily intake (PTDI)

Daily intakes of copper ranging from 2 to 32 mg in drinking water have been reported to cause symptoms of general gastric irritation. This low limit in water is of interest given that an intake of 2mg/day is equivalent to average intakes in Australia and New Zealand. This discrepancy may result from the fact that in water (and in supplements) copper is present in the ionic form whereas in food, copper is present in the form of organic compounds (ANZFA, 1999). While there is little doubt that the uncontrolled ingestion of soluble inorganic copper salts in milligram quantities should be regarded with caution, levels of copper in food up to around 13 mg/day (assuming a body weight of 70 kg; 0.2 mg/kg bw/day) seem to have no detrimental effect on human health (WHO, 1996; ANZFA, 1999). This will take account of the quantity likely to be consumed from the usual diet (<10mg/day) and will limit both the amount of copper that can be introduced by dietary fortification and the quantity of contaminating copper that can be regarded as tolerable.

US derived a NOAEL of 10 mg/day of copper on the basis of a double-blind study, where 10 mg copper as copper gluconate capsules was consumed daily for 12 weeks. Liver function tests were normal. From a case report, consumption of 30 mg/day as copper tablets for 2 years, followed by 60 mg/day for an additional period of time, resulted in acute liver failure. The NOAEL of 10 mg/day was considered protective of the general population. The UL does not apply to individuals with Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis.

The EU based the NOAEL on the same study as the US evaluation, however an uncertainty factor of 2 was considered appropriate on the NOAEL of 10 mg/day to allow for potential variability within the normal population.

High doses of copper can result in hepatoxicity. This effect is considered to be the most sensitive adverse effect induced by copper and is relevant for establishing an UL. Based on the data considered in the US and FAO/WHO evaluation, a level of 10 mg copper/day has been adopted as an UL. This UL does not apply to individuals with Wilson's disease, ICC, or ICT. In summary the ULs for **copper** in the various age groups are:

1-3 years 1.8 mg/day
4-8 years 3.0 mg/day
9-13 years 5.0 mg/day
14-18 years 8.0 mg/day
adults 10 mg/day

Permitted forms

The Applicant requested the following forms to be permitted for copper: copper gluconate, cupric sulphate, cupric citrate and cupric carbonate. Copper gluconate, cupric sulphate and cupric citrate are already permitted in Standard 2.9.1 – Infant Formula Products, and cupric carbonate is permitted in Standard 2.9.4 – Formulated Supplementary Sports Foods.

Within the assessment of copper toxicity by both the EU (European Commission Health & Consumer Protection Directorate-General, 2003b)and US (US Institute of Medicine, 2001b) copper toxicity was focussed on the copper II forms. All requested copper forms have a valency state of II. All four forms are easily dissociated and therefore, the toxicity would be similar.

In conclusion, the available evidence does not indicate that the different forms of copper have differences in toxicity. Therefore, the requested forms of copper are appropriate as permitted forms for copper.

Dietary intake

Intakes of copper were estimated at baseline and when formulated beverages are consumed. Estimated intakes were adjusted based on second day intake data from the NNSs.

The concentration of copper requested to be added to formulated beverages was 0.75 mg/600 ml reference quantity.

Copper was not included in the 1995 Australian NNS. Therefore, in order to estimate intakes for the Australian population, the concentration data from the New Zealand NNS were matched to the most appropriate Australian food codes, then these values were used to estimate dietary intakes for the Australian population groups.

Estimated intakes increased from baseline by around 0.5 mg/per day when FBs were consumed across the population groups assessed. The UL was not exceeded by any population groups assessed.

Table 15: Estimated dietary intakes of copper, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	0.9 (45)	1.1 (65)	1.2 (65)	1.8 (100)
4-8 years, Aus	0.9 (30)	1.3 (45)	1.3 (45)	2.0 (65)
5-6 years, NZ	^1.1 (**)	NA	#1.5 (**)	NA
7-10 years, NZ	^1.3 (**)	NA	#1.7 (**)	NA
9-13 years, Aus	1.2 (25)	1.7 (35)	1.6 (30)	2.2 (45)
11-14 years, NZ	^1.3 (**)	NA	#1.9 (**)	NA
14-18 years, Aus	1.5 (20)	2.0 (25)	2.0 (25)	3.0 (40)
15-18 years, NZ	1.5 (20)	1.9 (25)	2.3 (30)	3.0 (35)
≥19 years, Aus	1.7 (15)	2.0 (20)	1.9 (20)	2.3 (25)
≥19 years, NZ	1.5 (15)	1.6 (15)	2.2 (20)	2.6 (25)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.

^ mean adjusted intake, from MOH 2003, averaged for males and females.

[#] 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Dietary modelling indicates that intake for all population groups is predicted to be below the UL even for high consumers and applying a worst-case scenario where all specified products are replace with formulated beverages would be replaced by formulated beverages (Scenario 2).

All population groups, with the exception of 2-3 year olds, are estimated to have high consumer dietary intakes of copper below the UL. Estimated high consumer intakes for 2-3 year olds are at the UL (100%).

Copper intake from other sources includes drinking water. For the modelling, drinking water consumption is included in the dietary intake assessment using a copper concentration of 0.02 mg/L (from the 1997 New Zealand NNS). In Australia copper concentrations in drinking water range up to 0.8 mg/L with typical concentrations of about 0.05 mg/L (NHMRC and NRMMC, 2004). Therefore, intake of copper from drinking water has been included in the dietary intake assessment.

A number of conservative assumptions were used in the dietary modelling which may mean the 95th percentile intakes are still an overestimation to some extent. The conservative assumptions include that all drinks will be substituted for formulated beverages in the 2-3 year old.

The adverse effect on which the UL for copper was based is hepatoxicity. The UL was based on a 12-week study in healthy volunteers where copper supplementation at 10 mg/day did not result in effects on liver function. There is one case report, where consumption of 30 mg of copper tablets per day for 2 years, followed by 60 mg/day for an additional period of time, resulted in acute liver failure.

The UL represents a quantitative level of total intake at which, or below no harm is expected to occur assuming nutrient adequacy is met. Therefore an estimated intake level at the UL generally does not raise any safety concerns, particularly as the dietary intake assessment includes the contribution from water. In this case, the predicted high consumer intake for 2-3 year olds is still well below a level at which adverse effects might be observed. The dietary modelling also predicts that the higher intakes estimated for 2-3 year olds will not be sustained in the older age groups (e.g. 4-8 year olds).

Overall, the potential to exceed the UL, even for 2-3 year olds, is considered to be low, given the conservative assumption in the Scenario 2 dietary modelling.

In conclusion, for the general population the addition of copper to formulated beverages at a level of 0.75 mg per 600 ml serve poses no appreciable public health and safety risk.

Comparison of estimated intakes with the UL is not appropriate when considering the health risk for individuals with Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis, as typically they respond adversely to levels of intake that might fall below the UL and, in some cases, at levels that approximate normal dietary intakes. Such individuals may therefore potentially be at risk even from natural fluctuations in the copper levels in foods. For individuals with Wilson's disease, Indian childhood cirrhosis or idiopathic copper toxicosis, consumption of formulated beverages with copper added, would be inappropriate.

Iodine

Hazard identification and characterisation

Chemistry

Iodine is a non-metallic group VII element (a halogen) existing in the valency states –1 (iodide) to +7 but not occurring free in nature. Iodides and iodates, its mineral forms, occur ubiquitously in igneous rocks and soils. The iodides in the sea accumulate in seaweeds, sea fish and shellfish. On land small amounts of iodide are taken up by plants, which have no essential nutritional requirement for this element, the plants being subsequently ingested by herbivores.

Function

Iodine is an important trace element that is required for the synthesis of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). These hormones have a key role in influencing cellular metabolism and metabolic rate.

Sources

Diet is the major source of iodine intake for humans. The major food categories contributing to dietary intake include seafood, milk and eggs, with meat and cereals being secondary sources. The iodine content of food is reflective of background levels in the environment as well as the use of iodine and its compounds in food production, processing and manufacturing. In addition to dietary sources, various mineral supplements and medical preparations can further add to iodine intake.

Absorption, distribution, metabolism and excretion

Greater than 97% of ingested iodine is absorbed from the gastrointestinal tract, generally as iodide. Absorbed iodide enters the circulation where it is taken up primarily by the thyroid gland. The uptake of iodide by the thyroid gland is controlled by the thyroid-stimulating hormone (TSH) and is highly sensitive to dietary iodine intake. At low intakes representing iodine deficiency, uptake of iodide into the thyroid gland is increased and at very high intakes, iodine uptake into the thyroid gland decreases.

Once the physiological requirements for thyroid hormone synthesis have been met, the thyroid does not accumulate more iodine and any excess is excreted, primarily in the urine.

Iodine is largely excreted in the urine, mainly in the form of iodine. Very small amounts of iodine may be excreted in sweat, faeces and exhaled air.

Toxicity

A Final Assessment Report has been prepared for Application 493 – Iodine as a Processing Aid, which included a summary of available toxicity data of iodine. For a full review see this report (FSANZ, 2005).

A large number of human experimental, clinical, and epidemiological studies on the effects of excess iodine on human health have been reported and reviewed in detail by both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) ((WHO, 1989) and the Agency for Toxic Substances and Disease Registry (ATSDR, 2004). These studies indicate that the principal direct effects of excessive iodine ingestion are on the thyroid gland and regulation of thyroid hormone production and secretion. Some individuals may experience a sensitivity type reaction to excess iodine, which is unrelated to thyroid gland function. Such reactions are typically associated with large doses of iodine (>300 mg/day), which would not be typical from dietary sources. There are also reports in the literature of iodine poisoning, but such cases are rare and typically associated with intakes of many grams. The focus of this evaluation is on the effects of excess iodine on thyroid function.

Excess iodine can produce an enlargement of the gland (goitre) and/or affect the production of the thyroid hormones. A diminished production of the thyroid hormones is referred to as hypothyroidism (and may be accompanied by goitre) and increased thyroid hormone synthesis and secretion by the thyroid gland is referred to as hyperthyroidism.

The effect on the thyroid depends on the current and previous iodine status of the individual and any current or previous thyroid dysfunction. For example, individuals with a history of iodine deficiency may be prone to the development of iodine-induced hyperthyroidism if iodine exposure increases later in life.

The literature indicates that the human response to excess iodine can be quite variable. Some individuals can tolerate quite large intakes without exhibiting any adverse effects on thyroid gland function, while others may respond adversely to levels close to recommended intakes. Individuals responding adversely to levels close to recommended intakes typically have an underlying thyroid disorder or have a long history of iodine deficiency.

For the majority of healthy individuals, the most sensitive endpoint for iodine toxicity is sub-clinical hypothyroidism, which is defined as an elevation in TSH concentration while serum thyroid hormone concentration is maintained within the normal range of values for healthy individuals. While not clinically adverse, such an effect, if persistent, could lead to clinical hypothyroidism. In healthy individuals, such effects are generally associated with intakes of 24 μg/kg body weight/day (1700 μg/day for a 70 kg person).

Vulnerable groups

Individuals with thyroid disorders or a long history of iodine deficiency may respond adversely at levels of intake below the UL.

Evaluation

Iodine	UL in adults, µg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	1100	total	elevated TSH	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	500	Suppl	change in thyroid hormones	human
EU (European Commission Health & Consumer Protection Directorate-General, 2002a)	600	total	TSH levels	human
WHO/FAO (WHO, 1989)	1000	total	elevated TSH	human

* Guidance level

Intakes of approximately 1 mg iodine per day appear to be well tolerated by healthy adults. This level has been used by JECFA to establish a provisional maximum tolerable daily intake (PTDI) for iodine of 0.017 mg/kg bw. FSANZ has adopted this level as a safe intake level for the general healthy population. Individuals with thyroid disorders or a long history of iodine deficiency may respond adversely however at levels of intake below the UL. The adult UL of 1100 µg/day was adjusted on the basis of relative body weights.

In summary, the UL for **iodine** for the various groups are:

1-3 years 220 µg/day
4-8 years 350 µg/day
9-13 years 650 µg/day
14-18 years 1000 µg/day
Adults 1100 µg/day

Dietary intake

Intakes of iodine were estimated at baseline and when formulated beverages are consumed.

The concentration of iodine requested to be added to formulated beverages was 37.5 µg/600 ml reference quantity.

Iodine was not assessed in the 1995 Australian or the 1997 New Zealand NNSs therefore, there were not concentration data available for the foods consumed in the NNSs. Iodine concentrations were available for a restricted range of foods or food groups from survey data or food composition data. A model was set up in DIAMOND assigning iodine concentrations to wider food groups. This type of model did not allow second day adjustments of intake to be made.

The concentrations of iodine in foods were only available from a limited number of sources. For Australia, the intake estimate was based primarily on unpublished 22nd Australian Total Diet Survey (TDS) data. For New Zealand, the intake estimate was based primarily on the data from the 2003/2004 New Zealand TDS first and then the 1997/1998 New Zealand TDS. However, where data gaps existed in the Australian data, New Zealand data were used, and visa versa. Where there were no recent TDS data, unpublished data from the Australian or New Zealand food composition programs were used for the respective countries.

If data gaps still existed, international food composition data (German and UK) were used. For Australia, information from A493 – Iodine as a Processing Aid was also used.

Dietary iodine intakes were not assessed as a part of the 2002 New Zealand CNS, therefore, baseline estimates of intake were not available.

Estimated intakes increased from baseline by around 20 µg/per day when FBs were consumed across the population groups assessed. The UL was not exceeded for any population group assessed, except for Australian children aged 2-3 years at the 95th percentile intake when FBs are consumed. In reality, the UL is not likely to be exceeded, as unadjusted 95th percentile intakes are higher than those at the same level over a lifetime.

Table 16: Estimated dietary intakes of iodine, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake µg/day (%UL)		95th percentile intake µg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	106 (50)	124 (55)	206 (95)	232 (105)
4-8 years, Aus	109 (30)	131 (35)	217 (60)	243 (70)
5-6 years, NZ	N/A	NA	NA	NA
7-10 years, NZ	N/A	NA	NA	NA
9-13 years, Aus	130 (20)	156 (25)	276 (40)	314 (50)
11-14 years, NZ	N/A	NA	NA	NA
14-18 years, Aus	142 (15)	178 (20)	338 (35)	408 (40)
15-18 years, NZ	93 (9)	119 (10)	211 (20)	252 (25)
≥19 years, Aus	116 (10)	132 (10)	276 (25)	305 (30)
≥19 years, NZ	92 (8)	102 (9)	213 (20)	234 (20)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
NA = not assessed, because iodine was not included in the New Zealand 2002 CNS.

Risk characterisation
Healthy population

The data support the safety of iodine added to formulated beverages for the normal healthy population.

Dietary modelling indicates that intakes for all population groups is predicted to be below the UL even for high consumers and applying a worst-case scenario i.e. all products specified are replaced by formulated beverages.

All high consumer population groups, with the exception of 2-3 year olds, are estimated to have intakes of iodine below the UL. Estimated high consumer intakes for 2-3 year olds is estimated to only marginally exceed the UL (105%).

Due to the use of 24-hour dietary survey data, which tends to over-estimate habitual food consumption amounts for high consumers, it is likely that the 95th percentile dietary intake is an over-estimate. In addition, a number of conservative assumptions were used in the dietary modelling which may further add to the overestimation. For example, that all specified drinks would be substituted for formulated beverages for the 2-3 year old population group.

The UL represents a quantitative level of total intake at which, or below no harm is expected to occur assuming nutrient adequacy is met. Short-term excursions above the UL, particularly when these are of small magnitude (e.g. 105%), generally do not raise any safety concerns as the UL is not itself a threshold for toxicity. In this case, the predicted high consumer intake for 2-3 year olds is still well below a level at which adverse effects might be observed. The dietary modelling also predicts that the higher intakes estimated for 2-3 year olds will not be sustained in the older age groups (e.g. 4-8 year olds).

Overall, the potential to exceed the UL, even for 2-3 year olds, is considered to be low.

Vulnerable individuals

In relation to the vulnerable individuals identified in the hazard identification and characterisation, further consideration is necessary. Under certain circumstances these individuals may respond to excess iodine in the diet by developing thyrotoxicosis (also referred to as iodine-induce hyperthyroidism). Symptoms include rapid heartbeat, nervousness, weakness, heat intolerance, and weight loss. The most vulnerable are those over 40 years of age who have a long history of iodine deficiency, although individuals with underlying thyroid disorders may also be affected.

Comparison of estimated intakes with the UL is not appropriate when considering the health risk for these individuals, as typically they respond adversely to levels of intake that fall below the UL and, in some cases, at levels that approximate normal dietary intakes. Such individuals may therefore potentially be at risk even from natural fluctuations in the iodine levels in foods.

In the case of individuals with underlying thyroid disease, such as Graves' disease, consumption of formulated beverages with iodine would be inappropriate. In the case of individuals with a long history of iodine deficiency, there may be cause for greater concern as such individuals may not be aware of their condition.

Conclusion

For the vast majority of the population, the addition of iodine to formulated beverages at a level of 37.5 μg per 600 ml serve poses no appreciable public health and safety risk. However, for individuals with underlying thyroid disease or have a long history of iodine deficiency may respond adversely to levels of intake that are safe for the general healthy population.

Iron

Hazard identification and characterisation

ChemistryIron is a transition metal and ubiquitous in biological systems. In aqueous solution, it exists in one of two oxidation states, Fe^{2+}, the ferrous form, and Fe^{3+}, the ferric form. Iron has a particularly high redox potential in solution. The interconversion of iron oxidation states is a mechanism whereby iron participates in electron transfer, as well as a mechanism whereby iron can reversibly bind ligands. The common biological ligands for iron are oxygen, nitrogen, and sulfur atoms.

Function

Four major classes of iron-containing proteins exist in the mammalian system: iron containing haem proteins (haemoglobin, myoglobin, cytochromes, others), iron sulfur enzymes (flavoproteins, haem-flavoproteins), proteins for iron storage and transport (transferring, lactoferrin, ferritin, haemosiderin), and other iron-containing or activated enzymes (sulfur, nonheam enzymes). In haem proteins, iron is bound to porphyrin ring structures with various side chains. In humans, the predominant form of haem is protoporphyrin-IX.

The movement of oxygen from the environment to the tissues is one of the key functions of iron. Oxygen is bound to an iron-containing porphyrin ring, either as part of the prosthetic group of haemoglobin within erythrocytes or as part of myoglobin as the facilitator of oxygen diffusion in tissues.

Myoglobin is located in the cytoplasm of muscle cells and increases the rate of diffusion of oxygen from capillary erythrocytes to the cytoplasm and mitochondria. The concentration of myoglobin in muscle is drastically reduced in tissue iron deficiency, thus limiting the rate of diffusion of oxygen from erythrocytes to mitochondria.

The cytochromes contain haem as the active site with the iron-containing prophyrin ring functioning to reduce ferric iron to ferrous iron. Cytochromes act as electron carriers.

Sources of iron

Dietary sources of iron include liver, meat, beans, nuts, dried fruits, poultry, fish, whole grains or enriched cereals, soybean flour and most dark green leafy vegetables. Iron in foods occurs in two main forms: haem and non-haem. The major sources of haem iron in the diet are haemoglobin and myoglobin from meat, poultry and fish. Non-haem iron present as foods is in the ferric form.

Absorption, distribution, metabolism and excretion

Modulation of absorption of iron from the gastrointestinal tract is the primary mechanism for regulation of body iron levels. The amount of iron absorbed from the diet can vary widely and depends on body iron stores and physiological requirements (generally, the rate of erythrocyte production). Absorption of haem and non-haem iron involves different mechanisms. In general haem iron uptake, which is via a specific haem receptor, occurs approximately 2- to 3-fold more extensively than that of non-haem iron and is largely independent of other dietary components. The mechanism by which non-haem iron enters intestinal mucosal cells is not clearly established, although there appear to be separate mechanisms for the uptake of ferrous and ferric iron. Uptake of non-haem iron depends initially on a low pH to effect solubilisation. Iron chelators, such as ascorbic acid, increase absorption by maintaining iron in solution. In the absence of chelators, ferric iron is generally less well absorbed than ferrous iron, due to its low solubility at higher pH. Dietary supplements are mostly inorganic salts. Iron supplements are also available in the form of the iron protein complex, ferritin, but poor absorption is reported.

Iron absorption from a diverse diet has been estimated to be approximately 15%. Women and children generally have lower iron stores than men, and thus absorb a greater percentage of the amount ingested. This is particularly pronounced during pregnancy with absorption of dietary iron increasing throughout gestation. Conversely, absorption is lower in postmenopausal women, in whom iron stores are generally high.

Iron is transported by the plasma transport protein, transferrin. In healthy adults approximately one-third of the total iron binding capacity is saturated. In conditions of iron overload or atransferrinaemia, non-protein-associated iron may also be detected in the plasma. Turnover of the total plasma iron pool (approximately 3 mg) is more than 10-fold every day. Approximately 80% of iron leaving the plasma is delivered to erythroid bone marrow. Iron in circulating erythrocytes is returned to plasma transferrin by means of reticuloendothelial cell phagocytosis.

Iron uptake by cells (other than during absorption from the intestinal lumen) occurs via binding of transferrin to the transferrin receptor, which is subsequently internalised within an endocytic vesicle.

Recent studies have identified a number of novel proteins which are also likely to be involved in iron transport into and within cells, although the function of these proteins in iron transport has yet to be determined.

Little of the absorbed iron is excreted. Very small losses occur in the faeces, by desquamation of gastrointestinal cells, in haemoglobin and bile, and via the urine. Substantial iron loss can occur through loss of blood. Average, total daily iron losses for healthy adults are 1.0 mg for men and 1.3 mg for premenopausal women (assuming an average blood loss of 30 – 40 mL per menstrual cycle). Daily iron losses for children have not been measured directly but are estimated as 0.2 and 0.5 mg for infants and children aged 6 – 11 years, respectively.

Toxicity

Case reports of accidental poisoning with medicinal iron, especially in young children, indicate acute damage of gastrointestinal, hepatic, pancreatic and cardiovascular structures after ingestion of very high doses. An acute oral dose of 60 mg iron/kg body weight can be lethal but oral doses below about 10-20 mg iron/kg body weight do not cause acute systemic toxicity.

Adverse gastrointestinal effects (e.g. nausea, epigastric discomfort, constipation) have been reported following short-term oral dosage at 50-60 mg daily of supplemental non-haem iron preparations, particularly if taken without food.

Iron overload with clinical symptoms, including liver cirrhosis, has been reported in individuals receiving long-term, high-dose medical treatment with iron (160-1200 mg iron/day). Iron overload with clinical symptoms has also been found in subjects homozygous for hereditary haemochromatosis (a genetic disorder of iron storage), even at normal dietary iron intakes. Bantu siderosis, with liver cirrhosis and diabetes, has been attributed to chronic excess intake of highly available iron (50-100 mg iron/day) in beer; however, these adverse effects may be confounded by chronic alcohol intake and possibly by a genetic disorder.

Although a proportion of the population has serum ferritin levels indicative of elevated iron stores (above 200 μg/L for women and 300 μg/L for men), the point at which an elevated serum ferritin level becomes associated with an increased risk of adverse effects (such as liver fibrosis) is not known. The risk of adverse effects from iron overload in the general population, including those heterozygous for hereditary haemochromatosis, is considered to be low.

Epidemiological studies have reported associations between high iron intake and/or stores with increased risk of chronic diseases such as cardiovascular disease, type II diabetes and cancer of the gastrointestinal tract. However, these data are conflicting and do not provide convincing evidence of a causal relationship between iron intake or stores and such chronic diseases.

Vulnerable groups

A particularly sensitive subpopulation (up to 0.5% of the Caucasian population) are homozygous for hereditary haemochromatosis, who are susceptible to iron overload even at normal dietary iron intakes. Such individuals should avoid iron-supplements and highly iron-fortified foods. The majority of homozygotes are not diagnosed or identified, and they are not aware of their greater susceptibility until sufficient iron has accumulated to produce adverse effects.

Evaluation

Iron	UL, in adults mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	45	Total	gastrointestinal	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	17	Suppl.	gastrointestinal	human
EU (The Scientific Panel on Dietetic Products, 2005)	No UL		insufficient data	human

* Guidance level

The US identified a LOAEL of 60 mg/day of supplemental iron on the basis of a controlled, double blind study where gastrointestinal effects were examined in 97 Swedish male and female adults after intake of either a non-haem iron supplement (60 mg/day as iron fumarate), a supplement containing both haem iron and non-haem iron (18 mg/day, 2 mg from porcine blood and 16 mg as iron fumarate), or a placebo. The groups were similar with respect to gender, age, and basic iron status. The frequency of constipation and the total incidence of all side effects were significantly higher among those receiving non-haem iron than among those receiving either the combination of haem and non-haem iron or the placebo. Although most of the reported GI effects were minor, five individuals found them to be severe enough to stop taking the medication. Four of these withdrawals occurred during the non-haem containing iron treatment and one occurred just after changing from the non-haem-containing iron treatment to placebo.

The EU considered that the adverse gastrointestinal effects which have been reported after short-term oral dosage at 50-60 mg daily of supplemental non-haem iron preparations are not a suitable basis to establish an UL for iron from all sources. An UL could not be established for iron based on iron overload due to a poor correlation between iron intake and biochemical indicators of iron status, between biochemical indicators and actual body stores, or between body stores and adverse effects. Also the EU considered that an UL could not be established for iron (including haem iron) based on increased risk of chronic diseases such as cardiovascular disease, diabetes and cancer, due to the lack of convincing evidence of a causal relationship between iron intake or stores and chronic diseases.

The limited data indicate that supplemental intakes of non-haem iron at levels of 30 mg/day or more (in addition to iron intake from food) can be associated with indicators of high iron stores (e.g elevated serum ferritin) in older adults. However, the point at which an elevated serum ferritin level becomes associated with an increased risk of adverse effects (such as liver fibrosis) is not known. Furthermore, epidemiological associations between high iron intake and/or stores and increased risk of chronic diseases such as cardiovascular disease, type II diabetes and cancer of the gastrointestinal tract are conflicting and do not provide convincing evidence of a causal relationship between iron intake or stores and such chronic diseases.

FSANZ considers the EU evaluation as more appropriate, since the gastrointestinal effects observed in short term studies are transient, reversible and occurred with non-haem iron without food. Therefore, the US level is not appropriate for the establishment for an UL. Data on effects on iron overload or risk on chronic diseases are insufficient to set an UL.

In conclusion, there is **insufficient data to set an UL for iron**. The limited data indicate that supplemental intakes of non-haem iron at levels of 30 mg/day or more (in addition to iron intake from food) can be associated with indicators of high iron stores (e.g. elevated serum ferritin) in older adults. However, the point at which an elevated serum ferritin level becomes associated with an increased risk of adverse effects (such as liver fibrosis) is not known.

Dietary intake

Intakes of iron were estimated at baseline and when formulated beverages are consumed. Estimated intakes were adjusted based on second day intake data from the NNSs.

The concentration of iron requested to be added to formulated beverages was 3 mg/600 ml reference quantity.

Estimated intakes increased from baseline by around 1-2 mg/per day when FBs were consumed depending on the population groups assessed. There was no UL to compare the estimated intakes to.

Table 17: Estimated dietary intakes of iron, before and after FBs are introduced into the diet

	Mean intake mg/day		95th percentile intake mg/day	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	8.2	9.4	12.2	13.4
4-8 years, Aus	9.3	10.8	13.7	15.5
5-6 years, NZ	^9.4	NA	#11.8	NA
7-10 years, NZ	^11.1	NA	#14.4	NA
9-13 years, Aus	12.3	14.3	22.1	23.2
11-14 years, NZ	^11.6	NA	#16.7	NA
14-18 years, Aus	13.9	16.4	24.5	29.4
15-18 years, NZ	12.8	16.3	19.4	25.2
≥19 years, Aus	12.7	13.8	20.9	22.9
≥19 years, NZ	12.2	13.5	18.5	22.0

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.

[#] 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Dietary modelling indicated that when various drinks are substituted for formulated beverages, adolescents aged 14-18 years old would have the highest intake of iron (high level of intake 29.4 mg/day), which is still much lower than the concentrations found to result in adverse gastrointestinal effects. In older adults (>70 years), who represent a non-target group for formulated beverages, high consumers are estimated to have intakes of 17.5 mg of iron per day in Australia and 15.5 mg of iron per day in New Zealand. This level is below the level which is associated with indicate high iron store levels in older adults. Therefore, this would not be of concern.

A particularly sensitive subpopulation (up to 0.5% of the Caucasian population) are homozygous for hereditary haemochromatosis, who are susceptible to iron overload even at normal dietary iron intakes. Such individuals should avoid iron-supplements and highly iron-fortified foods. The majority of homozygotes are not diagnosed or identified, and are therefore not aware of their greater susceptibility until sufficient iron has accumulated to produce adverse effects.

In conclusion, for the general population the addition of iron to formulated beverages at a level of 3 mg per 600 ml serve poses no appreciable public health and safety risk. However, for individuals who are homozygous for hereditary haemochromatosis there is a potential increased risk of iron toxicity, especially for those individuals who are unaware of their increased susceptibility for iron overload.

Magnesium

Hazard identification and characterisation

Chemistry

Magnesium is a metallic element of group II of the periodic table and has an atomic weight of 24.3. Magnesium is the eighth most abundant element in the earth's crust. It does not occur as a pure metal in nature, but it is found in large deposits as magnesite, dolomite and other minerals.

Function

Magnesium is required as a cofactor for many enzyme systems. It is required for protein synthesis and for both anaerobic and aerobic energy generation and for glycolysis, either indirectly as a part of magnesium-ATP complex, or directly as an enzyme activator. Magnesium plays a multifunctional role in cell metabolism, (particularly at the level of key phosphorylations), and has a critical role in cell division. It has been suggested that magnesium is necessary for the maintenance of an adequate supply of nucleotides for the synthesis of RNA and DNA. Magnesium regulates the movement of potassium in myocardial cells and is also known to act as a calcium channel blocker. Magnesium is an important element in the metabolism and/or action of vitamin D, and is essential for the synthesis and secretion of parathyroid hormone.

Sources of magnesium

Magnesium is ubiquitous in foods, but the content varies substantially. Leafy vegetables, as well as grains and nuts, generally have a higher magnesium content (60-2700 mg/kg) than meats and dairy products (less than 280 mg/kg). A number of magnesium salts are used as food additives (see Standard 1.3.1 – Food Additives). Within Australia and New Zealand voluntary fortification with magnesium is allowed in various products up to 25% of the recommended daily intake (80 mg). In food derived from plant and animal sources, magnesium is mostly bound or chelated, e.g. to phytic acid, phosphates, chlorophylls or it is included in biological apatites (skeleton). In aqueous solutions, magnesium salts (e.g., sulphate, chloride, phosphate, citrate, and carbonate) are mostly dissociated depending on the concentration, pH and temperature. Most magnesium salts are hygroscopic and have a bitter taste.

Absorption, distribution, metabolism and excretion

The net absorption of magnesium from the diet is typically approximately 50 percent. High levels of dietary fibre from fruits, vegetables, and grains decrease magnesium absorption. Dietary protein is also known to influence intestinal magnesium absorption. Magnesium is absorbed along the entire intestinal tract, but the sites of maximal absorption appear to be the distal jejunum and ileum. It has been suggested that absorption occurs by both an unsaturable passive and saturable active transport system. Thus, in both adults and children, the fractional absorption of magnesium is inversely proportional to the amount ingested. Magnesium is absorbed much more efficiently from the normal concentrations found in the diet than it is from the higher doses found in non-food sources. The presence of food likely counteracts the osmotic effect of the magnesium salts in the gut lumen.

Magnesium is abundant in the body with the largest amounts found in bone. It is also found in a variety of other tissues including muscle, liver, heart and kidneys. In plasma, half of magnesium present is in the ionised form. About 20% is bound to proteins, the remaining 80% is unbound. Most intracellular magnesium is found bound to the endoplasmic reticulum.

In normal individuals, the kidney seems to maintain magnesium homeostasis over a rather wide range of magnesium intakes. Thus, hypermagnesemia has not been documented following the intake of high levels of dietary magnesium in the absence of either intestinal or renal disease.

Magnesium is excreted primarily in the urine. The extent of urinary excretion, and thereby the homeostasis of magnesium, is influenced by a wide variety of hormones, including calcitonin, thyroxine, glucocorticoids, glucagons and angiotensin. Under normal conditions, the kidney tubule reabsorbs 95% of the filtered load of magnesium and about 5% is excreted in urine.

Toxicity

Magnesium, when ingested as a naturally occurring substance in foods, has not been shown to exert any adverse effects. However, adverse effects of excess magnesium intake have been observed with intakes from non-food sources such as various magnesium salts used for pharmacologic purposes. Magnesium derived from plant or animal sources has not been demonstrated to induce diarrhoea or other adverse effects in healthy persons, probably as magnesium is bound to matrices and hence is mostly not easily dissociable. On the other hand easily dissociable magnesium salts (e.g. chloride or sulphate; included are compounds

like MgO becoming readily dissociable after the reaction with gastric hydrochloric acid) that are present in water many supplements and drugs exert dose-dependent laxative effects.

Easily dissociable magnesium salts, especially the sulphate are used as 'osmotic' and 'saline' laxatives, respectively. Nevertheless mild diarrhoea can be taken as the most sensitive non-desirable effect if magnesium supplements are taken for nutritional purposes. However it must be kept in mind that adaptation of the bowel to higher oral magnesium intake is known, that a mild laxative effect may be desirable ('four patients reported mild diarrhoea in the magnesium group, and a similar number felt that their bowel function improved with less constipation'), that mild laxative effects have been frequently observed also in the placebo groups (perhaps caused by taste adjusters, vehicles a.o.), that a given daily dose of magnesium is better tolerated when it is divided into several portions, and finally that the galenic form (aqueous solution, capsules, tablets, etc.) may play a role. Data from the literature included children, pregnant women, tetanic, hypertensive and cardiac patients as well as volunteers. Papers were only considered when the presence or absence of 'mild diarrhoea' was stated. Studies where magnesium was derived from plant or animal sources were not considered, since these forms are poorly dissociable (e.g. phytates).

As discussed, mild diarrhoea is the most sensitive non-desirable effect of orally administered easily dissociable magnesium salts. From the available data it can be concluded that mild diarrhoea occurs in a small percentage of adult subjects at oral doses of about 360/365 mg magnesium per day, this level being regarded as the LOAEL.

Larger pharmacological doses (e.g. doses > 2500 mg/day) of magnesium can clearly result in more serious adverse effects, such as metabolic alkalosis, hypokalemia, paralytic ileus and cardio respiratory arrest.

Vulnerable groups

Individuals with impaired renal function are at greater risk of magnesium toxicity. However, magnesium levels obtained from food are insufficient to cause adverse reactions even in these individuals. Patients with certain clinical conditions (e.g. neonatal tetany, hyperuricemia, hyperlipidemia, lithium toxicity, hyperthyroidism, pancreatitis, hepatitis, phlebitis, coronary artery disease, arrhythmia, and digitalis intoxication) may benefit from the prescribed use of magnesium in quantities exceeding the upper limit in the clinical setting.

Evaluation

Magnesium	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000a)	350	non-food	Osmotic diarrhoea	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	400	Suppl	Osmotic diarrhoea	human
EU (European Commission Health & Consumer Protection Directorate-General, 2001b)	250	not normally present in foods and beverages	Osmotic diarrhoea	human

* Guidance level only

Diarrhoea was chosen by the US, UK and EU as the most sensitive toxic manifestation of excess magnesium intake from non-food sources. Therefore, it is considered appropriate to set an UL for magnesium for readily dissociable magnesium salts (e.g., chloride, sulphate, aspartate, lactate) and compounds like MgO in nutritional supplements, water, or added to food and beverages.

The US established an upper level of 350 mg/day for adolescents and adults aged 9 and over. Although a few studies have noted mild diarrhoea and other mild gastrointestinal complaints in a small percentage of patients at levels of 360 to 380 mg/day, it is noteworthy that many other individuals have not encountered such effects even when receiving substantially more than this level of supplementary magnesium. It was assumed that children are as susceptible to the osmotic effects of non-food sources of magnesium as are adults. Thus, by adjusting the value for adults on a body-weight basis an UL for children at a magnesium intake of 5 mg/kg bw /day can be established. For children, aged 1-3 years, the upper level would be 65 mg/day, and aged 4-8 years 110 mg/day.

The EU established an upper level of 250 mg/day for children, adolescents and adults aged 4 and over, while for younger children no upper limit was established. Based on a NOAEL of 250 mg magnesium per day and an uncertainty factor of 1.0 an UL of 250 mg magnesium per day can be established for readily dissociable magnesium salts (e.g., chloride, sulphate, aspartate, lactate) and compounds like MgO in nutritional supplements, water, or added to food and beverages. This UL does not include magnesium normally present in foods and beverages. An uncertainty factor of 1.0 was justified in view of the fact that data are available from many human studies involving a large number of subjects from a spectrum of lifestage groups, including adults, pregnant and lactating women, and children. In addition, the NOAEL was based on a mild, transient laxative effect, without pathological sequelae, which is readily reversible and for which considerable adaptation can develop within days. This UL holds for adults, including pregnant and lactating women, and children from 4 years on.

As no data were available for children from 1 to 3 years, and since it was considered that extrapolation of the UL for older children and adults on the basis of body weight was inappropriate, no UL could be established for this age group.

FSANZ considered the UL established by the US as the most comprehensive and therefore the age-derived ULs for **magnesium, not naturally occurring in food** are:

1-3 years	**65 mg/day**
4-8 years	**110 mg/day**
9 and over	**350 mg/day**

Dietary intake

Intakes of magnesium were only assessed from added sources from food. Intakes were estimated when formulated beverages are consumed. Baseline intakes were not calculated because it was assumed that no food products are fortified with magnesium.

The concentration of magnesium requested to be added to formulated beverages was 80 mg/600 ml reference quantity.

Estimated intakes were adjusted based on second day intake data from the NNSs.

Dietary magnesium intakes were not assessed as a part of the 2002 New Zealand CNS, therefore, baseline estimates of intake were not available.

Estimated mean intakes were between 20 and 65 mg/per day and between 75 and 170 mg/day when FBs were consumed depending on the population groups assessed. The UL was not exceeded for any population groups assessed, except for Australian children aged 2-3 years at the 95th percentile intake when FBs are consumed.

Table 18: Estimated dietary intakes of magnesium from formulated beverages only, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake mg/day (%UL)	95th percentile intake mg/day (%UL)
Age group	**Scenario 2***	**Scenario 2***
2-3 years, Aus	33 (50)	95 (150)
4-8 years, Aus	44 (40)	105 (95)
5-6 years, NZ	NA	NA
9-13 years, Aus	54 (15)	123 (35)
7-10 years, NZ	NA	NA
11-14 years, NZ	NA	NA
14-18 years, Aus	63 (20)	169 (50)
15-18 years, NZ	45 (15)	120 (35)
≥19 years, Aus	32 (9)	106 (30)
≥19 years, NZ	22 (6)	76 (20)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
NA = not assessed, because magnesium was not included in the New Zealand 2002 CNS.

Risk characterisation

Dietary modelling was undertaken on the assumption that there is no baseline exposure to magnesium, since the adverse effects associated with magnesium are only observed to occur when magnesium is not in a food matrix. It could be assumed that magnesium would not be in a food matrix when added to formulated beverages, therefore the UL for magnesium, not naturally occurring in food, is applicable when assessing the risk of adding magnesium to formulated beverages. Formulated beverages could be consumed on an empty stomach, therefore, osmotic diarrhoea could occur at a high consumption level. Children aged 2-3 years with a high level of intake of magnesium are predicted to exceed the UL (50% of UL at mean intake and 150% at high level of intake).

The UL is based on a mild reversible adverse effect, osmotic diarrhoea. The age-specific UL was derived from the adult UL on a body weight basis, which might not be appropriate. For an adverse effect such as osmotic diarrhoea, the intake level at which the diarrhoea occurs might be more related to the concentration of magnesium in the intestines than to a daily dose.

It is unlikely that children aged 2 to 3 years would consume the daily reference quantity (600 ml) of formulated beverages in one serve on an empty stomach. Because of these assumptions in setting age-specific ULs for magnesium, not naturally occurring in food, the mildness and reversibility of the adverse effect, and the assumption that the intake would be in one serving on an empty stomach, the risk of adverse effects in 2-3 years old is considered to be relatively low.

For all other population groups, there was no appreciable risk of adverse effects related to high intake of magnesium.

In conclusion, the addition of magnesium to formulated beverages at a level of 80 mg per 600 ml serve poses no appreciable public health and safety risk.

Manganese

Hazard identification and characterisation

Chemistry

Manganese is an abundant metallic element that can exist in a variety of oxidation states. Mn^{2+} and Mn^{3+} are the most biologically important. Within this assessment, the word manganese refers to ionic manganese, except when specific manganese compounds are mentioned.

Function

Manganese is a component of a number of enzymes and activates a range of others. Glycosyl transferases are specifically activated by manganese.

Sources of manganese

Manganese is present both naturally and as a result of contamination in soils, sediments and water. Manganese is present in foods, particularly tea, green vegetables, nuts, bread and other cereals. The level of manganese in drinking water in Australia in reticulated supplies can range up to 0.25 mg/L, with typical concentrations of manganese usually less than 0.01 mg/L (NHMRC and NRMMC, 2004).

Absorption, distribution, metabolism and excretion

Absorption takes place in the small intestine via a carrier-mediated mechanism; passive diffusion may also occur. Absorption is generally low but appears to be higher in infants and young animals. Bioavailability of manganese from different food types is variable, but appears to be generally low, due to poor solubility.

In the portal blood manganese may bind to albumin and α_2 macroglobulin. A small proportion of manganese is oxidised to Mn^{3+}, and enters the systemic circulation, possibly by binding to transferrin. Manganese accumulates in mitochondria-rich tissues such as liver and pancreas. Manganese also accumulates in the brain, particularly in the globus pallidus, striatum and substantia nigra.

Manganese is excreted largely in the faeces, mostly as a result of biliary excretion, although some direct secretion also occurs. A small amount of manganese is excreted in the urine.

Toxicity

Manganese has low acute toxicity. Occupational exposure, for example in manganese mines and smelters, to high levels of inhaled manganese has been associated with manganism, a neurotoxic condition similar to Parkinson's disease. This condition occurs as a result of inhalation exposure to high levels of manganese and is not relevant to the assessment of lower levels of manganese in food. Drinking water contaminated with manganese has also been associated with neurological and behavioural effects. There is an association between manganese accumulation and liver disease but this may be due to impaired biliary excretion

caused by the liver disease rather than manganese toxicity. Effects on the immune system have been reported.

Manganese is a known neurotoxin at high occupational levels of inhalation exposure. However, it has also been suggested that exposure from lower levels in drinking water may result in more subtle neurological effects in human populations. The reported symptoms include muscle pain, fatigue, tremor, memory problems and impaired reflexes. Neurological effects have been reported at estimated intakes of 3.6-4.6 mg manganese from water, through comparable intakes have been negative in other studies. Other more limited data suggest that adverse effects may occur at even lower intake levels in children.

Animal data are also available and indicate similar neurotoxic effects to those reported in humans. However, the neurotoxic effects are inevitably of a less subtle nature than the symptoms assessed in human studies and so these have not been considered further. Animal studies have also reported adverse effects on haematology and reproductive parameters. In laboratory animals, adverse effects have been reported following long-term exposure to manganese at doses greater than 50-200 mg/kg bw/day. Detailed neurological examinations were performed in only one study in mice which detected effects at ~ 130 mg/kg bw/day.

The margin between oral effect levels in humans as well as experimental animals and the estimated intake from food is very low. Given the findings on neurotoxicity and the potential higher susceptibility of some subgroups in the general population, oral exposure to manganese beyond that normally present in food and beverages could represent an adverse health risk without evidence of any health benefit.

Vulnerable groups

Anaemic individuals may be vulnerable to the toxic effects of manganese due to the increased absorption that occurs in states of iron deficiency. Groups with impaired biliary clearance, such as patients with liver disease or older people, may also be susceptible to manganese accumulation and toxicity. It has also been reported that ethanol and long-term use of anti-psychotic drugs increases the susceptibility of humans to manganese toxicity.

Evaluation

Manganese	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	11	Total	neurotoxicity	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	4	Suppl	neurotoxicity	human
EU (European Commission Health & Consumer Protection Directorate-General, 2000i)**	No UL		neurotoxicity, insufficient data	

* Guidance level

** EU considered the available data not suitable for establishing an upper limit, however characterised the risk such that oral exposure above levels normally present in food could represent a risk of adverse health effects..

The US established a NOAEL of 11 mg/day of manganese from food based on the data presented by Greger (Greger, 1999). Greger reviewed information indicating that people eating Western-type and vegetarian diets may have intakes as high as 10.9 mg/day of manganese. Because no adverse effects due to manganese intake have been noted, at least in people consuming Western diets, 11 mg/day is a reasonable NOAEL for manganese from

food. A LOAEL of 15 mg/day can be identified on the basis of an earlier study by Davis and Greger (Davis and Greger, 1992).

At this dose, there were significant increases in serum manganese concentrations after 25 days of supplementation and in lymphocyte manganese-dependent superoxide dismutase activity after 90 days of supplementation. Because of the lack of evidence of human toxicity from doses less than 11 mg/day of manganese from food, an uncertainty factor of 1.0 was selected. The adult UL of 11 mg/day was adjusted for other age groups on the basis of relative body weights.

The EU decided there were limitations with the human data and the non-availability of NOAELs for critical endpoints from animal studies produced a considerable degree of uncertainty. Therefore, a UL could not be set. The margin between oral effect levels in humans as well as experimental animals and the estimated intake from food is very low. Given the findings on neurotoxicity and the potential higher susceptibility of some subgroups in the general population, oral exposure to manganese beyond the normally present in food and beverages could represent a risk of adverse health effects without evidence of any health benefit.

FSANZ considers the US evaluation as less appropriate, since adjustment on a body weight basis for age groups is inappropriate, when the UL is based on the level currently in a Western diet. If this basis is taken, it would be more appropriate to base the age-specific UL on their intake levels. Therefore, the EU approach is more appropriate. There are limitations with the human data and the margin between oral effect levels in humans as well as experimental animals and the estimated intake from food is very small. Oral exposure to manganese beyond the normally present in food and beverages could represent a risk of adverse health effects without evidence of any health benefit.

In conclusion, oral exposure to **manganese beyond the normally present in food and beverages could represent a risk of adverse health effects** without evidence of any health benefit.

Dietary intake

Intakes of manganese were only estimated at baseline. Estimated intakes were adjusted using second day intake data from the NNSs.

The concentration of manganese requested to be added to formulated beverages was 1.25 mg/600 ml reference quantity.

Manganese was not included in the 1995 Australian NNS. Therefore, in order to estimate intakes for the Australian population, the concentration data from the New Zealand NNS were matched to the most appropriate Australian food codes, then these values were used to estimate dietary intakes for the Australian population groups.

Estimated intakes for manganese were between two and five milligrams per day at the mean level of intake, and between four and eight milligrams per day at the 95th percentile of intake, depending on the population group.

Table 19: Estimated dietary intakes of manganese, before and after FBs are introduced into the diet

	Mean intake mg/day	95th percentile intake mg/day
Age group	**Baseline**	**Baseline**
2-3 years, Aus	2.7	4.9
4-8 years, Aus	3.0	5.5
5-6 years, NZ	^2.7	#3.5
7-10 years, NZ	^3.1	#4.0
9-13 years, Aus	3.5	6.5
11-14 years, NZ	^3.5	#4.5
14-18 years, Aus	3.9	7.3
15-18 years, NZ	3.8	6.4
≥19 years, Aus	4.6	7.9
≥19 years, NZ	4.6	7.6

^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.

Risk characterisation

The NHMRC has proposed an adequate intake for manganese in 2-3 years old to be at the same level as the UL (NHMRC, 2004). The adequate intake was based on current mean intake of manganese in Australia and New Zealand. This indicates that addition of manganese to formulated beverages is inappropriate, since there is a risk of adverse health effects without evidence of any health benefit.

For all other age groups, the margin between oral effect levels and the estimated intake from food is very small. Therefore, the addition of manganese to a formulated beverage could pose a public health and safety risk.

In conclusion, there are potential safety concerns with the addition of manganese to formulated beverages at a level of 1.25 mg in a 600 ml serve.

Molybdenum

Hazard identification and characterisation

Chemistry

Molybdenum (Mo) does not exist naturally in the metallic state, but occurs in association with other elements. Molybdenum exists in several valency states, e.g. $Mo^{II}O$, $Mo^{IV}S_2$, $Mo^{VI}O_3$, and as the stable salts $(NH_4)_2Mo^{VI}O_4$ (ammonium molybdate), $(NH_4)_6Mo^{VI}_7O_{24}.4H_2O$ (ammonium molybdate tetrahydrate) and $Na_2Mo^{VI}O_4.2H_2O$ (sodium molybdate dihydrate).

Function

Molybdenum is ubiquitous in food and water as soluble molybdates. Molybdenum-containing enzymes are found in many plants and animal organisms. In plants and lower organisms these enzymes are involved in the bacterial fixation of N_2, in the conversion of NO_3 to NH_3, in protein synthesis and in some redox reactions. In human and animal tissues the enzymes xanthine dehydrogenase (XD)/oxidase (XO), aldehyde oxidase (AO) and sulfite

oxidase (SO) require molybdopterin as cofactor and part of the enzyme molecule. In molybdopterin, molybdenum is bound by two S atoms to the pterin.

The redox potential of Mo^{V}/Mo^{VI} is appropriate for the electron exchange with flavinmononucleotides. Molybdenum is therefore an essential component of flavin- and Fe-containing enzymes.

Sources of molybdenum

Good food sources of molybdenum are sorghum, leafy vegetables (levels depending on soil content, those grown on neutral or alkaline soil are rich in molybdenum, those grown on leached acid soil are molybdenum deficient, legumes (beans), grains (cereals, wheat germ), organ meats, milk and eggs. Some 40% of molybdenum in cereals is lost on milling. Fruits, root vegetables, and muscle meat are pour sources. High concentrations have been found in shellfish.

Absorption, distribution, metabolism and excretion

Animals

The rate of gastrointestinal absorption of molybdenum depends on its chemical nature and the animal species. Ingested Mo^{VI} but not Mo^{IV} is readily absorbed from the duodenum and proximal jejunum. Water-soluble molybdates, thiomolybdates and oxothiomolybdates and molybdenum in herbage and green vegetables are absorbed to 75-97% by laboratory animals and ruminants. Insoluble MoS_2 is not absorbed; Mo^{IV} compounds are not readily absorbed. Intestinal absorption is inhibited by high intraluminal sulphate concentrations, probably because of competition for the common carrier. Silicates also inhibit the absorption of dietary molybdates.

Absorbed molybdenum rapidly appears in the blood loosely attached to the erythrocytes, specifically bound to α2-macroglobulins. In rodents it is distributed mainly to the liver, converted to molybdate and 36-90% of the total dose is excreted in the urine, less than 1% in the bile and only some in the faeces. In rabbits and guinea pigs molybdenum is deposited in the tissues within 4 hours after initial high blood and bile levels and eliminated within 72 hours by the kidneys. In horses, cattle and sheep faecal elimination is about half the urinary elimination because of limited absorption. Some bone storage was noted. Molybdenum crosses the placenta. Sulphate reduces the utilisation of molybdenum by some tissues and increases the urinary molybdenum excretion. Molybdenum is reabsorbed by the renal tubules but this reabsorption is reduced by S-containing and by acid proteins. The reabsorbed molybdenum deposits in liver, lung, bone and skin. It is responsible for fluoride storage and aids retention of fluoride in the bone of old rats as well as decreasing caries in rats. Small amounts of molybdenum increase antibody formation, e.g. agglutinins

^{99}Mo injected into dogs was concentrated in liver, kidney, pancreas, pituitary, thyroid and adrenals but none appeared in brain, white marrow or fat. The biological half-life varies from a few hours to several days in small laboratory animals and is related to the Cu and S metabolism.

Humans

Water-soluble molybdenum compounds and molybdenum in herbage and green vegetables are absorbed by humans at 40-50%. The absorption rate from drinking water may be the same as from food. Twenty five percent of absorbed molybdenum appears rapidly in the blood loosely attached to the erythrocytes, specifically bound to α2-macroglobulins, normal whole blood levels are 2-6 µg/L and serum levels are 0.55 µg/L. In man, the highest levels appear in kidney, liver and bone, raised levels appear also in adrenals, fat and omentum.

There is no bioaccumulation, with tissue levels rapidly returning to normal once exposure stops. Increased exposure at the work place or through drinking water is balanced by increased urinary excretion.

16-27% of intravenously administered ^{99}Mo to human subjects was excreted in 5 days in the urine. Faecal excretion over 10 days was 1-7%. Molybdenum was rapidly cleared from the blood within 24 hours.

Data on the molybdenum status of normal tissues are unreliable. Quoted blood and serum levels vary by 4 orders of magnitude. Serum levels of molybdenum rise in liver functional defects, hepatitis, hepatic tumours and after certain drugs. Raised blood levels are seen in uraemia, rheumatic disorders and cardiovascular disease. Human liver contains 1.3-2.9 mg molybdenum/kg dry matter, kidney 1.6 mg/kg dry matter, lung 0.15 mg/kg dry matter, brain and muscle 0.14 mg/kg dry matter, hair 0.07-0.16 mg/kg.

Toxicity

Molybdenum compounds appear to have low toxicity in humans. More soluble forms of molybdenum have greater toxicity than insoluble or less soluble forms. The UL in this report applies to all forms of molybdenum. There are limited toxicity data for molybdenum in humans; most of the toxicity data are for animals, especially ruminants. Ruminants are more sensitive to molybdenum than monogastric animals, but the basis for the toxicity of molybdenum in ruminants is not relevant for humans, because in ruminants this toxicity is always associated with 'conditioned' copper-deficiency. In monogastric laboratory animals, molybdenum has been associated with reduce growth or weight loss, renal failure, skeletal abnormalities, infertility, anaemia, diarrhoea, and thyroid injury. Since none of these effects have been observed in humans, it is impossible to determine which ones might be considered most relevant to humans.

Molybdenum toxicity in animals varies according to age, species, sex, and duration of exposure. In ruminants, the relative amounts of copper and sulfur in the diet are also important determinants of toxicity, but the effect of molybdenum on copper metabolism in humans is probably not significant.

There are no adequate human data for establishing a UL. Growth depression occurs in rats at 2-8 mg molybdenum/kg bw/day and skeletal changes at 7.5 mg molybdenum/kg bw/day. Reproductive and developmental changes were found in rats at 1.6-2 mg molybdenum/kg bw/day. In mice infertility and early pup deaths were noted at 1.5 mg molybdenum/kg bw/day. In rabbits skeletal changes and nephrotoxicity were found at 5 mg molybdenum/kg bw/day, while skeletal changes, bodyweight loss and anaemia were seen at 25-46 mg molybdenum/kg bw/day. Reduced growth occurred in guinea pigs at 75 mg molybdenum/kg bw/day. Adverse spermatogenic effects were seen in calves at 4 mg molybdenum/kg bw/day. Thiomolybdate intoxication can occur in experimental animals at intakes of 5 mg molybdenum/kg bw.

From these studies the critical effects of molybdenum in the rat and mouse appear to be effects on reproduction, particularly foetal development.

In a 9 weeks study in SD rats on the effects of molybdenum supplementation on oestrus activity, fertility and foetal development, 5 groups, each of 21 female weaning rats, were given for 6 weeks a basic diet containing 0.025 mg molybdenum/kg diet as well as 6.3 mg Cu/kg

diet, and additionally in their drinking water doses of 0, 5, 10, 50 and 100 mg molybdenum/L as sodium molybdate ($Na_2MoO_4.2H_2O$) for 3 weeks until the 21st day of gestation. Six animals in each group were sacrificed after 6 weeks to determine the oestrus cycle length. The remaining 15 animals in each group were mated with untreated males and allowed to continue gestation for 21 days. The average mean weekly supplementary molybdenum intakes were 0.0, 0.64, 1.12, 5.81 and 11.56 mg molybdenum/rat (equivalent to 0, 0.91, 1.6, 8.3 and 16.7 mg molybdenum/kg bw/day assuming an average rat weight of 100 g). There was no effect on fertility, food and water consumption. Oestrus cycle was prolonged from 1.6 mg/kg bw/day and higher supplementation. Gestational weight, litter size and foetal weights were less than controls for the groups fed 1.6 mg/kg bw/day and higher doses.

Histopathology showed delayed histological development of foetal structures, delayed oesophageal development, delayed transfer of foetal haematopoeisis from liver to bone marrow, and delayed myelination of the spinal cord at doses of ≥1.6 mg/kg bw/day. Foetal resorption increased at doses of 1.6 mg/kg bw/day and higher. Molybdenum supplementation at dose levels of 1.6 mg/kg bw/day and higher increased SO and XDH/XO activity, however this effect was less apparent in pregnant animals. The NOAEL was 0.9 mg molybdenum/kg bw/day ((Fungwe *et al*., 1989), reviewed by the EU).
This study in rats is pivotal because of its satisfactory design (according to EU), the use of an adequate number of test animals, demonstration of a clear dose-response relationship and clear toxicological endpoints.

Few data are available on human toxicity following ingestion. Food or water must contain more than 100 mg/kg to produce signs of toxicity, which include diarrhoea, anaemia and high levels of uric acid in the blood. Elevated uric acid levels, which are associated with the onset of gout, are hypothesised to be caused by stimulation of xanthine oxidase by high molybdenum intake.

Evaluation

Molybdenum	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2001b)	2	Total	reproductive effects	rat
UK (UK Expert Group on Vitamins and Minerals, 2003)*	0.23	Total	insufficient data	
EU (European Commission Health & Consumer Protection Directorate-General, 2000d)	0.6	Total	reproductive effects	rat

* Guidance level, the level is the current estimated maximum intake from the UK diet.

Because of deficiencies in human studies, inadequate data exist to identify a causal association between excess molybdenum intake in normal, apparently healthy individuals and any adverse health outcomes. In addition, studies have identified levels of dietary molybdenum intake that appear to be associated with no harm. Thus, the US and EU selected reproductive effects in rats as the most definitive toxicological indices, while the UK found the data inadequate to establish an UL.

Based on studies in rats and mice, the EU and US established a NOAEL of 0.9 mg/kg/day.

The US used an uncertainty factor of 30 (10 for interspecies and 3 for intraspecies), while the EU used an uncertainty factor of 100 (10 for interspecies and 10 for intraspecies).

The US used a UF of 3 for intraspecies variation that was based on the expected similarity in pharmokinetics of molybdenum among humans. The reason for this difference was explained by the US that the main concern for an intraspecies factor of 10 was based on concerns on possible interactions with copper and concerns about copper-deficient humans. Recent information suggests that molybdenum does not have any effect on copper metabolism in humans (Turnland and Keyes, 2000). The US used the NOAEL of 0.9 mg/kg bw/day and divided this by the overall uncertainty factor of 30 to obtain an UL of 30 μg/kg bw/day for humans. This value of 30 μg/kg bw/day was multiplied by the average of the reference bodyweight and the resulted UL for adults was rounded to 2000 μg/day. Since no specific data for other age groups are available the adult UL was adjusted on the basis of relative weight. The UL is also applicable for pregnant and lactating women, since the adverse effect was based on reproductive effects.

The EU used an uncertainty factor of 100. This comprised a factor of 10 for protecting sensitive human sub-populations with inadequate copper intake or with deficient copper metabolism in view of the species differences in antagonism between molybdenum and copper, and another factor of 10 to cover the lack of knowledge about reproductive effects of molybdenum in humans and incomplete data on the toxicokinetics in man. Because the exposure in this 9-week rat study is sufficient to cover the relevant period of foetal development, a further uncertainty factor is unnecessary. This provides an UL of approximately 0.01 mg/kg bw/day, equivalent to 0.6 mg/person/day for adults, which is also applicable to pregnant and lactating women. The UL for children was derived by extrapolating from the adult UL on a body weight basis. .

FSANZ evaluation
The US evaluation based the decreased uncertainty factor for intraspecies variation on recent information on the possible interaction between molybdenum and copper. However, this publication was not published in a peer-reviewed scientific paper, but in a book chapter. Since 2001 (US assessment), there haven't been any scientific publications on the interaction between molybdenum and copper. A reduced uncertainty factor may therefore be premature and so at this point in time the EU evaluation is considered the most appropriate. The adult UL was adjusted on a body weight basis for the various age groups.

In summary, the UL for **molybdenum** for the various groups are:

1-3 years	**13 kg**	**100 μg/day**
4-8 years	**22 kg**	**200 μg/day**
9-13 years	**40 kg**	**350 μg/day**
14-18 years	**61 kg**	**500 μg/day**
Adults	**69 kg**	**600 μg/day**

Dietary intake

There were no food composition data available to enable a comprehensive intake assessment to be conducted for molybdenum. Whilst there are small amounts of data available, these data were either not from Australian or New Zealand sources, were not extensive enough across the whole diet, were not in the correct format or had not been assessed for accuracy.

Risk characterisation

For molybdenum a UL of 600 μg/day for adults has been established based on reproductive effects in rats. Some food composition data are available for molybdenum although these are not sufficient to undertake a complete dietary intake assessment at the present time.

In the absence of a complete dietary intake assessment, it is not currently possible to evaluate the safety of the addition of molybdenum to formulated beverages.

Phosphorus

Hazard identification and characterisation

Chemistry

Phosphorus is a group 5 element of the periodic table and has an atomic weight of 30.97. Phosphorus is most commonly found in nature in its pentavalent form in combination with oxygen, as phosphate (PO_4^{3-}).

Function

Phosphorus is a constituent of all major classes of biochemical compounds. Structurally, phosphorus occurs as phospholipids, which are a major constituent of most biological membranes, and as nucleotides and nucleic acids. Phosphorus plays an important role in carbohydrate, fat and protein metabolism and is essential for optimum bone health. The energy that is required for most metabolic processes is derived from the phosphate bonds of adenosine triphosphate and other high energy phosphate compounds.

Clinical studies employing chronic phosphorus supplementation were the first to show that high phosphorus intakes influence the parathyroid-vitamin D axis, which maintains calcium balance in the body. The phosphorus loading in humans operates through mechanisms of nutritional or secondary hyperparathyroidism similar to those observed in animals fed excess phosphorus.

Sources of phosphorus

Dietary sources that are rich in phosphorus include red meats, dairy products, fish, poultry and bread and other cereal products. A number of phosphate salts are used in foods and soft drinks as additives.

Absorption, distribution, metabolism and excretion

Food phosphorus is a mixture of inorganic and organic forms. Intestinal phosphatase hydrolyze the organic forms contained in ingested protoplasm and thus most phosphorus absorption occurs as inorganic phosphate. On a mixed diet, net absorption of total phosphorus in various reports ranges from 55 to 70 percent in adults and from 65 to 90 percent in infants and children. There is no evidence that this absorption efficiency varies with dietary intake. There is no apparent adaptive mechanism that reduces phosphorus absorption at high intakes. A portion of phosphorus absorption is by way of a saturable active transport facilitated by 1,25-dihydroxyvitamin D. However, the fact that fractional phosphorus absorption is virtually constant across a broad range of intakes suggests that the bulk of phosphorus absorption occurs by passive, concentration-dependent processes. Phosphorus absorption is reduced by ingestion of aluminium-containing antacids and by

pharmacologic doses of calcium carbonate. There is no significant interference with phosphorus absorption by calcium at intakes within the typical adult range.

Approximately 80% of the body phosphorus is present in the skeleton and the remainder is distributed in soft tissues and extracellular fluid. About 70% of the phosphorus in blood is as a constituent of phospholipids; the remainder is present as inorganic phosphate, about 85% free and 15% protein-bound.

Excretion of endogenous phosphorus is mainly through the kidneys. Inorganic serum phosphate (P_i) is filtered at the glomerulus and reabsorbed in the proximal tubule. The transport capacity of the proximal tubule for phosphorus is limited; it cannot exceed a certain number of mmol per unit time. This limit varies inversely with parathyroid hormone (PTH) concentration; PTH thereby adjusts renal clearance of P_i. In the healthy adult, urine phosphorus is essentially equal to absorbed diet phosphorus, less small amounts of phosphorus lost in shed cells of skin and intestinal mucosa. This regulation of phosphorus excretion is apparent from early infancy. In infants, as in adults, the major site of regulation of phosphorus retention is at the kidney.

Toxicity

P_i rises as total phosphorus intake increases. Excess phosphorus intake from any source is expressed as hyperphosphatemia, and essentially all the adverse effects of phosphorus excess are due to the elevated P_i in the extracellular fluid. The principal effects that have been attributed to hyperphosphatemia are: 1) adjustments in the hormonal control system regulating the calcium economy, 2) ectopic (metastatic) calcification, particularly in the kidney, 3) in some animal models, increased porosity of the skeleton, and 4) a suggestion that high phosphorus intakes could reduce calcium absorption by complexing calcium in the chyme.

It has been reported that high intakes of polyphosphates, such as are found in food additives, can interfere with absorption of iron, copper, and zinc; however, described effects are small, and have not been consistent across studies. For this reason it was not considered feasible to use trace mineral status as an indicator of excess phosphorus intake.

Most of the studies that describe harmful effects of phosphorus intake used animal models. In extrapolating these data to humans, it is important to note that the phosphorus density of human diets represent the extreme low end of the continuum of standard diets for pets and laboratory animals.

The US stated that a UL can be defined as an intake associated with the upper boundary of adult normal values of serum P_i. No reports exist of untoward effects following high dietary phosphorus intakes in humans. Essentially all instances of dysfunction (and, hence, all instances of hyperphosphatemia) in humans occur for non-dietary reasons (for example, end-stage renal disease, vitamin D intoxication). Therefore, data on the normal adult range for serum P_i are used as the basis for deriving a UL for adults.

The higher values for serum P_i in infancy are manifestly tissue-safe levels, and if they are taken as an approximation of the upper normal human value (on the ground that there is no basis for assuming major differences in tissue susceptibility to metastatic mineralization at different ages), the corresponding ingested intake in an adult would be over 10.2 g (330 mmol)/day.

If the normal adult range is used, the upper boundary of adult normal values of serum P_i is reached at a daily phosphorus intake of 3.5 g. There is no evidence that individuals consuming this intake may experience any untoward effects. No benefit is evident from serum P_i values above the usual normal range in adults.

Vulnerable groups

Hyperphosphatemia from dietary causes becomes a problem mainly in patients with end-stage renal disease or in such conditions as vitamin D intoxication. When functioning kidney tissue mass is reduced to less than ~20 percent of normal, the glomerular filtration rate becomes too low to clear typical absorbed loads of dietary phosphorus, and then even sharply reduced phosphorus diets may still be excessive as they lead to hyperphosphatemia.

Evaluation

Phosphorus	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2000a)	4,000	Total	serum inorganic phosphorus levels	human
UK (UK Expert Group on Vitamins and Minerals, 2003)*	250	supplemental	gastrointestinal	human
EU	no assessment available			

* Guidance level only

Only the US set a UL for total phosphorus intake and is therefore more relevant than the UK evaluation.

The US stated that no benefit is evident from serum P_i values above the usual normal range in adults. Moreover, information is lacking concerning adverse effects in the zone between normal P_i and levels associated with ectopic mineralization. Therefore, the US kept with the pharmacokinetic practice where the relationship between intake and blood level is known, an uncertainty factor of 2.5 is chosen. An UL of 4.0 g/day for adults is calculated by dividing a NOAEL of 10.2 g/day by an uncertainty factor of 2.5.

The US calculated a UL for children up to 8 years of 3 g/day by dividing the NOAEL for adults (10.2 g/day) by an uncertainty factor of 3.3 to account for potentially increased susceptibility due to smaller body size. There is no evidence to suggest increased susceptibility to adverse effects during adolescence. Therefore, the same UL specified for adults was selected. Because of an increasing prevalence of impaired renal function after age 70, a larger uncertainty factor of 3.3 seems prudent, and the UL for adults of this age is set at 3.0 g/day. During pregnancy, absorption efficiency for phosphorus rises by about 15 percent, and thus, the UL associated with the upper end of the normal range will be about 15 percent lower, that is, about 3.5 g/day.

During lactation, the phosphorus economy of a woman does not differ detectably from the non-lactating state. Hence the UL for this physiologic state is not different from the non-lactating state, 4.0 g/day.

In summary, the UL for **phosphorus** for the various groups are:

1-3 years 3.0 g/day
4-8 years 3.0 g/day
9-13 years 4.0 g/day
14-18 years 4.0 g/day

19-70 years	**4.0 g/day**

71 years and over **3.0 g/day**
Pregnancy **3.5 g/day**
Lactation **4.0 g/day**

Dietary intake

Intakes of phosphorus were estimated at baseline and when formulated beverages are consumed. Estimated intakes were adjusted based on second day intake data from the NNSs.

The concentration of phosphorus requested to be added to formulated beverages was 250 mg/600 ml reference quantity.

Estimated intakes were calculated for two more specific population groups for phosphorus compared to other nutrients. This was because these groups had specific ULs. The additional groups assessed were older people aged 71 years and over, and women of child bearing age (16-44 years) as a proxy to represent pregnant and lactating women. Where respondents aged 71 years or over were included in the collated results for the age group of 19 years and above, they were assigned their own respective UL. Where the estimates were calculated for the general population that may have included females 16-44 (e.g. 14-18 years), the UL for the general population was used. Only when females aged 16-44 years were assessed in isolation was the UL for pregnancy used. (A separate comparison of intakes against the UL of 4 g/day for lactation was not calculated, as the pregnancy UL of 3.5 g/day was a worst case scenario).

Estimated intakes increased from baseline by around 100 mg/per day when FBs were consumed across the population groups assessed. The UL was not exceeded for any population group assessed.

Table 20: Estimated dietary intakes of phosphorus, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	1052 (35)	1150 (40)	1504 (50)	1655 (55)
4-8 years, Aus	1143 (40)	1270 (45)	1737 (60)	1860 (60)
5-6 years, NZ	^1020 (**)	NA	#1301 (**)	NA
7-10 years, NZ	^1164 (**)	NA	#1546 (**)	NA
9-13 years, Aus	1402 (35)	1549 (40)	2259 (55)	2375 (60)
11-14 years, NZ	^1339 (**)	NA	#1792 (**)	NA
14-18 years, Aus	1589 (40)	1758 (45)	2735 (70)	2980 (75)
15-18 years, NZ	1568 (40)	1685 (40)	2462 (60)	2585 (65)
16-44 years females, Aus	1374 (40)	1470 (40)	2145 (65)	2245 (65)
16-44 years females, NZ	1421 (40)	1494 (45)	2141 (60)	2231 (65)
≥19 years, Aus	1490 (40)	1574 (40)	2459 (65)	2608 (65)
≥19 years, NZ	1484 (40)	1541 (40)	2335 (60)	2427 (60)
71+ years, Aus	1247 (40)	1281 (45)	1941 (65)	1982 (65)
71+ years, NZ	1235 (40)	1254 (40)	1733 (60)	1765 (60)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.

** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

The main route of exposure to phosphorus is through the diet. Toxicological evaluation and dietary intake data indicate that both children and adult Australian and New Zealand consumers are unlikely to approach the UL set for phosphorus, at the high level of intake assuming use in formulated beverages (55-75% UL for children of the various age-groups and 65% UL for adult Australians 19 years and above and 60% UL for adult New Zealanders aged 19 years and above.

For pregnant women a UL of 3.5 g/day was established. Females of childbearing age (16-44 years) had at high level of intake of 2.2 g/day when formulated beverages are consumed (65% UL). For older adults (71 years and over) a lower UL was established of 3.0 g/day. This age group did not exceed the UL at the high level of intake (2.0 g/day for Australians or 65% UL and 1.8 g/day or 60% UL for New Zealanders, aged 71 and above). Therefore, dietary intake of phosphorus for consumers from all population groups is considered to be within the safe range of intake for both mean and high consumers.

It is concluded that addition of phosphorus to formulated beverages at a level of 250 mg in a 600 ml serve poses no appreciable public health and safety risk, assuming baseline levels of use in other foods.

Selenium

Hazard identification and characterisation

Chemistry

Selenium is a metallic group VI element that is abundant and which can exist in 4 oxidation states (-2, +1, +2 and +6).

Function

The biologically active form of selenium is selenocysteine. Selenocysteine is incorporated into selenoproteins, of which over thirty have been identified to date. The selenoproteins include the glutathione peroxidases, which protect against oxidative damage, the iodothyronine deiodinases (involved in the production of the hormone triiodothyronine from thyroxine), selenoprotein P (which is involved in antioxidant and transport functions) and the thioredoxin reductases (maintenance of the intracellular redox state). Selenium is essential to humans at low levels but potentially toxic at high levels of exposure. Selenium is widely distributed in rocks and soils; however, its distribution is uneven. Selenium was known as a toxicant before being recognised as a nutrient.

Sources of selenium

The selenium content of food varies depending on the selenium content of the soil where the animal was raised or the plant was grown: organ meats and seafood, 0.4-1.5 μg/g; muscle meats, 0.1 to 0.4 μg/g; cereals and grains, less than 0.1 to greater than 0.8 μg/g; dairy

products, less than 0.1 to 0.3 μg/g; and fruits and vegetables, less than 0.1 μg/g ((WHO, 1987). Thus the same foodstuffs may have more than a ten-fold difference in selenium content. Plants do not appear to require selenium and most selenium metabolism by plants occurs through sulphur pathways in which selenium substitutes for sulphur. Thus, plant content of selenium depends on the availability of the element in the soil where the plant was grown. Unlike plants, animals require selenium. Meat and seafood are therefore more reliable dietary sources of selenium.

Absorption, distribution, metabolism and excretion

Absorption of selenium is efficient and is not regulated. More than 90 percent of selenomethionine, the major dietary form of the element, is absorbed by the same mechanism as methionine itself. Although little is known about selenocysteine absorption, it appears to be absorbed very well also. An inorganic form of selenium, selenate (SeO_4^{2-}), is absorbed almost completely, but a significant fraction of it is lost in the urine before it can be incorporated into tissues. Another inorganic form of selenium, selenite (SeO_3^{2-}), has a more variable absorption, probably related to interactions with substances in the gut lumen, but is better retained, once absorbed, than is selenate. Absorption of selenite is generally greater than 50 percent. Although selenate and selenite are not major dietary constituents, they are commonly used to fortify foods and as selenium supplements.

Two pools of reserve selenium are present in humans and animals. One of them, the selenium present as selenomethionine, depends on dietary intake of selenium as selenomethionine. The amount of selenium made available to the organism from this pool is a function of turnover of the methionine pool and not the organism's need for selenium. The second reserve pool of selenium in the selenium present in liver glutathione peroxidase (GSHPx-1). In rats, 25 percent of total body selenium is present in this pool.

As dietary selenium becomes limiting for selenoprotein synthesis, this pool is downregulated by a reduction of GSHPx-1 messenger RNA concentration. This makes selenium available for synthesis of other selenoproteins.

Selenomethionine, derived mainly from plants, enters the methionine pool in the body and shares the fate of methionine until catabolised by the transsulfuration pathway. The resulting free selenocysteine is further broken down with liberation of a reduced form of the element, which is designated selenide. Ingested selenite, selenate, and selenocysteine are all apparently metabolised directly to selenide. This selenide may be associated with a protein that serves as a chaperone. The selenide can be metabolised to selenophosphate, the precursor of selenocysteine in selenoproteins and of selenium in transfer RNA, or it can be converted to excretory metabolites, some of which have been characterised as methylated forms.

The mechanism that regulates production of excretory metabolites has not been elucidated, but excretion has been shown to be responsible for maintaining selenium homeostasis in the animal. The excretory metabolites appear in the urine, primarily, but when large amounts of selenium are being excreted, the breath also contains volatile metabolites (e.g. dimethylselenide, garlic breath).

Toxicity

FSANZ[46] reviewed selenium toxicity in 1999 as part of Proposal P157 – Metal Contaminants (ANZFA, 1999). Since then new evaluations have become available and therefore the safety of selenium has been revisited.

[46] as the Australia New Zealand Food Standards Authority (ANZFA)

Selenium has a variety of toxic endpoints in both animals and humans. In humans, the first signs of chronic toxicity appear to be pathological changes to the hair and nails, followed by adverse effects on the nervous system. Common clinical features are hair loss and structural changes in the keratin of hair and of nails, the development of icteroid skin, and gastrointestinal disturbances. A positive association between dental caries and urinary selenium have been reported. Changes in biochemical parameters have also been reported. The available studies indicate the development of selenosis (chronic selenium poisoning) is associated with selenium intakes in excess of 0.85 mg/day (0.014 mg/kg bw for a 60 kg adult). Selenium toxicity is cumulative.

Supplementation studies in humans indicate that up to 0.3 mg/day additional selenium is not associated with overt adverse effects over a short period of time, although specific symptoms have not always been investigated. However, one study, which specifically considered symptoms of selenosis, indicated that 0.2 mg/day additional selenium for up to 10 years did not result in symptoms of selenosis. In addition to reduced growth rates, similar symptoms to those in humans are found in animals treated with selenium.

Selenium sulphide, which is not a permitted form in the Code, is carcinogenic but other selenium compounds are not. Selenium compounds are not mutagenic *in vivo*. Adverse effects have been reported on the reproductive system of various animals, though not primates. Reproductive toxicity is not an issue that has been examined in detail in the available human epidemiological studies.

The most sensitive indicators of selenium toxicity are changes in the nails and hair. In a study by Yang ((Yang *et al*., 1989a; Yang *et al*., 1989b) conducted in an area of China where dietary selenium exposure is high, selenium intakes were correlated with blood levels to determine the intakes at which marginal selenium toxicity occur. This was at a total intake of 0.91 mg/day selenium.

Children
Studies have shown that a human milk selenium concentration of 60 μg/L was not associated with known adverse effects. Therefore, this will give a conservative estimate to derive upper limits for children and adolescents.

Evaluation

Selenium	**UL in adults, mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US (US Institute of Medicine, 2000c)	0.40	Total	hair loss and changes in nail pathology	human
UK (UK Expert Group on Vitamins and Minerals, 2003)	0.45	Total	hair loss and changes in nail pathology	human
EU (European Commission Health & Consumer Protection Directorate-General, 2000e)	0.30	Total	hair loss and changes in nail pathology	human
WHO/FAO (WHO, 1987)#	0.40	Total	hair loss and changes in nail pathology	human
ANZFA (ANZFA, 1999)#	0.75	Total	hair loss and changes in nail pathology	human

Provisional Tolerable Daily Intake

The EU considered the study of Yang the most relevant study for selenium toxicity. A NOAEL of 850 μg/day was derived. The NOAEL used was derived from a study on a large number of subjects and is expected to include sensitive individuals. It was decided to use an uncertainty factor of 3 to account for the remaining uncertainties of the studies used in deriving an upper level. An upper limit of 0.30 mg/day was derived for adults. This value covers selenium intake from all sources of food, including supplements.

The US established a NOAEL of 800 μg/day, based on the Chinese studies, which is protective for the population in the United States and Canada. An uncertainty factor of 2 was selected to protect sensitive individuals. The toxic effect is not severe, but may not be readily reversible, so a UF greater than 1 is needed. An UL of 0.40 mg/day was derived for adults.

The UK concluded that the intake of 0.91 mg selenium/day produced slight effects and was close to a NOAEL. Because of this an uncertainty factor of 2 was applied for LOAEL to NOAEL extrapolation. Because this is based on a population study, an uncertainty factor for inter-individual variation is not required. An upper level for total selenium intake of 0.45 mg/day can therefore be derived.

The evaluation of FAO/WHO (FAO/WHO, 2002) for the upper limit of selenium was based on a risk assessment report from the International Programme on Chemical Safety (WHO, 1987).

A comprehensive account of the clinically significant biochemical manifestations of chronic and acute intoxication from selenium arising from high concentrations in food, drinking water, and the environment were published jointly by WHO and the United Nations Environment Programme and the International Labour Organisation (WHO, 1987). This report stresses that the signs and symptoms of human overexposure to selenium are not well defined. Common clinical features are hair loss and structural changes in the keratin of hair and of nails, the development of icteroid skin, and gastrointestinal disturbances. An increased incidence of nail dystrophy has been associated with consumption of high-selenium foods supplying more than 900 μg/day. These foods were grown in selenium-rich (seleniferous) soil from specific areas in China. A positive association between dental caries and urinary selenium output under similar circumstances was reported. Sensitive biochemical markers of impending selenium intoxication have yet to be developed. In their absence it is suggested that the upper tolerable nutrient intake level (UL) for selenium should be set, provisionally, at 400 μg/day for adults. It is noteworthy that a maximum tolerable dietary concentration of 2 mg/kg dry diet was suggested for all classes of domesticated livestock and has proved satisfactory in use (National Research Council, 1980). This suggests that the proposed UL of 400 μg/day for human subjects provides a fully adequate margin of safety.

The previous evaluation by FSANZ (as ANZFA) had established the level of 750 μg/day for a toxicological endpoint, which is not life-threatening. Homeostatic mechanisms present in adults act to compensate for excessive intakes of selenium and the toxicity at this level, and at higher levels (850-959 μg/day) associated with clinical signs of toxicity, were considered to be reversible. Chronic selenium intake of 750 μg/day was therefore proposed as the provisional tolerable daily intake for selenium. Insufficient data were available from which to estimate the safe upper limit to population mean intakes of selenium for most other age groups and for pregnant and lactating women.

The most sensitive indicators for selenium toxicity are changes in nails and hair. More severe adverse effects on the nervous system are difficult to analyse and therefore less easily detected. The effects of selenium toxicity, i.e. adverse effects on the nervous system, are serious and cumulative, and necessitate the setting of an upper limit. The most sensitive indicators of selenium toxicity are changes in nails and hair; therefore these endpoints are used for establishing an upper limit.

The more recent evaluations by the US and the FAO/WHO are considered the most comprehensive and have been used to derive the following upper limits for **selenium**:

1-3 years	**90 µg/day**
4-8 years	**150 µg/day**
9-13 years	**280 µg/day**
14-18 years	**400 µg/day**
adults	**400 µg/day**

Permitted forms

The Applicant requested the following forms to be permitted for selenium: seleno methionine, sodium selenate, and sodium selenite. Seleno methionine and sodium selenite are already permitted in Standard 2.9.1 – Infant Formula Products and sodium selenate is permitted in Standard 2.9.4 – Formulated Supplementary Sports Foods.

Within the assessment of selenium toxicity by both the EU (European Commission Health & Consumer Protection Directorate-General, 2000e) and US (US Institute of Medicine, 2000c) inorganic selenites and selenates as well as selenomethionine were included. The US stated that the limited data available in humans suggest that chronic toxicities from inorganic and organic forms have similar clinical features but differ in rapidity of onset and relationship to tissue selenium concentrations.

In conclusion, the available evidence does not indicate that the different forms of selenium have differences in toxicity. Therefore, the requested forms of selenium are appropriate as permitted forms for selenium.

Dietary intake

Intakes of selenium were estimated at baseline and when formulated beverages are consumed.

The concentration of selenium requested to be added to formulated beverages was 17.5 µg/600 ml reference quantity.

Selenium was not assessed in the 1995 Australian NNS. Therefore, a model was set up in DIAMOND assigning selenium concentrations to food groups in order to estimate selenium intakes for Australian population groups. The concentration data used in the dietary modelling were derived from Australian analytical surveys that were collected for the purposes of conducting dietary exposure assessments for P157 – Metal contaminants in foods, a previous proposal raised during the Review of the Code. Only Australian survey data were used for the assessment for Australia.

Selenium was assessed in the 1997 New Zealand NNS, therefore the concentration data were specific to New Zealand foods.

Estimated intakes for selenium were not adjusted for Australia, but were adjusted for New Zealand based on second day intake data from the 1997 NNS. Baseline intakes for New Zealanders aged 5-14 years from the 2002 Children's Nutrition Survey were also adjusted using second day intakes (Ministry of Health, 2003). The unadjusted estimated intakes for selenium for the Australian population groups will be higher at the 95th percentile than those for similar age groups that have adjusted intakes.

Estimated intakes increased from baseline around 10 to 20 µg/per day when FBs were consumed depending on the population group assessed. The UL was not exceeded for any population groups assessed.

Table 21: Estimated dietary intakes of selenium, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake µg/day (%UL)		95th percentile intake µg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	32 (35)	42 (45)	70 (80)	92 (100)
4-8 years, Aus	41 (30)	53 (35)	93 (60)	111 (75)
5-6 years, NZ	^28.3 (**)	NA	#37.7 (**)	NA
7-10 years, NZ	^35.3 (**)	NA	#52.6 (**)	NA
9-13 years, Aus	54 (20)	68 (25)	117 (40)	138 (50)
11-14 years, NZ	^42.6 (**)	NA	#63.4 (**)	NA
14-18 years, Aus	69 (15)	86 (20)	160 (40)	192 (50)
15-18 years, NZ	48 (10)	59 (15)	70 (20)	85 (20)
≥19 years, Aus	70 (15)	77 (20)	165 (40)	178 (45)
≥19 years, NZ	51 (15)	56 (15)	78 (20)	87 (20)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Dietary modelling indicates that selenium intakes for all population groups are predicted to be below the UL even for high consumers and applying a worst-case scenario i.e. all products specified are replaced by formulated beverages (Scenario 2).

All high consumer population groups, with the exception of 2-3 year olds, are estimated to have intakes of selenium below the UL. Estimated high consumer intakes for 2-3 year olds is estimated to be at the UL (100%).

Due to the use of 24-hour dietary survey data, which tends to over-estimate habitual food consumption amounts for high consumers, it is likely that the 95th percentile dietary intake is an over-estimate. In addition, a number of conservative assumptions were used in the dietary modelling which may further add to the overestimation. For example, that all specified drinks would be substituted for formulated beverages in the 2-3 year old population group.

The UL represents a quantitative level of total intake at which, or below no harm is expected to occur assuming nutrient adequacy is met. Therefore estimated intake levels at the UL, generally do not raise any safety concerns as the UL is not itself a threshold for toxicity. In this case, the predicted high consumer intake for 2-3 year olds is still well below a level at which adverse effects might be observed. The dietary modelling also predicts that the higher intakes estimated for 2-3 year olds will not be sustained in the older age groups (e.g. 4-8 year olds).

Overall, the potential to exceed the UL, even for 2-3 year olds, is considered to be low.

It is concluded that addition of selenium to formulated beverages at a level of 17.5 μg in a 600 ml serve poses no appreciable public health and safety risk.

Zinc

Hazard identification and characterisation

Chemistry

Zinc is an abundant group IIB post-transition metallic element. It occurs in nature in various forms. Zinc is present in the earth's crust and in seawater. Zinc is found in all plant and animal tissues, particularly inside the nuclei.

Function

Zinc is essential for growth and development, testicular maturation, neurological function, wound healing and immunocompetence. Over 300 zinc enzymes have been discovered covering all six classes of enzymes and in different species of all phyla. Zinc has structural, regulatory or catalytic roles in many enzymes. Additionally, it maintains the configuration of a number of non-enzymatic proteins such as pre-secretory granules of insulin, some mammalian gene transcription proteins and thymulin. Well known zinc containing enzymes include superoxide dismutase, alkaline phosphatase and alcohol dehydrogenase.

Sources of zinc

Zinc is found in all plant and animal tissue, particularly inside the nuclei. Good food sources of zinc include red meat, whole wheat, raisins, unrefined cereals (high content, low bioavailability) and fortified cereals.

Tap water can contain high concentrations of zinc as a result of corrosion of zinc-coated pipes and fittings (NHMRC and NRMMC, 2004). Zinc concentrations in galvanised iron rainwater tanks are typically 2 mg/L to 4 mg/L but have been reported as high as 11 mg/L. In major Australian reticulated supplies, the concentration of zinc ranges up to 0.26 mg/L, with a typical concentration of 0.05 mg/L. Drinking water guidelines in Australia and New Zealand (Ministry of Health, 2000) recommend concentrations should not exceed 3 mg zinc/L, based on aesthetic considerations (taste).

Other sources of zinc, excluding dietary intakes, include zinc supplements, inhalation of zinc metal or oxide fumes in industrial settings and storage of food and drink in galvanised containers.

Absorption, distribution, metabolism, and excretion

Absorption of zinc takes place in the small intestine and appears to be a carrier-mediated transport process which is not saturated under normal physiological conditions. At high intakes, zinc is also absorbed through a non-saturable process or passive diffusion. Absorption of dietary zinc ranges from 15 to 60%. Mechanisms for the transport of zinc across the intestinal wall, its export into plasma and its uptake into other tissues are uncertain. Once in plasma, zinc is carried by a number of proteins that include albumin, transferrin and caeruloplasmin. Most of the absorbed zinc is excreted in the bile and eventually lost in the faeces. There appears to be no specific zinc 'store' in the body.

Tissue content and activity of zinc-dependent processes are maintained over a wide range of dietary zinc intakes. When zinc intake is increased, the fractional absorption decreases and intestinal excretion increases while urinary losses remain fairly constant. Endogenous faecal zinc losses may increase several fold to maintain zinc homeostasis with high intakes. At very low zinc intakes, absorption can increase to between 59-84% and faecal and urinary losses decrease accordingly. When these primary homeostatic mechanisms are not sufficient to handle large dietary excesses of zinc, the excess zinc is lost via the hair. The kinetics of zinc absorption and elimination follow a two-component model. The initial rapid phase has a half-life in humans of 12.5 days and the slower pool turns over with a half-life of approximately 300 days.

Interactions with a number of dietary factors influence zinc uptake. Ligands, such as phytate, form insoluble complexes with zinc and prevent absorption. Calcium increases binding of zinc by phytate. Larger doses of calcium can decrease net zinc absorption. High iron content in the diet decreases zinc absorption. Earlier reports indicated that folic acid can also inhibit zinc retention and metabolism, but more recent evidence indicates that folic acid does not adversely affect zinc status. Copper and zinc compete for absorption but it appears unlikely that modestly increased intakes of copper interfere with zinc absorption. Histidine, methionine and cysteine are thought to facilitate zinc absorption (these amino acids remove zinc from the zinc-calciumphytate complexes).

Toxicity

FSANZ[47] reviewed zinc toxicity in 1999 as part of Proposal P157 – Metal Contaminants (ANZFA, 1999). Since then new evaluations have become available and therefore the safety of zinc has been revisited.

Animals

Very high doses of zinc in animal studies can cause neural degeneration, acinar cell necrosis and metaplasia in the pancreas, decreased haematocrit and decreased white blood cell count. Very high doses have also been shown to cause reproductive toxicity in rats. Lower doses have resulted in reduced ceruloplasmin activity and decreased haemoglobin levels.

[47] as the Australia New Zealand Food Standards Authority (ANZFA)

Zinc has been found to give positive results in some in vitro and in vivo genotoxicity tests. The weight of evidence from the in vitro and in vivo genotoxicity tests supports the conclusion that zinc, notwithstanding some positive findings at chromosome levels at elevated doses, has no biologically relevant genotoxicity activity. No data have been identified on the carcinogenicity of zinc.

Humans
Acute toxicity is infrequent in humans. Several cases of food poisoning are described resulting from storage of food or drink in galvanised containers. Symptoms of acute zinc toxicity include nausea, vomiting, epigastric pain, abdominal cramps and diarrhoea. One study reported symptoms of lethargy and light-headedness. This change in presenting symptoms could be a result of the type of zinc (in this case zinc sulphate) ingested. Zinc acetate (25-50 mg, three times per day), given to Wilson's disease patients to prevent copper accumulation was reported to cause less dyspepsia than equivalent doses of zinc sulphate. Emetic doses of zinc have been estimated to correspond to 225-450 mg. An industrial hazard associated with inhalation of zinc oxide fumes is 'metal fume fever'. Subjects present with malaise, fever, headache, nausea and dryness of mouth and throat.

Studies of chronic and sub-chronic toxicity of zinc are well documented. Prolonged intakes of zinc supplements ranging from 50 mg/day up to 300 mg/day have been associated with a range of biochemical and physiological changes. These changes include hypocupraemia, leucopaenia, neutropaenia, sideroblastic anaemia, decreased concentrations of plasma copper and decreased activity of the copper containing enzymes, superoxide dismutase and caeruloplasmin, altered lipoprotein metabolism and impaired immune function. Many of these biochemical and physiological changes are similar to those observed during copper deficiency. Nevertheless, there are problems with hazard identification in that these changes are not specific to copper deficiency and the clinical relevance of some are unknown.

Vulnerable groups

Sensitive sub-populations may include subjects with haemochromatosis and/or insulin dependent diabetes. A small study suggests that zinc supplementation increases the levels of glycosylated haemoglobin in diabetics.

Zinc excess in water may decrease iron absorption. Hepatic zinc concentration is increased in haemochromatosis and there is some evidence that zinc absorption may be increased

Evaluation

Zinc	UL in adults, mg/day	Total diet / suppl	Critical effect	human /animal data
US (US Institute of Medicine, 2001b)	40	Total	reduced copper status	human
UK (UK Expert Group on Vitamins and Minerals, 2003)	25	Suppl	reduction in copper absorption	human
EU (European Commission Health & Consumer Protection Directorate-General, 2003e)	25	Total	reduced copper status	human
FAO/WHO (FAO/WHO, 2002)	45	Total	reduced copper status	human
ANZFA (ANZFA, 1999)*	60	Total	reduced copper status	human

* Provisional Tolerable Daily Intake.

The selection of reduced copper status was chosen as the critical effect based on 1) the consistency of findings from studies measuring the interaction of zinc and copper, 2) the sensitivity of endothelial superoxide dismutase (ESOD) activity as a marker for this effect, and 3) the quality and completeness of the database for this endpoint. The data on the effects of zinc on HDL cholesterol concentration were not consistent from study to study and therefore were not used to derive a UL.

Systemic evidence of copper deficiency in humans may be observed at doses of 150 mg/day in humans, but doses as low as 50 mg/day may indicate a threshold effects, as observed by changes in biochemical markers of copper deficiency (ANZFA, 1999).

The US set a LOAEL of 60 mg/day based on a study of Yadrick and coworkers (Yadrick *et al*., 1989) who evaluated copper status after supplemental intake of 50 mg/day as zinc gluconate in 18 healthy female subjects (aged 25 to 40 years) for 10 weeks. ESOD activity was significantly lower than pretreatment values. Although no dietary zinc or copper intakes were reported, a level of dietary zinc can be estimated at approximately 10 mg/day for females. A LOAEL of 60 mg/day was calculated by adding the supplemental intake of 50 mg/day with the rounded estimate of dietary intake, 10 mg/day. Support for a LOAEL of 60 mg/day is provided by other studies showing altered copper balance after zinc supplementation.

The US selected an uncertainty factor of 1.5 to account for inter-individual variability in sensitivity and for extrapolation from a LOAEL to a NOAEL. Because reduced copper status is rare in humans, a higher UF was not justified.

For children a study in infants fed 5.8 mg/L of zinc for six months did not reveal effects of zinc on serum copper or cholesterol concentrations or other adverse effects. This would result in an intake of 4.5 mg/day for infants 0 through 6 months of age. This NOAEL was divided by a UF of 1.0 to obtain an upper limit of 4 mg/day (rounded down) for infants 0 through 6 months. No adverse effects of zinc in children and adolescents could be found. Due to a dearth of information, the UL for young infants was adjusted for older infants, children and adolescents on the basis of relative body weight. Values have been rounded down.

The EU set a NOAEL of 50 mg/day, based on the absence of any adverse effects on a wide range of relevant indicators of copper status (as the critical endpoint) in the various. Subjects were 25 and 21 healthy post-menopausal women and 19 healthy young men. Duration of supplementation was for 90 days and for 14 weeks. Total zinc and copper intakes were tightly controlled in the metabolic studies in which the zinc intake was 53 mg/day. Total zinc intake was 40 mg/day in the second study. An uncertainty factor of 2 is applied owing to the small number of subjects included in relatively short-term studies but acknowledging the rigidly controlled metabolic experimental conditions employed. EU recommended an UL of 25 mg/day.

Based on the data considered in the US evaluation the UL for **zinc** for the various age groups are:

1-3 years	**7 mg/day**
4-8 years	**12 mg/day**
9-13 years	**23 mg/day**
14-18 years	**34 mg/day**
adults	**40 mg/day**

Dietary intake

Intakes of zinc were estimated at baseline and when formulated beverages are consumed.

The concentration of zinc requested to be added to formulated beverages was 3 mg/600 ml reference quantity.

Estimated intakes were adjusted based on second day intake data from the NNSs. Dietary modelling has been conducted only for food intake. Intake through other sources (i.e. supplements and drinking water) was not included in the modelling.

Estimated intakes increased from baseline by between 1 and 2 mg/per day when FBs were consumed depending on the population groups assessed. The UL was not exceeded for the majority of population groups assessed, apart from Australian children aged 2-3 years at the mean level of intake, at baseline and when consuming FBs, and for Australian children aged 2 to 8 years at the 95th percentile level of intake, at baseline and when consuming FBs.

Table 22: Estimated dietary intakes of zinc, before and after FBs are introduced into the diet, and percent of upper level (UL)

	Mean intake mg/day (%UL)		95th percentile intake mg/day (%UL)	
Age group	**Baseline**	**Scenario 2***	**Baseline**	**Scenario 2***
2-3 years, Aus	7.5 (110)	8.8 (130)	10.4 (150)	11.9 (170)
4-8 years, Aus	8.2 (70)	9.7 (80)	11.7 (100)	13.7 (115)
5-6 years, NZ	^8.1 (**)	NA	#10.3 (**)	NA
7-10 years, NZ	^9.7 (**)	NA	#13.4 (**)	NA
9-13 years, Aus	10.9 (45)	12.9 (55)	16.5 (70)	18.2 (80)
11-14 years, NZ	^10.2 (**)	NA	#15.5 (**)	NA
14-18 years, Aus	12.7 (35)	15.3 (45)	21.3 (65)	25.6 (75)
15-18 years, NZ	13.0 (40)	16.6 (50)	22.3 (65)	26.4 (80)
≥19 years, Aus	11.9 (30)	13.0 (35)	18.4(45)	20.5 (50)
≥19 years, NZ	12.3 (30)	13.7 (35)	19.6 (50)	22.7 (60)

* Scenario 2 = when people substitute all water based flavoured drinks, bottled water and fruit juices and drinks they consumed with FBs.
^ mean adjusted intake, from MOH 2003, averaged for males and females.
# 90th percentile adjusted intake, from MOH 2003, averaged for males and females.
** not calculated, because the age groups in the summary report did not allow comparison of the mean or high percentile intake with the UL, and the raw data from the survey were not available to allow the age groups to be disaggregated to allow this calculation.
NA = not assessed, because the raw data from the New Zealand 2002 CNS were not in DIAMOND to allow scenario 2 estimates to be calculated.

Risk characterisation

Toxicological evaluation and dietary intake data indicate that children aged 2-3 years as well as children aged 4-8 years in Australia may be exceeding the UL for zinc, both at the mean and high level of dietary intake at baseline and for Scenario 2, when added to formulated beverages at 3 mg in a 600 ml serving. For these calculations, intake from other sources, e.g. galvanised containers and supplements, have not been included.

For adults in both Australia and New Zealand estimated zinc intakes, both at baseline and when added to formulated beverages, are below the UL.

In conclusion, children up to 8 years of age are predicted to exceed the UL at the high level of intake of dietary zinc for baseline and Scenario 2. At the high level of intake for adolescents up to the age of 18 years the intake is 80% of the UL of zinc for Scenario 2.

Chronic zinc toxicity is associated with symptoms of copper deficiency. These overt adverse effects (e.g. anaemia, neutropaenia, impaired immune responses) are evident only after feeding zinc in the form of dietary supplements in excess of 150 mg/day for long periods. It is much more difficult to identify the critical effect of zinc excess at intakes below 100-150 mg per day.

The UL for zinc is based on reduced copper status. The LOAEL was set at 60 mg/day based on a 10-week study in 18 healthy female subjects. At this level the endothelial superoxide dismutase activity (the most sensitive indicator of copper status) was significantly lower than pre-treatment values. Other studies support this LOAEL.

The UL for children was based on levels in infants that did not reveal effects of zinc on serum copper concentrations or other adverse effects. Due to a dearth of information, the UL for young infants was adjusted for older infants, children and adolescents on the basis of relative body weight.

Chronic zinc toxicity is associated with symptoms of copper deficiency. These adverse effects include anaemia, neutropaenia and impaired immune response. Furthermore, the potential contribution from other sources (e.g. dietary supplements) has not been taken into consideration in the dietary intake assessment. Therefore, there are potential safety concerns for children and adolescents up to the age of 18 years were the addition of zinc to FBs to be permitted.

For adults, addition of zinc to formulated beverages at a level of 3 mg per 600 ml serve poses no appreciable public health and safety risk.

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Attachment 7

Dietary Modelling Methodologies for Nutrient Intake Assessment Application A470 – Formulated Beverages

Introduction

An application was received by FSANZ requesting that a standard to be added to the Food Standards Code (the Code) for formulated beverages (FB), with an FB being a water–based, non-alcoholic flavoured drink with added vitamins and minerals. It was requested that the FB standard allow for the addition of vitamins and minerals at concentrations sufficient to allow claims of 'source of' or 'good source of'.

A dietary intake assessment was deemed necessary in order to determine the impact of permitting a range of nutrients to be added to FB. The impact was assessed in two ways:

1. determining whether the added nutrients would pose a risk to public health and safety; and
2. determining whether there is 'nutrient inadequacy' in the population, or whether there would be a 'health benefit' from allowing the addition of vitamins and minerals to FB. For example, would consumption of these products address the identified nutrient inadequacy, assuming they replaced specified beverages.

In order to assess safety, estimated intakes of the nutrients were compared with an upper level of intake (UL). To assess whether there is likely to be any inadequacy, the estimated dietary intakes were compared to estimated average requirements (EARs). Where inadequacy or potential health benefits for a nutrient of permitting FB with added vitamins and minerals were identified, nutrient intakes were then compared to the EAR to determine whether the consumption of FB has the capacity to address the inadequacy or provide a health benefit.

Results of the dietary intake assessments for nutrients can be found in other attachments. Attachment 6 Risk Assessment - Micronutrients, includes estimated intakes for nutrients and comparison with the ULs. Attachment 5 – Nutrition Assessment includes estimated intakes and comparison with EARs and an outline of the percentage of the population below this standard. These attachments also highlight specific information that was relevant to the modelling for each nutrient.

The methodologies and results for the exposure assessments for the food additives are at Attachment 8 – Risk Assessment - Food Additives.

Background

FB are currently sold in New Zealand under Dietary Supplements regulations. These products contain nutrients such as pantothenic acid and vitamin C. FB are not currently permitted to be manufactured in Australia and then sold on the Australian market, however, they can be imported from New Zealand under the Trans Tasman Mutual Recognition Arrangement (TTMRA) and sold on the Australian market.

The Applicant requested that FB be permitted to contain nutrients at the maximum claimable level of 25% of the recommended dietary intake (RDI) (except for vitamin C which is at 100% of the RDI). The Applicant provided a list of the requested quantities of vitamins and minerals in a reference quantity (600 ml) of FB. These concentrations were converted to mg/100 g, µg/100 g or mg/kg concentrations for use in the DIAMOND program. The requested nutrient concentrations are listed in Table 1.

Table 1: Proposed concentration levels of nutrients in formulated beverages, as requested by the Applicant

Type of Nutrient	Nutrient Name	Concentration Level to be used in FB	
		(units/600 ml)	units/100 g
Vitamin	Vitamin A (µg)	187.5	31.3
	Thiamin (mg)	0.275	0.046
	Riboflavin (mg)	0.425	0.071
	Niacin (mg)	2.5	0.42
	Folate (µg folic acid)	50	8.3
	Vitamin B_6 (mg pyridoxine)	0.4	0.07
	Vitamin B_{12} (µg)	0.5	0.08
	Vitamin C (mg)	40	6.7
	Vitamin D (µg)	2.5	0.42
	Vitamin E (mg)	2.5	0.42
	Biotin (µg)	7.5	1.25
	Pantothenic Acid (mg)	1.25	0.21
Mineral	Calcium (mg)	200	33
	Chromium (µg)	50	8.3
	Copper (mg)	0.75	0.13
	Iodine (µg)	37.5	6.3
	Iron (mg)	3	0.5
	Magnesium (mg)	80	13.3
	Manganese (mg)	1.25	0.21
	Molybdenum (µg)	62.5	10.4
	Phosphorus (mg)	250	41.7
	Selenium (µg)	17.5	2.9
	Zinc (mg)	3	0.5

Dietary intake assessment provided by the Applicant

The Application did not provide any estimates of nutrient intakes resulting from the consumption of FB. Therefore, FSANZ conducted dietary intake assessments for the nutrients requested.

Dietary modelling

The dietary intake assessments were conducted using dietary modelling techniques that combine food consumption data with food composition data to estimate the intake of the nutrient from the diet. The dietary intake assessment was conducted using FSANZ's dietary modelling computer program, DIAMOND.

Dietary intake = nutrient concentration x food consumption

The intakes were estimated by combining usual patterns of food consumption, as derived from national nutrition survey (NNS) data, with either naturally occurring nutrient levels, levels of nutrient fortification and/or proposed levels of use of the nutrients in foods.

The requested nutrients were assessed in two separate ways:

1. To assess the safety of the nutrient intakes – estimated nutrient intakes were compared to ULs (see results in Attachment 6 – Risk Assessment - Micronutrients).
2. Nutrients were assessed against the fortification policy. Where it may be determined that there is a need for additional levels of the nutrients in the diet due to inadequate intakes, or where it may be determined that fortification would provide a health benefit, intakes were compared to EARs (see results in Attachment 5 – Nutrition Assessment).

Where no UL had been set for a nutrient or where there were no safety concerns, no modelling to assess safety was conducted. Additionally, for some nutrients there were insufficient concentration data, therefore, modelling was unable to be conduced for these nutrients.

Dietary survey data

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

It is recognised that nutrient intakes in a 24-hour period are not representative of nutrient intakes over a longer period of time.

For both NNSs, a second day of food consumption information was collected from approximately 10% of respondents for Australia and 15% for New Zealand. FSANZ can take into account second day nutrient intakes by using factors for adjusting the first day intake to gain a more accurate reflection of what daily nutrient intakes would be across a population over a longer period of time. This information has been used for the majority of the intake assessments for nutrients in this Application. Second day adjustments will have little or no impact on estimated mean nutrient intakes, but would likely reduce estimated one-day 95th percentile nutrient intakes.

Second day nutrient adjustments were not calculated for some population groups for retinol (Australians aged 14 years and above and New Zealanders aged 19 years and above) or for some population groups for Vitamin D (for Australians aged 4-18 years) since an adjustment factor could not be obtained for these nutrient/age group combinations due to small consumer numbers of foods containing retinol. Second day nutrient adjustments were also not calculated for iodine (Australia and New Zealand) and selenium (Australia only). This is because iodine was not included in the NNS of either country and selenium was not included in the Australian NNS. Therefore, the nutrient intakes were calculated using a different methodology in DIAMOND. This methodology does not include a component for adjusting estimated intakes as it only includes consumption data from the first 24-hour recall.

Conducting dietary modelling based on 1995 or 1997 NNS food consumption data provides the best estimate of actual consumption of a food and the resulting estimated intake of a nutrient. However, it should be noted that limitations exist within the NNS data. These limitations relate to the age of the data and the changes in eating patterns that may have occurred since the data were collected.

Generally, consumption of staple foods such as fruit, vegetables, meat, dairy products and cereal products, which make up the majority of most people's diet, is unlikely to have changed markedly since 1995/1997 (Cook et al, 2001). However, there is uncertainty associated with the consumption of foods that may have changed in consumption since 1995 or 1997 or that have been introduced to the market since 1995/1997.

Additionally, there may be more foods on the market now that are fortified than was the case in 1995 or 1997 when the food composition databases for the NNSs were established, therefore, some of the baseline nutrient intakes for some nutrients may not take this into consideration.

Additional food consumption data or other relevant data

The 1995 and 1997 NNSs did not report any consumption of FB. Market share data were therefore required to enable dietary modelling to be conducted for this Application. The Applicant provided a report (Leatherhead Food International, 2003) that detailed the consumption of functional soft drinks in an international context. Using German data on the percentage of the soft drinks market held by functional soft drinks (4.1%), FSANZ assumed that formulated beverages will replace 5% of the non-alcoholic beverages market (excluding milk). These data were only used in the assessment of nutrient intakes not food additive exposures. How these data were used will be discussed below in more detail in "Scenarios for nutrient dietary modelling".

The Applicant also provided data on the types of beverages that are likely to be replaced by FB. These data were used in the assessment of nutrients and food additives.

No other information was required or identified for the purpose of using in the dietary intake estimates.

Scenarios for nutrient dietary modelling

For nutrients, three different scenarios were examined:

1. Baseline

'Baseline' nutrient assessments, based on the 1995/1997 NNSs' food consumption data, were conducted to estimate current nutrient intakes before permission before FB are permitted to be manufactured and sold in both Australia and New Zealand with added vitamins and minerals.

For the baseline assessment of folic acid, it was assumed that only breakfast cereals contained folic acid. The levels of folic acid in breakfast cereals were determined using the labelled quantities of folate in the cereals.

Baseline estimates were estimated for the nutritional inadequacy/health benefit assessment (see Attachment 5) and for the safety assessment (see Attachment 6).

2. Market Share Scenario (Scenario 1)

Scenario 1 assessed the impact on nutrient intakes over the long term and across the population. In this scenario, it was assumed that 5% of all non-alcoholic beverages (excluding milk and milk based beverages) would be replaced with FB.

The foods substituted include tea and coffee, cordials, carbonated drinks, fruit juices, fruit juice drinks, sports drinks, bottled water and tap water (as used as a beverage or to make up a beverage).

This scenario was used for the nutritional benefit assessment only (see Attachment 5). For assessing nutrient inadequacy or a health benefit, estimated nutrient intakes are compared to an EAR. For this type of modelling, the data used for the assessment and the assumptions made need to be as realistic as possible, so as to not overestimate intakes and therefore underestimate the extent of any possible level of deficiency.

3. 100% Substitution Scenario (Scenario 2)

Scenario 2 assessed nutrient intakes when people remove specified beverages from their diet and include formulated beverages in the place of these beverages. The food groups substituted were cordials (excluding those made up from powder), carbonated drinks, fruit juice drinks, sports drinks and bottled water.

This scenario was used for the safety assessment (see Attachment 6). For assessing the safety of nutrient intakes, estimated nutrient intakes are compared to ULs. For this type of modelling, a 'worst case' approach is normally taken in order to determine the upper end of possible nutrient intakes and therefore the likelihood of potential safety concerns.

There were several nutrients that were only assessed against the UL for the added sources of the nutrient. This was due to the ULs being applicable only to supplementary sources of the nutrient in the diet. These nutrients included folic acid, niacin (nicotinic acid) and magnesium. For scenario 2 for these nutrients, nutrient intakes from FB were included in the estimated intakes from added sources in the diet.

Population groups assessed

The dietary intake estimates were conducted for both the Australian and New Zealand populations and compared to EARs and/or RDIs and/or ULs, where relevant. Depending on the nutrient, the age groups listed against one of these reference health standards may differ from the age groups listed for another reference health standard. For many nutrients, there are different EARs and/or RDIs for males and females. Consequently, nutrient intakes were estimated for both males and females for all nutrients for comparison against the EAR and RDI. Generally, the ULs were not different for males and females for the nutrients examined in this application. Consequently, for comparison against ULs, nutrient intakes have been calculated for different age groups but not genders.

Nutrient concentration levels

The levels of nutrients in foods used in the intake assessments at baseline were from the nutrient datasets developed for each of the NNSs. Vitamin B_6, Vitamin B_{12}, Vitamin D, Vitamin E, manganese and copper were not examined in the 1995 Australian NNS. Therefore, in order to estimate intakes for the Australian population for these nutrients, the concentration data from the 1997 New Zealand NNS were matched to the most appropriate Australian food code and these values were used to estimate dietary intakes for the Australian population groups. Where no data from the New Zealand NNS were directly applicable for Australian NNS foods, nutrient concentration data, predominantly from the United States, were used.

US data were used as they were easily and freely accessible from the United States Department of Agriculture (USDA) website (http://www.nal.usda.gov/fnic/foodcomp/search/).

For the majority of nutrients, concentrations were assigned to each individual food from the NNSs in DIAMOND. Scenario concentrations for foods nominated as replacement beverages for FB were added by FSANZ and replaced the baseline concentration for the particular scenario being run. For example, food code 11330101 Fruit Drink, Apple from the 1995 Australian NNS has a calcium concentration of 3 mg/100 g at 'Baseline', 5 mg/100 g for Scenario 1, and 33 mg/100 g for Scenario 2, assuming apple drink was replaced by a FB for Scenario 1 and 2 according to assumptions discussed earlier.

The Applicant provided concentrations of nutrients in FB in units/reference quantity (600 ml). These were converted to mg/100 g or µg/100 g concentrations, or mg/kg concentrations for use in the DIAMOND program, depending on the dietary intake assessment methodology used.

Since the data were collected for the Australian and New Zealand NNSs, there have been significant changes to the Food Standards Code to allow more innovation in the food industry. As a consequence, some of the foods that are currently available in the food supply were either not available or were not as commonly available in 1995/1997. Since the data were collected for the NNSs, there has been an increase in the range of products that are fortified with nutrients. Therefore, if fortified foods have appeared on the market since 1995/1997, these foods were not taken into consideration in the nutrient intake assessment. An exception to this was the assessment for folic acid where it was assumed that only breakfast cereals are fortified with folic acid and that the level of folic acid in the breakfast cereal is equal to the labelled quantity of folate for those products. For nicotinic acid and magnesium, it was assumed that there were no foods with added sources of these nutrients at baseline.

For some nutrients, the form of the nutrient used in the assessment against the EAR or RDI differs from that used in the assessment against the UL. For example, total folates have been compared to the EAR while folic acid has been compared to the UL.

In the assessments for iodine (for Australia and New Zealand) and selenium (Australia only), analytical data from sources such as food composition data and surveys were used for the dietary intake assessment (see Appendix 1).

The concentrations of iodine in foods were only available from a limited number of sources. For Australia, the intake estimate was based primarily on unpublished 22nd Australian Total Diet Survey (TDS) data. For New Zealand, the intake estimate was based primarily on the data from the 2003/2004 New Zealand TDS and then the 1997/1998 New Zealand TDS. However, where data gaps existed in the Australian data, New Zealand data were used, and visa versa. Following the use of the most recent TDS data, unpublished data from the Australian or New Zealand food composition programs were used for the respective countries. If data gaps still existed, international food composition data (German and UK) were used. For Australia, information from A493 – Iodine as a Processing Aid was also used.

The concentrations for selenium for the Australian intake assessments were all based on survey data collected from a number of sources around Australia for proposal P157 – Metal Contaminants in Foods.

There were no food composition data available to enable a comprehensive dietary intake assessment to be conducted for chromium, molybdenum, biotin and pantothenic acid. Whilst there are small amounts of data available, these data were either not from Australian or New Zealand sources, were not extensive enough across the whole diet or were not in the correct format or had not been assessed for accuracy. Therefore, these nutrients were not able to be assessed in the dietary modelling.

How were the estimated dietary intakes calculated?

The DIAMOND program allows nutrient concentrations to be assigned to individual foods in the DIAMOND program within the 'nutrient intake model' (NIM). There were two nutrients (selenium for Australia only and iodine for both Australia and New Zealand) for which no nutrient concentration data were set up in the NIM in DIAMOND. Consequently, a 'chemical intake model' (CIM) was used in the assessment of these nutrients. In a CIM, foods are grouped according to raw commodity classification codes and analytical data are assigned to relevant raw commodity classification codes (see Appendix 1). This means that instead of individual foods in from the NNS being assigned an individual nutrient concentration level (as in the NIM), one concentration is used to represent a single raw commodity, which may be made up of one or more individual foods from the NNS. This means there is less variation in the nutrient concentrations for a food in the CIM. Where analytical information was available on individual raw commodities and these concentrations differed from that of the broader raw commodity group, the more specific nutrient concentrations were used. For example, the raw commodity group DF Dried Fruit has an iodine concentration of 13 μg/kg while DF0269 Dried Grapes has an iodine concentration of 17 μg/kg.

The intake of each nutrient was calculated for each individual in the NNSs using his or her individual food records from the dietary survey. The DIAMOND program multiplies the specified concentration of the nutrient by the amount of food that an individual consumed from that group in order to estimate the intake of the nutrient from each food. Once this has been completed for all of the foods containing the nutrient, the total amount of the nutrient consumed from all foods is summed for each individual. Population statistics (mean and high percentile intakes) are then derived from the individuals' ranked intakes.

For both NNSs, a second day of food consumption information was collected from approximately 10% of respondents for Australia and 15% for New Zealand. To take into account second day nutrient intakes, factors are calculated for adjusting the first day intake to gain a more accurate reflection of daily nutrient intakes over a longer period of time. The adjustment factor is calculated by taking into account several factors including each persons day 1 intake, the mean intake from the group on day 1, the standard deviation from the day 1 sample and the between person standard deviation from the day 2 sample. (For more information on the methodology of adjusting for second day intakes, see the Technical Paper on the National Nutrition Survey: Confidentialised Unit Record File (ABS, 1998). The nutrient adjustment factor is applied to each individuals' intake before population statistics are derived.

Where estimated intakes are expressed as a percentage of the reference health standard, each individual's adjusted nutrient intake is calculated as a percentage of the reference health standard (using the intake in units per day), the results are then ranked, and population statistics derived.

The percentage of each population group over or under a reference health standard was calculated by assessing each individuals' intake for a nutrient, and comparing it with the level of the relevant standard, then counting the number of respondents above or below the standard, then calculating that as a percent of the total number of respondents in the age/gender group being assessed.

Uncertainties in the nutrient intake assessments

Where there are uncertainties in the data used for dietary intake assessments, assumptions normally have to be made. Some of the uncertainly associated with the intake estimates for nutrients are outlined below.

It is not known what beverages consumers will actually substitute with an FB. Whilst the Applicant provided some information on the products currently on the market that would be substituted with FB, there is uncertainty about what consumers will actually do when given the choice between a beverage they may normally consume and an FB. Additionally, it is not known exactly what volume of FB people are consuming, as there are no data in the NNSs and no survey data available.

Assumptions in the nutrient dietary modelling

The aim of the dietary intake assessments was to make as realistic an estimate of dietary intake as possible. However, where significant uncertainties existed in the data, conservative assumptions were generally used to ensure that the dietary intake assessment did not underestimate intake. This was the case when the percent market share held by FB in Scenario 1 was rounded to be 5%, and when the maximum claimable concentrations of the nutrients in the FB were used in the dietary modelling.

Assumptions made in the dietary modelling include:

consumption of foods as recorded in the NNS represent current food consumption patterns;
in the 100% substitution scenario, if a consumer drank one or more types of substituted beverages, all of these beverages will be substituted with an FB product
consumers always select the FB containing nutrient being assessed;
consumers do not alter their food consumption habits besides to substitute non-FB with an FB;
consumers do not increase/decrease their consumption of foods/food groups upon FB becoming available;
all of the nutrients in the FB are absorbed by the body;
endogenous production of nutrients (where relevant) has not been included in the dietary intake assessment;
naturally occurring sources of nutrients have been included in the dietary intake assessment for most of the nutrients. This was not relevant for the assessment of added sources of niacin (nicotinic acid) and magnesium and for the assessment of folic acid;
concentrations of nutrients in the FB are the maximum claimable amounts, (which may be smaller than the added amounts as highlighted in the Application);

for iodine assessments, where the concentration of iodine in a food was reported as being less than the Limit of Detection (LOD) or Limit of Reporting (LOR), then the iodine concentration of the food was equal to half of the LOD or LOR value. The LOD is the lowest concentration of a chemical that can be qualitatively detected using a specified laboratory method and/or item of laboratory equipment (i.e. its presence can be detected but not quantified). The LOR used in this assessment has been established at the Limit of Quantification (LOQ) which is the lowest concentration of a chemical that can be detected and quantified, with an acceptable degree of certainty, using the specified laboratory method;

where there were no Australian nutrient concentration data for specific food groups, it was assumed that New Zealand data were representative of these food groups, and vice versa for New Zealand. (Many of the New Zealand food composition data and the data in the New Zealand NNS are based on Australian food composition data);

where Australian or New Zealand concentration data were not available for certain foods, it was assumed that other international data (from either the UK, Germany or the US) were representative of the Australian and New Zealand concentrations in these foods;

where a food was not included in the intake assessment (which is mostly applicable to the CIMs), it was assumed to contain a zero concentration of the nutrient being assessed;

there is a 5% market share for the use of FB in the Australian and New Zealand non-alcoholic beverage (excluding milks) market for scenario 1;

for the nutrients assessed using a CIM, where a food has a specified nutrient concentration, this concentration is carried over to mixed foods where the food has been used as an ingredient e.g. iodine in carrot which is used to make a carrot cake or coleslaw;

there is no consumption of iodine through discretionary salt use (since NNSs did not measure discretionary salt use);

there are no reductions in nutrient concentrations from food preparation or due to cooking;

for the purpose of this assessment, it is assumed that 1 millilitre is equal to 1 gram for all liquid and semi-liquid foods (e.g. milk, yoghurt); and

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

These assumptions are likely to lead to conservative estimates of dietary intake for nutrients.

Limitations of the dietary modelling

Whilst for the majority of nutrients an adjusted nutrient intake was able to be calculated using second day 24-hour recalls from the NNSs, for a small number of nutrients this was not possible. A limitation of estimating dietary intake over a period of time associated with the dietary modelling for these few nutrients is that 24-hour dietary survey data lead to over-estimates of habitual nutrient intakes for high consumers of those nutrients.

For example, daily food consumption amounts for occasionally consumed foods based on 24 hour food consumption data would be higher than daily food consumption amounts for those foods based on a longer period of time; for example, seafood.

Over time, there may be changes to the ways in which manufacturers and retailers make and present foods for sale. Since the data were collected for the Australian and New Zealand NNSs, there have been significant changes to the Food Standards Code to allow more innovation in the food industry. As a consequence, another limitation of the dietary modelling is that some of the foods that are currently available in the food supply were either not available or were not as commonly available in 1995/1997. Since the data were collected for the NNSs, there has been an increase in the range of products that are fortified with nutrients. Consequently, the nutrient databases from the NNSs may not be entirely representative of the nutrient levels in some foods that are now on the market.

There are no data in DIAMOND on the use of complementary medicines (Australia) or dietary supplements (New Zealand). Consequently, these could not be included in the dietary intake assessment. This will underestimate nutrient intakes for those people in the population who take vitamin or mineral supplements. This is a particularly relevant limitation for those nutrients that are assessed for safety against the ULs that are derived for supplemental or added sources in the diet.

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

FSANZ does not apply statistical population weights to each individual in the NNSs in order to make the data representative of the population. This prevents distortion of actual food consumption amounts that may result in an unrealistic intake estimate. Maori and Pacific Islanders were over-sampled in the 1997 New Zealand National Nutrition Survey so that statistically valid assessments could be made for these population groups. As a result, there may be bias towards these population groups in the dietary intake assessments because population weights were not used.

The recently approved application A493 (Iodine as a Processing Aid) that deals with the application of an iodine sanitiser wash to foods can cause the presence of additional iodine in foods due to residual iodine from the wash. These additional iodine concentrations have not been taken into consideration when assessing iodine intakes for this application. Calcium in fortified foods (such as orange juice and biscuits) have not been taken into account in the estimated intakes of calcium.

References

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Attachment 8

Risk Assessment – Food Additives
Application 470 – Formulated Beverages

Summary and conclusions

A risk assessment has been conducted on 57 food additives/additive groups requested by the Applicant to be added to formulated beverages. All of these food additives are currently permitted in Standard 1.3.1 – Food Additives.

Hazard identification and characterisation

FSANZ has not performed an independent hazard identification and characterisation of the 57 food additives, but has relied upon the assessment reports from the Joint FAO/WHO Expert Committee on Food Additives (JECFA). JECFA has established numerical Acceptable Daily Intakes (ADIs)[48] for some, and established an ADI 'not specified'[49] for many in this group. For several, there was not enough data available to perform an assessment.

Dietary exposure assessment

Dietary exposure assessments were conducted only on those food additives with a numerical ADI, i.e., those where there was a potential for safety concerns if the exposure significantly increased. For the majority of the food additives, the dietary exposure either did not change or changed very little when formulated beverages were included in the modelling.

Risk Characterisation

Food additives which have an ADI 'not specified' or and ADI which is sufficiently high to allow GMP use for the additive in food

For the additives with an ADI 'not specified'. dietary exposure assessments were not conducted, since these food additives are considered to have low toxicity and would not be expected to pose a public health and safety risk as a result of their use in formulated beverages.

Food additives, which have a numerical ADI

For the additives for which a numerical ADI existed, dietary exposure assessments were conducted. The risk characterisation concluded that the addition of the following food additives to formulated beverages at the requested concentration would pose no additional public health and safety risk: tartrazine, quinoline yellow, sunset yellow, azorubine, amaranth, ponceau 4R, allura red, indigotine, brilliant blue, fast green, brilliant black, brown HT, sorbates, sulphites, calcium disodium EDTA, sucrose acetate isobutyrate, glycerol ester of wood rosin, and dioctyl sodium succinate.

In the case of annatto, benzoates, acesulphame potassium (ace K), saccharin and alitame, the dietary exposure assessment predicted that there could be an increase in exposure as a result of their use in formulated beverages. This apparent increase is the result of the assumptions made about which beverages were substituted with formulated beverages in the dietary model used, and the current permissions in these particular beverages. Even taking into account these apparent increases in exposure, no public health and safety concerns were raised.

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[48] JECFA defined the ADI *as an estimate of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk*

[49] JECFA defined the term '*ADI not specified' to mean that, on the basis of available data (chemical, biochemical, toxicological, and other), the total daily intake of the substance, arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not represent a hazard to health.*

Overall conclusion of the risk assessment

On the basis of currently available information, even using very conservative modelling, it can be concluded that, the addition of the requested 57 food additives/additive groups to formulated beverages would not raise any public health and safety concerns.

Introduction
This Attachment details the risk assessment for those food additives proposed for use in formulated beverages (FBs).

The Applicant requested that 57 food additives/food additive groups be approved for use in FBs including colourings, intense sweeteners, preservatives, emulsifiers, modifying agents and flavourings. The additives and the maximum concentration levels to be used in FBs are shown in Table 1. Many of the requested concentrations are the same as those used in similar beverages, such as water-based flavoured drinks and fruit juice-based beverages.

Hazard identification and characterisation
FSANZ has not performed an independent hazard identification and characterisation of the requested food additives, but has relied upon the assessment reports from the FAO/WHO Joint Expert Committee on Food Additives (JECFA).

JECFA has assessed various food additives and for some of them established Acceptable Daily Intakes (ADIs). For others, not enough data was available to perform an assessment, and others have an ADI 'not specified'. The principles used by JECFA for assessing food additives are available in Environmental Health Criteria 70 (WHO, 1987a).

In the context in which JECFA uses it, the ADI is defined as an estimate (by JECFA) of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk.

There are occasions when JECFA considers the use of an ADI in numerical terms not to be appropriate. This situation arises when the estimated exposure to the additive is expected to be well below any numerical value that would ordinarily be assigned to it. Under such circumstances, JECFA uses the term ADI 'not specified'. The Committee defines this term to mean that, on the basis of available data (chemical, biochemical, toxicological, and other), the total daily exposure to the substance, arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health.

Table 1: Food Additives requested by the Applicant to be added to formulated beverages

Schedule 1[$]	Maximum proposed concentration levels to be used in FBs (mg/kg)	Schedule 2	Maximum proposed concentration levels to be used in FBs (mg/kg)
123 Amaranth	30	951 Aspartame	GMP
160b Annatto	10	955 Sucralose	GMP
200-203 Sorbic acid and sorbates	400	957 Thaumatin	GMP
210-213 Benzoic acid and benzoates	400	961 Neotame	GMP
220-225 Sulphur dioxide and sulphites	115		
242 Dimethyl dicarbonate	250		
281-282 Propionates	GMP		
385 Calcium disodium EDTA	33		
444 Sucrose acetate isobutyrate	200		
445 Glycerol ester of wood rosin	100		
480 Dioctyl sodium sulphosuccinate	10		
950 Acesulphame potassium	300		
954 Saccharin	80		
956 Alitame	40		
Schedule 3		**Schedule 4**	
100 Curcumins	GMP	102 Tartrazine	70
101 Riboflavins	GMP	104 Quinoline yellow	70
103 Alkanet (& Alkannin)	GMP	110 Sunset yellow	70
120 Cochineal and carmines	GMP	122 Azorubine	70
140 Chlorophylls	GMP	124 Ponceau 4R	70
141 Chlorophylls, copper complexes	GMP	129 Allura red	70
150a Caramel I – plain	GMP	132 Indigotine	70
150b Caramel II - caustic sulphite process	GMP	133 Brilliant blue	70
150c Caramel III - ammonia process	GMP	142 Green S	70
150d Caramel IV - ammonia sulphite process	GMP	143 Fast green	70
153 Vegetable carbon	GMP	151 Brilliant black	70
160a Carotenes	GMP	155 Brown HT	70
160c Paprika oleoresins	GMP		
160d Lycopene	GMP		
160e Carotenal, b-apo-8'-	GMP		
160f Carotenoic acid, b-apo-8'-, methyl or ethyl esters	GMP		
161a Flavoxanthin	GMP		
161b Lutein	GMP		
161c Kryptoxanthin	GMP		
161d Rubixanthin	GMP		
161e Violoxanthin	GMP		
161f Rhodoxanthin	GMP		
162 Beet Red	GMP		
163 Anthocyanins	GMP		
164 Saffron, crocetin and crocin	GMP		
171 Titanium dioxide	GMP		
172 Iron oxides	GMP		

$ The schedule number reflects to the various schedules in Standard 1.3.1 – Food Additives.

Dietary modelling

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

Dietary exposure = food chemical concentration x food consumption

The exposures were estimated by combining usual patterns of food consumption, as derived from national nutrition survey (NNS) data, with both current and proposed levels of use of the food chemicals in the foods.

Food consumption data from the 1995 Australian NNS and the 1997 New Zealand NNS were used for the dietary modelling, along with concentration data for the food additives from a variety of sources (including the Code, manufacturers' use data and analytical data from surveys). Populations were assessed as a whole as well as for children aged 2-6 years for Australia. Modelling was conducted to estimated exposures to food additives at baseline (i.e. current exposures) and following the consumption of FBs. Due to the uncertainties in some of the data used for the assessment, certain assumptions needed to be made. These assumptions are likely to lead overall, to a conservative estimate for food additive dietary exposures, in particular the assumption that all beverages in the specified types of beverages will be substituted by a FB and that all foods within a food groups will contain the additive being assessed.

Specific details of how the dietary modelling was conducted can be found at Appendix 1 to this attachment.

What food additives were assessed?

There were 57 additives/additive groups requested by the Applicant to be added to FBs. Of these, dietary modelling was conducted for 23 additive/additive groups, essentially those which have a numerical ADI. For the other additives, the ADI was either 'not specified' or sufficiently high such that the use of the food additive was not limited on the basis of safety considerations. In these cases, the additives are allowed to be used in food according to GMP, on the basis that the additive is very unlikely to be used at a level which would cause safety concerns.

Details of these 23 additives where dietary modelling was performed are shown in Table 2.

Table 2: Food Additives for which dietary exposure assessments were conducted

Schedule 1	Schedule 4
123 Amaranth	102 Tartrazine
160b Annatto	104 Quinoline yellow
200-203 Sorbic acid and sorbates	110 Sunset yellow
210-213 Benzoic acid and benzoates	122 Azorubine
220-225 Sulphur dioxide and sulphites	124 Ponceau 4R
385 Calcium disodium EDTA	129 Allura red
444 Sucrose acetate isobutyrate	132 Indigotine
445 Glycerol ester of wood rosin	133 Brilliant blue
480 Dioctyl sodium sulphosuccinate	143 Fast green
950 Acesulphame potassium	151 Brilliant black
954 Saccharin	155 Brown HT
956 Alitame	

Risk assessment of individual food additives, where dietary modelling was conducted

102 – Tartrazine (Schedule 4)

Hazard identification and Characterisation

Tartrazine was evaluated by the JECFA in 1964, and an ADI of 0-7.5 mg/kg bw was allocated (WHO, 1965). The report did not explain the basis on which the ADI was established.

Dietary exposure assessment

For the baseline estimate of exposure, some food groups were assumed to have concentrations at the maximum permitted level (MPLs) from Standard 1.3.1 – Food Additives in the Code. Some foods were assigned an analytical concentration from the South Australian (SA) food colours survey (South Australia Department of Health, personal communication). Based on information found in the FSANZ Food Additive Database, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 7.1.1 Plain breads, 11.4 Tabletop sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitutes, 14.1.3.2 Kola soft drinks and some category 4 foods (Fruits and vegetables) do not contain food colours. Tartrazine is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of tartrazine was present in bottled waters assuming these are replaced with FBs containing tartrazine at that concentration. Kola drinks also contained tartrazine at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to tartrazine between the baseline and the 'FB' scenario.

Table 3: Estimated dietary exposure to 102 – Tartrazine

				Mean consumer exposure	**95th %ile consumer exposure**
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13800	1.3 (15)	4.0 (55)
		"FB"	13808	1.3 (20)	4.0 (55)
	2-6 yrs	Baseline	987	2.9 (40)	7.3 (95)
		"FB"	987	2.9 (40)	7.3 (95)
New Zealand	15+	Baseline	4608	1.1 (15)	3.3 (45)
		"FB"	4610	1.1 (15)	3.3 (45)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation

The addition of tartrazine to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to tartrazine below the ADI.

In conclusion, the addition of tartrazine to FB would not pose a public health and safety risk.

104 – Quinoline Yellow (Schedule 4)

Hazard identification and Characterisation
Quinoline yellow was evaluated by the JECFA in 1984, and an ADI of 0-10 mg/kg bw was allocated (WHO, 1984c). JECFA based the ADI for quinoline yellow on data from a long-term study in mice, where no adverse effects were observed at the highest dose tested. A safety factor of 150 was used.

Dietary exposure assessment
For the baseline estimate of exposure, food groups were assumed to have concentrations at the MPLs. The SA food colours survey did not analyse foods for quinoline yellow, therefore there were no actual concentrations that could be used to make the estimated exposures more realistic. No manufacturers' use data were available. Based on information found in the Food Additive Database, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 7.1.1 Plain breads and some category 4 foods (Fruits and vegetables) do not contain food colours. Quinoline yellow is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of quinoline yellow was present in bottled waters assuming these are replaced with FBs containing quinoline yellow at that concentration.

There is no change in estimated dietary exposure to quinoline yellow between the baseline and the 'FB' scenario.

Table 4: Estimated dietary exposure to 104 – Quinoline yellow

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13809	2.4 (25)	6.8 (70)
		"FB"	13810	2.4 (25)	6.8 (70)
	2-6 yrs	Baseline	987	6.2 (60)	12.8 (130)
		"FB"	987	6.2 (60)	12.8 (130)
New Zealand	15+	Baseline	4610	1.8 (20)	4.6 (45)
		"FB"	4610	1.8 (20)	4.6 (45)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation

The addition of quinoline yellow to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of 2-6 year olds at the 95th percentile exposure, have estimated exposures to quinoline yellow below the ADI. Exposure for high consumers of quinoline yellow for 2-6 year olds is estimated to only marginally exceed the ADI (130%).

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of quinoline yellow, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured yellow, and alternative yellow colours could be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain quinoline yellow is <1%, which also suggests that the above model is highly conservative. Also, all food groups are assumed to contain quinoline yellow at the MPL, which would not be the case in reality. However, no manufacturers use data were available to refine the exposure estimates. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

In conclusion, the addition of quinoline yellow to FB would not pose a public health and safety risk.

110 – Sunset Yellow (Schedule 4)

Hazard identification and Characterisation
Sunset yellow was evaluated by the JECFA in 1982, and an ADI of 0-2.5 mg/kg bw was allocated (WHO, 1982). JECFA based the ADI for sunset yellow on the absence of adverse effects observed at the highest dose in long-term studies in rats and dogs. A safety factor of 250 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels used in the food additive review (ANZFA, 1998, ANZFA, 1999), it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.2.1.2 Butter products, 2.2.1.3 Margarine, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 8.4 Edible casings, 11.4 Tabletop sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitutes, 14.1.3.2 Kola soft drinks and some category 4 foods (Fruits and vegetables) do not contain food colours. Sunset yellow is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of sunset yellow was present in bottled waters assuming these are replaced with FBs containing sunset yellow at that concentration. Kola drinks also contained sunset yellow at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to sunset yellow between the baseline and the 'FB' scenario.

Table 5: Estimated dietary exposure to 110 – Sunset yellow

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	13772	1.4 (55)	4.2 (170)
		"FB"	13782	1.4 (55)	4.2 (170)
	2-6 yrs	Baseline	986	3.0 (120)	7.8 (310)
		"FB"	986	3.0 (120)	7.9 (310)
New Zealand	15+	Baseline	4583	1.1 (45)	3.3 (130)
		"FB"	4587	1.1 (45)	3.4 (140)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation

The addition of sunset yellow to FB would not result in an increase in estimated dietary exposure for any of the population groups assessed.

The ADI is exceeded for mean consumers aged 2-6 yrs for Australia, and for all population groups assessed for 95th percentile consumers of sunset yellow in Australia and New Zealand, for baseline and scenario estimates.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the specified population groups, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of sunset yellow, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured yellow, and alternative yellow colours may be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain sunset yellow is 10%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain sunset yellow, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of sunset yellow to FB would not pose a public health and safety risk.

122 – Azorubine (Schedule 4)

Hazard identification and Characterisation
Azorubine was evaluated by the JECFA in 1983, and an ADI of 0-4 mg/kg bw was allocated (WHO, 1983a). JECFA based the ADI for azorubine on the absence of adverse effects observed at the highest dose in long-term studies in rats, mice and pigs. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels used in the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.2.1.3 Margarine, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 11.4 Tabletop sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitutes, 14.1.3.2 Kola soft drinks and some category 4 foods (Fruits and vegetables) do not contain food colours. Azorubine is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of azorubine was present in bottled waters assuming these are replaced with FBs containing azorubine at that concentration. Kola drinks also contained azorubine at the mean concentration from the SA survey assuming these were also substituted.

There is no change in exposure to azorubine between the baseline and the 'FB' scenario.

Table 5: Estimated dietary exposure to 122 – Azorubine

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13597	0.5 (15)	2.1 (50)
		"FB"	13646	0.5 (15)	2.1 (50)
	2-6 yrs	Baseline	983	1.3 (30)	4.6 (110)
		"FB"	983	1.3 (30)	4.6 (110)
New Zealand	15+	Baseline	4550	0.4 (10)	1.7 (45)
		"FB"	4562	0.4 (10)	1.7 (45)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of azorubine to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of 2-6 year olds at the 95th percentile exposure, have estimated exposures to azorubine below the ADI. Exposure for high consumers of azorubine for 2-6 year olds is estimated to only marginally exceed the ADI (110%).

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of azorubine, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured red/maroon, and alternative red/maroon colours may be used.

For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain azorubine is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data. Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain azorubine, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of azorubine to FB would not pose a public health and safety risk.

123 – Amaranth (Schedule 1)

Hazard identification and Characterisation
Amaranth was evaluated by the JECFA in 1984, and an ADI of 0-0.5 mg/kg bw was allocated (WHO, 1984a). JECFA based the ADI for amaranth on adverse effects observed in rats, where high exposures were found to cause increased renal calcification and lesions in long-term studies, which included in utero exposure. A safety factor of 100 was used.

Dietary exposure assessment
Amaranth has restricted permissions for use in specific food groups as it is included in Schedule 1 of Standard 1.3.1 in the Code.

For the baseline dietary exposure estimate for amaranth, analytical concentration data from the SA food colours survey were used for a range of foods (South Australia Department of Health, personal communication). Manufacturers' use data were also used for some food groups. It was assumed that the category 14.1.3.2 Kola soft drinks does not contain amaranth, based on information on the market leaders in this food group, Coca Cola and Pepsi.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 30 mg/L of amaranth was present in bottled waters assuming these are replaced with FBs containing amaranth at that concentration. Kola drinks also contained amaranth at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to amaranth between the baseline and the 'FB' scenario.

Table 7: Estimated dietary exposure to 123 – Amaranth

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	10266	0.08 (15)	0.3 (60)
		"FB"	10964	0.09 (20)	0.3 (65)
	2-6 yrs	Baseline	922	0.2 (45)	0.6 (130)
		"FB"	926	0.2 (50)	0.7 (140)
New Zealand	15+	Baseline	3092	0.04 (8)	0.1 (30)
		"FB"	3278	0.05 (10)	0.2 (40)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of amaranth to FB would not result in a large increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of high consumers of amaranth aged 2-6 years from Australia, have estimated exposures to amaranth below the ADI. Exposure for high consumers of amaranth for 2-6 year olds is estimated to only marginally exceed the ADI (130-140%).

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the specified age groups, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of amaranth, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured red/purple, and alternative red/purple colours may be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain amaranth is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain amaranth, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of amaranth to FB would not pose a public health and safety risk.

124 – Ponceau 4R (Schedule 4)

Hazard identification and Characterisation
Ponceau 4R was evaluated by the JECFA in 1983, and an ADI of 0-4 mg/kg bw was allocated (WHO, 1983b). JECFA based the ADI for ponceau 4R on adverse effects observed in mice, where high exposures were found to cause foamy reticuloendothelial cells in liver and glomerulonephrosis in long-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels from the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.2.1.3 Margarine, 4.3 Processed fruits and vegetables, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 11.4 Tabletop sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitutes and 14.1.3.2 Kola soft drinks do not contain food colours. Ponceau 4R is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of ponceau 4R was present in bottled waters assuming these are replaced with FBs containing ponceau 4R at that concentration.

Kola drinks also contained ponceau 4R at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to ponceau 4R between the baseline and the 'FB' scenario.

Table 8: Estimated dietary exposure to 124 – Ponceau 4R

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13715	1.1 (25)	3.5 (90)
		"FB"	13731	1.1 (25)	3.6 (90)
	2-6 yrs	Baseline	985	2.2 (55)	6.4 (160)
		"FB"	985	2.2 (55)	6.4 (160)
New Zealand	15+	Baseline	4576	1.0 (25)	3.1 (75)
		"FB"	4580	1.0 (25)	3.1 (75)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of ponceau 4R to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of 2-6 year olds at the 95th percentile exposure, have estimated exposures to ponceau 4R below the ADI.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of ponceau 4R, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured red, and alternative red colours may be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain ponceau 4R is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain ponceau 4R, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of ponceau 4R to FB would not pose a public health and safety risk.

129 – Allura Red AC (Schedule 4)

Hazard identification and Characterisation
Allura red was evaluated by the JECFA in 1981, and an ADI of 0-7 mg/kg bw was allocated (WHO, 1980).

JECFA based the ADI for allura red on adverse effects observed in rats, where high exposures were found to decrease body weight in long-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey. Based on information found in the Food Additive Database and manufacturer use levels from the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.1.1 Olive oil, 7.1.1 Plain breads, 11.4 Table top sweeteners, 12.1.2 Reduces sodium salt mixture, 12.1.3 Salt substitute, 14.1.3.2 Kola soft drinks and some category 4 foods (Fruits and vegetables) do not contain food colours. Allura red is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of allura red was present in bottled waters assuming these are replaced with FBs containing allura red at that concentration. Kola drinks also contained allura red at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to allura red between the baseline and the 'FB' scenario.

Table 9: Estimated dietary exposure to 129 – Allura red

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13800	1.3 (20)	4.0 (55)
		"FB"	13808	1.3 (20)	4.0 (55)
	2-6 yrs	Baseline	987	2.8 (40)	7.1 (100)
		"FB"	987	2.8 (40)	7.1 (100)
New Zealand	15+	Baseline	4608	1.1 (15)	3.2 (45)
		"FB"	4610	1.1 (15)	3.3 (45)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of allura red to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to allura red at or below the ADI.

In conclusion, the addition of allura red to FB would not pose a public health and safety risk.

132 – Indigotine (Schedule 4)

Hazard identification and Characterisation
Indigotine was evaluated by the JECFA in 1975, and an ADI of 0-5 mg/kg bw was allocated (WHO, 1975). JECFA based the ADI for indigotine on adverse effects observed in rats, where high exposures were found to decrease body weight in long-term studies.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels from the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.1.1 Olive oil, 2.2.1.3 Margarine, 4.3 Processed fruits and vegetables, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 8.4 Edible casings, 11.4 Table top sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitute and 14.1.3.2 Kola soft drinks do not contain food colours. Indigotine is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of indigotine was present in bottled waters assuming these are replaced with FBs containing indigotine at that concentration. Kola drinks also contained indigotine at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to indigotine between the baseline and the 'FB' scenario.

Table 10: Estimated dietary exposure to 132 – Indigotine

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13715	1.1 (20)	3.5 (70)
		"FB"	13731	1.1 (20)	3.6 (70)
	2-6 yrs	Baseline	985	2.2 (45)	6.4 (130)
		"FB"	985	2.2 (45)	6.4 (130)
New Zealand	15+	Baseline	4576	1.0 (20)	3.1 (60)
		"FB"	4580	1.0 (20)	3.1 (60)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of indigotine to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of 2-6 year olds, have estimated exposures to indigotine below the ADI. Exposure for high consumers of indigotine for 2-6 year olds is estimated to only marginally exceed the ADI (130%).

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of indigotine, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured blue/purple/mauve, and alternative blue/purple/mauve colours may be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain indigotine is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain indigotine, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of indigotine to FB would not pose a public health and safety risk.

133 – Brilliant Blue (Schedule 4)

Hazard identification and Characterisation
Brilliant Blue was evaluated by the JECFA in 1969, and an ADI of 0-12.5 mg/kg bw was allocated (WHO, 1970). JECFA based the ADI for brilliant blue on the absence of adverse effects observed at the highest dose in long-term studies in rats. A safety factor of 250 was used.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs. Based on information found in the Food Additive Database, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 7.1.1 Plain breads and some category 4 foods (Fruits and vegetables) do not contain food colours. Brilliant blue is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of brilliant blue was present in bottled waters assuming these are replaced with FBs containing brilliant blue at that concentration.

There is no change in exposure to brilliant blue between the baseline and the 'FB' scenario.

Table 11: Estimated dietary exposure to 133 – Brilliant blue

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	13809	2.4 (20)	6.8 (55)
		"FB"	13810	2.4 (20)	6.8 (55)
	2-6 yrs	Baseline	987	6.2 (50)	12.8 (100)
		"FB"	987	6.2 (50)	12.8 (100)
New Zealand	15+	Baseline	4610	1.8 (15)	4.6 (35)
		"FB"	4610	1.8 (15)	4.6 (35)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of brilliant blue to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to brilliant blue at or below the ADI.

In conclusion, the addition of brilliant blue to FB would not pose a public health and safety risk.

143 – Fast Green FCF (Schedule 4)

Hazard identification and Characterisation
Fast green was evaluated by the JECFA in 1986, and an ADI of 0-25 mg/kg bw was allocated (WHO, 1987b). JECFA based the ADI for fast green on the absence of adverse effects observed at the highest dose in long-term studies in rats. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs. Based on information found in the Food Additive Database, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 7.1.1 Plain breads and some category 4 foods (Fruits and vegetables) do not contain food colours. Fast green is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of fast green was present in bottled waters assuming these are replaced with FBs containing fast green at that concentration.

There is no change in exposure to fast green between the baseline and the 'FB' scenario.

Table 12: Estimated dietary exposure to 143 – Fast green

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	13809	2.4 (10)	6.8 (25)
		"FB"	13810	2.4 (10)	6.8 (25)
	2-6 yrs	Baseline	987	6.2 (25)	12.8 (50)
		"FB"	987	6.2 (25)	12.8 (50)
New Zealand	15+	Baseline	4610	1.8 (7)	4.6 (20)
		"FB"	4610	1.8 (7)	4.6 (20)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of fast green to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to fast green below the ADI.

In conclusion, the addition of fast green FCF to FB would not pose a public health and safety risk.

151 – Brilliant Black (Schedule 4)

Hazard identification and Characterisation
Brilliant black was evaluated by the JECFA in 1981, and an ADI of 0-1 mg/kg bw was allocated (WHO, 1981). JECFA based the ADI for brilliant black on adverse effects observed in pigs, where high exposures were found to cause cysts containing mucus and fibrin in the mucosa of the ileum in short-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels used in the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.2.1.2 Butter products, 4.3 Processed fruits and vegetables, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 8.4 Edible casings, 11.4 Table top sweeteners, 12 Salts and condiments and 14.1.3.2 Kola soft drinks do not contain food colours. Brilliant black is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of brilliant black was present in bottled waters assuming these are replaced with FBs containing brilliant black at that concentration. Kola drinks also contained brilliant black at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to brilliant black between the baseline and the 'FB' scenario.

Table 13: Estimated dietary exposure to 151 – Brilliant black

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13782	1.1 (110)	3.6 (360)
		"FB"	13791	1.1 (110)	3.6 (360)
	2-6 yrs	Baseline	987	2.2 (220)	6.5 (650)
		"FB"	987	2.3 (230)	6.5 (650)
New Zealand	15+	Baseline	4598	1.0 (100)	3.1 (310)
		"FB"	4600	1.0 (100)	3.1 (310)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of brilliant black to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to brilliant black above the ADI, except for consumers of brilliant black at the mean exposure for New Zealand.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of brilliant black, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured black, and there are very few 'black' or very darkly coloured foods in the food supply. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain brilliant black is <1%, which is extremely small in comparison to some of the other food colourings and also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain brilliant black, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of Brilliant Black to FB would not pose a public health and safety risk.

155 – Brown HT (Schedule 4)

Hazard identification and Characterisation
Brown HT was evaluated by the JECFA in 1984, and an ADI of 0-1.5 mg/kg bw was allocated (WHO, 1984b). JECFA based the ADI for brown HT on adverse effects observed in mice, where high exposures were found to cause reduced body weight gain and heart weight, increased incidence of leucocyte infiltration and an increased incidence of cystic ovaries in long-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Some foods were assigned an analytical concentration from the SA food colours survey (South Australia Department of Health, personal communication). Based on information found in the Food Additive Database and manufacturer use levels used in the food additive review, it was assumed foods in classification codes 1.3 Condensed and evaporated milk, 1.4.2 Cream products, 1.5 Dried milk, 2.2.1.2 Butter products, 2.2.1.3 Margarine, 4.3 Processed fruits and vegetables, 7.1.1 Plain breads, 8.2 Processed meat in whole cuts, 8.3 Processed comminuted meat, 11.4 Table top sweeteners, 12.1.2 Reduced sodium salt mixture, 12.1.3 Salt substitutes and 14.1.3.2 Kola soft drinks do not contain food colours. Brown HT is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 70 mg/L of brown HT was present in bottled waters assuming these are replaced with FBs containing brown HT at that concentration. Kola drinks also contained brown HT at the mean concentration from the SA survey assuming these were also substituted.

There is little change in exposure to brown HT between the baseline and the 'FB' scenario.

Table 14: Estimated dietary exposure to 155 – Brown HT

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13715	1.1 (70)	3.5 (240)
		"FB"	13731	1.1 (70)	3.5 (240)
	2-6 yrs	Baseline	985	2.2 (140)	6.4 (430)
		"FB"	985	2.2 (150)	6.4 (430)
New Zealand	15+	Baseline	4576	1.0 (65)	3.1 (200)
		"FB"	4580	1.0 (65)	3.1 (210)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation

The addition of brown HT to FB would not result in an increase in dietary exposure for any of the population groups assessed.

The ADI for brown HT is exceeded for mean consumers aged 2-6 yrs for Australia, and for all population groups assessed for 95th percentile consumers in Australia and New Zealand.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the specified population groups, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of brown HT, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured brown, and alternative brown colours could have been used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain brown HT is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Whilst the SA food colours survey provided some information on actual concentrations in some food groups, it did not cover all the food groups that could potentially contain tartrazine, nor did it provide any indication of the exact proportion of each food category to contain the additive.

In conclusion, the addition of Brown HT to FB would not pose a public health and safety risk.

160b – Annatto Extracts (Schedule 1)

Hazard identification and Characterisation
Annatto extracts were most recently evaluated by the JECFA in 2003 (WHO, 2004). JECFA could not establish a generic ADI for the various annatto extracts on the basis of the data submitted and therefore established a temporary ADI for each of the individual preparations tested. With the application of a 200-fold safety factor to the NOEL for each of the annatto preparations, the following ADIs were allocated:

Annatto B: 0-7.0 mg/kg bw, based on adverse effects observed in rats, where high exposures were found to cause urinary effects (elevated concentrations of protein in urine and crystals in urine sediment).

Annatto C: 0-0.4 mg/kg bw, based on adverse effects observed in rats, where high exposures were found to cause increases in liver weight accompanied by hepatocellular hypertrophy and necrosis.

Annatto E: 0-4.0 mg/kg bw, based on adverse effects observed in rats, where high exposures were found to cause increases in thyroid and kidney weights and decreased spleen weights.

Annatto F: 0-0.4 mg/kg bw, based on adverse effects observed in rats, where high exposures were found to cause increases in kidney weights, haematological changes and alterations in serum proteins.

No data on the potential toxicity of Annatto D or Annatto G were available, and no ADI could be established. An additional safety factor of 2 was applied to the NOELs, because of deficiencies in the database.

JECFA adopted tentative specifications for the four annatto extracts tested, with the following minimum essay values:

Annatto extract (solvent-extracted bixin) – Annatto B: not less than 85% pigment (as bixin, of which not more than 2.5% is norbixin).

Annatto extract (solvent-extracted norbixin) – Annatto C: not less than 85% pigment (as norbixin).

Annatto extract (aqueous processed bixin) – Annatto E: not less than 25% pigment (as bixin, of which not more than 7% is norbixin).

Annatto extract (alkali-processed norbixin) – Annatto F: not less than 35% pigment (as norbixin).

JECFA also adopted tentative specifications with minimum assay values as proposed for the commercial products annatto D and G, which has not been tested biologically.

For the purpose of this assessment, the ADI for 2 norbixin extracts at a level of 0.4 mg/kg bw was used, which was at a lower level than the ADI for the bixin extracts.

Dietary exposure assessment
Annatto extracts have restricted permissions for use in specific food groups, given in Schedule 1 of Standard 1.3.1 in the Code.

For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Most foods were assigned manufacturer use levels from the food additive review (ANZFA, 1998; ANZFA, 1999). It was also assumed that 40% of yoghurts and 10% of ice cream and edible ice products contained Annatto. Annatto is only currently permitted in fruit juice based beverages. At baseline, annatto was not permitted in water based flavoured drinks or bottled waters as per Standard 1.3.1.

For the 'FB' Scenario the requested maximum level of 10 mg/kg of annatto has been assigned to water based flavoured drinks and bottled waters assuming that a person will replace these beverages with a fruit juice based FB.

The MPLs in the Code do not specify to which annatto extract they apply. FSANZ has some manufacturers use data for annatto extracts specified as being either 'bixin' or 'norbixin' for some foods. However, it is unknown as to what bixin or norbixin extract they apply to. With a lack of any other relevant data on the concentrations of annatto extracts in foods, all manufacturers' use data on annatto extracts available to FSANZ were used in the exposure assessment, without making a distinction between bixin and norbixin. Therefore, there are some significant limitations with the exposure estimates for annatto extracts.

There is an increase in exposure to annatto between the baseline and the 'FB' scenario.

Table 15: Estimated dietary exposure to 160b – Annatto

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	13515	0.07 (20)	0.2 (60)
		"FB"	13621	0.1 (30)	0.4 (100)
	2-6 yrs	Baseline	981	0.2 (55)	0.6 (150)
		"FB"	983	0.4 (95)	0.9 (230)
New Zealand	15+	Baseline	4570	0.05 (10)	0.1 (35)
		"FB"	4582	0.07 (20)	0.2 (55)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of annatto to FB would result in an increase in dietary exposure for all the population groups assessed.

All population groups assessed, with the exception of 2-6 year olds, have estimated exposures to annatto at or below the ADI.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that for every food category that was assigned a numerical concentration of annatto, every product in that category contained the colour, which in reality is not the case. Only a small proportion of the category would be coloured yellow, and alternative yellow colours may be used. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain annatto is 10%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

For annatto there was a difference in estimated exposures between baseline, representing current permissions, and the scenario model assuming annatto was permitted in FBs. This is because at baseline, neither the bottled water or water based flavoured drinks (e.g. cordial, soft drink) contain annatto. Whereas, when it is assumed that water based flavoured drinks are replaced with FBs that do contain annatto, exposure goes up significantly since beverages are consumed in larger quantities in comparison to solid foods, and if a food additive is in a beverage, the exposure to that additive is likely to be higher.

For annatto a conservative approach was taken with the hazard identification and characterisation, i.e. the lowest available ADI, as established by JECFA, for the various annatto extracts was used. Whether this form of annatto is representative for annatto used in Australia and New Zealand is currently unknown.

In conclusion, the addition of annatto FB would not pose a public health and safety risk.

200 – Sorbic Acid and Sorbates (Schedule 1)

Hazard identification and Characterisation
Sorbates were evaluated by JECFA in 1985, where a group ADI of 0-25 mg/kg bw for sorbic acid and its calcium, potassium and sodium salts was allocated (WHO, 1986). JECFA based the ADI for sorbates on the absence of adverse effects observed at the highest dose in long-term studies in rats. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Most foods were assigned an analytical concentration from the unpublished 21st ATDS results (FSANZ, unpublished). Kola drinks were assumed not to contain sorbates based on information from manufacturers'. This was confirmed by assessing the labels of the two market leaders of kola drinks, Coca Cola and Pepsi, neither of which use sorbates in their products. Sorbates are not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 400 mg/kg of sorbates was present in bottled waters assuming these are replaced with FBs containing sorbates at that concentration. Kola drinks also then contained sorbates at the mean concentration from the ATDS.

There is little change in exposure to sorbates between the baseline and the 'FB' scenario.

Table 16: Estimated dietary exposure to 200-203 – Sorbic acid and sorbates

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	13802	3.6 (15)	10.6 (40)
		"FB"	13808	3.6 (15)	10.7 (45)
	2-6 yrs	Baseline	988	9.1 (35)	22.8 (90)
		"FB"	988	9.2 (35)	22.9 (90)
New Zealand	15+	Baseline	4604	2.8 (10)	8.8 (35)
		"FB"	4607	2.9 (10)	8.9 (35)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of sorbates to FB would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to sorbates below the ADI.

In conclusion, the addition of sorbic acid and sorbates to FB would not pose a public health and safety risk.

210 – Benzoic Acid and Benzoates (Schedule 1)

Hazard identification and Characterisation
Benzoates were most recently evaluated by JECFA in 1996, and an ADI for benzoic acid and sodium benzoate of 0-5 mg/kg bw was allocated (WHO, 1996b). JECFA based the ADI for benzoic acid and its salts on short-term (90 days) and long-term (lifetime) exposure in rats where the adverse effect observed at a low dose level was testicular tubular atrophy. Other adverse effects such as decreased body weight and neurological changes occurred at higher dose levels. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Most foods were assigned an analytical concentration from the unpublished 21st ATDS results (FSANZ, unpublished). Based on market leaders, Coca Cola and Pepsi, it was assumed that regular sugar sweetened kola drinks do not contain benzoates, however artificially sweetened kola drinks do. Benzoates are not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 400 mg/kg of benzoates was present in bottled waters assuming these are replaced with FBs containing benzoates at that concentration. Kola drinks also then contained benzoates at the mean concentration from the ATDS.

There is an increase in exposure to benzoates between the baseline and the 'FB' scenario.

Table 17: Estimated dietary exposure to 210-213 – Benzoic acid and benzoates

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	12807	1.3 (25)	5.2 (100)
		"FB"	12912	1.7 (35)	6.5 (130)
	2-6 yrs	Baseline	966	4.3 (85)	12.0 (240)
		"FB"	967	4.8 (95)	13.5 (270)
New Zealand	15+	Baseline	4177	0.6 (10)	2.4 (45)
		"FB"	4214	0.8 (15)	3.4 (70)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The ADI is exceeded for 95th percentile consumers aged 2 years and above for the FB scenario, and for children aged 2-6 years for Australia at baseline and for the FB scenario.

The addition of benzoates to FB would result in an increase in dietary exposure for all the population groups assessed.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons.

Firstly, it was assumed that where benzoates are used in a food category, all foods within that category contained benzoates at the specified level, which in reality is not the case. Only a small proportion of the category would contain benzoates. For example, the Food Additive Database indicates the maximum proportion of the products in the database that contain benzoates is 5%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

For benzoates there was a difference in estimated exposures between baseline, representing current permissions, and the scenario model assuming benzoates was permitted in FBs. This is because at baseline, neither the bottled water or sugar-sweetened kola drinks contain benzoates. Whereas, when it is assumed that these drinks are replaced with FBs that do contain benzoates, exposure goes up significantly since beverages are consumed in larger quantities in comparison to solid foods, and if a food additive is in a beverage, the exposure to that additive is likely to be higher.

Benzoates were identified during the Review (ANZFA, 1998; ANZFA, 1999) as a cause for concern and placed on the list for future monitoring, which is why benzoates are currently being assessed in the 21st ATDS (FSANZ, unpublished).

In conclusion, the addition of benzoic acid and benzoates to FB would not pose a public health and safety risk.

220 – Sulphur Dioxide and Sulphites (Schedule 1)

Hazard identification and Characterisation
Sulphur dioxide and sulphites were most recently re-evaluated by JECFA in 1998, where the previously allocated group ADI of 0.7 mg/kg bw was maintained (WHO, 1999). JECFA based the ADI for sulphites on adverse effects observed in rats and pigs, where high exposures were found to cause gastric lesions in long-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, some food groups were assumed to have concentrations at the MPLs. Most foods were assigned an analytical concentration from the unpublished 21st ATDS results (FSANZ, unpublished). Based on market leaders, Coca Cola and Pepsi, it was assumed all kola drinks do not contain sulphites. Sulphites are not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 115 mg/kg of sulphites was present in bottled waters assuming these are replaced with FBs containing sulphites at that concentration. Kola drinks also then contained sulphites at the mean concentration from the ATDS.

There is little change in exposure to sulphites between the baseline and the 'FB' scenario.

Table 18: Estimated dietary exposure to 220-225 – Sulphur dioxide and sulphites

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	13365	0.5 (75)	1.9 (270)
		"FB"	13445	0.6 (80)	2.0 (280)
	2-6 yrs	Baseline	981	1.2 (180)	4.0 (570)
		"FB"	981	1.3 (180)	4.0 (570)
New Zealand	15+	Baseline	4453	0.3 (45)	1.1 (160)
		"FB"	4464	0.3 (50)	1.2 (170)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of sulphites to FB would not result in a large increase in dietary exposure for all the population groups assessed.

The ADI is exceeded for mean consumers of sulphites aged 2-6 yrs for Australia, and for all population groups assessed for 95th percentile consumers for Australia and New Zealand.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was assumed that where sulphites are used in a food category, all foods within that category contained sulphites at the specified level, which in reality is not the case. Only a small proportion of the category would contain sulphites. For example, the Food Additive Database indicates the maximum proportion of the products in that database that contain sulphites is 10%, which also suggests that the above model is highly conservative. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

Sulphites were identified during the Review (ANZFA, 1998; ANZFA, 1999) as a cause for concern and placed on the list for future monitoring, which is why they are currently being assessed in the 21st ATDS (FSANZ, unpublished).

JECFA based the ADI for sulphites on adverse effects observed in rats and pigs, where high exposures were found to cause gastric lesions in long-term studies. As the occurrence of gastric lesions is more likely related to sulphite concentrations in foods than total dietary exposure, potential adverse effects are more likely to be associated with those foods with high concentrations of sulphites. The proposed concentration for sulphite in FB is at a maximum level of 115 mg/kg. This concentration is considerably lower, than that permitted in some other foods (e.g. dried fruits).

In conclusion, the addition of sulphur dioxide and sulphites to FB would not pose a public health and safety risk.

385 – Calcium Disodium EDTA (Schedule 1)

Hazard identification and Characterisation
Calcium disodium EDTA was evaluated by the JECFA in 1973, and an ADI of 0-2.5 mg/kg bw was allocated, calculated as calcium disodium EDTA, no excess of disodium EDTA should remain in foods (WHO, 1974). JECFA based the ADI for calcium disodium EDTA on the absence of adverse effects observed at the highest dose in long-term studies in rats. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs. No survey or manufacturers' use data were available to use in the exposure assessment. Calcium disodium EDTA is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 33 mg/L of calcium disodium EDTA was present in bottled waters assuming these are replaced with FBs containing calcium disodium EDTA at that concentration.

There is no change in exposure to calcium disodium EDTA between the baseline and the 'FB' scenario.

Table 19: Estimated dietary exposure to 385 – Calcium disodium EDTA

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	10444	0.3 (10)	1.0 (40)
		"FB"	10548	0.3 (10)	1.0 (40)
	2-6 yrs	Baseline	826	0.8 (30)	2.3 (90)
		"FB"	828	0.8 (30)	2.3 (90)
New Zealand	15+	Baseline	3590	0.2 (7)	0.6 (25)
		"FB"	3603	0.2 (7)	0.6 (25)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of calcium disodium EDTA to FBs would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to calcium disodium EDTA below the ADI.

In conclusion, the addition of calcium disodium EDTA to FB would not pose a public health and safety risk.

444 – Sucrose Acetate Isobutrate (Schedule 1)

Hazard identification and Characterisation
Sucrose acetate isobutrate was most recently evaluated by the JECFA in 1996, and an ADI of 0-20 mg/kg bw was allocated (WHO, 1997). JECFA based the ADI for sucrose acetate isobutrate on the absence of adverse effects observed at the highest dose in long-term studies in rats and dogs. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs. No survey or manufacturers use data were available to use in the exposure assessment. Sucrose acetate isobutrate is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 200 mg/L of sucrose acetate isobutrate was present in bottled waters assuming these are replaced with FBs containing sucrose acetate isobutrate at that concentration.

There is little change in exposure to sucrose acetate isobutrate between the baseline and the 'FB' scenario.

Table 20: Estimated dietary exposure to 444 – Sucrose acetate isobutrate

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	10229	1.6 (8)	5.4 (25)
		"FB"	10340	1.6 (8)	5.5 (25)
	2-6 yrs	Baseline	822	4.4 (20)	13.0 (65)
		"FB"	824	4.5 (20)	13.1 (65)
New Zealand	15+	Baseline	3452	0.8 (4)	3.2 (15)
		"FB"	3470	0.8 (4)	3.3 (15)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of sucrose acetate isobutrate to FBs would not result in a large increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to sucrose acetate isobutrate below the ADI.

In conclusion, the addition of sucrose acetate isobutrate to FB would not pose a public health and safety risk.

445 – Glycerol Ester of Wood Rosin (Schedule 1)

Hazard identification and Characterisation
Glycerol ester of wood rosin was most recently evaluated by the JECFA in 1996, and an ADI of 0-25 mg/kg bw was allocated (WHO, 1996c). JECFA based the ADI for glycerol ester of wood rosin on the absence of adverse effects observed at the highest dose in a 13-week study in rats. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs. No survey or manufacturers use data were available to use in the exposure assessment. Glycerol ester of wood rosin is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 100 mg/L of glycerol ester of wood rosin was present in bottled waters assuming these are replaced with FBs containing glycerol ester of wood rosin at that concentration.

There is little change in exposure to glycerol ester of wood rosin between the baseline and the 'FB' scenario.

Table 21: Estimated dietary exposure to 445 – Glycerol ester of wood rosin

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	10229	0.8 (3)	2.7 (10)
		"FB"	10340	0.8 (3)	2.7 (10)
	2-6 yrs	Baseline	822	2.2 (9)	6.5 (25)
		"FB"	824	2.2 (9)	6.5 (25)
New Zealand	15+	Baseline	3452	0.4 (2)	1.6 (6)
		"FB"	3470	0.4 (2)	1.6 (7)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of glycerol ester of wood rosin to FBs would not result in an increase in dietary exposure for any of the population groups assessed.

All population groups assessed have estimated exposures to glycerol ester of wood rosin well below the ADI.

In conclusion, the addition of glycerol ester of wood rosin to FB would not pose a public health and safety risk.

480 – Dioctyl Sodium Sulphosuccinate (DSS) (Schedule 1)

Hazard identification and Characterisation
DSS was most recently evaluated by the JECFA in 1995, and an ADI of 0-0.1 mg/kg bw was allocated (WHO, 1995). JECFA based the ADI for DSS on adverse effects observed in rats, where high exposures were found to cause reduction in parental body weight as well as weanling pup weight in reproduction studies. A safety factor of 500 was used, because of the limited toxicological database on DSS.

Dietary exposure assessment
For the baseline estimate of exposure, all food groups were assumed to have concentrations at the MPLs apart from one. A manufacturers' use level obtained during the food additives review was assigned to water based flavoured drinks (ANZFA, 1998; ANZFA, 1999). No other survey or manufacturers use data were available to use in the exposure assessment. DDS is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 10 mg/L of DSS was present in bottled waters assuming these are replaced with FBs containing DSS at that concentration.

There is little change in exposure to DSS between the baseline and the 'FB' scenario.

Table 22: Estimated dietary exposure to 480 – Dioctyl sodium sulphosuccinate (DSS)

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	10229	0.1(95)	0.3 (320)
		"FB"	10340	0.1(100)	0.3 (320)
	2-6 yrs	Baseline	822	0.2 (250)	0.7 (690)
		"FB"	824	0.3 (250)	0.7 (690)
New Zealand	15+	Baseline	3452	0.06 (60)	0.2 (200)
		"FB"	3470	0.06 (60)	0.2 (200)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of DDS to FB would not result in a large increase in dietary exposure for any of the population groups assessed.

All population groups assessed, with the exception of mean consumers of DSS aged 2-6 years from Australia, have estimated exposures to DSS below the ADI. All population groups have estimated exposures that exceed the ADI at the 95th percentile exposure.

Whilst, in this conservative model, the estimated exposures exceeded the ADI for the consumers in the 2-6 year groups at the 95th percentile, this is highly unlikely to occur in reality for two reasons. Firstly, it was it was assumed that for every food category that was assigned a numerical concentration of DSS, every product in that category contained DSS, which in reality is not the case.

For example the Food Additive Database did not contain any food products where DSS was used, which also suggests that the model above is highly conservative. This may also indicate that there is very little use of the additive in the food supply, suggesting the actual exposure to DSS would be much lower than predicted. Secondly, the 95th percentile is an overestimate of exposure over a long period of time as it is based on 24-hour food consumption data.

In conclusion, the addition of DSS to FB would not pose a public health and safety risk.

ESTIMATED EXPOSURES FOR INTENSE SWEETENERS

The *Consumption of Intense Sweeteners in Australia and New Zealand: Benchmark Survey 2003* ('The Sweetener Survey')(FSANZ, 2003) was used to obtain concentrations of sweeteners used in food groups. At the time of the survey, concentrations of the sweeteners added to the products (by brand and flavour) were obtained from manufacturers for almost all products on the market that contained intense sweeteners at the time. The mean concentration of each sweetener in each food group was calculated from the compiled database of manufacturers concentrations for use in the dietary modelling for the sweeteners being assessed in this application. The concentrations were assigned to the relevant food groups in DIAMOND for dietary modelling purposes.

It was not possible to use the sweetener survey data directly to undertake predictive modelling for the proposed use of intense sweeteners in FBs for a number of reasons. The sweetener survey collected consumption data using a 7-day diary of intense sweetened foods consumed by brand and flavour. These consumption data are not in a format (e.g. in DIAMOND) to allow dietary exposure assessments to be conducted. Also, other food products (such as the bottled water and fruit juice based products) needed to be included in the scenario modelling, for which consumption data were not collected as a part of the sweetener survey. The sweetener survey only included respondents 12 years of age and above. The dietary modelling for this application needed to include children younger than 12 years of age, therefore, this had to be done using the 1995 NNS consumption data and DIAMOND.

950 – Acesulphame Potassium (Ace K) (Schedule 1)

Hazard identification and Characterisation
Ace K was most recently evaluated by the JECFA in 1990, and an ADI of 0-15 mg/kg bw was allocated (WHO, 1991). JECFA based the ADI for Ace K on the absence of adverse effects observed at the highest dose in long-term studies in rats. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, only food groups that were identified in the 2003 sweetener survey as containing Ace K were included in the exposure assessment (FSANZ, 2003). The concentration data collected for the sweetener survey were for almost all of the products on the market at the time that contained intense sweeteners. Therefore, where there may have been a permission in the Code to allow Ace K in a food group, if there were no data from the sweetener survey on these food groups, a zero concentration was assigned in the modelling. Ace K is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 300 mg/L of Ace K was present in bottled waters and sugar sweetened water based flavoured drinks assuming these are replaced with FBs containing Ace K at that concentration.

There is an increase in exposure to Ace K between the baseline and the 'FB' scenario.

Table 23: Estimated dietary exposure to 950 – Acesulphame potassium (Ace K)

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	4877	1.1 (7)	3.6 (25)
		"FB"	8596	3.1 (20)	9.8 (65)
	2-6 yrs	Baseline	494	2.2 (15)	6.8 (45)
		"FB"	817	7.6 (50)	20.3 (140)
New Zealand	15+	Baseline	1230	0.7 (5)	2.0 (15)
		"FB"	2376	1.9 (15)	5.9 (40)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of Ace K would result in an increase in dietary exposure for all population groups assessed.

All population groups assessed have estimated exposures for consumers of Ace K below the ADI, except for children aged 2-6 years at the 95th percentile exposure when FBs are consumed, where exposures only marginally exceed the ADI (140%).

Whilst the estimated exposures in this model exceed the ADI for high consumers of Ace K in the 2-6 year age group at the 95th percentile when FBs are consumed, it is not considered that the actual exposure to Ace K would exceed the ADI. It was concluded from the sweetener survey (FSANZ 2003) that there are no public health and safety risk associated with exposures to Ace K. This was determined for people identified in the survey as 'high consumers' of intense sweetened foods. For the sweetener survey respondents recorded, for seven days, all foods they consumed that contained intense sweeteners. The concentration of the intense sweetener by brand and flavour was then matched to the consumption in order to estimate exposure for each respondent. For this Application, 24-hour recall consumption data were used, and combined with a mean concentration of the sweetener for each food group. The dietary modelling for this Application therefore is not as realistic as the modelling conducted for the sweetener survey.

For the sweetener survey, exposures were estimated for high consumers of foods containing intense sweeteners aged 12 years and above. Mean exposures for consumers of Ace K were 4% of the ADI for Australia and 3% of the ADI for New Zealand. Estimated 95th percentile exposures for consumers of Ace K were 9% of the ADI for Australia and 11% of the ADI for New Zealand. These estimates are lower than those estimated for this Application.

In addition, it was assumed for this Application, that for every food category that was assigned a numerical concentration of Ace K, every product in that category contained the sweetener, which in reality is not the case. Only a small proportion of the category would contain intense sweeteners and Ace K in particular. Of the 531 products in the sweetener survey database, 33% contained Ace K.

For Ace K there was a difference in estimated exposures between baseline, representing current permissions, and the scenario model assuming annatto was permitted in FBs. This is because of the way the modelling has been conducted and the assumptions made about what beverages were substituted with FBs. It is assumed that people substitute bottled water and sugar sweetened water-based flavoured drinks with an FB that contains Ace K, therefore increasing estimated exposure.

In conclusion, the addition of Ace K to FB would not pose a public health and safety risk.

954 – Saccharin (Schedule 1)

Hazard identification and Characterisation
Saccharin and its salts was most recently evaluated by the JECFA in 1993, and a group ADI of 0-7.5 mg/kg bw was allocated for saccharin and its calcium, potassium, and sodium salts (WHO, 1993). JECFA based the ADI for saccharin on adverse effects observed in rats in a two-generation study, where high exposures were found to cause decreased body weight gain in the presence of increased food consumption, which were probably related to inhibitory effects of saccharin on carbohydrate and protein digestion. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, only food groups that were identified in the 2003 sweetener survey as containing saccharin were included in the exposure assessment (FSANZ, 2003). The concentration data collected for the sweetener survey were for almost all of the products on the market at the time that contained intense sweeteners. Therefore, where there may have been a permission in the Code to allow saccharin in a food group, if there were no data from the sweetener survey on these food groups, a zero concentration was assigned in the modelling. Saccharin is not permitted in bottled waters.

The data for concentrations of sweeteners in foods from the sweetener survey was collected during the 2 year 'transition period' between the old Australian Food Standards Code and the current Code. This meant that during that period, manufacturers could manufacture their products to meet the regulations in either Code (not a mixture of both). As a consequence of the review, the MPLs for saccharin were reduced in some food groups. Therefore, some of the concentration data collected from manufacturers at the time, would now exceed the MPL in the new Code. Therefore, mean concentrations derived for these foods from the manufacturers' data, if they exceeded the current MPL, were 'capped' at the MPL for dietary modelling purposes.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 80 mg/L of saccharin was present in bottled waters and sugar sweetened water based flavoured drinks, assuming these are replaced with FBs containing saccharin at that concentration.

FSANZ is currently considering another application (A469 – Saccharin in water-based flavoured drinks) requesting the concentration of saccharin permitted to be added to water based flavoured drinks be raised from 80 mg/kg to 150 mg/kg. The dietary modelling for this Application used the current maximum permitted level in the Code of 80 mg/kg as A469 had not been approved at final assessment at the time the modelling for this application was conducted.

There is an increase in exposure to saccharin between the baseline and the 'FB' scenario.

For the New Zealand population, the baseline estimate of exposure is higher than exposure when assuming FBs are consumed (FB scenario).

Table 24: Estimated dietary exposure to 954 – Saccharin

				Mean consumer exposure	95th %ile consumer exposure
Country	**Population sub-group**	**Scenario**	**No. of Consumers**	**mg/kg bw/day (% ADI)**	**mg/kg bw/day (%ADI)**
Australia	2+	Baseline	2020	1.0 (20)	2.8 (55)
		"FB"	7224	1.0 (20)	3.0 (60)
	2-6 yrs	Baseline	84	1.3 (25)	2.8 (55)
		"FB"	707	2.1 (40)	5.5 (110)
New Zealand	15+	Baseline	392	1.7 (35)	6.5 (130)
		"FB"	1880	0.9 (15)	2.6 (50)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of saccharin to FB would result in an increase in dietary exposure for the population groups assessed, except for the New Zealand population, which saw a decrease in saccharin exposure.

All population groups assessed, with the exception of 2-6 year olds for the FB scenario and at baseline for the New Zealand consumers, have estimated exposures to saccharin below the ADI. Exposure for high consumers of saccharin for the FB scenario for 2-6 year olds is estimated to only marginally exceed the ADI (110%).

Whilst the estimated exposures in this model exceed the ADI for high consumers of saccharin in the population groups outlined, it is not considered that the actual exposure to saccharin would exceed the ADI. It was concluded from the sweetener survey (FSANZ, 2003) that there are no public health and safety risks associated with exposures to saccharin. This was determined for people identified in the survey as 'high consumers' of intense sweetened foods. For the sweetener survey respondents recorded, for seven days, all foods they consumed that contained intense sweeteners. The concentration of the intense sweetener by brand and flavour was then matched to the consumption in order to estimate exposure for each respondent. For this Application, 24-hour recall consumption data were used, and combined with a mean concentration of the sweetener for each food group. The dietary modelling for this Application therefore is not as realistic as the modelling conducted for the sweetener survey.

For the sweetener survey, exposures were estimated for high consumers of foods containing intense sweeteners aged 12 years and above. Mean exposures for consumers of saccharin were 10% of the ADI for Australia and 6% of the ADI for New Zealand. Estimated 95th percentile exposures for consumers of saccharin were 51% of the ADI for Australia and 24% of the ADI for New Zealand. These estimates are lower than those estimated for this Application.

In addition, it was assumed that for every food category that was assigned a numerical concentration of saccharin, every product in that category contained the sweetener, which in reality is not the case. Only a small proportion of the category would contain intense sweeteners and saccharin in particular. Of the 531 products in the sweetener survey database, 20% contained saccharin.

There is an increase in exposure to saccharin between the baseline and the 'FB' scenario. This is because of the way the modelling has been conducted and the assumptions made about what beverages were substituted with FBs. It is assumed that people substitute bottled water and sugar sweetened water based flavoured drinks with an FB that contains saccharin, therefore increasing potential exposure.

For the New Zealand population, the baseline estimate of exposure is higher than exposure when assuming FBs are consumed (FB scenario). This is because of the way DIAMOND is programmed, and how consumers of specific food chemicals are counted. At baseline, only a few food products contained saccharin, and therefore only a part of the population is considered to be a consumer at baseline. However, for modelling it was assumed that all of the following beverages wee replaced: cordials, carbonated drinks, fruit juices, fruit juice drinks, sport drinks and bottled water. This would increase the number of saccharin consumers. The exposure estimates based on the baseline exposures and FB scenario exposures are derived from different numbers of consumers of saccharin and therefore, different distributions of individual exposures. This results in different mean and 95th percentile exposures being derived, and in some cases higher exposures for the baseline model.

In conclusion, the addition of saccharin to FB would not pose a public health and safety risk.

956 – Alitame (Schedule 1)

Hazard identification and Characterisation
Alitame was most recently evaluated by the JECFA in 1996, and an ADI of 0-1 mg/kg bw was allocated (WHO, 1996a). JECFA based the ADI for alitame on adverse effects observed in dogs, where high exposures were found to cause decreased body weight gain and increased liver weight in long-term studies. A safety factor of 100 was used.

Dietary exposure assessment
For the baseline estimate of exposure, only food groups that were identified in the 2003 sweetener survey as containing alitame were included in the exposure assessment (FSANZ, 2003). Only two products in the sweetener survey contained alitame. The concentration data collected for the sweetener survey were for almost all of the products on the market at the time that contained intense sweeteners. Therefore, where there may have been a permission in the Code to allow alitame in a food group, if there were no data from the sweetener survey on these food groups, a zero concentration was assigned in the modelling. Alitame is not permitted in bottled waters.

When estimating exposures based on the 'FB' Scenario, it was additionally assumed that the requested maximum level of 40 mg/L of alitame was present in bottled waters and sugar sweetened water based flavoured drinks, assuming these are replaced with FBs containing alitame at that concentration.

There is an increase in exposure to alitame between the baseline and the 'FB' scenario.

Table 25: Estimated dietary exposure to 956 – Alitame

Country	Population sub-group	Scenario	No. of Consumers	Mean consumer exposure mg/kg bw/day (% ADI)	95th %ile consumer exposure mg/kg bw/day (%ADI)
Australia	2+	Baseline	3653	0.1 (10)	0.3 (30)
		"FB"	8667	0.4 (40)	1.2 (120)
	2-6 yrs	Baseline	360	0.2 (20)	0.5 (50)
		"FB"	797	1.0 (100)	2.6 (260)
New Zealand	15+	Baseline	1449	0.1 (9)	0.2 (20)
		"FB"	2670	0.2 (25)	0.7 (75)

NB: Total number of respondents: Australia 2+ = 13858; Australia 2-6 years = 989; New Zealand 15+ = 4636.
Mean body weight: Australia 2+ = 67 kg; Australia 2-6 years = 19 kg; New Zealand 15+ = 71 kg.

Risk characterisation
The addition of alitame to FB would result in an increase in dietary exposure for all the population groups assessed.

All population groups assessed, with the exception of the 95th percentile consumers aged 2 years and above for the FB scenario and 2-6 year olds for the FB scenario only, have estimated exposures to alitame below the ADI.

Whilst the estimated exposures in this model exceed the population groups mentioned, it is not considered that the actual exposure to alitame would exceed the ADI. It was concluded from the sweetener survey (FSANZ, 2003) that there are no public health and safety risks associated with exposures to alitame. This was determined for people identified in the survey as 'high consumers' of intense sweetened foods. For the sweetener survey respondents recorded, for seven days, all foods they consumed that contained intense sweeteners. The concentration of the intense sweetener by brand and flavour was then matched to the consumption in order to estimate exposure for each respondent. For this Application, 24-hour recall consumption data were used, and combined with a mean concentration of the sweetener for each food group. The dietary modelling for this Application therefore is not as realistic as the modelling conducted for the sweetener survey.

For the sweetener survey, exposures were estimated for high consumers of foods containing intense sweeteners aged 12 years and above. Mean exposures for consumers of alitame were 2% of the ADI for both Australia and New Zealand. A 95th percentile exposure for consumers of alitame was not presented. It could not be calculated due to the small number of consumers of alitame. These estimates are lower than those estimated for this Application.

In addition, it was assumed that for every food category that was assigned a numerical concentration of alitame, every product in that category contained the sweetener, which in reality is not the case. Only a small proportion of the category would contain intense sweeteners and alitame in particular. From the sweetener survey, there were only 3 products (in 2 food groups) that contained alitame. There were 531 products in total in the sweetener survey database.

There is an increase in exposure to alitame between the baseline and the 'FB' scenario. This is because of the way the modelling has been conducted and the assumptions made about what beverages were substituted with FBs. It is assumed that people substitute bottled water and sugar sweetened water based flavoured drinks with an FB that contains alitame, therefore increasing exposure.

In conclusion, the addition of alitame to FB would not pose a public health and safety risk.

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Appendix 1

Details of how the dietary modelling for food additives was conducted

Dietary exposure assessment provided by the Applicant

The Applicant did not provide any estimates of exposure to the food additives that could result from the consumption of FBs. Therefore, FSANZ conducted dietary exposure assessments for the food additives.

What food additives were assessed?

There were 57 additives/additive groups requested by the Applicant to be added to FBs. Of these, dietary modelling was conducted for 23 additives/additive groups. 'Selection criteria' were developed in order to determine when a dietary exposure estimate was required. Dietary modelling was not conducted in cases where:

1. additives had no numerical ADI (see hazard identification/characterisation);
2. additives had no numerical permissions in the Food Standards Code, such as those that have GMP permissions, and no numerical concentration data were available on actual use levels by manufacturers to be used for modelling (e.g. those in Schedule 2 and Schedule 3 of Standard 1.3.1,);
3. if the Applicant requested a GMP permission for the additive, and a numerical concentration was not available to be used for dietary modelling.

Dietary survey data

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

Estimated exposures to food additives were based on a single 24-hour recall for all survey respondents.

The NNS data used for the exposure assessments were from 1995 and 1997, which are the best, most comprehensive data available for dietary modelling purposes. Therefore, conducting dietary modelling based on these data provides the best estimate of actual consumption of a food and the resulting estimated exposure to a food chemical. However, it should be noted that limitations exist within the NNS data. These limitations relate to the age of the data and the changes in eating patterns that may have occurred since the data were collected. Generally, consumption of staple foods such as fruit, vegetables, meat, dairy products and cereal products, which make up the majority of most people's diet, is unlikely to have changed markedly since the NNSs were conducted (Cook *et al*., 2001). However, there is an increasing level of uncertainty associated with the consumption of other foods where these may have changed in consumption since 1995 or 1997, or where new foods are now available on the market that were not available in 1995 or 1997.

Despite FBs currently being permitted to be manufactured in New Zealand under the Dietary Supplement regulations, there was no reported consumption of the products in the 1997 New Zealand NNS.

Population groups assessed

The dietary exposure assessments for food additives were conducted for both the Australian and New Zealand populations. An assessment was conducted for the whole population, as well as for children aged 2-6 years for Australia only. Dietary exposure assessments were conducted for the whole population as a proxy for lifetime exposure. An exposure assessment was conducted on children as they tend to have higher exposures per kilogram of body weight due to their smaller body weight, and they consume more food per kilogram of body weight compared to adults. It is important to note that, while children aged 2-6 years have been assessed as a separate group, this group has also been included in the dietary exposure assessment for the whole population estimate for Australia.

Food additive concentration levels

The concentrations of the food additives in foods that were used in the dietary exposure assessments were derived from a range of sources, including the MPLs in the Code, manufacturers use data and analytical concentrations from surveys. Proposed concentrations of additives in FBs were provided by the Applicant (see Table 1). The concentrations requested by the Applicant were in most cases the same for equivalent beverage products in the Code. For example, if fruit drinks are permitted to contain additive X at 200 mg/kg, it was requested by the Applicant that the fruit drink based FBs have the same concentration. This was based on the assumption made by FSANZ that the additives will have the same technological function in the FB and therefore will need to be used at the same concentration to achieve the desired effect.

Concentrations of food additives were assigned to food groups using DIAMOND food classification codes. These codes are based on the Australian New Zealand Food Classification System (ANZFCS) used in Standard 1.3.1 Food Additives (for example 14.1.3 represents Water-based flavoured drinks).

Additives in Schedule 1 of Standard 1.3.1 of the Code have specific permissions in a restricted range of foods.

Many of the colourings being assessed were in Schedule 4 of Standard 1.3.1, meaning they are permitted to be used in a broad range of processed foods and beverages at 70 mg/kg in beverages and 290 mg/kg in foods other than beverages. It is unrealistic to assume that all foods in every classification code will contain a colour at the MPL, or that every food within each classification contains the colouring. However, there are limited data available that reflect more accurate uses that can be used to refine the exposure estimates. Where more specific data were available, these were used to refine the estimates.

For example, where concentrations from an analytical survey were available, these were used for the relevant food classification. If there were no analytical data, manufacturers' use data were used, if available. If manufacturers' use data were not available, the MPL from food standards (Standard 1.3.1 of the Code) was used.

Where an analytical level or manufacturers' use level was available for a drink being substituted by FBs, the FB was assumed to contain the specific use level and not the maximum requested level, as it was assumed that the additive would have the same technological function in the FB and therefore would be used at the same level.

Two recent surveys were available that had analytical data for foods. The first, the 21st Australian Total Diet Survey (ATDS) (FSANZ, unpublished), and the South Australian Food Colouring Survey (South Australia Department of Health, personal communication).

Analytical concentration data for the preservatives (sorbates, benzoates and sulphites) were obtained from the 21nd Australian Total Diet Survey, which is currently being undertaken by FSANZ (FSANZ, unpublished). Multiple analytical results were available for each food analysed. The mean concentration derived from the analysed composite samples was derived and assigned to the most relevant classification code in DIAMOND for dietary modelling purposes. Where there were analytical samples whose result was 'not detected', an 'upper bound' mean concentration was derived for the food. This was calculated assuming that not detected results were at the limit of reporting (LOR) for the analytical method. The LOR is the lowest concentration of a chemical that can be detected and quantified, with an acceptable degree of certainty, using a specified laboratory method and/or item of laboratory equipment. An upper bound mean is a worst case scenario, as it concentration could be anywhere between the LOR and zero.

In 2004, the South Australian (SA) Department of Health conducted a compliance survey for food colourings. The results from this survey were provided to FSANZ for dietary modelling purposes (South Australia Department of Health, personal communication). The colours that were assessed included tartrazine, allura red, indigotine, sunset yellow, azorubine, amaranth, ponceau 4R, brown HT and brilliant black. The food groups analysed included fruit drinks, ice cream, cordials, soft drinks, flavoured milk, cheese, confectionery, breakfast cereals, biscuits, jams, meat pies, cakes, toppings and sauces, snack foods, alcoholic beverages, jelly, yoghurt and dairy snacks, table spreads and margarine. There were 255 individual samples analysed in total. The mean concentration from individual samples for a food group was derived and assigned to the most appropriate classification code in DIAMOND for dietary modelling purposes. Where there were analytical samples whose result was 'not detected', an 'upper bound' mean concentration was derived for the food and used for the exposure assessments.

Manufacturers' use data had previously been obtained from certain manufacturers' in 1998-1999, when dietary exposure assessments were being conducted by FSANZ for the Review of the Code, for proposal P150 – Food Additives (ANZFA, 1998; ANZFA, 1999). This information was provided by a number of major food manufacturers through personal communication via meetings and other correspondence. A smaller amount of data for other additives were obtained from manufacturers following the review when it was required for other projects, such as amaranth.

The *Consumption of Intense Sweeteners in Australia and New Zealand: Benchmark Survey 2003* ('The Sweetener Survey') (FSANZ, 2003) was used to obtain concentrations of sweeteners used in food groups. More information on how these survey data were used for the dietary modelling for this Application can be found in the main report.

Additional food consumption data or other relevant data

The 1995 Australian NNS did not include any consumption information for formulated beverages. The New Zealand 1997 NNS did not report any consumers of FBs.

For the purposes of the dietary modelling for food additives, it was necessary to determine what beverages a person may take out of their diet and substitute with an FB. The Applicant provided data on the types of beverages that are likely to be replaced by FBs. These data were used in the assessment exposure to food additives. The food groups assumed to be substituted were cordials (excluding those made up from powder), carbonated drinks, fruit juice drinks, sports drinks and bottled water.

Over the past few years, FSANZ has compiled a Food Additive Database, recording the food additives used in over 2200 food products, primarily processed foods and beverages. The database itself is by no means complete or considered representative of the whole food supply, however, it does provide a guide to likely proportions of each food category in the food supply that may contain certain additives. Each product entered into the database is given a code relevant to the classification numbering system used in Standard 1.3.1 of the Code. From the database, FSANZ was able to determine how the proportion of products within a classification code, that contained the food additive of interest. In the absence of other specific data on the proportion of each food category that contains the additive, the information from this database was used qualitatively to put into context the estimated exposures. The data from the database were of most use for the assessments for food colourings.

Scenarios for dietary modelling

A baseline estimate of exposure was calculated, in order to determine current food additive exposures before any additional level of exposure from the additives in FBs is included. A '100% substitution' approach was also modelled ('FB scenario'). For this scenario it was assumed that people will take a beverage out of the diet and replace it with a FB. It was assumed that all of the following beverages were replaced: cordials, carbonated drinks, fruit juices, fruit juice drinks, sports drinks and bottled water. The consumption amount of the FB remained the same as the beverage it replaced.

How were the estimated dietary exposures calculated?

The DIAMOND program allows food additive concentrations to be assigned to food groups. For intense sweetened foods, the food chemical level is only normally assigned to intense sweetened food groups, where these were reported separately. For the 'FB' scenario, however, it was assumed that the normal counterpart of a beverage (i.e. a sugar sweetened soft drink) could be substituted with an FB that contains the intense sweetener being assessed.

Exposure to the food additives was calculated for each individual person in the NNSs using his or her individual food records from the dietary survey. The DIAMOND program multiplies the specified concentration of the food additive by the amount of food that an individual consumed in order to estimate the exposure to the additive from each food. Once this has been completed for all of the foods specified to contain the additive, the total amount of the additive consumed from all foods is summed for each individual.

Population statistics (mean and high percentile exposures) are then derived from the individuals' ranked exposures.

Where estimated dietary exposures are expressed per kilogram of body weight, each individuals' total dietary exposure is divided by their own body weight, the results ranked, and population statistics derived. A small number of NNS respondents did not provide a body weight. These respondents are not included in calculations of estimated dietary exposures that are expressed per kilogram of body weight.

Where estimated exposures are expressed as a percentage of the reference health standard (ADI), each individual's total exposure is calculated as a percentage of the reference health standard (using the total exposures in units per kilogram of body weight per day), the results are then ranked, and population statistics derived.

Food consumption amounts for each individual take into account where each food in a classification code is consumed alone and as an ingredient in mixed foods. For example, ice cream eaten 'as is' or in a thickshake are all included in the consumption of ice cream. Where a higher-level food classification code (e.g. 14.1.3 Water based flavoured drinks) is given an additive concentration, as well as a sub-category (e.g. 14.1.3.2 Kola soft drinks), the consumption of the foods in the sub-classification is not included in the higher level classification code.

In DIAMOND, all mixed foods in classification codes 20 and 21 have a recipe. Recipes are used to break down mixed foods into component ingredients that are in classification codes 1-14. The data for consumption of the ingredients from the recipe are then used in models and multiplied by the additive concentrations for each of the raw ingredients. This only occurs if the *Mixed food* classification code (classification code 20) is not assigned its own additive permission. If the *Mixed foods* classification is assigned an additive concentration, the total consumption of the mixed food is multiplied by the specified level, and the recipes are not used for that food group.

When a food that does not have a recipe is classified in two food groups in classification codes 1-14, and these food groups are assigned different permissions, DIAMOND will assume the food is in the food group with the highest assigned additive level (worst-case scenario). If the food groups have the same permitted additive concentration, DIAMOND will assume the food is in the food group that appears first, based numerically on the ANZFCS.

In DIAMOND, hydration factors are applied to some foods to convert the amount of food consumed in the dietary survey to the equivalent amount of the food in the form to which a food chemical permission is given. For example, consumption figures for cordial concentrate are converted into the equivalent quantities of cordial beverage as consumed.

Uncertainty associated with the exposure assessment

Where there are uncertainties in the data used for dietary exposure assessments, assumptions normally have to be made. Some of the uncertainly associated with the exposure estimates for food additives are outlined below.

It is not known what the current consumption pattern and volume of FBs is by consumers, as there are no data in the NNSs and no survey data available.

It is not known what beverages consumers will substitute with a FB. Whilst the Applicant provided some information on the products currently on the market that would be similar to FBs, and these were assumed to be substituted, there is uncertainty about what consumers will actually do when given the choice between a beverage they may normally consume and a FB.

Whilst additives are used at specific concentrations in order to perform a specific technological function, there is uncertainly around the range of concentrations manufacturers use.

In relation to the exposure assessments for food colourings, there is uncertainly around the food groups that actually contain colours. There may be a broad range of food groups permitted to contain a colour, however, some of these food groups may never contain the colour. Also, the percent of each category that actually contains the colour is unknown.

Assumptions in the dietary modelling

The aim of the dietary exposure assessment was to make as realistic an estimate of dietary exposure as possible. However, where significant uncertainties in the data existed, conservative assumptions were generally used to ensure that the dietary exposure assessments did not underestimate exposure.

Assumptions made in the dietary modelling include:

where a permission is given to a food classification code, all foods in that group contain the additive;

all the foods within the group contain the additive at the levels specified in DIAMOND. Unless otherwise specified, the maximum permitted level of the additive in each food category has been used;

where a food has a specified additive concentration, this concentration is carried over to mixed foods where the food has been used as an ingredient;

where the concentration of the additives used were from analytical data and the concentration was reported as being less than the LOR, then the additive concentration in the food was equal to the LOR value;

where Australian foods were analysed for certain additives (sorbates, benzoates and sulphites), it was assumed that New Zealand foods had the same concentrations, which is a realistic assumption, as Australia and New Zealand have the same additive permissions, food manufacturers common to both countries and a similar food supply;

where a food was not included in the exposure assessment, it was assumed to contain a zero concentration of the additive being assessed;

where a food or food group has a GMP concentration of the additive, it was assumed to have a zero concentration of the additive, unless manufactures use data or survey data were available;

for food colourings, it was assumed that for certain food groups, there was no colour added. These food groups are outlined in the discussion for each individual colour in the main part of this report;

consumption of foods as recorded in the NNS represent current food consumption patterns;
if FBs were available, consumers always substitute the 'like' beverages and select the FB containing the additive;
consumers substitute all of the 'like' beverages with the FB, even if they have had more than one of them on the day of the NNS;
consumers do not alter their food consumption amount besides to substitute a non-FB with an FB;
the number of serves per day recommended or bottle size of FBs does not influence the amount consumed and therefore, FBs are consumed in the same volume as the beverage that the person replaces; and
for the purpose of this assessment, it is assumed that 1 millilitre is equal to 1 gram for all liquid and semi-liquid foods (e.g. milk, yoghurt).

These assumptions are likely to lead overall, to a conservative estimate for food additive dietary exposures, in particular the assumption that all beverages in the specified types of beverages will be substituted by a FB and that all foods within a food groups will contain the additive being assessed.

Limitations of the dietary modelling

A limitation of estimating dietary exposure over a period of time associated with the dietary modelling is that only 24-hour dietary survey data were available, and these tend to over-estimate habitual food consumption amounts for high consumers. Therefore, predicted high percentile exposures are likely to be higher than actual high percentile exposures over a lifetime.

Daily food consumption amounts for occasionally consumed foods based on 24 hour food consumption data would be higher than daily food consumption amounts for those foods averaged over a longer period of time.

Over time, there may be changes to the ways in which manufacturers and retailers make and present foods for sale. Since the data were collected for the Australian and New Zealand NNSs, there have been significant changes to the Food Standards Code to allow more innovation in the food industry. As a consequence, another limitation of the dietary modelling is that some of the foods that are currently available in the food supply were either not available or were not as commonly available in 1995/1997.

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

FSANZ does not apply statistical population weights to each individual in the NNSs in order to make the data representative of the population. This prevents distortion of actual food consumption amounts that may result in an unrealistic exposure estimate. Maori and Pacific Islanders were over-sampled in the 1997 New Zealand National Nutrition Survey so that statistically valid assessments could be made for these population groups.

As a result, there may be bias towards these sub-population groups in the dietary exposure assessment because population weights were not used.

The DIAMOND computer program only contains food consumption data from the NNSs. Therefore, the predicted exposure estimates for sweeteners for A470 were not able to utilise the more detailed 7-day consumption data obtained in the sweetener survey. Therefore, the modelling for this Application for the requested sweeteners using DIAMOND will be different to the results obtained in the Sweetener Survey.

There is a lack of actual concentration data for the use of additives across all food groups, as well as a lack of data on the proportion of each category each additive is used in. This is mostly an issue for colourings and means the exposure estimates are for colours are worst case. For preservatives and sweeteners there are extensive concentration data available that were used to calculate refined estimates of exposure.

Attachment 9

Food Technology Report
Application A470 – Formulated Beverages

The use of food additives is regulated by Standard 1.3.1 – Food Additives, with permissions provided by Schedules 1 to 4. Schedule 1 of this Standard permits the use of food additives at specified levels in specific foods. Maximum permitted levels are prescribed for additives where risk assessment indicates a need to restrict usage levels to protect public health and safety. Schedule 2 lists food additives that may be used to levels determined by Good Manufacturing Practice (GMP) where permitted by Schedule 1. Schedule 3 lists colours that are permitted to GMP levels where permitted in Schedule 1. Schedule 4 lists colours that are restricted to 70 mg/kg for liquids and to 290 mg/kg for solid foods and which may be further restricted by Schedule 1. Schedule 5 lists the permitted technological functions to be performed by food additives as distinct from processing aids (Standard 1.3.3) and vitamins and minerals (Standard 1.3.2).

The Applicant has requested permission for use of a wide range of food additives in Formulated Beverages (FB). Some of these requests are covered by the general permissions in Schedule 2 of Standard 1.3.1 and colours have been requested for use in accordance with Schedules 3 and 4. The levels requested for other additives are compliant with the permissions currently available for non-alcoholic beverages in Schedule 1 under the categories of 14.1.2.2 – Fruit and vegetable juice products and of 14.1.3 – Water based flavoured drinks.

A table containing a list of the requested food additives and their maximum requested levels for FB is given at the Appendix at the back of this report, compared to the current permissions in the two existing categories 14.1.2.2 – Fruit and vegetable juice products and 14.1.3 – Water based flavoured drinks. The requested permissions have been amended from the original Application to correct some errors and inconsistencies which had been resolved after communications between FSANZ and the Applicant. The Applicant confirmed they wished the food additive permissions to be consistent with the current permissions for these comparable beverages. The Applicant is not requesting any increase in maximum permitted levels or new permissions.

Schedule 1 of Standard 1.3.1 is currently under review to address complaints and to provide clarification of permissions in Proposal P279 – Review of Schedule 1 and Related Clauses – Standard 1.3.1 – Food Additives. Any changes arising from P279 will need to be incorporated into the assessment for this Application, A470.

Technological justification for the requested food additives

Intense sweeteners

The Applicant has requested approval for a variety of intense sweeteners.

An intense sweetener is a food additive defined by Schedule 5 of Standard 1.3.1 as:

'replaces the sweetness normally provided by sugars in foods without contributing significantly to their available energy'.

The Applicant has requested approvals for the intense sweeteners currently permitted in categories 14.1.2.2 – Fruit and vegetable juice products and 14.1.3 – Water based flavoured drinks in Schedule 1 of Standard 1.3.1.

The different intense sweeteners have different properties including advantages and disadvantages compared to each other and to sucrose (Smith, 1991). These different properties include comparable sweetness to sucrose, cost, flavour profile to replicate that of sucrose in the drink matrix and stability in the drink (including different pH, temperatures and storage times). Manufacturers of commercial products will make decisions on which individual intense sweetener or combination of sweeteners to use taking these considerations into account and the results of trial products. Examples of disadvantages that some intense sweeteners have are that cyclamate has accelerated decomposition in the presence of water soluble vitamins at elevated temperature, while thaumatin's taste is reduced by mono- and divalent salts (Smith, 1991).

Aspartame (INS 951), sucralose (INS 955), thaumatin (INS 957) and neotame (INS 961) are intense sweeteners which are currently listed in Schedule 2 of Standard 1.3.1, which allows their use in accordance with GMP. These intense sweeteners are only approved with the limitation 'technological use consistent with clause 4 only'. This means that such intense sweeteners may only be added to food in an amount necessary to replace the sweetness normally provided by sugars or as a flavour enhancer. This limitation would apply to any approvals if this Application is successful.

Acesulphame potassium (INS 950), saccharin (INS 954) and alitame (INS 956) have also been requested as intense sweeteners at the same permitted levels as is currently permitted in comparable drinks in Schedule 1.

The current permissions for acesulphame potassium (INS 950) in the Code are 500 mg/kg for fruit and vegetable juice products, and 3,000 mg/kg for both low joule fruit and vegetable juice products, and water based flavoured drinks. The Applicant has confirmed that they are seeking permission for acesulphame potassium at 3,000 mg/kg for FB comparable to water based flavoured drinks.

The Applicant has not requested approval for cyclamate (INS 952) as an intense sweetener for FB.

Preservatives

A variety of preservatives are currently approved in categories 14.1.2 – Fruit and vegetable juices and fruit and vegetable juice products and 14.1.3 – Water based flavoured drinks in Schedule 1 of Standard 1.3.1. These preservatives are sorbic acid and sorbates (INS 200, 201, 202 and 203), benzoic acid and benzoates (INS 210, 211, 212 and 213), sulphur dioxide and sulphites (INS 220, 221, 222, 223, 224, 225 and 228) and dimethyl dicarbonate (INS 242). Sodium and calcium propionate (INS 281 and 282 respectively) are approved at GMP for category 14.1.2 - Fruit and vegetable juices and fruit and vegetable juice products.

The different preservatives have different properties and antimicrobial activity (Smith 1991) relevant to their use in currently produced drinks and proposed use in FB. Sorbic acid and sorbates have broad spectrum activity against fungi, with less activity against bacteria. Benzoic acid and benzoates have activity against yeasts and moulds, food poisoning bacteria, and spore-forming bacteria. Sulphur dioxide and sulphites has activity against most bacteria and less activity against yeast and moulds. Propionic acid and propionates have activity against moulds but not yeasts. Dimethyl dicarbonate is used as a yeast inhibitor for beverages (Ash and Ash, 2002).

A combination of sulphites with another preservative, e.g., sorbates or benzoates, is frequently used for fruit juices where the sulphite acts to control chemical spoilage reactions, and lactic and acetic acid fermentations, whilst the second preservative acts as a longer lasting agent against yeasts and moulds (Encyclopedia, 2003, p 4778).

A qualification listed in the Code for fruit and vegetable juice products, which will need to be considered if this Application is successful is that the 'GMP principle precludes the use of preservatives in juices represented as not preserved by chemical or heat treatment'.

Sequestrants

Calcium disodium EDTA (INS 385) is a sequestrant (also called a metal chelating agent) which is used for beverages which contain fruit flavouring, juice or pulp or orange peel extract. Calcium disodium EDTA is approved within the Code for carbonated fruit drink products under category 14.1.2.2 – Fruit and vegetable juice products and category 14.1.3 - Water based flavoured drinks for products containing fruit flavouring, juice or pulp or orange peel extract only.

Sequestrants are used to ensure flavour retention (Smith, 1991). Free metal ions which naturally occur at low levels in beverages can readily form inactive complexes with flavour compounds so reducing the active flavour concentration and hence reduced perceptible flavour. Calcium disodium EDTA acts to selectively bind up metal ions preventing them from reacting with flavourings.

The current restrictions for EDTA will need to be considered if the Application is successful.

Colourings

The Applicant has requested that the colours permitted in Schedule 3 and Schedule 4 be approved for FB. These colours are currently permitted in categories 14.1.2.2 – Fruit and vegetable juice products and 14.1.3 – Water based flavoured drinks in the Code.

Annatto extracts (INS 160b) are currently approved for category 14.1.2.2 – Fruit and vegetable juice products. Annatto is available in a water soluble form. It is a well established food colour (producing yellow to red colour) due to its superior technical properties compared to other colours (Watson, 2002). Permission to use annatto extracts has only been sought by the Applicant for fruit and vegetable juice FB.

The situation with the colouring annatto extracts is complicated by the fact that there are a number of different types of extracts that can be produced and used commercially.

The FAO/WHO Joint Expert Committee on Food Additives (JECFA) recently re-evaluated the toxicology of the various annatto extracts in 2003, and assigned different temporary Acceptable Daily Intakes (ADI) for a number of different annatto extracts, while others have no ADI established (discussed in Attachment 8 – Safety Assessment – Food Additives).

Annatto extracts are obtained from the annatto seed, using a number of different extraction methods including water, vegetable oil, solvent and alkaline extraction. Bixin is the principle pigment of oil-soluble annatto extracts, while norbixin is the principle pigment of alkaline water-soluble annatto extracts.

JECFA designated six different types of annatto extracts in their 2003 evaluation:

Annatto B Annatto extract (solvent-extracted bixin)
Annatto C Annatto extract (solvent-extracted norbixin)
Annatto D Annatto extract (oil-processed bixin suspension)
Annatto E Annatto extract (aqueous-processed norbixin)
Annatto F Annatto extract (alkali-processed norbixin)
Annatto G Annatto extract (alkali-processed norbixin, not acid-precipitated)

The specific type of annatto extract used by Australian and New Zealand food manufacturers, specifically for fruit and vegetable juice products is important to ensure that the correct ADI is used for dietary modelling work.

Clause 5 – Maximum permitted levels of additives of Standard 1.3.1 may require amendment, due to consideration of the 2003 JECFA report, where it refers to annatto, *viz*

> **annatto** and annatto extracts shall be calculated as bixin

in Proposal P279 – Review of Schedule 1 and related clauses – Standard 1.3.1 – Food Additives.

FSANZ will seek advice from food manufacturers and the Applicant on which of the six forms of annatto extracts (for example, alkali-processed norbixin) is used in food manufactured in Australia and New Zealand, specifically category 14.1.2.2 – Fruit and vegetable juice products in Schedule 1 of Standard 1.3.1.

Amaranth (INS 123) is currently approved in categories 14.1.2.2 – Fruit and vegetable juice products and 14.1.3 – Water based flavoured drinks in the Code. Amaranth is a water soluble colour which produces a dark red to purple colour (Ash and Ash, 2002).

Emulsifiers

An emulsifier as defined in Schedule 5 of Standard 1.3.1 of the Code:

'facilitates the formation or maintenance of an emulsion between two or more immiscible phases'.

In general this means a food additive that improves the solubility or mixing of an aqueous phase and an oil phase. To achieve this emulsifiers usually have a hydrophilic group (aqueous loving) and a lipophilic group (oil loving) within the molecule.

For beverages this can mean compounds that improve the solubilisation and dispersion of flavours and colours which normally have poor solubilities in aqueous solutions or would form cloudy emulsions. Emulsifiers can help to produce clear solutions of the resultant beverage mixture (Smith, 1991).

Sucrose acetate isobutyrate (INS 444), glycerol esters of wood rosins (INS 445) and dioctyl sodium sulphosuccinate (INS 480) are currently approved as emulsifiers (or stabilisers) in fruit drinks under category 14.1.2.2 – Fruit and vegetable juice products and category 14.1.3 – Water based flavoured drinks within Schedule 1 of Standard 1.3.1.

Sucrose acetate isobutyrate is used as an emulsion stabiliser for flavouring oils in non-alcoholic beverages (Ash and Ash, 2002). Glycerol esters of wood rosins are listed as having functional use as emulsifiers and stabilisers/density adjustment agents for flavouring oils in beverages (Food and Agriculture Organisation, 1992). Dioctyl sodium sulphosuccinate use includes being an emulsifier, a wetting agent, dispersant and diluent in food colourants (Ash and Ash, 2002).

Flavourings

Flavourings (excluding quinine and caffeine) are included in Schedule 2 of Standard 1.3.1 so are permitted in both categories 14.1.2.2 – Fruit and vegetable juice products and category 14.1.3 – Water based flavoured drinks at GMP. Permitted flavourings are regulated by clause 11 of Standard 1.3.1.

Permitted flavourings currently approved in such beverages as above should also be allowed in FB if this Application is approved.

Quinine is permitted in Schedule 1 to 100 mg/kg in category 14.1.3 for tonic, bitter and quinine drinks only. However quinine is not requested for addition in FB in this Application.

Carbon dioxide

The Applicant has indicated that FB will not be carbonated. That is they have confirmed that they have not requested permission for addition of carbon dioxide for FB. This needs to be included in any permissions within Schedule 1 of Standard 1.3.1 if this Application is successful. The complication is that carbon dioxide (INS 290) is listed in Schedule 2 of Standard 1.3.1 so any products that allow additives in Schedule 2 do have permissions for carbon dioxide addition.

Conclusion

The requested food additives are technologically justified for their proposed use in formulated beverages in the same way as they are technologically justified for their current use in comparable fruit and vegetable juice products and water based flavoured drinks.

Consideration of the current restrictions in Schedule 1, and any changes resulting from P279, for a number of food additives will need to be considered if the Application is successful. The Application has also not sought permissions for some additives which need to be addressed. The important areas of difference between current permissions in the Code and requested permissions for FB for this Application are listed below.

No permissions sought for quinine.
No permissions sought for cyclamate.
No permissions sought for carbon dioxide.
Permissions for acesulphame potassium at 3,000 mg/kg comparable to water based flavoured drinks.
Permissions for sodium and calcium propionate for fruit and vegetable juices and fruit and vegetable juice products only at GMP.
Permission for calcium disodium EDTA for products containing fruit flavouring, juice or pulp or orange peel extract only.
Permission for annatto extracts for fruit and vegetable products only.

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Appendix

TABLE OF REQUESTED FOOD ADDITIVES
A470 – FORMULATED BEVERAGES

INS	Food additive name	Current approval in 14.1.2.2- Fruit and vegetable juice products mg/kg	Current approval in 14.1.3- Water based flavoured drinks mg/kg	A470 requested approval mg/kg	Comments and qualifications for A470 requested permissions
123	Amaranth	30	30	30	
160b	Annatto extracts	10	-	10	for fruit and vegetable products only
200 201 202 203	Sorbic acid and sodium, potassium and calcium sorbates	400	400	400	for fruit and vegetable juice products the GMP principle precludes use of preservatives in products not treated by chemicals or heat.
210 211 212 213	Benzoic acid and sodium, potassium and calcium benzoates	400	400	400	for fruit and vegetable juice products the GMP principle precludes use of preservatives in products not treated by chemicals or heat.
220 221 222 223 224 225 228	Sulphur dioxide and sodium and potassium sulphites	115	115	115	for fruit and vegetable juice products the GMP principle precludes use of preservatives in products not treated by chemicals or heat.
242	Dimethyl dicarbonate	250	250	250	for fruit and vegetable juice products the GMP principle precludes use of preservatives in products not treated by chemicals or heat.

INS	Food additive name	Current approval in 14.1.2.2- Fruit and vegetable juice products mg/kg	Current approval in 14.1.3- Water based flavoured drinks mg/kg	A470 requested approval mg/kg	Comments and qualifications for A470 requested permissions
281	Sodium propionate	GMP	-	GMP	for fruit and vegetable juice products only, GMP principle precludes use of preservatives in products not treated by chemicals or heat.
282	Calcium propionate	GMP	-	GMP	for fruit and vegetable juice products only, GMP principle precludes use of preservatives in products not treated by chemicals or heat.
385	Calcium disodium EDTA	fruit drink 33 (carbonated products only)	33 (products containing fruit flavouring, juice or pulp or orange peel extract only)	33	for products containing fruit flavouring, juice or pulp or orange peel extract only
444	Sucrose acetate isobutyrate	fruit drink 200	200	200	for fruit drink and water based flavoured drinks only
445	Glycerol esters of wood rosins	fruit drink 100	100	100	for fruit drink and water based flavoured drinks only
480	Dioctyl sodium sulphosuccinate	fruit drink 10	10	10	for fruit drink and water based flavoured drinks only
950	Acesulphame potassium	fruit and vegetable juice products (500), low joule fruit and vegetable juice products (3,000)	3,000	3,000	for water based flavoured drinks (3,000 mg/kg)

INS	Food additive name	Current approval in 14.1.2.2- Fruit and vegetable juice products mg/kg	Current approval in 14.1.3- Water based flavoured drinks mg/kg	A470 requested approval mg/kg	Comments and qualifications for A470 requested permissions
951	Aspartame	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, schedule 2	use consistent with clause 4 of Standard 1.3.1 only
954	Saccharin	low joule fruit and vegetable juice products 80	80	80	for water based flavoured drinks and low joule fruit and vegetable juice products only
955	Sucralose	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, schedule 2	use consistent with clause 4 of Standard 1.3.1 only
956	Alitame	40	40	40	
957	Thaumatin	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, schedule 2	use consistent with clause 4 of Standard 1.3.1 only
961	Neotame	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, Schedule 2 use consistent with clause 4 of Standard 1.3.1 only	GMP, schedule 2	use consistent with clause 4 of Standard 1.3.1 only
	Schedule 3 colours	permitted at GMP	permitted at GMP	requested	covered by the use of the asterisk, Schedule 3 colours are approved for use at GMP
	Schedule 4 colours	permitted to prescribed limits in Schedule 4	permitted to prescribed limits in Schedule 4	requested	covered by the use of the asterisk, Schedule 4 colours are approved for use to specified limits
	flavourings	permitted, Schedule 2	permitted, Schedule 2	requested	covered by the use of the asterisk, flavourings (excluding quinine and caffeine) are permitted in Schedule 2

Attachment 10

Summary of Submissions to the Initial Assessment Report
Application A470 – Formulated Beverages

FSANZ received 19 submissions in response to the Initial Assessment Report on Application A470 – Formulated Beverages, during the six-week public consultation period of 15 January to 26 February 2003. A summary of submitter comments is provided in the table below.

Two regulatory options were presented in the Initial Assessment Report:

Option 1 – Maintain *status quo*; and
Option 2 – Include regulations specific to formulated beverages in the Code.

No.	Submitter	Submission Comments
1	**Australian Food and Grocery Council**	Supports Option 2 Characteristics • Should be considered as general purpose foods. • Policy guidance required from the ANZFRMC to guide FSANZ in considering fortification of foods. • Recommends that all non-alcoholic water-based beverages, including formulated caffeinated beverages, be included in the definition of FBs. Consumption • Estimated New Zealand consumption for the year to June 2001 was 0.14 litres per capita, and 0.39 litres per capita for the year to June 2002. Composition • Considers there is adequate risk management for the addition of medicinal herbs to FBs, through the control of restricted botanicals and in consideration of Proposal P260 – Medicinal Herbs. • The beverage vehicle should be considered a mere carrier of the added micronutrients such that the composition of the beverage is incidental and therefore of no regulatory issue. • Recommends that rather than constraining the use of terms such as 'daily dose', 'daily quantity' or 'one-day quantity', Standard 1.3.2 be reviewed to permit a more rational approach to FBs.

No.	Submitter	Submission Comments
		• Does not consider the use of FBs as ingredients in other foods a concern. Food Additives • Considers food additives raise no additional safety concerns for their intended use. • Considers the list of additives requested to be appropriate as they are present for a technological purpose. Labelling • Supports that FBs be permitted to carry claims, based on the principle that if they are present in the FB then consumers have a right to know. • Consumer's rights to useful information would be denied if per cent of RDI were not permitted. • Does not consider mandatory statements are necessary. • Label statements that advise against regarding a product as a substitute for a healthy diet could apply to all foods, and the AFGC does not support the use of such label statements on FBs. Impact Analysis Option 1: • *Likely to cost consumers more than if local manufacturer of FBs were permitted.* • No information to suggest any possible harm to consumers outside the target market. • Will continue to disadvantage Australian industry. • Potential cost of enforcing food standards in Australia. Option 2: • Likely price benefit to Australian consumers. • Unlikely that an increase in availability of FBs would result in unintended consumption and thus result in excessive intake of certain nutrients. Believes substitution for unfortified drinks tends to be the pattern of consumption rather than increased consumption. • Will benefit Australian industry. • Would contribute significantly to Australian exports of FBs, through the use of concentrates with overseas bottling plants. • Considers it possible that FBs and non-beverage products such as dietary supplements could be substituted. • Initial reduction in New Zealand exports of FBs to Australia. • Potential competitive advantage to New Zealand industry while the *New Zealand Dietary Supplements Regulations 1985* is still in place.

2	**Australian Beverages Council** (formerly the Australasian Soft Drink Association Ltd) - The Applicant Ms Melanie McPherson	Supports Option 2 ***Note: the following comments have been provided by the Applicant*** General Comments • Concerned with the emphasis placed on the issue of botanical extracts, as ASDA is not seeking approval for the addition of herbal extracts. Characteristics • Should be considered as general purpose foods, as consumers purchase them as part of their normal diet. • Composition is their defining feature, and they fit as a subset of water-based non-alcoholic beverages. • Suggests the definition 'a water-based product, that may be sweetened and/or flavoured; may or may not contain juice; and that contains a mix of added vitamins and/or minerals'. Consumption • Provided consumption data as part of their Application. • Target groups are those consumers who are looking for these types of beverages, rather than consumers who are purchasing these products imported from or through New Zealand. Composition • ASDA has sought levels of vitamins and minerals that are currently permitted in a range of other beverages. • All vitamins and minerals are listed at levels established as safe. • Vitamin K has been excluded in consideration of health and technological issues. Food Additives • All levels of food additives are consistent with current approvals for additives, taking into consideration safety and technological need. Labelling • Seek permission to use the current provisions of 'a source' and 'a good source' in order to provide consumers with adequate information on the content of the beverage. • Consider using a statement regarding maximum daily consumption is appropriate to manage the risk associated with the use of one-day quantities. • Vitamin and mineral information displayed in quantitative terms only will not give consumers meaningful information.

		• No need for FBs to have a prescribed name. • Should not be labelled with statements that advise against regarding FBs as substitutes for a healthy diet. Impact Analysis • Not aware of any credible data showing substitution of other beverage products with water-based beverages • Consumer's use of these products is more likely to be as an addition to their current diet. • No evidence of progressive replacement resulting in a lowering of other nutrients. • No issues for enforcement agencies. • Labelling will provide consumers with information that can be expected to all but eliminate unintended consumption. • The 20% rate of growth is based on a small base. Hence, a small volume growth will initially appear to be a larger percentage growth, than for a product sold in a mature market. From estimations of overseas markets this growth is sustainable. • Refer to the Allen Consulting Report, regarding likely economic expansion. • Expect there to be some substitution of other water-based beverages only, however there is no data available. • Overseas experience shows the predominant growth of these products appears to be consumption additional to current diets. • Reduction in the volume of product imported from New Zealand. • Significant market is available to manufacturers in exporting product to Singapore and other Asian countries. This market can be expected to develop in the medium to longer term.
3	**Australian Self-Medication Industry** Mr Jonathan Breach	<u>Supports Option 1</u> Characteristics • Should be treated as supplementary foods, and as such remain within the scope of the FTDS discussions. • Lack of clarity between those FBs that will be used for general-purpose verses those that are supplementary. • The primary purpose of some FBs is likely to be 'hydration', and others 'functional' or health benefit related. • Appears lack of insight as to who is currently buying FBs, for what purpose and how the composition and presentation influences their decision. • Regulatory controls should be based on both a compositional and functional approach. • Consider FBs are the same in function as multivitamin pills, where the medicines manufacturing industry must comply with strict manufacturing practice standards, none of which is applicable to the foods manufacturing industry.

		Consumption • Refers to a submission by the Australasian Soft Drink Association Ltd to the Productivity Commission Citrus Growing and Processing Inquiry in 2001 which comments on market growth and sales for still water and energy drinks – provided as an attachment to their submission. • Refers to other market trend data over the past two years for mineral water, still water and energy drinks – provided as an attachment to their submission. • The level of consumption potentially becomes a public health and safety concern in context to the proposed composition of the FB covered by this application. Composition • Level of selenium is inappropriate for a food. If a TTDS were to contain the proposed level of selenium it would be scheduled as a Pharmacist Only Medicine due to safety risk. • The level of vitamin A proposed would require a mandatory warning if used as an ingredient in a Complementary Medicine. The vitamin A limit is a potential public health risk as these products could be used in a manner other than supplementary to the diet. • Reasonable expectation of the consumer that any vitamins and minerals formulated within these products would remain at the label stated amounts at the end of shelf life. • Lack of clarity over the identity of the role of the carrier. • One-day quantity may be an appropriate basis for regulation in context to supplementary use. However, products presented in context to the still water market may be consumed in larger quantities, and doubt exists as to the effectiveness of consumer labelling recommending restricted intake. • Should not be used as an ingredient in other foods, due to concern regarding the stability and therefore nutritive value of the vitamins and minerals if further altered. Food Additives • Need for safety assessments of the requested maximum limits, taking into account the potential for some products to be consumed in greater quantities than may occur for 'supplementary use'. Labelling • Potential for false and misleading labelling to occur in vitamin, mineral and herbal content claims (and the implied health benefits). • Use of the terms 'source' and 'good source' are only applicable if the formulation ensures adequate bioavailability and

		stability of the vitamins and minerals, including at the end of shelf life. • Content and nutrition based claims for FTDS should only be acceptable where there is sufficient quantity i.e. 25% of the RDI. However, quantification should still be mandated at levels below this amount. • Maximum consumption limits are only useful when the total presentation of a product is considered, and whether the product is viewed for supplementary or general use. • Refers to 'Performance Based Labelling' that is gaining interest in the medicines arena, as a means to ensure correct consumer interpretation of a label and appropriate use of product from the label. Impact Analysis • Retail World (Vol 55, No 24, December 2002) – Still waters (including FBs such as Mizone) experienced a 20% growth in market value and 14% growth in market volume from 2001. • Public health concern is whether an increase in water based beverage consumption will result in unreasonably widespread consumption of formulated waters not containing the same nutritional complexity as may be found in fruit based drinks. • Children will be a potential target market of some manufacturers. • To create a separate standard for FBs would prematurely create another interface between foods and medicines that needs to be interpreted and enforced, without suitable resolution to other similar functional FTDS products. • The claim regarding market potential is not reasonable because of the regulatory environments of Australia and the US differ significantly. • Concern that the formulation of vitamins, minerals, amino acids and medicinal herbs at levels comparable to that found in Complementary Medicines may increase the incidence of adverse reactions to particular substances and increase the potential for food-medicine interactions, especially if used as part of the general food supply rather than strictly for supplemental purposes. • Questions whether the market growth is due to greater numbers of the population consuming FBs or that individual consumers are increasing their levels of consumption, and whether this poses health risks based on maximum daily intake. • Any increase in the capacity to manufacture FBs may be offset by a corresponding decline in manufacture of other beverages. • Any shift in consumers using FBs as a source of supplementary intake of vitamins and minerals may result in a decline in manufacture, sales and thus employment in the local medicines manufacturing industry. • Australia has always had the capacity to supply FBs and other FTDS products to export market, even though not approved for sale in Australia. • Difficult to postulate a 20% growth without a firm identification of who the target consumer is, the purchase motivation and in what quantities it will be consumed. • Unclear how these products are perceived by consumers with regard to their total diet and how this may affect dietary education. • Suggests that currently available multivitamin and mineral products sold as effervescent tablets and powders in sachets, which are added to water to produce as liquid beverage to be consumed for supplementary purposes, are comparable products to FBs.

		• Herb containing FBs imported from NZ will still have a promotional advantage over Australian manufactured products unless Australian manufacturers include herbal ingredients under the pre-text of being 'flavours'.

4	**Australian Dairy Corporation** Dr Anita Wells	Supports Option 1 Regulatory Principles • Considers this Application not compatible with nationally endorsed guidelines on healthy eating, and therefore does not meet the Regulatory Principles for Addition of Vitamins and Minerals to Food. • Not consistent with the national guidelines of 'encourage water as a drink' and 'eat only a moderate amount of sugars and foods containing added sugars'. Consumption • The Australian Dairy Corporation commissioned a Newspoll survey among a nationally representative cohort of 1,200 adults aged 18 years and over (Beanham et al, 2003). In light of survey results the Australian Dairy Corporation believes that approval of Application A470 is likely to lead to (evidence provided): - an increase in consumption of fruit drinks/soft drinks; and - a decline in the consumption of milk. Health Impact • In light of previous research (references provided) and the Newspoll survey, the Australian Dairy Corporation believes the approval of Application A470 would not be in the interest of public health as: - dental caries and dental erosion would be likely to increase; - it is likely to adversely affect bone health; and - it may have a detrimental effect on Australia's growing obesity problem. Composition • Does not consider soft drinks and fruit drinks to be suitable vehicles for voluntary fortification. Cited References • Beanham S et al. Australian dairy Corporation Issues Research: Calcium-Fortified Drinks Executive Summary, February 2003. • Other references provided throughout the submission.
5	**Blackmores Ltd** Ms Lynda McFarlane	Supports Option 2 General Comments • Supports a specific standard to ensure there are adequate controls in place to characterise and regulate FBs. • It is not in the interests of either consumers or industry to extend permissions without adequate consideration to the public health and safety consequences, particularly for children and teenagers who are currently high demand consumers for other water-based beverages.

		Characteristics • Should be considered 'supplemental foods', have a separate standard, and their purpose could be 'formulated supplemental beverages'. • Should be defined using parameters of both composition and purpose, to avoid confusion with other food products and medicines. • The definition could encompass both carbonated and non-carbonated water based premade drinks. These drinks could include flavours and fruit additives. Consumption • Not aware of any additional consumption data. • Potential target groups are any groups that currently consume soft-drinks and other dietary supplement beverages (New Zealand made or imported), and includes all age groups. Composition • Identifies safety concerns regarding current restrictions on selenium and chromium contained within the Therapeutic Goods Regulations. • A safety assessment needs to be made to establish the appropriate range and content of vitamins and minerals. • The quality of the base beverages should be considered, given that there is potential for large quantities to be consumed. • Likely to be used by consumers as thirst quenchers, energy boosters and in social situations as an alternative to alcohol or other beverages. • One-day quantity is appropriate. • Seems reasonable to limit the use of FBs in other foods unless there is data available on their usage and consumption in order to make an appropriate safety assessment. • The level of claimed vitamin and mineral content should be maintained during the shelf life of the product, so that consumers are not mislead. Labelling • Explicit or implied health or therapeutic claims should not be made, however should be free to state the presence of vitamins and minerals in the beverage. • The vitamin and mineral content should be displayed on the packaging and be consistent with the current requirements for other foods. They should be disclosed as a mandatory requirement to inform consumers. • Considers the one-day quantity statement to be reasonable, but that it needs to be examined further. • Suggested some alternative/additional statements used for traditional vitamin and mineral supplement products. • Supports use of a prescribed name for identification and enforcement purposes. • Labelling with statements that advise against regarding FBs as substitutes for a healthy diet or as providing health benefits is appropriate and consistent with complementary medicines and other food categories.

		• Where products contain substances that have been evaluated by other government agencies and require safety warnings, then those same warnings should be required on FBs to ensure consumers are aware of any risks. Impact Analysis Option 2: • *Known documented risks on excess consumption of specific vitamins and minerals - selenium, vitamin A, zinc, vitamin B6, iodine and iron.* • Consumers may substitute more traditional vitamin and mineral supplement products such as complementary medicines for FBs, particularly if they perceive they have some health benefit. Advertising • Strongly support a co-regulatory system of advertising controls to ensure that FBs are responsibly promoted, especially to children and teenagers.
6	**Community Nutrition Team, Central Sydney Area Health Service** Ms Ruth Kharis	<u>Supports Option 1</u> General Comments • To maintain public health, a sustainable food supply and help address the increasing incidence of obesity and overweight, they request that A470 is not progressed further. • Appears this is a vitamin/mineral tablet in a liquid form posing as a beverage. • Proposal P235 is yet to be determined and the decisions made regarding how to distinguish a FTDS from TTDS. • The high kilojoule content contributes further to the increasing incidence of overweight and obesity. Consumers do not need more choices of high kilojoule drinks, there are ample already. • There must be a demonstrated need for the product, including that the nutritional requirements cannot be met by existing supplements. • It is important to keep the roles and intake of tablets and food separate, to avoid nutritional harm through displacement of foods and excessive consumption of vitamins and minerals. • A470 is premature, as New Zealand is currently reviewing and may rescind the law that allows FBs to be imported and exported from New Zealand. Characteristics • No suitable purpose category. Meeting consumer demand is not a purpose category the warrants the development of additional food standards. • Do not meet several criteria of the FSANZ regulatory principles including, adequate nutritional rationale, they are not a 'food category' and the carrier product is devoid of naturally occurring vitamins and minerals. • Are not general purpose foods. They naturally lack nutrients in sufficient quantities, contain high levels of vitamins and minerals like a tablet, and some population groups would be at risk if they consumed FBs. • Are not special purpose foods or a food type dietary supplement (reasons provided). • Possibility to use the Therapeutic Goods Act to assess these products.

		• FSANZ should not regulate to allow a liquid vitamin and mineral tablet to pose as a food. • Are not functional foods, as they do not provide health benefits beyond simple nutrition. • Do not sufficiently differ from a vitamin and mineral tablet to warrant defining. • If accepted, the definition must at least include a nutritional purpose of the product that relates to the composition of the product alleviating a disease. Both composition and purpose would be defining features. Consumption • Possible that current supplement users may consume FBs instead. • No appropriate target consumer groups as people's diets are adequate with respect to fluid intake and for most vitamins and minerals. • Concern that the excessive level of kilojoules in the proposed product is likely to contribute further to the increasing incidence of obesity. • Concern regarding the expected average consumption of 500 ml per day, and the subsequent high kilojoule content of this product. Composition • FBs would not be an effective method to address dietary gaps. The high kilojoule content and presence of sugars and food acids would harm the consumer's health. • Likely to be marketed as a 'healthy soft drink'. • Need to limit the percentage of juice, sugar, kilojoules and volume size. • Regulatory control over the nutritional quality of the beverage vehicle is needed, given that the Applicant has sought permission to make claims. • Safety concerns regarding the lack of controls to protect the public from consuming and over consuming the product. • Particular concern for children, pregnant and lactating women who are at risk of over consumption of nutrients. For children the requested amounts exceed the RDI for vitamin A, thiamin, riboflavin, B6, folate, vitamin C and magnesium. For pregnant and lactating women the RDI is exceeded for thiamine, riboflavin, B6 and vitamin C. • Concerns regarding kilojoule content, where 500 ml soft drink provides 8-18% of the RDI for adult and 1-2 year olds respectively. Also concern regarding links with diet and obesity and type-2 diabetes. • The range of vitamins and minerals proposed is not appropriate and is unnecessary. • The nutritional quality of the base beverage must be considered, as it has a much more significant role in the diet than just being a carrier for added vitamins and minerals. • The suggested one-day quantities are in excess of the RDI and people will also be obtaining these nutrients from other foods. • The use of FBs as ingredients in other foods should be prohibited. Food Additives • Some safety concerns regarding the type and amounts of proposed food additives. • Sensitive individuals with asthma, hyperactivity and chronic allergy are known to react with benzoic acid, sulphur dioxide and annatto (Briggs et al 1985, Hanssen et al 1989). • Sulphur dioxide is known to destroy thiamin in food.

		Labelling • Should restrict labelling of vitamin and mineral claims, as the base product is nutritionally poor, they are high kilojoule products, and the nutrients are not naturally present. • If the proposal goes ahead mandatory warning statements are essential to ensure informed consumer choice. Suggested warning statements: 'a healthy diet provides other essential components as well as vitamins and minerals', 'this product is not a meal or food replacement', 'to meet your nutritional needs you will still need to eat a healthy diet on the same day as drinking this beverage', 'not to be consumed by children, pregnant women and lactating women'. • People with poor maths skills will not understand the percentage daily intake information, and it is open to abuse in terms of marketing. • If the percentage daily intake is made mandatory then warning statements should also be mandatory, explaining that more of a vitamin/mineral is not always better and that a healthy diet is sufficient. • Prescribed name is needed to distinguish them from soft drinks given that they are more like a tablet. • Should be labelled with statements that advise against regarding them has substitutes for a healthy diet or as providing health benefits. <u>Advertising</u> • Should not be promoted on television, and if it is then equal time must be given to the health warnings. • Access to the product should be restricted to avoid unintended over consumption of the vitamins and minerals in the product, e.g. not sold in vending machines or school canteens. Impact Analysis • Disagree that consumers automatically 'benefit substantially from exercising choice', as there are many barriers to people exercising choice, e.g. language, literacy, how to read food labels. Cited Research • Briggs D, Wahlqvist M. Eating matters food additives – facts for consumers. Methuen Haynes North Ryde 1985, pages 122, 124 and 161. • Hanseen M, Marsden J. The new additive code breaker. Lothian Publishing Company Melbourne 1989, pages 22, 42, 46, 62-64, 78-79 and 92-83. • Other references provided throughout submission.

7	**Complementary Healthcare Council of Australia**	Supports Option 1 General Comments • Currently no equivalent standard for such beverages in any other country. • Such a standard would only facilitate the provision of sugar water as a carrier of supplemental vitamin and minerals. • Understands that there is no fundamental nutritional value in the proposed FBs. Characteristics • Strongly opposes incorporation into general purpose foods on the grounds that: daily intake will be firmly influenced by marketing companies; the possible mass dosing of consumers; lack of controls over claims/safety/quality; and poor enforcement of standards. • Appear to be of a supplementary composition and could more appropriately meet the proposed standard for FTDS. • Neither composition nor purpose are defining features. Consumption • Normally sold in New Zealand as sports waters and consumption levels appear high. • Likely target group is 14-35 years old, as they are more susceptible to advertising of perceived health type foods and supplements. **Composition** • Concern about the toxicity of selenium at the level proposed. • Iron limit appears high and is likely to be a safety issue, particularly for children. • Vitamin A at the proposed level may pose a risk to pregnant women when included in addition to the normal diet. • There are many minerals that are not appropriate to be included in FBs including phosphorus. • The combination of phosphorus, magnesium and iron makes little sense as phosphorus acts to bind to magnesium and iron making them unavailable for absorption. • The nutritional quality of the base beverage must be addressed as the proposed food vehicle has no basic nutritional role. The request to contain sugar at unspecified amounts is contrary to the principles of a healthy diet. The request to contain fruit juice etc appears to be there principally as a flavouring agent. • Consumers perceive FBs as 'pick-me up', 'feel-good' and 'contains vitamins and minerals, therefore must be good for me' products. Perceive them as a way to meet the recommended 1-2 litres of water per day. Doubtful that they would consider them as part of a nutrition plan. • Strongly opposes use of FBs as an ingredient in other foods. Labelling • Should not permit products to be labelled with 'source of' or 'good source' or any other claims, as with potentially high sugar content they are of an unhealthy composition.

		• Prescribed name is appropriate to allow identification of the product. Impact Analysis Option 2 • Potential economic loses for the Complementary Medicines sector, and the economic impact would be cost neutral. • Difficult for government to monitor the safety aspects associated with FBs (e.g. stability, quality) • High risk of excess consumption, especially by teenagers, which could result in adverse health outcomes. • Difficult to formulate a stable vitamin-mineral preparation. • Less costly to produce under a food standard compared with the Therapeutic Goods Regulations.
8	**Dietitians Association of Australia**	<u>Supports Option 1</u> Characteristics • Recommends regulation as general purpose foods, to restrict the ability of manufacturers to add vitamins and minerals to these beverages. • No definition required. Consumption • Not aware of any data on per capita consumption of FBs. • Concern that FBs may promote consumption of excess kilojoule intake, and therefore further contributing to Australia and New Zealand's escalating rate of obesity and overweight in children and adults. • Cited research (Ludwig et al, 2001) showing an association between sugar-sweetened drinks and the development of obesity in children in the United States. • Poppitt et al, 1996 showed that energy from drinks adds to total energy intake and does not displace energy from other foods. • Mattes, 1996 showed that compensation at subsequent meals for energy consumed in the form of a liquid is less complete than for energy consumed from foods. • Based on advertising and popularity, the target groups are likely to be children and teenagers. • Concerned about the potential for FBs to replace more nutritious beverages, such as milk and water, in these groups. Composition • Not aware of any safety concerns. However, consider the level of iron proposed of potential concern for haemochromatosis sufferers, and the proposed levels could also present a risk for children and pregnant and lactating women. • Does not support the application to add more than recommended dietary intake levels for vitamin B12, vitamin C, folate, thiamin, riboflavin, niacin and vitamin B6. • Believes it unnecessary to add any of the proposed vitamins and minerals, as the base of the beverages is likely to be nutritionally poor. • Considers the nutritional quality of the base beverage is important should the application proceed.

		• Concerned about further increasing the range and consumption of sugar sweetened beverages. • Considers a 'one-day' quantity more appropriate than a 'daily dose', and a need to state the target group for whom this one-day quantity was established (if the application proceeds). • Use of FBs as ingredients in other foods should be prohibited. If not, they could be used inappropriately to circumvent the current food standards for the addition of vitamins and minerals to foods. Food Additives • Although not in support of this application, they consider the proposed maximum levels appropriate considering they are allowed for other non-alcoholic beverages in the Food Standards Code. • Not aware of any safety concerns, however recommend FSANZ seek comment from food technology experts. Labelling **(if the Application proceeds)** • Believes all claims for vitamins and minerals should be prohibited. • Believes labelling with percentage daily intake information will provide consumers with a misleading perception that FBs are a healthy addition to the diet. • Information should be listed in quantitative terms only. • Considers the warning statement provided to be appropriate. • Supports the use of a prescribed name on the label of FBs. • Consider statements on product labels that advise against regarding FBs as a substitute for a healthy diet or as providing health benefits should be mandatory. Cited Research • Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective observational analysis. Lancet 2001;357:505-508. • Poppitt SD, Prentice AM. Energy density and its role in the control of food intake: evidence from metabolic and community studies. Appetite 1996;26:153-174. • Mattes RD. Dietary compensation by humans for supplemental energy provided as ethanol or carbohydrates in fluids. Physiol Behav 1996;59:179-187.

9	**FORK** Ms Diane Temple	<u>Support Option 1</u> Characteristics • No additional supplemental food categories are needed. • Are not general purpose foods because of the high level of vitamin and mineral supplementation, use of a high kilojoule carrier, and due to the nutritional concerns associated with an increase in intake of sugar and the increase in incidence of overweight and obesity. • However, if FSANZ proceeds to put FBs into a purpose category then they best fit with general purpose foods, as this would require them to comply with Standard 1.3.2. • Do not fit the food type dietary supplements category because of the poor nutritional quality of the carrier product, the product is not designed for a specific nutritional deficiency, the product is likely to be used as a fancy expensive soft drink, and they do not fit the category for formulated caffeinated beverages. • FBs do not belong in the Code as they are a water based carrier of a mineral/vitamin tablet and are not a food. • If FBs are approved, then both composition and purpose should be defining features. Consumption • No evidence of consumer demand. • As there is no demonstrated nutritional need for this product there is no target consumer group. • Likely consumer groups are the worried well with disposable cash who the marketing companies reach by trading on people's fear of ill health and people who drink soft drinks. Composition • Safety concerns regarding the presence of trace elements (copper, chromium, iodine, manganese, selenium), vitamin D and some vitamins well in excess of the RDI (thiamin, riboflavin, B6, folate, B12 and vitamin C). • No demonstrated need for such an excessive level of so many vitamins and minerals to fortify food. • At risk groups include high intake consumers, children and adolescents, and pregnant and lactating women. • Do not need vitamin D supplemented, due to the sunny climate. • Nutritional quality of base beverage is important given the increasing incidence of obesity. If people need to take vitamins and minerals it is better that it does not come with extra kilojoules. The presence of food acids and sugar are a concern for dental health. • Should not be used as ingredients in other foods. Labelling • All claims for vitamins and minerals should be prohibited, as the carrier does not naturally contain these nutrients and any claim is likely to persuade the misinformed to consume this product unnecessarily. • A safety warning should be present, for example, 'This product is not a substitute for a healthy diet/healthy foods. More vitamins and minerals are not always good for health. Excessive vitamins and minerals can harm your health'.

		• People may have difficulty understanding and interpreting a percentage daily intake label. For those who can understand percentage labelling, it will assist them to make an informed choice. Stating levels of nutrients alone would be meaningless, as people do not know what the RDI is for a particular nutrient. • The vitamin and mineral content should be stated within the context of the RDI and a healthy diet. • Suggests limiting package size and purchase quantity to 100-200 ml and only 10% of the RDI for the various nutrients as an alternative means of managing the risk associated with the use of one-day quantities. • If approved, FBs would need a prescribed name. Impact Analysis Option 2 • Government enforcement agencies would have a significant responsibility to ensure FB advertising, food labelling and composition laws are not breached. In addition, these agencies would need to provide consumer education. • Having a greater choice of 'dubious nutritional quality' is not a benefit to consumers and is not a benefit in the long-term sustainability of our food supply. • The product itself is unsustainable. • No export opportunities when ethical and sustainability issues are considered.
10	**Food Technology Association of Victoria Inc** Mr David Gill	<u>Supports Option 2</u> • Questioned if the calcium levels per reference quantity requested in the current Application and those proposed in the draft variation to Standard 1.3.2 for Application A424 are consistent.
11	**Heyhoe & Associates on behalf of Johnson & Johnson Pacific Pty Ltd** Mr Tom Heyhoe	<u>Supports Option 2</u> General Comments • Supports Option 2 as a means of addressing and partially rectifying the regulatory contradiction that the *New Zealand Dietary Supplements Regulations 1985* provide. Composition • Permission to use all currently permitted intense sweeteners in combination with sugars would allow management of product sugar content without loss of taste quality, as per ASDA's request. Food Additives • Considers the proposed additives and their maximum permitted use levels are both responsible and appropriate.

12	**Nestlé Australia Ltd** Ms Robyn Banks	Supports Option 2 General Comments • Supports the AFGC submission, where Nestle is a member. Additional comments are: Composition • Should be permitted to contain other foods and not restricted to a certain few ingredients. • Permission to add 'medicinal herbs' should be provided, if they are permitted in the Code to be added to other foods. Those botanicals that are prohibited under the Code should not be permitted. Food Additives • The additives permitted for non-alcoholic water-based beverages should be applicable to FBs. Labelling • Claims for vitamins and mineral content should be permitted. • No need for a prescribed name.
13	**New South Wales Health, Food Branch** Mr Michael Apollonov	Supports Option 1 General Comments • Strongly opposes the Application. • Opposes the Applicant's reason for the request, stating 'this is not a valid argument for the creation of yet another standard in a product area that is already crowed with standards and the wrong way to address what amounts to an exploitation of a blatant loophole in the Dietary Supplement Regulations'. • Need to remove the loophole that permits the manufacture of foods as 'dietary supplements'. • The addition a 'formulated beverage' to the already existing formulated caffeinated beverages, formulated supplementary sports foods etc would add to the confusion of regulators and consumers.

14	**New Zealand Food Safety Authority**	Supports Option 1 General Comments • Does not support proceeding with A470 at this stage, until policy guidance for the fortification of foods and for food type dietary supplements are developed by FRSC. • Recommends FSANZ consider data on the contribution of sweetened drinks to the overall energy intakes of New Zealand children that will be available in late 2003. • By recognising high energy/high sugar foods as potential sources of a range of nutrients and hence promoting possible health benefits, we are possibly increasing the potential risk of overweight and obesity. • Not clear if these products would replace consumption of other sweetened beverages or increase current levels of consumption of sweetened beverages due to the potential benefits of added nutrients. • Need to consider dental health if there is a potential for increased consumption of sweetened beverages. • Suggests use of dietary modelling, particularly for children.
15	**New Zealand Juice Association** Mr John Robertson	Supports Option 2 Characteristics • Should not be considered general purpose foods. • Should include all non-alcoholic beverages excluding white milk but including juices, fruit drinks non-fruit drinks and sports water type products. Composition • Is aware of safety concerns regarding the proposed maximum levels, and consequently support the use of a maximum daily consumption statement. • No need to address the nutritional quality of the base beverage as nutrition panels remove the possibility of deceiving the consumer. • Use of one-day quantity is appropriate. • Should not be ingredients in other foods. Food Additives • The same additives allowed in other non-alcoholic beverages should be permitted. Labelling • Should not be restricted in making nutrition claims. • Use of percentage RDI more appropriate than quantitative amounts, to assist with consumer understanding.

		• Should not have a prescribed name as this would have no meaning to the consumer. • The proposed warning statements are only required if all other foods also require this labelling. Impact Analysis • No history of problems of unintended consumption based on data from the last 4-5 years of consumption of similar products. • Export markets have already been established by New Zealand manufacturers.
16	**PB Foods Ltd** Ms Monica Witsch	Supports Option 2 *General Comments* • Strongly recommends that FSANZ review the overall principles for adding vitamins, minerals and other bioactive ingredients to general purpose, special purpose, medical foods and dietary supplements to simplify the standards instead of developing a new standard in isolation. • Understands that FBs were allowed as part of R9 before ANZFA incorporated minimum macronutrient criteria as part of Standard 2.9.3 and changed the definition of formulated supplementary foods. PB Foods consider that it was not the intention of ANZFA to prohibit liquid formulated supplementary foods. • Comments that the policy frameworks for fortification and functional foods have not been finalised, and until this time they cannot adequately comment on this proposal. • Recommends removing the minimum macronutrient criteria for formulated supplementary foods, which will then allow for FBs as part of Standard 2.9.3 until the policy guidelines are finalised. • Recommends that the formulated supplementary foods standard be reviewed to allow the development of liquid formulated supplementary foods.
17	**Public Health Services, Queensland Health** Mr Gary Bielby	Supports Option 1 *General Comments* • Strongly opposes the manufacture and sale of formulated beverages. • Opposes Application A470 as FRSC has established a working group to develop a policy on the fortification of food, and progressing this application may compromise any future decision made by this group. • FBs have significant potential to mislead or deceive consumers. *Characteristics* • Should not be considered general purpose foods, as they have a supplemental purpose. • Composition and purpose are defining features, where non-alcoholic water-based beverages should only encompass those of an appropriate nutritional profile (e.g. low sugar, low saturated fat).

		Consumption • Data on consumption of flavoured mineral water and electrolyte drinks from the 1995 National Nutrition Survey showed largest intake by males across all age groups, with largest volume intake by those aged between 16 and 24 years. • The Queensland Health Youth Oral Health Survey (2002) found that of the 2203 13-15 year old children surveyed, 34% consumed soft drinks, 29% juice, 10% cordial and 7% sports drinks while at school. • Likely target groups are children and youth, as well as other vulnerable groups such as women of child-bearing age. Composition • Opposes all additions of vitamins and minerals to the proposed beverages. • Concerned that the proposed addition of niacin, folate, magnesium, copper and manganese are at or above the upper limit for some at risk groups, notably children. • Concern of toxicity with excess consumption of fat soluble vitamins. • Excess vitamin D, C and E can have adverse health outcomes and/or affects on medications. • Without estimated consumption data it is difficult to estimate the impact of their consumption on total vitamin/mineral intake. • The nutritional quality of the base beverage is important, with major concern that the proposed products are likely to be very high in sugar. • One-day quantity is only appropriate if it is adequately labelled and policed. Serving size is a vital consideration in the potential impact of such beverages on calorie consumption. • Use of FBs as ingredients in other foods should be prohibited. **Labelling** • All vitamin and mineral claims should be prohibited, particularly given the doubtful nutritional quality of the beverages in question. • Percentage labelling enables the consumer to make a more informed choice, as few consumers would be aware of the quantitative RDIs and be able to interpret them. • Require a prescribed name so that they could be distinguished from other beverages. • Should be labelled with statements that advise against using them as substitutes for a healthy diet or as providing health benefits. Impact Analysis Option 1 • Most likely that consumers would consume FBs for their vitamin and mineral content.

		• Notes that just because there is no information to suggest any possible harm from unintended consumption by consumers outside the target market, does not mean that there is no harm. • Concern regarding the potential impact on rates of overweight and obesity. Option 2 • Consumers are currently overawed by the number of food products on supermarket shelves which have increased from around 6000-40000 from 1960 to 2000. As such the addition of FBs is hardly a benefit. • Risks of unintended consumption relate to concerns regarding overweight and obesity and excess consumption of vitamins and minerals. • The potential market for FBs is likely to be huge. • The addition of vitamins and minerals and the promotion of this may encourage some groups to consume even more of these high sugar drinks. • Need to consider the impact on nutrition and oral health education regarding the appropriate use of FBs, where government and non-government resources are already stretched to their limit.
18	**Sanitarium Health Food Company** Dr Sidney Cole, Ms Trish Guy and Ms Ruth Truswell	**Supports Option 2** *General Comments* • Sanitarium currently markets a range of vitamin and mineral fortified beverages that are produced under the New Zealand Dietary Supplements Regulations. • Sanitarium generally supports the proposal, but would like to prevent poor nutritional quality beverages from qualifying as FBs. <u>Characteristics</u> • Should be designated as Special Purpose Foods, as per formulated sports drinks and formulated caffeinated beverages. • Notes that the FBs Sanitarium are interested in do have a 'supplemental' function, and therefore may best fit under food type dietary supplements. • Their purpose is to provide an enhanced water based product that will improve consumer nutrition by encouraging the consumption of greater quantities of water as part of the daily food intake. In addition they will provide consumers with vitamin and minerals required for replacement of lost nutrients e.g. after exercise. They will provide a water product that will simultaneously provide a well balanced mineral and vitamin supplementation. • Should be defined using a combination of composition and purpose features, with purpose the most important aspect. • To define composition they suggest, 'a water product which supplies a good balance of vitamins and minerals'. <u>Composition</u> • Not aware of any safety issues with the levels of vitamins and minerals proposed.

		• Levels of biotin, pantothenic acid, calcium, iron, magnesium, phosphorous and zinc are all higher in the current supplementary sports foods, and know of no evidence why the higher levels should not be permitted for FBs. • The regulations need to address the possibility that a manufacturer may have an agenda encouraging the consumption of amounts of vitamins and minerals which may be excessive, for example through use of artificially low serving sizes. If manufacturers base the vitamin and mineral composition on reasonable maximum daily consumption there is not danger of excessive intake of these nutrients. • Serving size should be regulated to prohibit the use of artificially low volumes, as this would increase the maximum amount consumed in a day. Suggest a cut-off point of 700-800 ml may be suitable. • The range of vitamins and minerals requested is satisfactory. • The range of vitamins and minerals allowed should be the same as that allowed in formulated supplementary sports foods, as the types of consumers and the purpose of FBs in relation to vitamin and mineral supplementation is very similar. • Prefers that a maximum claimed amount is specified for those vitamins and minerals where there is evidence that high intakes may have negative impact. • The nutritional quality of the base beverage should be addressed. • If the energy content of a food is low, even large intakes will not have a significant dilution effect on other nutrients. • Concerned about the energy content that may be allowed in FBs to which vitamins and minerals are added, particularly if this misleads consumers that the food has been made 'healthy' by the addition of vitamins and minerals. This should be addressed by limiting FBs to those with low energy content, and perhaps using prescribed maximum sugar and fat levels. • Used by consumers as a thirst quenching drink that they believe will also supply reasonable levels of a broad range of vitamins and minerals. Many consumers of Sanitarium water products are using them to replace vitamin and mineral supplement pills. • One-day quantity is appropriate, however the quantity supplied per normal serve is a more important regulatory principle. • The use of FBs as ingredients in other foods should be prohibited. <u>Food Additive</u> • The proposed maximum levels are appropriate. • Would like the permissions to allow for the addition of new additives that may be approved in the future, and that these be automatically allowed for use in FBs, for example artificial sweeteners. • All permitted natural colouring, including food caramel, should be permitted. • Not aware of any need to do further safety assessments. <u>Labelling</u> • Some restrictions to labelling of vitamin and mineral claims should be in place. The principles established for the vitamin and mineral regulation should be the basis for this restriction (Standard 1.3.2).

		• Some restriction for beverages that are not classified as low energy drinks may be appropriate. • Claims should be permitted only on the basis of per serve quantities of nutrients. Claims on the basis of maximum daily consumption should not be allowed. • Does not support limiting claims to an expression of content only, e.g. 'good source'. • Supports use of percentage RDI claims, as these are readily understood and used by consumers to interpret the nutritional information. • Information on the quantity of vitamins and mineral present in a normal serve should be made mandatory and the percent RDI information could be optional. • If no RDI is established, then the claim should be limited to claims of content only. • Possibility of distortion of nutritional information by inappropriate values assigned to the serving size. A normal serve could be defined as the total contents of the package which the beverage is contained up to a bottle size of 750 ml. For larger size packages their label should define the size of a normal serve, for example 300 ml. • Use of the statement 'consume no more than….per day' is not appropriate, as it is too strong a statement and will tend to give the consumer a false assessment of the type of risk. Instead suggest 'recommended maximum daily intake no more than (amount of 1 day quantity)' • Ingredient and nutrition panel information are sufficient to identify FBs. • Unreasonable for FBs to be required to carry a warning or statements that advise against using them as substitutes for a healthy diet.
19	**Unilever Australasia** **<u>Ms Julie Newlands</u>**	**Supports Option 2** *General Comments* • Fully supports the AFGC submission. • Supports consideration of all Standards within the Food Standards Code relevant to this submission, including Standards 1.3.1, 1.3.2, 2.6.2, 2.6.4, 2.9.4 and the reviews of P235 and P260. • Supports Option 2 to include regulations specific to FBs in the Code, however opposes developing a specific prescribed standard. Characteristics • Should be considered as general purpose foods, as this is how these beverages are being consumed. • Does not agree with Table 1 of the Initial Assessment Report. • Should be defined to include the existing more specific standards for Formulated Caffeinated Beverages and Formulated Supplementary Sports Foods.

		• Should be established under Standard 2.6 – Non-alcoholic Beverages, with the relevant additive and vitamins and mineral permissions in Standards 1.3.1 and 1.3.2. Composition • A similar allowance made for medicinal herbs in the Formulated Caffeinated Beverages standard should be made for FBs, even though this is outside the scope of the Application. • Supports the use of a one-day quantity. • Questions the appropriateness of the range and levels of vitamins and minerals. Suggest that the range and levels appropriate for caffeinated beverages and sports foods be reviewed to determine levels appropriate for FBs. Food Additives • Supports use of the same food additive permissions for FBs as permitted for non-alcoholic beverages. Labelling • Labelling should be consistent with other product labelling requirements to promote consumer understanding and prevent complexity and potential confusion. • If vitamins and minerals are permitted to be added then a claim should also be permitted. The same rationale applies to percentage daily intake information. • Generic naming provisions are adequate, particularly where additional information such as claims, mandatory nutrition information panel and an ingredient list will all be present. • Unnecessary to include a statement to advise against regarding FBs as substitutes for a healthy diet or as providing health benefits, as the label will provide complete product information.