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

6-04
4 August 2004

PRELIMINARY FINAL ASSESSMENT REPORT

PROPOSAL P242

FOOD FOR SPECIAL MEDICAL PURPOSES

DEADLINE FOR PUBLIC SUBMISSIONS to FSANZ in relation to this matter:
15 September 2004
(See 'Invitation for Public Submissions' for details)

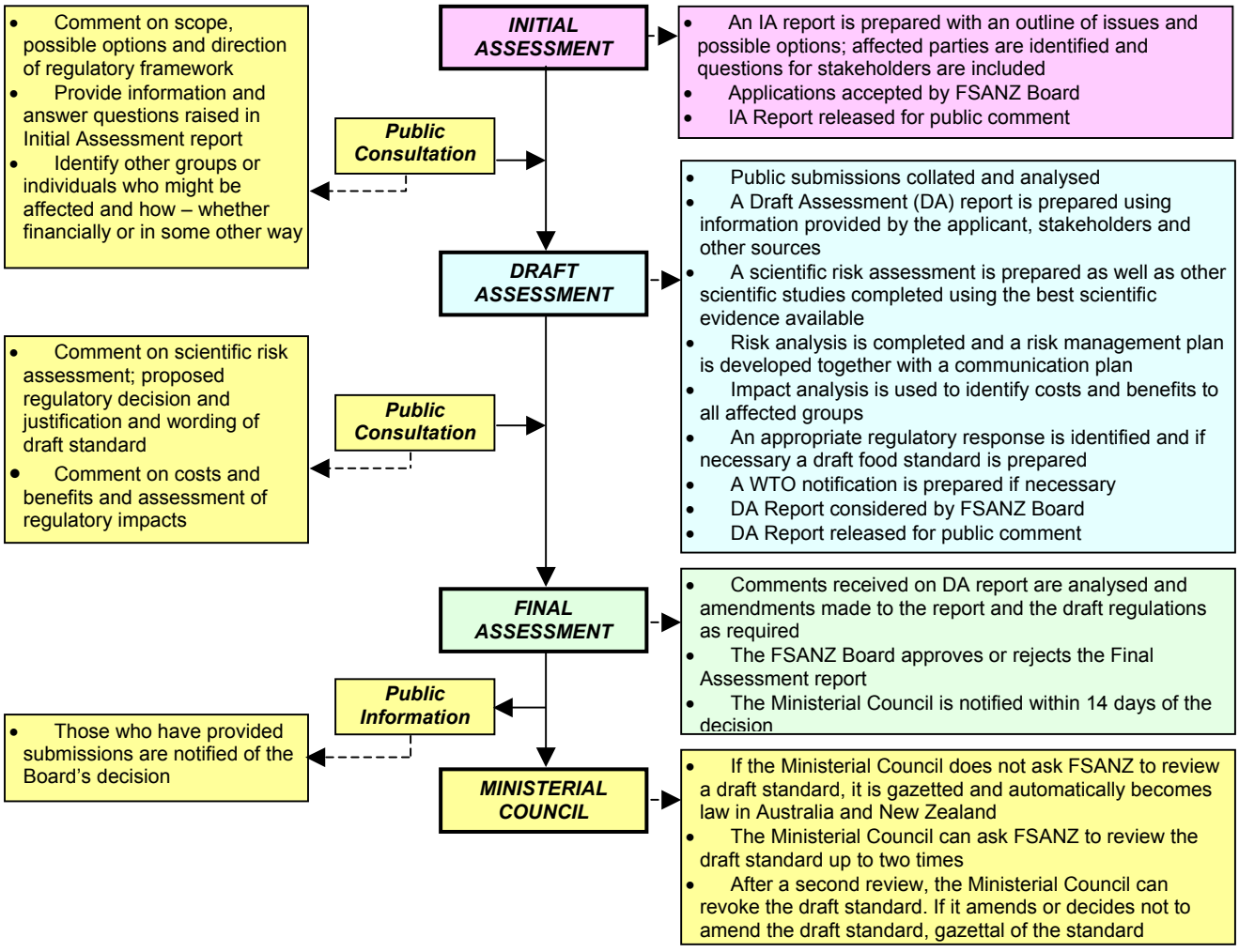
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

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 Commonwealth; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

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

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

The process for amending the *Australia New Zealand Food Standards Code* 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 Preliminary Final Assessment Report of Proposal P242 – Food for Special Medical Purposes; and prepared a draft variation to the *Australia New Zealand Food Standards Code* (the Code).

FSANZ invites public comment on this Preliminary Final 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 a Final Assessment of this Proposal. 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 should be received by FSANZ **by 15 September 2004**.

Submissions received after this date may not be considered, unless the Project Manager has given prior agreement for an extension.

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. Alternatively, requests for paper copies of reports or other general inquiries can be directed to FSANZ's Information Officer at either of the above addresses or by emailing info@foodstandards.gov.au.

CONTENTS

EXECUTIVE SUMMARY AND STATEMENT OF REASONS 6

REGULATORY PROBLEM 6
OBJECTIVES 6
ISSUES 7
OPTIONS 7
CONSULTATION 7
CONCLUSION AND RECOMMENDATION 8

1. INTRODUCTION 9

2. BACKGROUND 10

2.1 CURRENT REGULATORY FRAMEWORK 10
2.2 CURRENT MARKET AND DISTRIBUTION 11
2.3 PREVIOUS CONSIDERATION OF FOOD FOR SPECIAL MEDICAL PURPOSES 12

3. REGULATORY PROBLEM 12

4. OBJECTIVES 13

5. RELEVANT ISSUES 13

5.1 RISK ASSESSMENT OF NUTRITIONAL AND SAFETY ISSUES 13
5.2 MANAGING THE RISKS TO PUBLIC HEALTH AND SAFETY 16
5.3 APPLICATION OF OTHER GENERIC STANDARDS 22
5.4 OTHER ISSUES RAISED IN SUBMISSIONS 25

6. REGULATORY OPTIONS 30

6.1 OPTION 1 – STATUS QUO 30
6.2 OPTION 2 – REGULATION OF FSMP BY A DISCRETE STANDARD WITH THE APPLICATION OF AN OVERARCHING RISK MANAGEMENT FRAMEWORK. 30

7. IMPACT ANALYSIS 31

7.1 AFFECTED PARTIES 31
7.2 COST-BENEFIT ASSESSMENT OF REGULATORY OPTIONS 31

8. CONSULTATION 32

8.1 PUBLIC CONSULTATION 32
8.2 STAKEHOLDER CONSULTATIONS 33
8.3 WORLD TRADE ORGANIZATION (WTO) 33

9. CONCLUSION AND RECOMMENDATION 33

10. IMPLEMENTATION AND REVIEW 34

ATTACHMENT 1 - DRAFT VARIATIONS TO THE *AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE* 35

ATTACHMENT 2 - COMPOSITIONAL ASSESSMENT 46

ATTACHMENT 3 - SAFETY ASSESSMENT REPORT 62

ATTACHMENT 4 - LABELLING ASSESSMENT 109

ATTACHMENT 5 - FOOD TECHNOLOGY REPORT 128

ATTACHMENT 6 - MICROBIOLOGICAL EVALUATION 132

ATTACHMENT 7 - SUMMARY OF SUBMISSIONS 138

Executive Summary and Statement of Reasons

As part of the transition into the joint Australian and New Zealand food regulatory system, Food Standards Australia New Zealand (FSANZ) is required to complete the review and development of harmonised Australian and New Zealand regulations covering food for special medical purposes (FSMP), which is the subject of this Preliminary Final Assessment Report.

FSMP are principally formulated food products, used under the supervision of medical or other health professionals for the dietary management of individuals with certain medical conditions, disease states or disability. They include 'complete nutrition' formulas (i.e. intended for use as the sole source of nutrition), either consumed orally or through an enteral route (e.g. naso-gastric tube), as well as specialised dietary supplement formulas or foods, and very low energy diet formulas (VLED) used in the dietary management of morbid obesity.

There is minimal local manufacture of FSMP as it is estimated that 99% of products are imported, mainly from the European Union (including UK) and the United States of America. On a world scale, the Australian and New Zealand markets are comparatively small.

Regulatory Problem

By their nature, FSMP are products specifically formulated for use under medical or other health professional supervision, for the dietary management of individuals with particular medical conditions. These vulnerable individuals rely either fully or partially on FSMP to meet their specific nutritional requirements that cannot be satisfied by a normal diet. It is therefore essential that FSMP are available to, as well as safe and effective in meeting the needs of, the intended target population. There are inherent risks associated with the consumption of FSMP, although these risks are generally minimised by the supervision and guidance provided by a medical or other health professional.

The current regulatory status of FSMP in both Australia and New Zealand is unclear. The Code does not explicitly recognise FSMP and therefore, unlike other special-purpose foods, there are no permissions for composition of FSMP or specific labelling requirements. This regulatory uncertainty creates difficulties for enforcement agencies at the border and occasionally causes delays in the importation of FSMP.

Objectives

The specific objectives of Proposal P242 are to:

- protect public health and safety by ensuring the safe and appropriate use of FSMP; continued availability of FSMP for intended consumers; and prevention of misuse of FSMP by unintended users;

- provide health professionals and consumers with sufficient information to make appropriate choices about the safe and effective use of FSMP; and

- develop a uniform food standard applying to FSMP in Australia and New Zealand, that is, wherever possible, consistent with relevant international regulations.

Issues

In developing standards for FSMP, there are a number of issues that require consideration, including issues raised through consultation. Issues considered in this Preliminary Final Assessment include:

- defining features and purpose of FSMP;
- the inherent risks associated with the use of FSMP;
- the management of identified risks to public health and safety;
- access to FSMP including a proposed restriction on the sale and advertising of FSMP to the general public;
- the harmonisation of compositional and labelling requirements with international regulations; and
- applicability of other generic standards to FSMP including food additive permissions and microbiological limits.

Options

Two options are proposed at Preliminary Final Assessment:

- Option 1 – maintain *status quo* i.e. no specific regulation of FSMP in the Code; and

- Option 2 – regulation by a discrete standard in the Code incorporating specific compositional and labelling requirements, which are in general, consistent with relevant overseas regulations, in addition to the application of an overarching risk management framework consisting of mandatory advisory labelling for use under medical supervision, and restrictions on the sale and advertising of FSMP.

Consultation

Public consultation for Proposal P242 was conducted from 18 December 2002 to 24 March 2003. Seventeen separate submissions were made during this period; a summary of the issues raised in these submissions is at Attachment 7. In addition, FSANZ has conducted targeted consultation with both industry and health professional stakeholders.

Given the number and complexity of the issues raised at, and the lapse in time since, Draft Assessment (December 2002), FSANZ has included an additional round of public comment to allow further consultation on the proposed regulation of FSMP.

Therefore this Preliminary Final Assessment Report discusses issues relevant to the development of standards for FSMP and seeks further comment on the proposed draft variations to the Code, including draft Standard 2.9.5 – Food for Special Medical Purposes (Attachment 1). Comments received will assist in the preparation of the final assessment of the draft standards for FSMP in Australia and New Zealand.

Conclusion and Recommendation

By maintaining the *status quo* as per Option 1, consumers are unlikely to be aware of any impact except where imported FSMP may be delayed at national borders, whereas there will continue to be negative impacts for both industry and government caused by the current regulatory uncertainty for FSMP.

However when compared to Option 1, Option 2 provides greater benefits for all affected parties.

In addition to providing greater regulatory certainty for both industry and government, Option 2 minimises the risks to consumers by ensuring continued access to FSMP for intended consumers; reduced potential for misuse by unintended consumers; and assures the provision of sufficient information to allow health professionals and consumers to make choices about the safe and effective use of FSMP.

Option 2 provides clarity of regulation for industry and enforcement agencies, resulting in a uniform FSMP standard applying to Australia and New Zealand, which in general, harmonises with relevant overseas regulations and consequently will not unduly restrict trade.

For these reasons, Option 2 is considered the more suitable option in meeting the regulatory objectives.

Therefore, it is recommended that the proposed amendments (Attachment 1), incorporating a draft standard for FSMP, be approved for the following reasons:

- the inclusion of a standard for FSMP in the Code provides clear, uniform regulation of FSMP in Australia and New Zealand;

- the explicit recognition of FSMP in the Code provides regulatory certainty for industry and for government enforcement agencies;

- the regulation of FSMP provides assurance for consumers of protection of public health and safety, particularly for the target group being a vulnerable population;

- the inclusion of FSMP as a 'special purpose food' recognises that these foods are designed for a particular vulnerable target group;

- the inclusion of restriction on the sale and advertising of FSMP to the general public protects the public health and safety of both intended and unintended users of FSMP, particularly in the absence of medical or health professional supervision; and

- there is consistency with international regulations, wherever possible, to prevent potential barriers to trade that could jeopardise the supply of FSMP products to Australia/New Zealand.

1. Introduction

On 1 July 1996, an Agreement between Australia and New Zealand (the Treaty) came into force that established a joint Australian New Zealand food standards system, which served to underpin the development of the *Australia New Zealand Food Standards Code* (the Code). In December 2000, the Code came into effect in Australia and New Zealand and the former Australian *Food Standards Code* (Volume 1) and the New Zealand *Food Regulations 1984* (NZFR) were repealed at end of 2002, when the Code became the sole set of food standards for the two countries (except for those areas outside of the scope of the treaty e.g. food safety).

As part of the transition into this new joint food regulatory system, Food Standards Australia New Zealand (FSANZ) is required to complete the review and development of harmonised Australian and New Zealand food standards covering food for special medical purposes (FSMP), which is the subject of this Preliminary Final Assessment Report.

FSMP are principally formulated food products, used under the supervision of medical or other health professionals (e.g. dietitians, nurses and pharmacists), for the dietary management of individuals (including children) with either ongoing chronic medical or disability conditions or during acute phases of illness, injury or disease states. They include 'complete nutrition' formulas (i.e. intended for use as the sole source of nutrition), either consumed orally or through an enteral route (e.g. naso-gastric tube), as well as specialised dietary supplement formulas or foods, and very low energy diet formulas (VLED) used for the dietary management of morbid obesity.

Total parenteral nutrition (TPN) products are formulated to be administered intravenously and therefore fall outside the definition of food in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). For this reason, TPN is not considered part of the scope of this Proposal. Additionally, due to the complexity of the issues involved with the regulation of specialised infant formula products, these products are also excluded from the scope of this Proposal. FSANZ expects to consider specialised infant formula products under a separate proposal following the completion of Proposal P242.

In October 2001, FSANZ [then the Australia New Zealand Food Authority (ANZFA)] released an Initial Assessment Report for Proposal P242 and invited public submissions. The comments and information received assisted to progress this Proposal to Draft Assessment. A Draft Assessment Report was released for public comment in December 2002. A summary of submissions received following Draft Assessment is at Attachment 7.

Given the complexity of the issues involved in this Proposal and the lapse in time since Draft Assessment, FSANZ has included an additional round of public comment to allow further consultation on the proposed standard for FSMP. Therefore this Preliminary Final Assessment Report discusses issues relevant to the development of a standard for FSMP, particularly issues raised at Draft Assessment, and seeks further comment on the proposed draft variations to the Code, including draft Standard 2.9.5 – Food for Special Medical Purposes (Attachment 1). Comments received will assist in the preparation of the final assessment of the draft standard for FSMP in Australia and New Zealand.

2. Background

2.1 Current Regulatory Framework

2.1.1 Australia

In Australia, FSMP are currently not specifically regulated, as there is no explicit recognition of FSMP within the Code. As a result, the regulation of FSMP is unclear causing difficulties for industry, the State and Territories enforcement agencies and the Australian Quarantine and Inspection Service (AQIS).

2.1.2 New Zealand

Under the NZFR there was no specific regulation solely for FSMP, although some products may have fallen under Regulation 237 - Special Purpose Foods. The NZFR was repealed in late 2002 and Standard 1.1A.6 – Transitional Standard for Special Purpose Foods incorporates the provisions of Regulation 237 in the Code until such time as a Standard for FSMP are developed.

However, FSMP could also fall under the New Zealand Dietary Supplement Regulations (NZDSR); a set of regulations that 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. It is possible that some FSMP, due to the addition of further ingredients, do not comply with Regulation 237 in the NZFR, but may comply with the NZDSR (in relation to composition). FSANZ is currently reviewing the regulation of food-type dietary supplements through Proposal P235, which is currently stalled at Draft Assessment pending policy advice from the Ministerial Council.

2.1.3 International and other National Regulations

There are number of international and other national regulations that are relevant to the Australia/New Zealand regulation of FSMP. These are:

- Codex standards for 'The Labelling of and Claims for Foods for Special Medical Purposes' (CODEX STAN 180-1991), and for 'Formula Foods for use in Very Low Energy Diets for Weight Reduction' (CODEX STAN 203-1995);

- European Commission Directives on 'dietary foods for special medical purposes' (Directive 1999/21/EC) and 'on substances that may be added for specific nutritional purposes in foods for particular nutritional uses' (PARNUTS) (2001/15/EC);

- United States of America federal legislation: the Orphan Drug Amendments 1988, and the Nutrition Labeling and Education Act 1990 (NLEA); as well as a final ruling by the United States Food and Drug Administration (FDA) in 1993 clarifying the NLEA; and

- Canadian *Food and Drug Regulations 1954*, Division 24 – Foods for Special Dietary Use, specifically regulations on 'Formulated Liquid Diets' (B.24 100 – 103) and 'Foods Represented for Use in Very Low Energy Diets' (B.24 300 – 306).

2.1.4 Therapeutic Goods/Medicines

In Australia, the Therapeutic Goods Administration (TGA) is responsible for the regulation of therapeutic goods under the *Therapeutic Goods Act 1989*. When first introduced, this legislation placed a number of products in the position of being classified as either a food or a therapeutic good. Products designed to nourish people with medical conditions were considered as foods. However, in the absence of any explicit recognition of FSMP within the Code, FSMP potentially fall in the regulatory interface of therapeutic goods and food.

Similarly in New Zealand, FSMP are not considered as medicines, because they are not used for a therapeutic purpose i.e. they help to improve or maintain the nutritional condition of a person, rather than being used to treat or cure any disease state. Although again the level of formulation of FSMP and their unique role of nourishing individuals receiving medical therapy for particular health conditions can cloud their distinction as foods rather than as therapeutic goods.

Australia and New Zealand are in the process of establishing a bi-national organisation to regulate therapeutic goods. When harmonised legislation for therapeutics is developed, it is likely that, if there is no explicit recognition of FSMP in the Code, the current ambiguity between FSMP and therapeutic goods will remain.

2.2 Current Market and Distribution

There are four multi-national companies that almost exclusively supply the total Australian and New Zealand market of FSMP-type products. There is minimal local manufacture with an estimated 99% of FSMP products being imported. Products are mainly manufactured in either the European Union (including UK) or the United States of America. The domestic market is estimated at approximately AUD$ 40 million per annum for Australia and between NZ$5 to $8 million per annum for New Zealand, which collectively on a world market scale is comparatively small.

With very few FSMP manufactured in domestic markets, there are no significant trade arrangements in place between Australia and New Zealand. Some transfer of products may occur between Australia and New Zealand to balance product shortfalls or excesses, however the multi-national manufacturers of FSMP ultimately treat both nations as one market.

The local FSMP market is growing mostly as a result of improved technology, an ageing population, earlier patient discharge from hospital and a greater recognition of the importance of nutritional support in medical therapy. Volume sales vary from product to product with general nutritional support products such as formulated high energy/high protein supplements being consumed in much higher volumes than highly specialised foods for rare disease states that may only be supplied to a very small number of people.

2.2.1 Australia

The majority of FSMP (90%) are provided through healthcare settings (e.g. public and private hospitals, nursing homes), under the supervision of health professionals such as dietitians, nurses or medical staff. The supply of FSMP to healthcare facilities most often occurs through either state-wide or regional health service tendering procedures.

Generally, tenders outline requirements for the supply of specific FSMP including composition and price. FSANZ is aware that health services at times seek guidance from the Code (e.g. labelling requirements) when preparing tender specifications.

FSMP, particularly the highly specialised products, can be very expensive to the consumer; a problem that is often compounded by long-term dependence on such products. Individuals who require these products within a home/community setting either obtain supplies through regional health services (hospitals), or are able to order directly from suppliers. Consumers can also purchase products through retail pharmacies without a medical prescription. Currently, FSMP are not sold through supermarkets or convenience stores. The level of financial assistance that is offered to support the purchase of products varies considerably between each State and Territory. A very small number of specialised products, predominately for metabolic disorders, are listed on the Pharmaceutical Benefits Scheme.

2.2.2 New Zealand

It is estimated that 95% to 99% of the FSMP market is distributed via a prescription (authorised by a medical practitioner). The remaining section of the market is available over the counter in pharmacies and similar to Australia, FSMP are currently not available through supermarkets or convenience stores.

The majority of foods for special dietary use in New Zealand (including low protein pastas and some gluten free foods) are currently listed on the NZ Pharmaceutical Schedule, administered by PHARMAC (the Pharmaceutical Management Agency Ltd). PHARMAC has the task of managing pharmaceutical subsidies on behalf of the District Health Boards to ensure that all New Zealanders have access to safe, cost effective, quality medicines to meet reasonable health needs. Due to the listing of FSMP by PHARMAC, it is more cost effective for consumers to access products via a prescription and this is one of the main reasons why over the counter sales are very low.

2.3 Previous Consideration of Food for Special Medical Purposes

Previously Proposal P49 – Formula Food for Very Low Energy Diets (FFVLED)(P49) considered the development of standards for FFVLED in the former Australian *Food Standards Code.* However, P49 was stalled in 1995. The initiation of Proposal P242 therefore, allowed for the formal abandonment of P49 and renewed consideration of FSMP in the context of the joint Australia/New Zealand food regulatory system.

3. Regulatory Problem

By their nature, FSMP are products specifically formulated for use under medical or other health professional supervision, for the dietary management of individuals with particular medical conditions. These vulnerable individuals rely either fully or partially on FSMP to meet their specific nutritional requirements that cannot be satisfied by a normal diet. It is therefore essential that FSMP are available to, as well as safe and effective in meeting the needs of, the intended target population. There are inherent risks associated with the consumption of FSMP, although these risks are generally minimised by the supervision and guidance provided by a medical or other health professional.

The current regulatory status of FSMP in both Australia and New Zealand is unclear. The Code does not explicitly recognise FSMP and therefore, unlike other special-purpose foods, there are no permissions for composition of FSMP or specific labelling requirements. This regulatory uncertainty creates confusion for industry in complying with the Code, in addition to difficulties for enforcement agencies at the border, which on occasions causes delays in the importation of FSMP.

4. Objectives

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

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

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

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

The specific objectives of Proposal P242 are to:

- protect public health and safety by ensuring the safe and appropriate use of FSMP; continued availability of FSMP for intended consumers; and prevention of misuse of FSMP by unintended users;
- provide health professionals and consumers with sufficient information to make appropriate choices about the safe and effective use of FSMP; and
- develop a uniform food standard applying to FSMP in Australia and New Zealand, that is, wherever possible, consistent with relevant international regulations.

5. Relevant Issues

5.1 Risk Assessment of Nutritional and Safety Issues

There are inherent risks associated with the use of FSMP that primarily relate to nutritional adequacy and safety, and can be categorised into five areas:

- the inadequate provision of nutrition when FSMP do not contain sufficient quantities of vitamins and minerals;
- safety concerns from the excess intake of certain vitamins and minerals;
- macronutrient requirements in VLED;
- the safety of reducing minimum micronutrient requirements to cater for certain medical conditions; and

- the safety of various nutritive substance forms.

A summary of these risks is provided in the following sections. A full discussion of these nutritional and safety risks is provided in Attachments 2 and 3.

5.1.1 Nutritional considerations on minimum levels of vitamins and minerals

The nutritional issues associated with the use of FSMP are discussed in detail as part of the compositional assessment provided at Attachment 2.

FSMP can be consumed either as a supplement to the diet of an individual (nutritionally incomplete formula), or as the sole source of nutrition over an indefinite period of time (nutritionally complete formula). Those FSMP consumers who consume nutritionally complete formulas rely on the micronutrient contents of these foods for maintenance of an adequate nutritional status, whereas nutritionally incomplete formulas are consumed along with other foods in the diet. Consumers of nutritionally incomplete formulas are thus at a lower risk of consuming inadequate amounts of micronutrients, as other foods in the diet potentially contribute to providing sufficient micronutrients.

However, there is a significant risk of an insufficient micronutrient intake with the use of nutritionally complete formula, should such a formula contain inadequate amounts of micronutrients. Inadequate nutrition support can prolong a medical condition with possible adverse consequences on morbidity and mortality for the patient. This is a serious risk for public health and safety and therefore minimum nutritional requirements are proposed for nutritional complete products for most vitamins and minerals, in line with overseas standards.

For nutritionally incomplete products no minimum requirements are proposed, since these products would be normally consumed in conjunction with other foods.

5.1.2 Safety considerations on maximum levels of vitamins and minerals

A detailed report on the safety issues associated with high vitamins and minerals intake is provided in Attachment 3**.**

A safety assessment has been conducted for the purpose of establishing upper limits for vitamins and minerals used in FSMP. In this Proposal, restrictions on the sale of FSMP are proposed, and products are intended to be sold under medical supervision. Therefore, effects of an acute nature that are easily detected, such as diarrhoea, were not considered relevant in establishing an upper limit.

It should be noted that the upper limits in this Report have been established specifically for the setting of a standard for FSMP, and are not intended to be used generally as upper limits for other purposes.

As a result of this safety assessment, for most vitamins and minerals an upper limit is not considered necessary for FSMP. However, the following vitamins and minerals are identified as having potential safety concerns within the context of their use in FSMP and therefore an upper limit is considered necessary. These micronutrients are vitamins A, B_6, D, selenium, iodine, zinc, calcium, manganese and copper. The table below specifies the adverse effects on which the upper limit for these vitamins and minerals was based.

Vitamin or mineral	Daily upper limit	Adverse effect
Vitamin A, µg RE	3000	Teratogenicity, hepatotoxicity
Vitamin B_6, mg	25	Neuropathy
Vitamin D, mg	0.050	Hypercalcaemia
Selenium, mg	0.40	Brittle nails and hair pathology, adverse effects nervous system
Iodine, mg	1.0	Sub-clinical hypothyroidism
Zinc, mg	40	Reduced copper status
Calcium, mg	2500	Milk-alkali syndrome and renal stone formation
Manganese, mg	11.5	Neurotoxicity
Copper, mg	10	Hepatotoxicity

5.1.3 Macronutrient requirements in VLED

There are risks associated with an inadequate macronutrient profile in VLED, due to the possible use of these products in semi-starvation regimes. Insufficient provision of protein, fat and carbohydrate in a VLED can result in a substantial loss of lean body mass and may significantly alter normal metabolic processes. Furthermore, unsuitable macronutrient formulations of early VLED have sometimes produced deleterious effects in the past[1,2].

5.1.4 Safety concerns with minimum micronutrient requirements for certain medical conditions

Although nutritionally complete FSMP represent a risk to the health of the patient if they contain inadequate amounts of micronutrients (See Section 5.1.1), in certain medical conditions there is the need to reduce some micronutrients below levels required for the maintenance of normal nutrition in healthy people. In such circumstances, the upper intake limits of safety for the condition could be below normal minimum requirements. For this reason, specific consideration has been given to sodium, potassium and phosphorus, as low intakes of these nutrients are required for the management of certain medical conditions e.g. renal disease.

It is therefore concluded that if medically indicated, a decrease in the minimum requirement for sodium, potassium and phosphorus content of FSMP is appropriate.

5.1.5 Safety considerations on permitted forms of nutritive substances

At Draft Assessment, the proposed list of permitted forms of nutritive substances was mainly based on European legislation, as the European Union is the only major overseas region supplying FSMP to the domestic market that has undertaken a safety and nutritional assessment on a wide range of substances appropriate for addition to FSMP.

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1 ADA (American Dietetic Association), 1990. Position of the American Dietetic Association: Very-low-calorie weight loss diets. *Journal of the American Dietetic Association*, 90(5): p722-726.

2 NTPTO (Nutritional Taskforce on the Prevention and Treatment of Obesity), 1993. Very Low-Calorie Diets. *Journal of the American Medical Association*, 270(8): p967-974.

Therefore, permitting the inclusion of more nutritive substances for use in FSMP requires that these substances are safe. The permitted forms for use in infant formula products, listed in Standard 2.9.1, are regarded as suitable for use in FSMP, since these products are safe for use by infants, another vulnerable group. However, the safety of permitted forms listed in Standard 1.1.1 – Preliminary Provisions – Application, Interpretation and General Prohibitions, cannot be guaranteed for use in FSMP, as these provisions are intended to apply to a normal healthy population.

Following Draft Assessment, submitters requested certain additional forms of nutritive substances. The European Scientific Committee on Food has recently performed a safety assessment for the use of L-serine, and the double amino acid salts L-arginine-L-aspartate, L-lysine-L-aspartate, and L-lysine-L-glutamate dihydride for use in FSMP. Their conclusion was that these products are safe for use in FSMP. These products will therefore be included as permitted forms in the Code.

A safety assessment has been conducted for the purpose of assessing the safety of some other nutritive substances (Attachment 3).

The use of N-acetyl-L-methionine and L-asparagine monohydrate in FSMP is unlikely to give rise to adverse health effects and therefore, these substances will be permitted as nutritive substances for FSMP. Based on the different solubility of chromium acetate compared to other chromium III forms, its toxicological profile could not be determined. Therefore it is proposed that this form should not be permitted for FSMP. Since the characteristics of chromium potassium sulfate dodecahydrate are similar to the already permitted form chromium sulfate, it is proposed that chromium potassium sulfate dodecahydrate be permitted as a chromium compound.

5.2 Managing the Risks to Public Health and Safety

5.2.1 Availability of FSMP

At Draft Assessment, the majority of submitters, including both industry and health professionals, expressed concerns that the prescriptive nature of the proposed composition and labelling requirements, would adversely impact on the cost and availability of FSMP. This is because products, produced for a global market, would be unlikely to be reformulated or relabelled for the relatively small local FSMP market. Industry indicated that 95% of current FSMP would be non-compliant with the proposed draft standard.

In addition, a number of submitters disagreed that FSMP are unsafe in the current unregulated environment and that FSANZ had failed to demonstrate market failure requiring regulation. It was also suggested that the supervision provided by health professionals lessens the risk associated with FSMP.

Assessment

At Draft Assessment, the proposed composition and labelling requirements were considered appropriate to address the risks associated with FSMP. However following further consultation, FSANZ recognises that certainty of supply is an important consideration for individuals who rely on FSMP to meet their nutritional needs.

In addition, as FSMP are intended for use under medical supervision FSANZ accepts that the inherent risks associated with FSMP are reduced with this professional care. However, in the absence of medical or other health professional supervision there are potential risks for both intended and non-intended consumers.

Furthermore, in the current environment where there is greater demand for foods with health-related properties, a lessening of a conservative approach to FSMP standards could have undesirable impacts for the regulation of similar type foods. For example, there is the possibility that similar type foods (e.g. food-type dietary supplements) – more appropriately regulated under other food standards – would be inappropriately positioned under this Standard to avoid the application of certain prohibitions, restrictions and requirements within the Code.

Therefore to reduce the potential risks associated with the inappropriate and unsupervised use of FSMP, and to clearly distinguish FSMP from other similar foods, it is proposed that the standard for FSMP include an overarching risk management framework consisting of:

- the requirement for labelling with a mandatory advisory statement to the effect that FSMP are to be used only under medical supervision;

- a restriction on the retail sale of FSMP by permitting the sale of FSMP only from medical practitioners, pharmacies, hospitals, nursing homes and wholesalers; and

- a restriction on advertising directly to consumers i.e. permission to advertise only to health professionals, wholesalers, healthcare facilities e.g. hospitals and nursing homes and to members of disease and disorder support groups.

The intent of regulating the sale and advertising of FSMP is to maintain current access arrangements wherever possible, so as not to disadvantage users of FSMP, but also to be a disincentive for the inappropriate positioning of products to take advantage of fewer regulatory controls.

5.2.1.1 Use under medical supervision

FSMP are by definition intended for use under medical or other health professional supervision. It is recognised that medical supervision can manage many of the inherent risks associated with the use of FSMP. It is therefore appropriate to mandate the labelling of FSMP products with an advisory statement to clearly distinguish FSMP from other foods and reduce the risks associated with the unsupervised and inappropriate use of FSMP. Further discussion on this labelling requirement as a risk management strategy is included in the Labelling Assessment at Attachment 4.

5.2.1.2 Restriction on the Sale and Advertising of FSMP

Legislative basis of restrictions

Paragraphs 9(1)(k) and 9(1)(l) of the FSANZ Act permit the development of food standards to relate to restrictions on the:

- premises at which, and the persons by whom, particular food may be sold or otherwise supplied; and
- publications that may contain advertisements for particular food.

In addition, Paragraph 9(1)(ca) provides more generally that standards may relate to the prohibition of the sale of food either in all or specified circumstances, and either conditionally or unconditionally.

Restriction on the sale of FSMP

There are currently no restrictions on where FSMP can be sold in either Australia or New Zealand. Individuals requiring FSMP in both Australia and New Zealand primarily access products through healthcare institutions, or purchase them from pharmacies or directly from suppliers.

At Draft Assessment it was considered unnecessary to change the current unrestricted access to FSMP, as there was believed to be little incentive for non-target groups to consume these products. Submitters at Draft Assessment, on the whole, agreed with this approach. However given the proposed lessening of prescribed compositional and labelling requirements, a restriction on the sale of FSMP is now considered a necessary part of the overall risk management framework for FSMP.

Therefore, FSANZ is proposing to permit the retail sale of FSMP only from pharmacies, hospitals, nursing homes, medical practitioners and wholesalers of FSMP. Restricting the sale of FSMP to these premises is not expected to dramatically alter the current access arrangements for consumers but should, however, have the intended effect of discouraging manufacturers or importers from inappropriately positioning products as FSMP to take advantage of less restrictive compositional and labelling requirements.

Restriction on the advertising of FSMP

At Draft Assessment a restriction on advertising of FSMP to the general public was proposed as a means of managing the public health and safety risks associated with the unsupervised and inappropriate use of FSMP, in particular VLED. The proposed restriction permitted the advertising of FSMP in health professional publications only. This restriction was considered consistent with Codex regulations[3] that include a prohibition on the advertising of FSMP to the general public.

Public comment on the proposed advertising restriction was mixed. Health professional submitters were, in general, supportive of the restriction, whereas industry, on the basis of no evidence of market failure, did not consider that a restriction on advertising of FSMP was warranted. As an alternative, the **Australia New Zealand Enteral Nutrition Manufacturers Association** (ANZENMA) provided information on several advertising codes of practice (CoP) that could apply to FSMP[4,5].

[3] Codex Standard for the Labelling of and Claims for Foods for Special Medical Purposes (CODEX STAN 180-1991)
[4] Weight Management Code Administration Council of Australia (1999) 2nd Ed; *Weight Management Code of Practice*. http://www.weightcouncil.org/butts/Code.html
[5] New Zealand Advertising Standards Authority (1999); *Code for Therapeutic Advertising*. http://www.asa.co.nz/codes/codes.htm

In addition a number of submitters expressed concern that the term 'health professional publications' was too narrow and that this should include advertising: to patient support and specific disease consumer groups; at trade displays, conferences, and educational forums; in product leaflets; and electronic mediums such as websites. Also a few submitters asked for clarification of the disciplines covered by 'health professional' and it was suggested that this could be defined similar to the definitions given in the Australian *Therapeutic Goods Regulations 1990*[6].

The risk of unsupervised and inappropriate use of FSMP, particularly for VLED, is a concern. Australian and New Zealand studies have found that, across different geographical regions and age groups, a significant proportion of those who attempt to lose weight will resort to extreme and often dangerous dietary behaviours[7,8,9].

Females are the most likely group that will use dangerous techniques to achieve weight loss, particularly adolescent girls. In its review of Australian literature on the issue of weight loss techniques, the NHMRC Working Party on the Prevention of Overweight and Obesity concluded that although the occurrence was low, the number of women resorting to extreme health-threatening weight loss methods was of concern[10].

A restriction on advertising reduces the opportunity to promote FSMP to the general public thereby reducing the risk of unsupervised use of FSMP. In addition it also acts as a disincentive to manufacturers who may wish to inappropriately market their products to the general public.

Due to the diversity of FSMP products available, including VLED, FSANZ does not consider advertising CoP, as supported by industry, to be able to effectively manage the potential risks associated with the unsupervised and inappropriate use of FSMP.

Therefore FSANZ is proposing to maintain the prohibition on advertising to the general public, as proposed at Draft Assessment, and permit advertising to relevant health professionals (as adapted from the *Therapeutic Goods Regulations 1990* i.e. medical practitioners, psychologists, dentists, pharmacist, physiotherapists, dietitians, nurses, speech pathologists or scientists working in medical laboratories), wholesalers of FSMP, hospital purchasing officers and members of disease and disorder support groups.

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[6] *Therapeutics Goods Regulations 1990*, Part 2, Division 1(4) defines 'health professionals' as medical practitioners, psychologists, dentists, veterinary surgeons, pharmacists, physiotherapists, dietitians, scientists working in medical laboratories, and nurses.

[7] Crawford D, Owen N, Broom D, Worcester M, Oliver G (1998); *Weight-control practices of adults in a rural community*; Aust NZ J Public Health, 22(1): 73-79.

[8] O'Dea JA, Abraham S, Heard R (1996); *Food habits, body image and weight control practices of young male and female adolescents*; Aust J Nutr Diet, 53((1): 32-38.

[9] Worsley A, Worsley AJ, McConnon S, Silva P (1990); *The weight control practices of 15 year old New Zealanders*; J Paediatr Child Health, 26(1): 41-45.

[10] National Health and Medical Research Council (NHMRC) (1997); *Acting on Australia's Weight: a strategic plan for the prevention of overweight and obesity*; Australian Government Publishing Services, Canberra; p149-159.

Conclusion

The application of local regulatory requirements that deviate from international regulations is likely to adversely impact on the cost and availability of FSMP in the Australian and New Zealand market. However there are still significant potential risks associated with the unsupervised and inappropriate use of FSMP by both intended and unintended consumers of FSMP. Therefore as a means of managing these risks, rather than applying highly prescriptive compositional and labelling requirements, FSANZ proposes the application of an overarching risk management framework that includes the mandatory requirement to label FSMP as for use only under medical supervision, in addition to a restriction on sale and advertising of FSMP to the general public.

5.2.2 Composition of FSMP

Given that FSANZ is now proposing to primarily manage the risks associated with the unsupervised and inappropriate use of FSMP through the application of an overarching risk management framework (see Section 5.2.1), management of the inherent compositional risks as identified in Section 5.1 can be readily achieved by the application of specific composition requirements, which are, in general consistent with overseas FSMP regulations.

A full discussion on the issues concerning composition of FSMP, including issues raised by submitters is at Attachment 2.

In summary, FSANZ has proposed the following compositional requirements for inclusion in draft revised Standard 2.9.5:

- Prescribed minimum micronutrient limits for nutritionally complete FSMP as proposed at Draft Assessment and derived from the EU directive on FSMP (See Table 1 of the Appendix to Attachment 2).

- The minimum micronutrients for VLED to reflect Codex VLED parameters. In line with Codex, no minimum requirements have been proposed for biotin, pantothenic acid, vitamin K and manganese (See Table 2 of the Appendix to Attachment 2).

- Prescribed maximum micronutrient limits for nutritionally complete FSMP only for those micronutrients assessed as presenting a risk to safety from excessive intake (See Attachment 3). Maximum limits to apply to vitamin A, vitamin B6, vitamin D, calcium, zinc, iodine, manganese, copper and selenium (See Tables 1 and 2 of the Appendix to Attachment 2).

- Maximum limits to not apply to non-nutritionally complete FSMP.

- Prescribed macronutrient requirements for VLED based on the Codex Standard for VLED. This Standard provides minimum quantities for protein; carbohydrate; energy; and the essential fatty acids, linoleic acid and α-linolenic acid.

- Permission to deviate from the prescribed minimum limits for sodium and potassium to be extended to phosphorus to allow for the formulation of FSMP for particular medical conditions.

- Extending the list of permitted forms of nutritive substances (see Tables 3 and 4 of the Appendix to Attachment 2) to include permitted forms from:

    - Schedule 1 of Standard 2.9.1 – Infant Formula Products of the Code; and
    - Codex Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Children (CAC/GL 10-1979); and
    - Some additional nutritive substance forms that have been assessed for safety (See Section 5.1.5).

- Revising the unit of expression for VLED compositional requirements from daily quantity to per energy basis. The compositional requirements for all nutritionally complete FSMP to be expressed as per megajoule (MJ).

5.2.3 Labelling of FSMP

At Draft Assessment it was proposed that the majority of generic labelling requirements would apply to FSMP to meet FSANZ's statutory objectives of protecting public health and safety; providing adequate information to enable consumers to make informed choices; and to prevent misleading and deceiving conduct. However the possible impacts of withdrawal of FSMP from domestic markets, due to highly prescriptive labelling requirements, as previously discussed, is likely to have a greater impact on public health and safety than withdrawing the application of generic labelling requirements.

A detailed report on the issues associated with labelling FSMP, including issues raised by submitters, is at Attachment 4.

In the context of the aforementioned proposed overarching risk management approach for FSMP, FSANZ has reassessed the labelling requirements for FSMP and now proposes to ensure that information essential to the use of FSMP is available to consumers by applying a specific set of labelling provisions, which will include generic labelling requirements wherever the current range of FSMP can accommodate them.

Therefore, it is proposed that draft revised Standard 2.9.5 include:

- specific application of the following generic labelling requirements:

    - food identification requirements for FSMP allowing the name of the local supplier to be included on transportation outers or in accompanying documentation;
    - flexible ingredient labelling requirements for FSMP;
    - date marking for FSMP and allow flexibility in the format;
    - directions for use and storage of FSMP;
    - nutrition information requirements for FSMP and allow more flexibility in the presentation of this information; and
    - requirement to label FSMP with the condition, disease or disorder for which they have been specifically formulated.

- the following mandatory advisory statement and additional labelling:

    - that FSMP are to be used 'only under medical supervision'; and

- with a statement ‘advising if the product has been formulated for a specific age group’.

- for nutritionally complete FSMP (other than VLED) the mandatory advisory statement ‘not for parenteral use’.

- for VLED:

  - a warning statement ‘This product is for the dietary management of obesity’
  - the advisory statement ‘it is important to maintain an adequate daily fluid intake while using this product’; and
  - Insert the qualifier ‘except where medically indicated’ in the proposed advisory statement ‘the product may not be suitable for pregnant, lactating women or by infants, children, adolescents or the elderly’.

- exemption from:

  - mandatory allergen declaration;
  - percentage labelling requirements;
  - relevant aspects of the transitional standard on health claims; and
  - country of origin labelling.

5.3 Application of other Generic Standards

In addition to the Standards in Chapter 1 of the Code that relate to composition and labelling, there are a number of other generic Standards that are relevant to the development of regulations applying to FSMP. These include certain standards from the following sections of the Code:

- Part 1.3 - Substances Added to Foods (encompassing food additives and processing aids);

- Part 1.5 - Foods Requiring Pre-Market Clearance; and

- Part 1.6 - Microbiological and Processing Requirements.

5.3.1 Food additives and processing aids

A detailed food technology report is provided at Attachment 5.

A food additive is any substance not normally consumed as a food in itself and not normally used as an ingredient of food, but which is intentionally added to a food to achieve one or more technological functions specified in Schedule 5 of Standard 1.3.1 - Food Additives of the Code. A food additive may only be added to food where expressly permitted in Standard 1.3.1, and in order to achieve an identified technological function according to Good Manufacturing Practice (GMP).

As FSMP represent processed foods which are a general class of specific foods that are composed of a number of food ingredients, the use of all Schedule 2, 3 and 4 additives is technologically justified.

This can be achieved by including an entry for FSMP into Schedule 1 of Standard 1.3.1, which then provides Schedule 2, 3 and 4 permissions. As with all processed foods, the proportion of the additive used in any food must not exceed the maximum level necessary to achieve one or more technological functions under conditions of GMP. In simpler terms, additives that are not needed should not be added. For example, an approval to use flavour enhancers does not mean they have to be used.

All additives permitted in Category 0.1 – Preparations of food additives will be permitted in FSMP by virtue of the carry-over clause (Clause 7, Standard 1.3.1), where the preparations are used in an individual FSMP. That is, a flavoured product will be permitted to contain flavours and the additives permitted in the category, provided that the levels in the final food are no greater than would be introduced by the use of the flavour ingredient under proper technological conditions and GMP. This situation would be similar for a coloured FSMP or a FSMP that contains baking compounds.

Similarly, all additives permitted as antioxidants for edible oils will be permitted in individual FSMP by carry-over, if an edible oil which can contain the antioxidant is used as an ingredient. Foods that contain the preservatives, sorbates and benzoates can also be used as ingredients in FSMP, with similar carry-over permissions.

A processing aid is defined in Standard 1.3.3 as a substance used in the processing of raw materials, foods or ingredients, to fulfil a technological purpose relating to treatment or processing, but does not perform a technological function in the final food and the substance is used in the course of manufacture of a food at the lowest level necessary to achieve a function in the processing of a food, irrespective of any maximum permitted level specified.

Processing aids are prohibited for use in foods unless the provisions in Standard 1.3.3 give explicit permission to do so. As mentioned above, all Schedule 2 additives are generally permitted processing aids. FSMP are composed of ingredients or raw materials that are foods. The FSMP industry should not have any technological need for the use of processing aids outside of the current permissions.

5.3.1.1 Conclusion

The food additive permissions listed in Schedule 1, 2, 3 and 4 of Standard 1.3.1 – Food Additives, and the permissions for processing aids in Standard 1.3.3 are considered technologically justified and applicable to FSMP.

5.3.2 Foods requiring pre-market clearance

Part 1.5 of the Code contains standards for foods requiring pre-market clearance, namely:

- Standard 1.5.1 – Novel Foods;
- Standard 1.5.2 – Foods Products Using Gene Technology; and
- Standard 1.5.3 – Irradiation of Food.

These Standards require foods and ingredients to be approved as safe for consumption prior to sale if they are either novel, or produced using gene or irradiation technologies. They also contain, where prescribed, certain labelling requirements and other conditions of use.

Two submitters commented on the application of these Standards to FSMP. **BioActive Technologies** supported the application of pre-market clearance standards, however concern was expressed that the definition of 'novel foods' was too restrictive and would require the evaluation of ingredients that would otherwise be accepted with the use of a broader definition e.g. acceptance of foods that have a history of use in the global community, rather than just New Zealand and Australia. The **New Zealand Dietetic Association** commented that FSMP labels should contain information on genetic modification and irradiation.

5.3.1.2 Assessment

There are no apparent reasons why FSMP should be exempted from the requirements of these Standards, particularly given the formulated nature of the products involved and their targeted use by vulnerable individuals. FSMP, like all other foods, should meet the requirements of these Standards. Therefore, FSMP are expected to comply with the requirements of the Code in respect of novelty and the use of gene and irradiation technologies.

The Novel Foods Standard will be reviewed by FSANZ having regard to policy guidance from the Ministerial Council issued in December 2003. The review of the Standard will give consideration to the definitions for both 'non-traditional food' and 'novel food'.

5.3.1.3 Conclusion

FSMP will be required to comply with all of the requirements within the Part 1.5, which contains Standards for the pre-market clearance for novel foods, foods produced using gene technology and irradiated foods.

5.3.3 Microbiological standards

A detailed assessment of the microbiological issues for FSMP is at Attachment 6.

FSMP may be the sole source of nutrition for 'at-risk' individuals and therefore it is critical that these products are of high microbiological quality. The **New Zealand Dietetic Association** supported high microbiological standards given the higher risk status of the target consumer.

FSMP include ready-to-use liquid products and powdered formulas. Ready-to use liquid products are commercially sterile and if handled and prepared hygienically, pose no particular microbiological concern. Powdered products pose a higher microbiological risk than commercially sterile liquid products, as powdered products cannot be produced to be commercially sterile. However, a high microbiological quality should be achieved through adherence to good manufacturing and hygienic practices at the manufacturing facility.

As FSMP are highly specialised products, and there are only four multi-national companies that almost exclusively supply the Australian and New Zealand market for FSMP-type products, microbiological standards/criteria are not the best approach to manage their safety.

Instead, microbiological guidelines for FSMP are proposed to aid manufacturers in producing safe FSMP products. Such guidelines ensure preventive measures are implemented through the entire production and handling chain, and are to be published in 'The User Guide - Microbiological Limits for Food'[11].

5.3.3.1 Conclusion

To aid manufacturers in producing safe FSMP products microbiological guidelines for powdered FSMP are proposed (see Table 1 of Attachment 6)

5.4 Other Issues raised in Submissions

5.4.1 FSMP as a special purpose food

At Draft Assessment it was proposed that the FSANZ definition of special purpose foods, as applied to the Code, be broadened (bolded text) to incorporate FSMP, as per the Codex definition of foods for special dietary uses[12]:

> *foods that are specially processed or formulated to satisfy particular dietary requirements that exist because of a particular physical or physiological need* ***and/or specific diseases and disorders and which are presented as such***.

This definition was intended to be included as part of a commentary to *Part 2.9 – Special Purpose Foods* of the Code, to explicitly acknowledge the nature of the standards contained in Part 2.9[13], and of the underpinning regulatory principles for special purpose foods that consider not only the primary objective of safety but also efficacy.

Only one submitter, the **Australian Food and Grocery Council** (AFGC), commented on this matter indicating support for the broadening of the definition of special purpose foods. However, the AFGC also maintained that the acknowledgement of underpinning regulatory principles for special purpose foods is, in effect, the creation of government policy, which is no longer the responsibility of FSANZ. The AFGC recommended that advice be sought from the Ministerial Council for appropriate policy guidance in developing standards for special purpose foods, particularly FSMP.

5.4.1.1 Assessment

In developing or varying a food standard, the FSANZ Act sets specific objectives (see Section 4 above) for FSANZ, as well as matters the Authority must have regard to. These include having regard to: the promotion of consistency between domestic and international food standards; and any written policy guidelines formulated by the Ministerial Council and notified to FSANZ.

[11] http://www.foodstandards.gov.au/assistanceforindustry/userguides/microbiologicallimit1410.cfm
[12] Section 2.1 Codex General Standard for the Labelling of and Claims for Pre-packaged Foods for Special Dietary Uses, CODEX STAN 146-1985
[13] Part 2.9 contains standards for infant formula products (Standard 2.9.1), foods for infants (Standard 2.9.2), formulated meal replacements and supplementary foods (Standard 2.9.3), and formulated supplementary sports foods (Standard 2.9.4),

The general principles of the Codex Standard for the labelling of and claims for FSMP[14] require demonstration that FSMP are *safe and beneficial in meeting the nutritional requirements of persons for whom they are intended*. In addition, as FSMP target a vulnerable section of the population that has particular nutritional requirements because of medical conditions or disability, FSANZ considers it to be appropriate that the definition of special purpose foods, as currently applied to the Code, be broaden to include FSMP, in accordance with Codex.

The Ministerial Council recently (May 2004) endorsed a policy guideline on the fortification of foods with vitamins and minerals[15], the scope of which excludes special-purpose foods, including FSMP. At the same time, the Ministerial Council agreed to review the scope and intent of Part 2.9 of the Code to ensure that interpretation of special purpose foods is agreed and clear.

As previously indicated, FSANZ originally intended, as part of this Proposal, to preface Part 2.9 of the Code with a commentary, which would include the expanded definition of special purpose foods (bolded), as follows:

> *The Standards in Part 2.9 recognise special purpose food in the food supply, which differ from other food because they provide nutrition to at-risk groups whose dietary requirements cannot always be satisfied by a normal (solid food) diet.*
>
> ***Special purpose food is food that has been specially processed or formulated to satisfy particular dietary requirements that exist because of a particular physical or physiological need, and / or specific diseases and disorders**. In this case, the phrase particular dietary requirements refers to nutritional requirements that cannot be met by consumption of a normal diet. Physical and physiological need includes reference to normal states in the life cycle such as pregnancy and lactation, as well as physical (including lifestyle) and physiological conditions that occasion the use of special purpose food.*
>
> *Special purpose food may be permitted to contain added nutritive substances (as defined under Standard 1.1.1) that are not permitted for addition to other food.*
>
> *The compositional provisions in these Standards for special purpose food are complemented by additional labelling requirements to advise on the safe and appropriate use of such food including, where necessary, labelling requirements for use under health professional supervision and advice where relevant against inappropriate use. Other requirements include restrictions on access and advertising of certain special purpose food.*

Given that the Ministerial Council is now to consider special purpose foods, and in particular Part 2.9 of the Code, FSANZ has deferred inclusion of the above commentary pending policy guidance from the Ministerial Council.

[14] Codex Standard for the Labelling of and Claims for Foods for Special Medical Purposes (CODEX STAN 180-1991)
[15] http://www.foodsecretariat.health.gov.au/policydocs.htm

5.4.1.2 Conclusion

The proposal to broaden the definition of special purpose foods, in accordance with Codex, to incorporate FSMP, has been maintained as at Draft Assessment. However the proposed inclusion of a commentary to Part 2.9 has been deferred pending ministerial policy advice.

5.4.2 Definitions

5.4.2.1 The definition of FSMP

At Draft Assessment the following definition was proposed:

> '**food for special medical purposes** means a category of special-purpose food specifically processed or formulated and presented for the dietary management of persons for use solely under medical supervision. Food for special medical purposes are those intended for –
>
> (a) the exclusive or partial feeding of persons with limited or impaired capacity to take, digest, absorb or metabolise ordinary food or certain nutrients in the food; or
> (b) persons who have other special medically-determined nutrient requirements whose dietary management cannot be achieved solely by modification of the normal diet or by using other special-purpose food whether or not combined with the normal diet'.

The majority of submitters were supportive of this definition, although the following editing changes (bold type) were suggested:

- Expansion of 'medical supervision' to include supervision by dietitians;
- '…**and/or** presented for the dietary management of persons and **should be** used under medical supervision…';
- '…impaired capacity to take, digest, absorb, metabolise **or excrete** ordinary food…'; and
- '…dietary management **may not** be achieved solely…'.

The **South Australian Department of Human Services** did not support the definition in the proposed format as it excludes VLED. It was mentioned that obese patients do not have a limited capacity to take, absorb or metabolise ordinary food; and that obesity can be readily managed by a normal diet.

Assessment

The definition provided at Draft Assessment was developed through the adoption of the Codex definition of FSMP, including minor edits to ensure consistency with the remainder of the Code. Therefore, in the interests of harmonising with an internationally accepted definition, further changes can only be made where it is determined that the definition does not suitably reflect the purpose, use, or range of FSMP.

The term 'use under medical supervision' is recognised as a defining feature of FSMP and these words are included in all international FSMP regulations. Although the provision of FSMP by other health professionals is common practice, medical practitioners still provide overall supervision of patient care. In this situation, the words 'medical supervision' remain applicable and do not exclude the provision of, or advice on the use of, FSMP by other health professionals.

The inclusion of 'and/or' or 'should be' within the sentence on medical supervision removes the necessity to provide these products under medical guidance and cannot, therefore, be accepted.

The EC Directive (Directive 1999/21/EC) on 'dietary foods for special medical purposes' has adopted the Codex definition of FSMP but incorporates minor changes including *'or excrete'*. Therefore in the interest of harmonising with relevant overseas regulations *'or excrete'* is a suitable inclusion in the definition as revised at Preliminary Final Assessment.

The suggested replacement of 'cannot' by 'may not' in part b) of the definition is inappropriate. FSMP are usually the last essential dietary option for the nutritional support of individuals with medical conditions or disorders. Foods that only assist the management of special diets rather than act as an essential dietary component are more appropriately regulated under other standards e.g. Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods. The inclusion of 'may not' would potentially expand the scope of draft Standard 2.9.5 to include these foods.

For a food to comply with the definition proposed at Draft Assessment, it must conform with the first sentence as well as one of the criteria in parts a) or b). VLED comply with this definition as they are formulated for use under medical supervision (first sentence), and meet the criteria in part b) through their main function of being used only for the dietary management of morbid obesity.

As discussed above, Standard 2.9.3 applies more to products that are non-essential for the dietary management of a medical condition and complement normal dietary patterns. VLED, as captured under draft Standard 2.9.5, are not for use with weight conditions that can be managed by dietary modification to the normal diet, as these products replace the entire diet. It will be necessary for a supervising health professional to determine whether an obese condition is severe enough to warrant the use of VLED.

Conclusion

The definition proposed at Draft Assessment is to be revised by including the words 'or excrete' before 'ordinary foods' in part a). This change will bring the definition in line with other relevant overseas regulations.

5.4.2.2 The definition of protein

The definition of 'protein' provided in draft Standard 2.9.5 reads: '**protein** means protein which has a protein digestibility-corrected amino acid score of 1 when determined by the method prescribed in Schedule 4'. **Nestlé Australia** submitted that both the definition of protein and the method provided in Schedule 4 were inappropriate for all FSMP, as neither is provided in other parts of the Code or in overseas regulations.

Assessment

A definition of protein has been provided in draft Standard 2.9.5 because there is evidence demonstrating that an adequate intake of quality protein is important during a very low energy diet to prevent serious complications occurring from malnutrition[16,17]. Codex [18] regulations do contain prescribed compositional requirements for both quantity and quality of protein in VLED. Schedule 4 has been provided as a means of incorporating these compositional requirements into draft Standard 2.9.5.

VLED are the only class of FSMP in draft Standard 2.9.5 that have a specific reference to protein requirements. Therefore, as this reference is absent from compositional requirements for other FSMP, the Schedule 4 protein requirements do not apply to these foods.

Conclusion

To protect the health of VLED consumers, it is necessary for these products to provide adequate amounts of high quality protein. Therefore the requirement to meet specified protein quality criteria remains. However, for clarification purposes draft Standard 2.9.5 will be revised to ensure that this requirement only applies to the compositional requirements for VLED.

5.4.2.3 Regulating VLED under a FSMP standard

The **South Australian Department of Human Services** commented in their submission that VLED have different risks and issues from those identified for FSMP. Therefore, it was recommended that VLED be included as a separate category in Part 2.9 of the Code.

Assessment

VLED have been included under the proposed FSMP standard as they have very similar attributes in their sale and use. In particular, VLED can be categorised by the defining feature of requiring use under medical supervision. It is therefore reasonable to include VLED within a FSMP standard, and separating the two categories would only result in duplicating standards with the potential for unnecessary regulatory confusion.

Conclusion

Given that VLED are regarded as having attributes of FSMP, it is appropriate to regulate VLED as FSMP.

[16] Nutritional Taskforce on the Prevention and Treatment of Obesity; (1993); *Very Low-Calorie Diets*; JAMA, Vol 270(8): 967-974.

[17] Pi-Sunyer FX (1994); *Obesity* in: Shils ME (ed) Olsen JA (ed) Shike M (ed) (1994), 8th Edition; *Modern Nutrition in Health and Disease;* Lea & Febiger, Philadelphia; p96.

[18] Codex Standard on Formula Foods for use in Very Low Energy Diets for Weight Reduction (CODEX STAN 203-1995)

5.4.2.4 Transitional arrangements

It was proposed at Draft Assessment that the FSMP standards would have a transition period of two years and a stock-in-trade period of one year, to allow manufacturers and distributors of FSMP sufficient time to modify their products accordingly. Comments received from industry submitters have indicated that the transition period is too short and should be extended to four years, with a further stock-in-trade period of two years due to the long shelf life of FSMP products.

Assessment

It is understood from industry submissions that an extension to the transition period has been requested as a means of adjusting to the prescriptive requirements proposed at Draft Assessment. As draft Standard 2.9.5 has been significantly modified at Preliminary Final Assessment to reduce its level of prescription, it is anticipated that FSMP manufacturers will no longer require a transition period beyond that allowed for the implementation of other food standards. The two-year transition period is consistent with the recent implementation of Standard 2.9.1 – Infant Formula Products, which contains more prescriptive requirements than draft Standard 2.9.5.

Conclusion

A two-year transition period has already been applied to other similar products with more prescriptive regulatory requirements than draft Standard 2.9.5, and it is therefore appropriate to apply a similar transition period to FSMP.

6. Regulatory Options

Since Draft Assessment the options for the regulation of FSMP have been further refined. The option (Option 2 at Draft Assessment) of regulating FSMP with a discrete standard including prescribed compositional and labelling requirements has been re-considered and further developed on the basis of submitters' comments. There are two options being proposed at Preliminary Final Assessment.

6.1 Option 1 – Status Quo

This option maintains the *status quo* as there would be no specific regulation of FSMP in the Code, and therefore no overt recognition of FSMP under food law in either Australia or New Zealand.

6.2 Option 2 – Regulation of FSMP by a discrete standard with the application of an overarching risk management framework.

Under this option, a discrete Standard for FSMP would be included in Part 2.9 - Special Purpose Food of the Code incorporating specific compositional and labelling requirements, which are in general, consistent with relevant overseas regulations, in addition to the application of an overarching risk management framework consisting of mandatory advisory labelling for use under medical supervision, and restrictions on the sale and advertising of FSMP to the general public.

7. Impact Analysis

7.1 Affected Parties

The parties affected by this Proposal are: **consumers** in general (i.e. unintended users) and **target consumers** with medical conditions including very vulnerable groups such as the disabled and chronically ill (i.e. intended users); Australian and New Zealand **industry** including importers of FSMP, retail outlets such as pharmacies and a small number of local FSMP manufacturers; and the **Governments** of New Zealand and Australia, including the States and Territories, in particular enforcement agencies and government provided health services.

7.2 Cost-Benefit Assessment of Regulatory Options

In order to determine the most cost-effective regulatory option for FSMP, FSANZ is required to assess the relative costs and benefits of each option as it impacts on the identified affected parties.

Option 1 - Status Quo

Under this option there would be no change to the current regulatory situation for FSMP.

It is likely that **consumers** will be unaware of any impact of this option, as it is expected that they will continue to access the current range of products, some of which are only consumed by a small number of individuals with very special dietary requirements. However, **consumers** may experience possible interruptions to supply through product delays at the border resulting from the regulatory uncertainty for enforcement. Such delays could expose **consumers** to higher public health and risks, although it is known that this problem only occurs intermittently.

As the vast majority of products are imported from either the European Union or the United States of America, the regulatory requirements of the exporting market overseas will, in general, continue to provide adequate public health and safety protection for the Australian and New Zealand population. However, some **consumers** may perceive the lack of specific domestic regulations under Option 1 as poor assurance of the protection of health and safety for FSMP consumers, who are mostly a vulnerable population group.

The **industry** will be able to continue local manufacture under Option 1, albeit minimal, and import currently available products as well as new FSMP products. However, the lack of specific regulations for FSMP means that there is no guidance for **industry** in complying with the Code, and there is greater likelihood that the supply of FSMP products will be interrupted by enforcement activities, creating greater expense for **industry** importers of FSMP. Domestic manufacturers will not incur this expense, as local production represents a very minor component of the FSMP market.

By maintaining the status quo it is likely that the **government** health care system will continue to access the currently available FSMP products. However, the uncertainty caused by the lack of recognition of FSMP in the Code will remain, and will continue to require government agencies to devote time and resources into clarifying the enforcement of FSMP, which currently impairs **industry's** ability to operate in an efficient and effective manner.

In addition, the lack of regulatory certainty disadvantages **government**-provided health services that may seek to use compliance with the Code as a quality indicator when negotiating tender contract with suppliers of FSMP.

Option 2 - Regulation by a discrete standard in the Code.

Overall, Option 2 will provide greater clarity in the regulatory environment by establishing uniform regulations between Australia and New Zealand as well as, harmonising with international regulations where possible.

For **industry**, there is likely to be significantly less confusion under Option 2, as clear regulations would provide certainty on compliance with domestic regulations, and legal recognition for new innovative products and technological advances. The clarity of regulations may make enforcement easier for **governments**, thereby using fewer resources, and is likely to minimise importation delays resulting in less expense to **industry** importers of FSMP.

The impact of Option 2 on **target consumers** is likely to be minimal as the proposed regulation involving mandatory advisory labelling, and restrictions on the sale and advertising to the general public are not expected to affect the current access arrangements or costs of FSMP to consumers. Similarly, **industry**, specifically direct suppliers of FSMP such as pharmacies and wholesalers, will not be disadvantaged, as consumers will continue to access FSMP through these suppliers.

The risks to unintended **consumers** of FSMP will be reduced, as there is less likelihood that unintended **consumers** will access FSMP and consume products unsupervised. In addition the restriction on sale and advertising of FSMP will act as a disincentive for the inappropriate positioning of products as FSMP to take advantage of fewer regulatory controls, and therefore protects **consumers** from being misled and maintains the integrity and reputation of the *bona fide* FSMP **industry**.

There may be costs to **industry** associated with any minor reformulation or labelling changes required by Option 2. However this is likely to be very minimal given the flexible approach being applied to compositional and labelling requirements, which in general, harmonise with international standards. This harmonisation also means that trade is not jeopardised for **industry**.

8. Consultation

8.1 Public Consultation

Public consultation for Proposal P242 was conducted from 18 December 2002 to 24 March 2003. Seventeen separate submissions were made during this period; a summary of the issues raised in these submissions can be found at Attachment 7. The comments and information provided in submissions has assisted with the preparation of this Preliminary Final Assessment Report.

At Draft Assessment there was support for inclusion of a discrete standard in the Code, although, the majority of submitters expressed significant concern that a prescriptive standard would adversely impact on the cost and availability of FSMP.

On the basis of comments received, FSANZ has reconsidered the proposed approach to regulation of FSMP.

Given the complexity of issues involved and the significant change to the proposed regulation of FSMP, FSANZ is now seeking further comment on this Preliminary Final Assessment prior to making a Final Assessment on a preferred regulatory approach to FSMP.

8.2 Stakeholder Consultations

In addition to public consultation, FSANZ held targeted consultations with both industry and health professional stakeholder groups in Australia and New Zealand. This consultation has assisted FSANZ in revising the proposed approach to regulation of FSMP at Preliminary Final Assessment. Stakeholders have indicated support of the proposed regulatory approach at Preliminary Final Assessment as being least likely to affect the cost and availability of FSMP, but also in managing the risks associated with the inappropriate use of FSMP.

8.3 World Trade Organization (WTO)

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

The WTO was notified of Proposal P242 through Technical Barrier to Trade (TBT) notifications G/TBT/N/AUS/13 and G/TBT/N/NZL/12. The only response received on these notifications was from the European Commission that included concerns relating to the ability for FSMP to deviate from compositional requirements. These concerns have been addressed within the assessment of compositional issues provided at Attachment 2.

9. Conclusion and Recommendation

By maintaining the *status quo* as per Option 1, consumers are unlikely to be aware of any impact except where imported FSMP may be delayed at national borders, whereas there will continue to be negative impacts for both industry and government caused by the current regulatory uncertainty for FSMP.

However when compared to Option 1, Option 2 provides greater benefits for all affected parties.

In addition to providing greater regulatory certainty for both industry and government, Option 2 minimises the risks to consumers by ensuring continued access to FSMP for intended consumers; reduced potential for misuse by unintended consumers; and assures the provision of sufficient information to allow health professionals and consumers to make choices about the safe and effective use of FSMP.

Option 2 provides clarity of regulation for industry and enforcement agencies, resulting in a uniform FSMP standard applying to Australia and New Zealand, which in general, harmonises with relevant overseas regulations and consequently will not unduly restrict trade.

For these reasons, Option 2 is considered the more suitable option in meeting the regulatory objectives. Therefore, it is recommended that the proposed amendments (Attachment 1), incorporating a draft standard for FSMP, be approved for the following reasons:

- the inclusion of a standard for FSMP in the Code provides clear, uniform regulation of FSMP in Australia and New Zealand;

- the explicit recognition of FSMP in the Code provides regulatory certainty for industry and for government enforcement agencies;

- the regulation of FSMP provides assurance for consumers of protection of public health and safety, particularly for the target group being a vulnerable population;

- the inclusion of FSMP as a 'special purpose food' recognises that these foods are designed for a particular vulnerable target group;

- the inclusion of restriction on the sale and advertising of FSMP to the general public protects the public health and safety of both intended and unintended users of FSMP, particularly in the absence of medical or health professional supervision; and

- there is consistency with international regulations, wherever possible, to prevent potential barriers to trade that could jeopardise the supply of FSMP products to Australia/New Zealand.

10. Implementation and review

Following further consultation, a Final Assessment Report for this Proposal will be prepared for consideration by the FSANZ Board. If approved by the FSANZ Board, notification will be made to the Ministerial Council and it is anticipated that the proposed revised draft standard would come into effect shortly thereafter upon gazettal, subject to any request from the Ministerial Council for a review.

FSANZ expects that a transition period of two years would apply to allow manufacturers and importers of FSMP sufficient time to comply with the proposed new standard for FSMP.

Monitoring and review of the impact of this regulatory change is likely to occur, in due course, as part of the general evaluation program that FSANZ has in place to evaluate the effectiveness of new standards.

ATTACHMENTS

1. Draft Variation to the *Australia New Zealand Food Standards Code*
2. Compositional Assessment
3. Safety Assessment
4. Labelling Assessment
5. Food Technology Report
6. Microbiological Evaluation Report
7. Summary of Submissions

Attachment 1

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

To commence: on gazettal

[1] ***The Australia New Zealand Food Standards Code*** *is varied by omitting from the* Table of Contents*, Part 2.9, substituting –*

PART 2.9 Special Purpose Food

Standard 2.9.1 Infant Formula Products
Standard 2.9.2 Foods for Infants
Standard 2.9.3 Formulated Meal Replacements and Formulated Supplementary Foods
Standard 2.9.4 Formulated Supplementary Sports Foods
Standard 2.9.5 Food for Special Medical Purposes

[2] ***Standard 1.1.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in the table to clause 8 –*

MJ	megajoule

[3] ***Standard 1.1A.6*** *of the Australia New Zealand Food Standards Code is varied by omitting clause 2, substituting –*

(1) Subject to subclause (2), for the matters regulated in this Standard, food produced in or imported into New Zealand must comply with this Standard or Standard 2.9.5, but not a combination of both.

(2) This Standard does not apply to food produced in or imported into Australia.

(3) This Standard ceases to have effect two years from the commencement of Standard 2.9.5.

[4] ***Standard 1.2.3*** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *inserting in the* Table to clause 2 –

Food for special medical purposes	Statement to the effect that the product must be used under medical supervision
Nutritionally complete food for special medical purposes, other than formula for very low energy diets	Statement to the effect that the product is not for parenteral use
Formula for very low energy diets	Statements to the effect that – 1. except where medically indicated, the product may not be suitable for pregnant or lactating women, or for infants, children, adolescents or the elderly; and 2. it is important to maintain an adequate daily fluid intake when using the product

[3.2] *inserting in the* Table to clause 3 –

Formula for very low energy diets	This product is for the dietary management of obesity

[5] ***Standard 1.2.8*** *of the Australia New Zealand Food Standards Code is varied by omitting paragraph 3(p), substituting –*

(p) kava as standardised in Standard 2.6.3; or
(q) a food standardised in Standard 2.9.5.

[6] ***Standard 1.2.10*** *of the Australia New Zealand Food Standards Code is varied by omitting paragraph 2(4)(i), substituting –*

(i) alcoholic beverages standardised in Part 2.7 of this Code; or
(j) food standardised in Standard 2.9.5.

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

[6.1] *omitting from* Schedule 1, Item 13 FOODS INTENDED FOR PARTICULAR DIETARY USES, *substituting –*

13 SPECIAL PURPOSE FOOD

[6.2] *inserting in Schedule 1 after Item 13.4.2 –*

13.5 Food for special medical purposes*

[8] ***The Australia New Zealand Food Standards Code*** *is varied by inserting after* Standard 2.9.4 –

STANDARD 2.9.5

FOOD FOR SPECIAL MEDICAL PURPOSES

Purpose

This Standard provides for the compositional (including nutritional) and labelling requirements of food specially formulated for the dietary management of individuals with certain medical conditions, disease states or disabilities. Food regulated in this Standard is characterised by the need for medical supervision in their use. This Standard does not apply to Infant Formula Products as they are regulated by Standard 2.9.1, nor does it apply to Formulated Meal Replacements and Formulated Supplementary Foods as they are regulated by Standard 2.9.3.

The formulation of food for special medical purposes should be based on sound medical and nutritional principles. The use of the food should have been demonstrated, by scientific evidence, to be safe and effective in meeting the particular nutritional requirements of persons for whom the food is intended.

Standard 1.1.1 defines 'nutritive substance' and 'average quantity' for the purposes of this Code. General labelling requirements contained in Part 1.2 do not apply to food for special medical purposes unless specified in this Standard. Standard 1.3.1 contains permissions for food additives that may be used. Standard 1.3.4 contains specifications for permitted nutritive substances and particular fatty acids. Standard 1.5.1 contains provisions relating to the sale of novel food and novel food ingredients.

Table of Provisions

Division 1 – Preliminary
1 Interpretation
2 Application

Division 2 – Composition
3 General restrictions on composition
4 Permitted nutritive substances
5 Additional compositional requirements for formula for very low energy diets

Division 3 – Sale, Advertising and Labelling
6 Restriction on premises at which and the persons by whom food for special medical purposes may be sold
7 Prohibition on sale if advertising directed to consumers
8 Application of labelling requirements

Schedule 1 Nutritive substances and their permitted forms
Schedule 2 Minimum and maximum vitamin, mineral and electrolyte amounts for nutritionally complete food for special medical purposes other than formula for very low energy diets
Schedule 3 Minimum and maximum vitamin, mineral and electrolyte amounts for formula for very low energy diets
Schedule 4 Prescribed method of analysis for protein

Division 1 – Preliminary

Clauses

1 Interpretation

(1) In this Code –

food for special medical purposes means a category of special purpose food specifically processed or formulated, and presented, for the dietary management of persons for use solely under medical supervision. Food for special medical purposes are those intended for –

(a) the exclusive or partial feeding of persons with limited or impaired capacity to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients in the food; or

(b) persons who have other special medically determined nutrient requirements whose dietary management cannot be achieved solely by modification of the normal diet or by using other special purpose food whether or not combined with the normal diet.

formula for very low energy diets means food for special medical purposes that is a nutritionally complete formula presented for use in energy restricted diets for the dietary management of obesity.

nutritionally complete means a formulation which may constitute the sole source of nutrition for the persons for whom the formulation is intended when it is used in accordance with the manufacturer's directions.

(2) In this Standard –

advertisement directed to consumers means any advertisement other than one directed exclusively to –

(a) medical practitioners, psychologists, dentists, pharmacists, physiotherapists, dietitians, nurses, speech pathologists or scientists working in medical laboratories; or

(b) persons who are –

(i) engaged in the business of wholesaling food for special medical purposes; or

(ii) purchasing officers in hospitals; or

(c) members of disease and disorder support groups.

retail sale means sale to the public.

(3) Food for special medical purposes do not include infant formula products or formulated meal replacements and formulated supplementary food standardised in this Code.

2 Application

(1) Food for special medical purposes is taken to comply with this Standard for a period of 24 months after the commencement of this Standard.

(2) Subclause 1(2) of Standard 1.1.1 does not apply to food for special medical purposes.

Editorial note:

This means that food for special medical purposes will have a two year transitional period to comply with this standard.

Division 2 - Composition

3 General restrictions on composition

A vitamin, mineral or other nutritive substance must not be added to food for special medical purposes unless expressly permitted in this Standard.

4 Permitted nutritive substances

(1) A nutritive substance listed in column 1 of Schedule 1 of this Standard or Standard 2.9.1 may be added to food for special medical purposes provided that the nutritive substance is in one or more of the corresponding forms listed in column 2 of Schedule 1 of this Standard or Standard 2.9.1.

(2) Nutritionally complete food for special medical purposes, other than formula for very low energy diets –

(a) may contain vitamins, minerals and electrolytes only in the corresponding amount range specified in Schedule 2; and
(b) may vary in the minimum amount of sodium, potassium and phosphorus specified in Schedule 2 to satisfy particular medical conditions.

(3) Formula for very low energy diets –

(a) may contain vitamins, minerals and electrolytes only in the corresponding amount range specified in Schedule 3; and
(b) may have added to them, L-amino acids listed in column 1 of Schedule 1 only in an amount necessary to comply with paragraph 5(2)(c).

5 Additional compositional requirements for formula for very low energy diets

(1) Formula for very low energy diets must contain no less than 1.88 MJ and no more than 3.35 MJ in a recommended daily intake of the food.

(2) Formula for very low energy diets must contain, in a recommended daily intake of the food, no less than –

(a) 3 g linoleic acid and 0.5 g alpha-linolenic acid, and have a ratio of linoleic acid to alpha-linolenic acid of between 5 and 15; and
(b) 50 g available carbohydrate determined in accordance with the definition of carbohydrate under Standard 1.2.8; and
(c) 50 g protein that has a protein digestibility – corrected amino acid score of 1 when determined by the method prescribed in Schedule 4.

Division 3 – Sale, Advertising and Labelling

6 Restriction on premises at which and the persons by whom food for special medical purposes may be sold

Food for special medical purposes may only be sold by way of retail sale –

(a) from a pharmacy, hospital or nursing home; or
(b) by a medical practitioner; or
(c) by a person otherwise engaged in the business of wholesaling food for special medical purposes to medical practitioners, pharmacies, hospitals or nursing homes.

7 Prohibition on sale if advertising directed to consumers

Food for special medical purposes must not be sold if it is promoted by any advertisement directed to consumers.

8 Application of labelling requirements

The label on a package of food for special medical purposes must include the information prescribed in this clause.

(2) The labelling requirements contained in Standards in Parts 1.1A and 1.2 of this Code do not apply to food for special medical purposes, except for the Standards listed in column 1 of the Table to this subclause subject to any conditions or variations listed in column 2 of the Table to this subclause.

Table to subclause 8(2)

Column 1	Column 2
Standard	**Conditions**
Standard 1.1A.2, except subclause (3)(d)	
Standard 1.2.2	The information required by clause 3 is only required on the transportation outer or in documentation accompanying the food
Clause 2 of Standard 1.2.3	Only as it relates to advisory statements for food for special medical purposes
Clause 3 of Standard 1.2.3	Only as it relates to warning statements for food for special medical purposes
Standard 1.2.4	Food for special medical purposes must comply with Standard 1.2.4, Article 6 of Directive 2000/13/EC of the European Parliament and of the Council as at the date of commencement of this Standard, or 21CFR101.4 of the US Code of Federal Regulations as at the date of commencement of this Standard, but not a combination of any of these
Standard 1.2.5	An expiry date may be used as an alternative to a use-by date
Standard 1.2.6	
Clauses 15 and 16 of Standard 1.2.8	

(3) The label on a package of food for special medical purposes must include, in the form of a table or otherwise, the following information –

(a) the average or minimum energy content expressed per given quantity of the food; and

(b) the average or minimum quantity of protein, fat and carbohydrate expressed per given quantity of the food; and

(c) the average or minimum quantity of vitamins, minerals and electrolytes expressed per given quantity of the food; and

(d) the average or minimum quantity of other nutritive substances except L-amino acids added in accordance with paragraph 4(3)(b), if added to the food, expressed per given quantity of the food.

(4) The label on a package of food for special medical purposes, other than a formula for very low energy diets, must include a statement advising if the product has been formulated for a specific age group.

(5) Where food for special medical purposes have been specifically formulated for a condition, disease or disorder, the label on the package of the food must include a statement indicating the condition, disease or disorder, and any nutritional modifications for which the food has been specifically formulated.

SCHEDULE 1

NUTRITIVE SUBSTANCES AND THEIR PERMITTED FORMS

Column 1	Column 2
Nutritive Substance	**Permitted Form**
Vitamins	
Niacin	Nicotinic acid
Vitamin B_6	Pyridoxine dipalmitate
Vitamin E	d-alpha-tocopherol
Pantothenic acid	sodium pantothenate
Minerals	
Chromium	Chromium chloride
	Chromium potassium sulphate
Chlorine	Choline chloride
	Sodium chloride, iodised
	Hydrochloric acid
Copper	Copper-lysine complex
	Cupric carbonate
Fluoride	Potassium fluoride
	Sodium fluoride
Iodine	Sodium iodate
Iron	Carbonyl iron
	Electrolytic iron
	Ferric citrate
	Ferric gluconate
	Ferric orthophosphate
	Ferric pyrophosphate, sodium
	Ferric saccharate
	Ferric sodium diphosphate
	Ferrous carbonate
	Ferrous carbonate, stabilised
	Iron, reduced (ferrum reductum)

Magnesium	Magnesium acetate
	Magnesium citrate
	Magnesium glycerophosphate
	Magnesium hydroxide
	Magnesium hydroxide carbonate
	Magnesium lactate
Manganese	Manganese glycerophosphate
Molybdenum	Ammonium molybdate
Phosphorus	Magnesium phosphate, tribasic
	Potassium glycerophosphate
Potassium	Potassium lactate
Selenium	Sodium hydrogen selenite
	Sodium selenate
Zinc	Zinc carbonate
	Zinc citrate
	Zinc lactate
Other Nutritive Substances	
Amino acids	Cystine
	Glycine
	L-alanine
	L-arginine
	L-asparagine
	L-aspartic acid
	L-citrulline
	L-cysteine
	L-glutamic acid
	L-glutamine
	L-lysine acetate
	L-ornithine
	L-proline
	L-serine
	L-arginine-L-aspartate
	L-lysine-L-aspartate
	L-lysine-L-glutamate
	N-acetyl-L-methionine
	Cystine hydrochloride
	Glycine hydrochloride
	L-alanine hydrochloride
	L-arginine hydrochloride
	L-asparagine hydrochloride
	L-aspartic acid hydrochloride
	L-citrulline hydrochloride
	L-cysteine hydrochloride
	L-glutamic acid hydrochloride
	L-glutamine hydrochloride
	L-lysine hydrochloride
	L-ornithine hydrochloride
	L-proline hydrochloride
	L-serine hydrochloride
	Sodium cystine
	Sodium glycine
	Sodium L-alanine
	Sodium L-arginine
	Sodium L-asparagine
	Sodium L-aspartic acid
	Sodium L-citrulline

	Sodium L-glutamic acid
	Sodium L-glutamine
	Sodium L-lysine acetate
	Sodium L-ornithine
	Sodium L-proline
	Sodium L-serine
	Potassium cystine
	Potassium glycine
	Potassium L-alanine
	Potassium L-arginine
	Potassium L-asparagine
	Potassium L-aspartic acid
	Potassium L-citrulline
	Potassium L-glutamic acid
	Potassium L-glutamine
	Potassium L-lysine acetate
	Potassium L-ornithine
	Potassium L-proline
	Potassium L-serine
Carnitine	L-carnitine
	L-carnitine hydrochloride
Choline	Choline
	Choline bitartrate
	Choline chloride
	Choline citrate
	Choline hydrogen tartrate
Inositol	Inositol
Nucleotides	Adenosine 5'-monophosphate
	Adenosine 5'-monophosphate sodium salt
	Cytidine 5'-monophosphate
	Cytidine 5'-monophosphate sodium salt
	Guanosine 5'-monophosphate
	Guanosine 5'-monophosphate sodium salt
	Inosine 5'-monophosphate
	Inosine 5'-monophosphate sodium salt
	Uridine 5'-monophosphate
	Uridine 5'-monophosphate sodium salt
Taurine	Taurine

SCHEDULE 2

MINIMUM AND MAXIMUM VITAMIN, MINERAL AND ELECTROLYTE AMOUNTS FOR NUTRITIONALLY COMPLETE FOOD FOR SPECIAL MEDICAL PURPOSES OTHER THAN FORMULA FOR VERY LOW ENERGY DIETS

Column 1	Column 2	Column 3
Nutrient	**Minimum Amount per MJ**	**Maximum Amount per MJ**
Vitamins		
Vitamin A	84 μg retinol equivalents	345 μg retinol forms only
Thiamin	0.15 mg	No maximum set
Riboflavin	0.2 mg	No maximum set
Niacin	2.2 mg niacin equivalents	No maximum set
Vitamin B_6	0.2 mg	2.9 mg
Folate	25 μg	No maximum set
Vitamin B_{12}	0.17 μg	No maximum set

Column 1	Column 2	Column 3
Nutrient	**Minimum Amount per MJ**	**Maximum Amount per MJ**
Vitamin C	5.4 mg	No maximum set
Vitamin D	1.2 μg	5.7 μg
Vitamin E	0.5 mg alpha-tocopherol equivalents per g of polyunsaturated fatty acids expressed as linoleic acid, but in no case less than 10 mg alpha-tocopherol equivalents per MJ	No maximum set
Biotin	2 μg	No maximum set
Pantothenic Acid	0.35 mg	No maximum set
Vitamin K	8.5 μg	No maximum set
Minerals		
Calcium	84 mg	287 mg
Magnesium	18 mg	No maximum set
Iron	1 mg	No maximum set
Phosphorus	72 mg	No maximum set
Zinc	1 mg	4.6 mg
Manganese	0.12 mg	1.32 mg
Copper	0.15 mg	1.15 mg
Iodine	15.5 μg	115 μg
Chromium	3 μg	No maximum set
Molybdenum	7 μg	No maximum set
Selenium	6 μg	46 μg
Electrolytes		
Sodium	72 mg	No maximum set
Potassium	190 mg	No maximum set
Chloride	72 mg	No maximum set

SCHEDULE 3

MINIMUM AND MAXIMUM VITAMIN, MINERAL AND ELECTROLYTE AMOUNTS FOR FORMULA FOR VERY LOW ENERGY DIETS

Nutrient	Minimum Amount per MJ	Maximum Amount per MJ
Vitamins		
Vitamin A	319 μg retinol equivalents	896 μg retinol forms only
Thiamin	0.43 mg	No maximum set
Riboflavin	0.6 mg	No maximum set
Niacin	5.9 mg niacin equivalents	No maximum set
Vitamin B_6	1.1 mg	7.5 mg
Folate	106 μg	No maximum set
Vitamin B_{12}	0.53 μg	No maximum set
Vitamin C	16 mg	No maximum set
Vitamin D	1.3 μg	14.9 μg
Vitamin E	5 mg alpha-tocopherol equivalents	No maximum set
Minerals		
Calcium	266 mg	746 mg
Magnesium	186 mg	No maximum set
Iron	9 mg	No maximum set

Phosphorus	266 mg	No maximum set
Zinc	3 mg	11.9 mg
Manganese	No minimum set	3.43 mg
Copper	0.8 µg	3 µg
Iodine	74.5 µg	298.5 µg
Selenium	No minimum set	119 µg
Electrolytes		
Sodium	306 mg	No maximum set
Potassium	1649 mg	No maximum set

SCHEDULE 4

PRESCRIBED METHOD OF ANALYSIS FOR PROTEIN

The protein digestibility – corrected amino acid score is to be determined by the method set out in section 8 of the *FAO (Food and Agriculture Organization) Food and Nutrition Paper No. 51 (1991) Protein quality evaluation,* Report of Joint FAO/WHO Expert consultation, FAO, Rome.

The data for determining the protein digestibility-corrected amino acid score may be derived from one or more of the following:

(i) the manufacturer's analysis of the food; and
(ii) calculation from the actual quantity and proportion of amino acids in the ingredients used; and
(iii) calculation from generally accepted amino acid data.

Tables 8 and 11 of the *FAO (Food and Agriculture Organization) Food and Nutrition Paper No. 51 (1991) Protein quality evaluation,* Report of Joint FAO/WHO Expert consultation, FAO, Rome, may be used as a reference for selecting an appropriate true protein digestibility factor.

A true protein digestibility factor of 1 can be assigned to L-form amino acids in the calculation of the protein digestibility-corrected amino acid score.

To commence: two years after gazettal

[9] ***The Australia New Zealand Food Standards Code*** *is varied by –*

[9.1] *omitting from the* Table of Contents, Standard 1.1A.6

[9.2] *omitting* Standard 1.1A.6

[10] ***Standard 2.9.5*** *is varied by –*

[10.1] *omitting from the* Table of Contents, *clause 2, substituting –*

2 Deleted

[10.2] *omitting clause 2, substituting –*

2 Deleted

Attachment 2

Compositional Assessment

PROPOSAL P242 - FOODS FOR SPECIAL MEDICAL PURPOSES

The purpose of this assessment is to consider the risks associated with the composition of FSMP, and to determine the most appropriate regulatory measures for addressing these risks.

Background

At Draft Assessment, the following compositional regulation of food for special medical purposes (FSMP) was proposed:

- minimum micronutrient limits for nutritionally complete FSMP, including formulas for very low energy diets (VLED);
- maximum micronutrient limits for all FSMP;
- macronutrient requirements for VLED; and
- a list of permitted forms of nutritive substances for use in FSMP.

International regulations [19,20] were used as a basis for these requirements, wherever possible, to allow for harmonisation with overseas regulations, and with the overseas risk assessments that have informed the development of these regulations. In addition, the Tolerable Upper Intake Limits (UL) set by the US Institute of Medicine (IOM) were used as a primary reference for setting maximum limits. In the absence of an UL for a nutrient, European Commission (EC) maximums were used as an alternate reference source.

Changes to Compositional Requirements at Preliminary Final Assessment

On the basis of submitter comments at Draft Assessment, FSANZ has reconsidered the proposed risk management approach to FSMP and has determined that, amongst other proposed regulatory measures, highly prescriptive compositional requirements have the potential to adversely impact on the availability and cost of FSMP. Consequently, FSANZ is now proposing to primarily manage the risks associated with the unsupervised and inappropriate use of FSMP by applying a:

- requirement for mandatory advisory labelling of FSMP as for 'use under medical supervision'; and
- restriction on the sale and advertising of FSMP to the general public.

Discussion on the rationale for this proposed risk management framework is provided in Section 5.2.1 of this Preliminary Final Assessment Report.

Because of this change in approach, this assessment will focus on a revision of the proposed compositional requirements for FSMP, in the context of a reduced need for prescriptive compositional regulation.

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[19]Codex Standard on Formula Foods for use in Very Low Energy Diets for Weight Reduction (CODEX STAN 203-1995).
[20]EC Directive on dietary foods for special medical purposes (Directive 1999/21/EC).

Prescribed Minimum Micronutrient Requirements

In general, submitters at Draft Assessment supported the proposed minimum micronutrient limits for nutritionally complete non-VLED FSMP. There was, however, concern from industry that some of the prescribed minimum levels were not compatible with the current product range.

Comment was also received from the **Australia New Zealand Enteral Nutrition Manufacturers Association (ANZENMA)** stating that VLED should be permitted to contain potassium, chromium and fluoride, similar to the minimum micronutrient permissions available for other FSMP.

Assessment

At Draft Assessment, the proposed minimum micronutrient limits were based on harmonising with overseas regulations[21], which were based on an assessment of their appropriateness for FSMP. Any further reductions in the proposed minimum limits must therefore be justified on the grounds that they will not compromise the dietary intake of Australian and New Zealand target consumers.

Currently, there is no evidence to suggest that FSMP are failing to provide sufficient amounts of nutrition. However, available literature indicates that patients admitted to hospital (a representative group of FSMP consumers) are often malnourished[22,23], and that inadequate nutrition support will prolong this condition with adverse consequences on the morbidity and mortality of patients. This evidence lends support to the position that, where feasible, the minimum nutritional quality of FSMP should be maintained at the highest possible level.

Consumers of nutritionally complete FSMP are likely to have the greatest nutritional requirements of all FSMP consumers. Minimum micronutrient levels are important for nutritionally complete FSMP to meet these increased requirements, as well as ensuring that all nutritionally complete FSMP are of a known and consistent minimum nutritional quality. Therefore, on this basis, the degree of regulatory control over minimum micronutrient limits remains necessary for nutritionally complete FSMP as determined at Draft Assessment.

In respect to VLED, the absence of prescribed minimum limits for particular micronutrients does not prevent the presence of these substances in a product. As proposed at Draft Assessment, a nutritive substance can be present in FSMP provided it is in a form listed in Schedule 1 of draft Standard 2.9.5. Minimum and maximum levels are prescribed to restrict the quantities of the micronutrients within a product, but do not control the presence of the micronutrient itself.

[21]EC Directive on dietary foods for special medical purposes (Directive 1999/21/EC).
[22]Gallager-Allred CR, Coble Voss A, Finn SC, McCamish MA (1996); *Malnutrition and clinical outcomes: the case for medical nutrition therapy*; JADA, 96(4): 361-366.
[23]McWhirter JP, Pennington CR (1994); *'Incidence and recognition of malnutrition in hospital'*; BMJ, 308:945-948.

At Draft Assessment, the VLED minimum micronutrient limits were based on European regulation[24]. However, Codex VLED regulations[25] include minimum compositional requirements, and FSANZ is now of the opinion that it is more appropriate to adopt Codex regulations wherever possible. Therefore, Codex VLED micronutrient minimum limits will be adopted into revised draft Standard 2.9.5. This will mean that minimum limits will no longer be prescribed for biotin, pantothenic acid, vitamin K and manganese, however these micronutrients will be permitted voluntarily; and a minimum for potassium will be added. It is not expected that these changes will have a negative impact on the current range of Australian and New Zealand VLED products.

Conclusion

At Preliminary Final Assessment, the application of minimum micronutrient limits for nutritionally complete FSMP (including VLED) is still considered an important regulatory measure for ensuring a basic and consistent level of nutritional quality for nutritionally complete FSMP. Therefore it is recommended that draft Standard 2.9.5 maintain the prescribed minimum micronutrient limits for nutritionally complete FSMP as proposed at Draft Assessment (See Tables 1 and 2 of the Appendix). The minimum micronutrient limits for VLED will, however, be modified to reflect Codex VLED regulations.

Prescribed Maximum Micronutrient Limits

In submissions at Draft Assessment, concern was raised that the proposed maximum micronutrient limits were overly prescriptive, particularly for non-nutritionally complete FSMP where the risks are lessened by consumption of other foods in the diet. In addition, submitters commented that the risk from excessive intakes of micronutrients is managed by the use of FSMP under medical supervision, and because consumers of FSMP are often nutritionally compromised. There were also comments that the UL (which formed the basis of maximum limit setting) are more applicable to healthy population groups.

Assessment

It is no longer considered necessary to be as prescriptive in the control of maximum micronutrient limits as was proposed at Draft Assessment. This revised position has been taken because FSANZ is now proposing to primarily manage the risks associated with FSMP through a risk management framework involving mandatory advisory labelling and restrictions on the sale and advertising of FSMP. Instead FSANZ is now proposing to apply maximum limits on micronutrients where there is a demonstrated risk of harm from excessive intake.

Nutritionally complete FSMP represent a significant risk to public health and safety from excessive micronutrient intakes, as these foods provide the sole source of nutrition for nutritionally vulnerable individuals. For this reason FSANZ has undertaken a safety assessment (see Attachment 3), to identify nutrients with potential safety concerns from excessive intake. This safety assessment identified and recommended maximum limits in nutritionally complete FSMP for the following micronutrients: vitamin A (retinol forms only), vitamin B_6, vitamin D, calcium, zinc, iodine, manganese, copper and selenium.

[24]EC Directive on food intended for use in energy-restricted diets for weight reduction (Directive 96/8/EC).
[25]Codex Standard on Formula Foods for use in Very Low Energy Diets for Weight Reduction (CODEX STAN 203-1995).

In contrast, non-nutritionally complete FSMP are generally used under supervision of a health professional to supplement the daily intake of individuals who would normally consume other foods. Consumers of these products are considered to have a lower exposure to the micronutrients in FSMP products than individuals who rely on FSMP as a sole source of nutrition, and as such they are subsequently at a much lower risk from an excessive intake of micronutrients. Therefore, FSANZ is no longer proposing to apply maximum micronutrient limits to non-nutritionally complete FSMP.

Conclusion

The maximum micronutrient limits as proposed at Draft Assessment have been reassessed as too prescriptive. Therefore, the maximum micronutrient limits have been revised on the basis of safety, with maximum limits now proposed for identified high-risk micronutrients namely: vitamin A, vitamin B_6, vitamin D, calcium, zinc, iodine, manganese, copper and selenium (See Tables 1 and 2 of the Appendix). The maximum limit for vitamin A applies only to its retinol forms, while the minimum vitamin A requirement applies to all forms of vitamin A (i.e. retinol and carotenoid). For nutritionally incomplete FSMP, the potential for exposure to excessive micronutrient intakes is low and maximum limits are no longer considered necessary for this class of FSMP.

Prescribed Macronutrient Requirements for VLED

At Draft Assessment there was support for the prescribed macronutrient requirements for VLED. However, industry submitters indicated that health professionals sometimes use VLED to supplement the diets of patients who are returning to a normal eating pattern. In this case, the use of VLED could result in daily energy intakes greater than the prescribed maximum energy content of 3350 kJ per recommended daily quantity.

Assessment

The proposed FSMP standard will apply only to the manufacture and sale of FSMP. The impact on consumption patterns and use of the food are considered in the development of all food regulations; however, food regulations cannot anticipate all consumer behaviour. Therefore, if a VLED formula is manufactured in compliance with prescribed requirements (including composition), then the manner in which the product is used under health professional supervision is not so relevant to regulation but is more an issue of patient management.

Conclusion

The macronutrient requirements for VLED as proposed at Draft Assessment will remain unchanged at Preliminary Final Assessment.

Compositional Requirements Associated with Certain Medical Conditions

There is scientific evidence indicating that decreases in sodium and potassium intakes below normal nutritional requirements are necessary for a number of medical conditions. Chronic renal disease, heart failure, and ascites are the primary conditions that require a low sodium intake.

In all of these conditions it is the relationship between sodium intake and fluid balance that is of importance, often because a normal sodium intake causes hypertension that in turn exacerbates the severity of the condition[26,27,28]. A reduced intake of potassium is also required for chronic renal disease, as the ability to regulate potassium balance decreases with a deterioration in the condition. The change in potassium balance increases likelihood of hyperkalaemia developing – a physiological state that can have severe health consequences[28].

On the basis that certain medical conditions required very low dietary intakes of sodium and potassium, permission was given at Draft Assessment for nutritionally complete non-VLED FSMP to deviate from the prescribed minimum limits for these micronutrients.

Submissions to the Draft Assessment from the **European Commission** (EC) and ANZENMA indicated that the permission to deviate from the prescribed minimum sodium and potassium limits should be extended to all minimum and maximum micronutrient limits. ANZENMA further indicated that permission should at least be given to deviate from the minimum limit for phosphorus, as a reduction in phosphorus can also be necessary for the nutritional management of renal disease.

Assessment

The Code operates through the provision of discrete measurable criteria that foods can be evaluated against, i.e. a 'standard'. Although European FSMP regulations provide permission to deviate where necessary from prescribed micronutrient requirements, the application of such a permission in the Australian and New Zealand regulatory context does not produce a 'standard'. Permission for widespread deviation would, in effect, make prescribed micronutrient requirements voluntary and unenforceable.

There is scientific evidence in addition to that for sodium and potassium, which indicates that a decrease in phosphorus intake below normal human requirements is appropriate for the management of renal disease[29,30]. A reduction in the functioning of the kidney limits the ability to excrete phosphorus from the body ultimately resulting in hyperphosphataemia, a condition that contributes to the development of hyperparathyroidism, vascular calcifications and increased cardiovascular mortality. Therefore, applying a permission to deviate from the prescribed minimum phosphorus limit is appropriate for FSMP used in the management of renal disease.

Conclusion

Permitting FSMP to deviate from a small number of prescribed minimum micronutrient requirements (i.e. sodium, potassium and phosphorus) will enable the current range of FSMP that are used with certain disease states to comply with the proposed FSMP regulations.

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[26] Arroyo V (2002); *'Pathophysiology, diagnosis and treatment of ascites in cirrhosis'*; Ann Hepatol, 1(2): 72-79.

[27] Futterman LG and Lemburg L (2001); *'Heart failure: update on treatment and progression'*; Am J Crit Care, 10(4): 285-293.

[28] Kopple JD *'Nutrition, Diet and the Kidney'*; in Shils ME (ed), Olson JA (ed), Shike M (ed) (1994); *'Modern Nutrition in Health and Disease'*; 8th Ed; Lea & Febiger, Sydney, p1102-1134.

[29] Indridason OS and Quarles LD (2002); *'Hyperphosphatemia in end-stage renal disease'*; Adv Ren Replace Ther, 9(3): 184-192.

[30] Slatopolsky E, Brown A, Dusso A (2001); *'Role of phosphorus in the pathogenesis of secondary hyperparathyroidism'*; Am J Kidney Dis, 37(1)(Supp 2): S54-S57.

However, extending this permission to all prescribed micronutrient compositional requirements will undermine the integrity of the proposed FSMP standard, and is therefore inappropriate.

Permitted Forms of Added Nutritive Substances

At Draft Assessment, the proposed list of permitted nutritive substances was mainly based on European legislation (PARNUTS) [31], as the EC is the only major overseas region supplying FSMP to the domestic market that has undertaken a toxicological and nutritional assessment on a wide range of substances appropriate for addition to FSMP. Submissions to the Draft Assessment supported harmonising with European legislation; however, several submitters clarified this support by stating that:

- the proposed Schedule of permitted forms should be extended to include other nutritive substances permitted under Standard 1.1.1 – Preliminary Provisions - Application, Interpretation and General Prohibitions; and Standard 2.9.1 – Infant Formula Products of the Code; and
- FSMP regulations should be flexible enough to accommodate new ingredients or future innovation in nutritive substances.

ANZENMA also requested the inclusion of the following additional substances:

- Sodium, potassium and magnesium salts of the amino acids listed in the Schedule to Standard 2.9.5, and their hydrochlorides. These amino acid forms are permitted in PARNUTS;
- L-serine, and the double amino acid salts L-arginine–L-aspartate, L-lysine–L-aspartate, and L-lysine–L-glutamate dihydride. The European Scientific Committee on Food released an opinion in April 2003[32] that supported the addition of these amino acids to FSMP on the basis of a safety assessment;
- N-acetyl-L-methionine;
- Ferric orthophosphate;
- L-asparagine monohydrate;
- chromium potassium sulphate dodecahydrate and chromium acetate; and
- all hydrates of the various permitted forms of minerals.

Assessment

The PARNUTS list of permitted forms is based on scientific assessments for the addition of substances specifically to FSMP. Therefore, any expansion in the range of permitted forms should occur only where it can be identified that the additional substances have a similar level of safety and efficacy.

With this condition in mind, the permitted forms listed in Standard 2.9.1 are regarded as suitable for application to FSMP, since infants represent a similarly vulnerable population group to FSMP consumers.

[31]EC Directive on Substances that may be added for Specific Nutritional Purposes in Foods for Particular Nutritional Uses (2001/15/EC) (PARNUTS).
[32]Statement of the European Scientific Committee on Food on L-serine and some amino acid-amino acid salts for use in foods for particular nutritional purposes (Statement SCF/CF/ADD/NUT55).

However, the safety and efficacy of the permitted forms listed in Standard 1.1.1 cannot be guaranteed for FSMP consumers, as these permissions were originally developed for a healthy, normal population.

Codex has an advisory list of permitted forms of vitamins and minerals for use in foods for children and infants[33], which is based on sound science and can therefore also be applied to FSMP.

ANZENMA has requested certain additional forms that are not currently permitted elsewhere. Therefore, it has been necessary to evaluate these forms as part of the Safety Assessment at Preliminary Final Assessment (see Attachment 3). FSANZ's safety assessment has concluded that N-acetyl-L-methionine; and L-asparagine can be included as permitted forms. As there is a lack of toxicological information on chromium potassium sulphate and chromium acetate, these particular forms of chromium have not been permitted.

The request for inclusion of ferric orthophosphate does not require further assessment, as it is included in the Codex advisory list mentioned above, and can therefore be permitted for addition to FSMP.

The sodium, potassium and magnesium salts of amino acids, and the hydrochlorides of amino acids are included in PARNUTS. These forms were inadvertently omitted at Draft Assessment, and will therefore be included at Preliminary Final Assessment.

The physical nature of any substance added to food is regulated under Standard 1.3.4 – Identity and Purity of the Code, where substance specification requirements are listed. Hydrated varieties of a mineral substance are regulated under Standard 1.3.4, as they only reflect the substance's physical and purity attributes. Therefore for the purposes of FSMP regulations, the hydration variants of a mineral substance are considered to be the same substance so long as they comply with Standard 1.3.4.

By broadening the number of permitted forms on the basis of public health and safety considerations, the permitted form list proposed at Preliminary Final Assessment does provide scope for innovation.

Conclusion

The permitted forms list as proposed at Draft Assessment is to be extended to also include permitted forms from Schedule 1 to Standard 2.9.1 – Infant Formula Products of the Code, the Codex Advisory Lists (CAC/GL 10-1979), and several additional amino acid forms requested by industry submitters (see Tables 3 and 4 of the Appendix).

Units of Expression for Compositional Requirements

At Draft Assessment, VLED micronutrient requirements were expressed per daily quantities to maintain consistency with overseas VLED regulations. This related to a proposed requirement for the labelling of a statement on VLED indicating the recommended daily consumption amount, to ensure that VLED consumers would consume the correct intake of micronutrients.

[33]Codex Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Children (CAC/GL 10-1979)

However submitters' comments indicated that the labelling of a recommended daily consumption amount was inappropriate, as supervising health professionals should be responsible for managing the daily consumption of VLED.

Assessment

The requirement to label VLED with a recommended daily consumption amount has been reassessed as highly prescriptive especially as overseas VLED regulations do not prescribe this requirement (see Attachment 4 – Labelling Assessment). Therefore, it is no longer necessary for micronutrient requirements for VLED to be expressed per daily quantities. Instead, FSANZ is proposing to express the micronutrient requirements for VLED similar to those for non-VLED nutritionally complete FSMP i.e. per unit energy content.

In addition, to improve the practical application for expressing the minimum and maximum limits of all nutritionally complete FSMP (including VLED) on a per energy basis, values will be expressed per megajoule (MJ) rather than per 100 kJ as at Draft Assessment (see Tables 1 and 2 of the Appendix).

Conclusion

The units of expression for VLED compositional requirements will now be expressed per energy content, with the compositional requirements for all nutritionally complete FSMP being expressed per megajoule (MJ).

Summary of Recommendations for Compositional Requirements

As FSANZ is now proposing to primarily manage the risks associated with the unsupervised and inappropriate use of FSMP through the application of an overarching risk management framework (see Section 5.3 of the Preliminary Final Assessment Report), it is no longer considered necessary to apply highly prescriptive compositional requirements.

Therefore it is recommended that the following compositional requirements be included in revised draft Standard 2.9.5 at Preliminary Final Assessment:

- prescribed minimum micronutrient limits for nutritionally complete FSMP as proposed at Draft Assessment. The minimum micronutrients for VLED to reflect Codex VLED parameters (See Tables 1 and 2 of Appendix);

- prescribed maximum micronutrient limits for nutritionally complete FSMP only for those micronutrients assessed as presenting a risk to safety from excessive intake. Maximum limits to apply to vitamin A, vitamin B_6, vitamin D, calcium, zinc, iodine, manganese, copper and selenium (See Tables 1 and 2 of Appendix) as identified by FSANZ's safety assessment (See Attachment 3);

- maximum limits to not apply to non-nutritionally complete FSMP;

- permission to deviate from the prescribed minimum limits for sodium and potassium to be extended to phosphorus;

- extending the list of permitted forms of nutritive substances (see Tables 3 and 4 of Appendix) to include permitted forms from:

    - Schedule 1 of Standard 2.9.1 – Infant Formula Products of the Code; and
    - Codex Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Children (CAC/GL 10-1979); and
    - some additional nutritive substance forms that have been assessed for safety;

- revising the unit of expression for VLED compositional requirements from per daily quantity to per energy basis. The compositional requirements for all nutritionally complete FSMP to be expressed as per megajoule (MJ).

Appendix to Attachment 2

Table 1: Minimum and Maximum Vitamin, Mineral and Electrolyte Amounts for non-VLED Nutritionally Complete FSMP

Column 1	Column 2	Column 3
Nutrient	**Minimum Amount / MJ***	**Maximum Amount / MJ****
Vitamins		
Vitamin A	84 μg retinol equivalents	345 μg retinol forms only
Thiamin	0.15 mg	No maximum set
Riboflavin	0.2 mg	No maximum set
Niacin	2.2 mg niacin equivalents	No maximum set
Vitamin B_6	0.2 mg	2.9 mg
Folate	25 μg	No maximum set
Vitamin B_{12}	0.17 μg	No maximum set
Vitamin C	5.4 mg	No maximum set
Vitamin D	1.2 μg	5.7 μg
Vitamin E	0.5 mg alpha-tocopherol equivalents per g of polyunsaturated fatty acids expressed as linoleic acid, but in no case less than 10 mg alpha-tocopherol equivalents per MJ	No maximum set
Biotin	2 μg	No maximum set
Pantothenic Acid	0.35 mg	No maximum set
Vitamin K	8.5 μg	No maximum set
Minerals		
Calcium	84 mg	287 mg
Magnesium	18 mg	No maximum set
Iron	1 mg	No maximum set
Phosphorus	72 mg	No maximum set
Zinc	1 mg	4.6 mg
Manganese	0.12 mg	1.32 mg
Copper	0.15 mg	1.15 mg
Iodine	15.5 μg	115 μg
Chromium	3 μg	No maximum set
Molybdenum	7 μg	No maximum set
Selenium	6 μg	46 μg
Electrolytes		
Sodium	72 mg	No maximum set
Potassium	190 mg	No maximum set
Chloride	72 mg	No maximum set

* Minimum values = the minimum per 100 kJ listed in Table 2 of the Annex to EC Directive 1999/21/EC multiplied by 10 for per megajoule.

** Maximum values = the maximum daily value recommended by FSANZ Safety Assessment (Attachment 3) divided by 8.7 (i.e. assumed 8700 kJ reference daily intake for an adult).

Table 2: Minimum and Maximum Vitamin, Mineral and Electrolyte Amounts for VLED

Nutrient	Minimum Amount / MJ	Maximum Amount / MJ
Vitamins		
Vitamin A	319 μg retinol equivalents	896 μg retinol forms only
Thiamin	0.43 mg	No maximum set
Riboflavin	0.6 mg	No maximum set
Niacin	5.9 mg niacin equivalents	No maximum set
Vitamin B_6	1.1 mg	7.5 mg
Folate	106 μg	No maximum set
Vitamin B_{12}	0.53 μg	No maximum set
Vitamin C	16 mg	No maximum set
Vitamin D	1.3 μg	14.9 μg
Vitamin E	5 mg alpha-tocopherol equivalents	No maximum set
Minerals		
Calcium	266 mg	746 mg
Magnesium	186 mg	No maximum set
Iron	9 mg	No maximum set
Phosphorus	266 mg	No maximum set
Zinc	3 mg	11.9 mg
Manganese	No minimum set	3.43 mg
Copper	0.8 μg	3 μg
Iodine	74.5 μg	298.5 μg
Selenium	No minimum set	119 μg
Electrolytes		
Sodium	306 mg	No maximum set
Potassium	1649 mg	No maximum set

* Minimum values = the minimum value listed in Clause 3.2.4 of CODEX STAN 203-1995 divided by 1.88 (lowest permitted energy content for VLED)

** Maximum values = the maximum value recommended by FSANZ Safety Assessment (Attachment 3) divided by 3.35 (highest permitted energy content for VLED).

Table 3: Schedule of Permitted Forms in Standard 2.9.1

Column 1	Column 2
Vitamins or minerals	**Permitted Forms**
Vitamin A	Retinol Forms vitamin A (retinol) vitamin A acetate (retinyl acetate) vitamin A palmitate (retinyl palmitate) retinyl propionate Carotenoid Forms beta-carotene
Vitamin C	L-ascorbic acid L-ascorbyl palmitate calcium ascorbate potassium ascorbate sodium ascorbate
Vitamin D	vitamin D_2 (ergocalciferol) vitamin D_3 (cholecalciferol) vitamin D (cholecalciferol-cholesterol)
Thiamin	thiamin hydrochloride thiamin mononitrate

Column 1	Column 2
Vitamins or minerals	**Permitted Forms**
Riboflavin	riboflavin riboflavin-5'-phosphate, sodium
Niacin	niacinamide (nicotinamide)
Vitamin B_6	pyridoxine hydrochloride pyridoxine-5'-phosphate
Folate	folic acid
Pantothenic acid	calcium pantothenate dexpanthenol
Vitamin B_{12}	cyanocobalamin hydroxocobalamin
Biotin	d-Biotin
Vitamin E	dl-α-tocopherol d-α-tocopherol concentrate tocopherols concentrate, mixed d-α-tocopheryl acetate dl-α-tocopheryl acetate d-α-tocopheryl acid succinate dl-α-tocopheryl succinate
Vitamin K	vitamin K_1, as phylloquinone (phytonadione) phytylmenoquinone
Calcium	calcium carbonate calcium chloride calcium citrate calcium gluconate calcium glycerophosphate calcium hydroxide calcium lactate calcium oxide calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic calcium sulphate
Chloride	calcium chloride magnesium chloride potassium chloride sodium chloride
Chromium	chromium sulphate chromium potassium sulphate
Copper	copper gluconate cupric sulphate cupric citrate
Iodine	potassium iodate potassium iodide sodium iodide
Iron	ferric ammonium citrate ferric pyrophosphate ferrous citrate ferrous fumarate ferrous gluconate ferrous lactate ferrous succinate ferrous sulphate

Column 1	Column 2
Vitamins or minerals	**Permitted Forms**
Magnesium	magnesium carbonate magnesium chloride magnesium gluconate magnesium oxide magnesium phosphate, dibasic magnesium phosphate, tribasic magnesium sulphate
Manganese	manganese chloride manganese gluconate manganese sulphate manganese carbonate manganese citrate
Molybdenum	sodium molybdate VI dehydrate
Phosphorus	calcium glycerophosphate calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic magnesium phosphate, dibasic potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic
Potassium	potassium bicarbonate potassium carbonate potassium chloride potassium citrate potassium glycerophosphate potassium gluconate potassium hydroxide potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic
Selenium	sodium selenite seleno methionine
Sodium	sodium bicarbonate sodium carbonate sodium chloride sodium chloride iodised sodium citrate sodium gluconate sodium hydroxide sodium iodide sodium lactate sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic sodium sulphate sodium tartrate

Column 1	Column 2
Vitamins or minerals	**Permitted Forms**
Zinc	zinc acetate zinc chloride zinc gluconate zinc oxide zinc sulphate

Table 4: Additional Permitted Forms supplementary to Schedule 1 of Standard 2.9.1

Column 1	Column 2
Nutritive Substance	**Permitted Form**
Vitamins	
Niacin	Nicotinic acid
Vitamin B_6	Pyridoxine dipalmitate
Vitamin E	d-alpha-tocopherol
Pantothenic acid	sodium pantothenate
Minerals	
Chromium	Chromium chloride
Chlorine	Choline chloride
	Sodium chloride, iodised
	Hydrochloric acid
Copper	Copper-lysine complex
	Cupric carbonate
Fluoride	Potassium fluoride
	Sodium fluoride
Iodine	Sodium iodate
Iron	Carbonyl iron
	Electrolytic iron
	Ferric citrate
	Ferric gluconate
	Ferric orthophosphate
	Ferric pyrophosphate, sodium
	Ferric saccharate
	Ferric sodium diphosphate
	Ferrous carbonate
	Ferrous carbonate, stabilised
	Iron, reduced (ferrum reductum)
Magnesium	Magnesium acetate
	Magnesium citrate
	Magnesium glycerophosphate
	Magnesium hydroxide
	Magnesium hydroxide carbonate
	Magnesium lactate
Manganese	Manganese glycerophosphate
Molybdenum	Ammonium molybdate
Phosphorus	Magnesium phosphate, tribasic
	Potassium glycerophosphate
Potassium	Potassium lactate
Selenium	Sodium hydrogen selenite
	Sodium selenate
Zinc	Zinc carbonate
	Zinc citrate
	Zinc lactate

Column 1	Column 2
Nutritive Substance	**Permitted Form**
Other Nutritive Substances	
Amino acids	Cystine
	Glycine
	L-alanine
	L-arginine
	L-asparagine
	L-aspartic acid
	L-citrulline
	L-cysteine
	L-glutamic acid
	L-glutamine
	L-lysine acetate
	L-ornithine
	L-proline
	L-serine
	L-arginine-L-aspartate
	L-lysine-L-aspartate
	L-lysine-L-glutamate
	N-acetyl-L-methionine
	Cystine hydrochloride
	Glycine hydrochloride
	L-alanine hydrochloride
	L-arginine hydrochloride
	L-asparagine hydrochloride
	L-aspartic acid hydrochloride
	L-citrulline hydrochloride
	L-cysteine hydrochloride
	L-glutamic acid hydrochloride
	L-glutamine hydrochloride
	L-lysine hydrochloride
	L-ornithine hydrochloride
	L-proline hydrochloride
	L-serine hydrochloride
	Sodium cystine
	Sodium glycine
	Sodium L-alanine
	Sodium L-arginine
	Sodium L-asparagine
	Sodium L-aspartic acid
	Sodium L-citrulline
	Sodium L-glutamic acid
	Sodium L-glutamine
	Sodium L-lysine acetate
	Sodium L-ornithine
	Sodium L-proline
	Sodium L-serine
	Potassium cystine
	Potassium Glycine
	Potassium L-alanine
	Potassium L-arginine
	Potassium L-asparagine
	Potassium L-aspartic acid
	Potassium L-citrulline
	Potassium L-glutamic acid

Column 1	Column 2
Nutritive Substance	**Permitted Form**
	Potassium L-glutamine
	Potassium L-lysine acetate
	Potassium L-ornithine
	Potassium L-proline
	Potassium L-serine
Carnitine	L-carnitine
	L-carnitine hydrochloride
Choline	Choline
	Choline bitartrate
	Choline chloride
	Choline citrate
	Choline hydrogen tartrate
Inositol	Inositol
Nucleotides	Adenosine 5’-monophosphate
	Adenosine 5’-monophosphate sodium salt
	Cytidine 5’-monophosphate
	Cytidine 5’-monophosphate sodium salt
	Guanosine 5’-monophosphate
	Guanosine 5’-monophosphate sodium salt
	Inosine 5’-monophosphate
	Inosine 5’-monophosphate sodium salt
	Uridine 5’-monophosphate
	Uridine 5’-monophosphate sodium salt
Taurine	Taurine

Attachment 3

Safety Assessment Report

Proposal P242 – Foods for Special Medical Purposes

Summary and Conclusion

A safety assessment has been conducted for the purpose of 1) identifying those vitamins and minerals for which an upper limit is necessary when used in Foods for Special Medical Purposes (FSMP), and in those cases making recommendations on the upper limit to be used, and 2) assessing the safety of three nutritive substances. As restrictions for sale are proposed, and the products can only be sold under medical supervision, effects of an acute nature that are easily detected, such as diarrhoea, were not considered relevant for the setting of an upper limit.

It should be noted that the upper limits set in this report have been established solely on the basis of the use of the substances in FSMP, and are not intended to be used generally as upper limits.

As a result of this safety assessment, for most vitamins and minerals an upper limit is not considered necessary for FSMP. However, the following vitamins and minerals are identified as having potential safety concerns within the context of their use in FSMP and therefore an upper limit is considered necessary. These chemicals are vitamins A, B_6, and D, Selenium, Iodine, Zinc, Calcium, Manganese and Copper (see also the table).

Vitamin A

High doses of vitamin A can result in teratogenicity and hepatotoxicity. Teratogenicity and hepatotoxicity are considered relevant effects for FSMP. Because of the severity of these effects, an upper limit for vitamin A when used in FSMP is appropriate. The upper limit considered most appropriate is 3000 μg retinol equivalents per day for vitamin A in adults. This upper limit does not apply for pro-vitamin A forms.

Vitamin B_6

High doses of vitamin B_6 can result in peripheral neuropathy in humans. The effect is dependent on both the dose and the duration of exposure.

The neurotoxicity of pyridoxine is considered a relevant adverse effect for FSMP based on a review of the evaluations of the US, EU and the UK. The upper limits of both the EU and US were based on human data, using total dietary intake, and therefore are considered more relevant than the upper limit derived by the UK. The upper limit from the EU report is considered the most relevant, because it was derived from longer-term studies in humans as compared to the US upper limit. Therefore, an upper limit for vitamin B_6 of 25 mg/day has been established for FSMP.

Vitamin D

High vitamin D intake has been shown to be associated with reduced renal function and hypercalcaemia even when the exposure period was relatively short (6 weeks).

An upper limit of 0.050 mg/day for vitamin D is considered appropriate for FSMP. This level is based on the upper limits of the US and EU, since these values were based on total dietary intake.

Selenium

High doses of selenium can result in severe adverse effects on the nervous system, however these effects are difficult to analyse and therefore not easily detected. The most sensitive indicators for selenium toxicity are changes in nails and hair.

The effects of selenium toxicity, i.e. adverse effects on the nervous system, are serious and cumulative, therefore it is necessary to set an upper limit for FSMP. The most sensitive indicators of selenium toxicity are changes in nails and hair, therefore these endpoints are used for establishing an upper limit. The level of 0.40 mg/day, established by both the WHO and US, is considered appropriate as an upper limit for selenium in FSMP.

Iodine

High doses of iodine can result in sub-clinical hypothyroidism. This is a relevant adverse effect for the purpose of setting an upper limit for FSMP. A level of 1.0 mg/day is appropriate as an upper limit for iodine for the purpose of developing a standard for FSMP.

Zinc

High doses of zinc can result in secondary copper deficiency. Based on the severity of the effect, and having regard to the most vulnerable group (diabetics), an upper limit for zinc in FSMP is necessary. A level of 40 mg/day, based on the US limit which takes into account the total dietary intake of zinc, is considered appropriate as an upper limit for the purpose of developing a standard for FSMP.

Calcium

High calcium intake has been shown to be associated with kidney stone formation, reduced renal function and hypercalcaemia even when the exposure period was relatively short. Therefore, an upper limit for calcium is appropriate for FSMP.

A level of 2500 mg/day, based on the upper limits established by the US and EU, which take into account total dietary intake, is considered appropriate as an upper limit.

Manganese

High doses of manganese can result in neurotoxicity. This is a serious adverse effect, with the elderly especially sensitive. The margin between the recommended daily intake and adverse effects levels are small, therefore an upper limit is necessary.

A level of 11.5 mg manganese/day (mean of UK and US) has been established as an upper limit for the purpose of developing a standard for .

Copper

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 upper limit for FSMP. An upper limit of 10 mg copper/day has been established, based on the US and WHO evaluations.

Nutritive Substances

The use of N-acetyl-L-methionine and L-asparagine monohydrate in FSMP is unlikely to give rise to adverse health effects. Therefore, these substances will be permitted as nutritive substances for FSMP.

Based the different solubility of chromium acetate compared to other chromium III forms, its toxicological profile could not be determined. Therefore it is proposed that this form should not be permitted for FSMP.

Since the characteristics of chromium potassium sulfate dodecahydrate are similar to the already permitted form chromium sulfate, it is proposed that chromium potassium sulfate dodecahydrate be permitted as a chromium compound. Therefore, the following chromium compounds are permitted: chromium sulphate, chromium chloride and chromium potassium sulfate dodecahydrate.

Table: Upper limits for vitamins and minerals used in FSMP

	Upper limit for FSMP	**Organisation on which Limit based**	**Adverse effect which is the basis for an upper limit**
Vitamin A, µg RE/day*	3000	US, EU	teratogenicity, hepatoxicity
Niacin, mg/day	no upper limit		flushing, hepatoxicity
Vitamin B_6, mg/day	25	EU	neuropathy
Folate, mg/day	no upper limit		masking vitamin B_{12} deficiency
Vitamin C	no upper limit		diarrhoea
Vitamin D, mg/day	0.050	US, EU	hypercalcaemia
Vitamin E, mg/day	no upper limit		blood clotting related to vitamin K deficiency
Vitamin K,	no upper limit		-
Biotin	no upper limit		-
Pantothenic acid	no upper limit		-
Selenium, mg/day	0.40	WHO	brittle nails and hair pathology, adverse effects nervous system
Iodine, mg/day	1.0	WHO	sub-clinical hypothyroidism
Zinc, mg/day	40	US	reduced copper status
Calcium, mg/day	2500	US, EU	milk-alkali syndrome and renal stone formation
Magnesium	no upper limit		diarrhoea
Iron, mg/day	no upper limit		diarrhoea
Phosphorus, mg/day	no upper limit		diarrhoea

Manganese, mg/day	11.5	US, UK	neurotoxicity
Copper, mg/day	10	UK, US, WHO	hepatotoxicity
Molybdenum	no upper limit		reproductive effects (rat)
Sodium	no upper limit		blood pressure
Potassium	no upper limit		acid-base balance
Thiamin	no upper limit		-
Riboflavin	no upper limit		-
Chromium	no upper limit		absence of data

* The upper limit applies to retinol forms of vitamin A only

Introduction

In the Draft Assessment Report of P242 – Foods for Special Medical Purposes (FSMP), the maximum amount per 100 kJ for various vitamins and minerals was proposed for nutritionally complete foods (FSANZ 2002). Most of the values were derived from the US upper limits or where there was no upper limit available the EU limits for FSMP were used (United States Institute of Medicine, 2000a-c, 2001a; European Commission Directives 1999). For the upper limits of the EU, a general rule was to set the upper limit to about 3 times the population reference dose. However, following the consultation round after the Draft Assessment Report of Proposal P242, it was considered appropriate that upper limits where they are considered necessary should be based on safety concerns. Safety assessments have therefore been conducted for all vitamins and minerals and an upper limit has been set where there are specific safety concerns within the use of FSMP.

Exposure to FSMP products

There is relatively little information available on the general use of FSMP products. In a survey in Victoria (Acute Health Division, 1997) it was indicated that 64 percent of the persons who were using home enteral feeding products were using the products longer than 6 months. There was no information available on which proportion of the FSMP users are using home enteral feeding products.

Studies performed between 1996-1998 in the UK by the British Association for Parenteral and Enteral Nutrition indicate that a large proportion of the users of home enteral feeding products use the products over 1.5 years (Elia et al, 1998). The overall patient status one year after starting home enteral tube feeding (n=8832) was as follows: 22% died whilst on home enteral tube feeding, 13.6% returned to oral feeding, 62% continued to receive the products, and 2% withdrew/refused home enteral tube feeding or were in hospital at the time of assessment. The age distribution of 14,284 patients starting home enteral tube feeding between 1996 and 1998 was bimodal, with a peak in the first decade of life and a second larger peak in the seventh decade. The most common overall diagnosis was cerebrovascular accident, which accounted for 31% of all diagnoses, and 50% of diagnoses in patients over the age of 70 years. Multiple sclerosis was the commonest diagnosis in patients aged 30-40 years (20%), oesophageal cancer in those aged 50-60 years (32%) and cerebral palsy in children (19%).

Based on above studies it can be assumed that a significant proportion of the FSMP users will be dependent solely on FSMP for a long-term period.

Upper tolerable nutrient intake level

Upper tolerable nutrient intake levels (ULs) have been defined by FAO/WHO (FAO/WHO, 2001) as the maximum intake from food that is unlikely to pose risk of adverse health effects from excess in almost all (97.5 percent) apparently healthy individuals in an age and sex-specific population group.

ULs have been established for the general population for vitamins and minerals by a number of countries as well as by the Food and Agriculture Organisation of the United Nations and World Health Organisation (FAO/WHO, 2001). Australia and New Zealand have currently no established upper limits for the general population for vitamins and minerals.

The ULs established by the United Kingdom (UK; Expert Group on Vitamins and Minerals, 2003), the United States (US; United States Institute of Medicine, 2000a-c, 2001a), the European Union (EU; Scientific Committee on Food, 2003) and FAO/WHO (FAO/WHO, 2001) were compared and considered for their thoroughness and appropriateness for application to FSMP. The UK set ULs for 24 micronutrients, which were generally for supplemental intake only, although a total intake upper safety level was set for four micronutrients. Most of the levels set were guidance levels, rather than absolute levels. The US has set ULs, which were generally for total intake. The ULs set by the EU were slightly less comprehensive in the range of nutrients considered, and the FAO/WHO were not as comprehensive in terms of the range of nutrients and the range of age/gender groups considered as those levels set by the UK and US. Total intake ULs were considered preferentially where both supplemental and total ULs were set.

For the safety assessment of vitamins and minerals in FSMP it has been assumed that the products could be used for a long-term period (see above). Therefore in the safety assessment upper limits are based preferentially on long-term effects. As restrictions for sale are proposed, and the products can only be sold under medical supervision, effects of an acute nature that are easily detected, such as diarrhoea, were not considered relevant for setting a standard for FSMP.

The upper limits set in this report have been established solely on the basis of the use of the substances in FSMP, and are not intended to be used generally as upper limits.

During the second round of consultation interested parties have requested the inclusion of three nutritive substances, N-acetyl-methionine; L-asparagine monohydrate; chromium acetate and chromium potassium sulfate dodecahydrate in the FSMP standard. Therefore, a safety assessment of these chemicals was also performed.

VITAMINS AND MINERALS

Vitamin A

Vitamin A is a micronutrient essential to most mammalian species. The term vitamin A describes a group of lipid soluble compounds related metabolically to all-trans-retinol. Vitamin A is essential to the process of vision, reproduction, embryonic development, morphogenesis, growth and cellular differentiation.

Vitamin A	Upper limit µg/day	Total diet / supplementation	Critical effect	human /animal data
US	3000	Total diet	teratology	human
UK*	1500	Total diet	bone fracture and teratology	human
EU	3000	Total diet	teratology and hepatotoxicity	human

* Guidance level; the UK did not derive an upper limit, 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.

Safety Data

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 15,000 µg 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/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 are recognised: 1) reduced bone mineral density, 2) teratogenicity, and 3) liver abnormalities. High β-carotene intake has not been shown to cause hypervitaminosis A. Therefore, only adverse effects of preformed vitamin A or retinol are investigated.

The evidence regarding the effects on bone mineral density is limited and not easily used for deriving an upper limit. Liver abnormalities are reported after chronic intake of higher levels of vitamin A, as compared to the effects on teratogenicity, and therefore this adverse effect is considered less relevant for deriving an upper limit for FSMP.

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 lever 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 mg retinoid equivalents (RE) or less and foetal malformation.

The prospective study of Rothman et al. (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 mg 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 mg 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 mg RE/day than for those ingesting 1500 mg RE/day. The authors fitted a regression curve to their data, which indicated a rise in the ration of prevalence of birth defects associated to the cranial-neural crest at doses greater than 3000 mg 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 is suggested by both the EU and US.

Evaluation

Because of the severity of the toxic end points, teratogenicity and hepatotoxicity, an upper limit for vitamin A in FSMP is appropriate.

A level of 3000 μg retinol equivalents per day for vitamin A in adults has been adopted as an upper limit for the purpose of developing a standard for FSMP. This upper limit does not apply for pro-vitamin A forms.

Niacin

The term niacin refers to nicotinamide (nicotinic acid amide), nicotinic acid (pyridine-3-carboxylic acid), and derivatives that exhibit the biological activity of nicotinamide. The amino acid tryptophan is converted in part to nicotinamide and thus can contribute to meeting the requirement for niacin. In the form of the coenzymes NAD and NADP, niacin functions in many biological redox reactions.

Niacin	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	35	Suppl	flushing	human
UK*	17 nicotinic acid 500 nicotinamide	Suppl. Suppl.	flushing no adverse effects	human
EU	10	Total diet	flushing	human

* Guidance level

Safety data

There is no evidence of adverse effects from the consumption of naturally occurring niacin in foods. Therefore the safety data are limited to evidence resulting from intake of niacin as a supplement, food fortificant, or pharmacological agent.

Reports of nicotinic acid toxicity in humans stem, in the main, from its use in the treatment of hypercholesterolemia. Most adverse effects are dose-related and generally subside with a reduction in dose or the cessation of treatment. Symptoms of acute toxicity include flushing, itching of the skin, nausea, vomiting and gastrointestinal disturbances. Additionally, jaundice, hyperglycaemia, abdominal pain, elevated serum bilirubin, alkaline phosphatase and aminotransferase levels can be seen with ingestion of high levels of nicotinic acid (generally intakes of 3,000 mg/day or more) for long periods of time.

In a small number of cases, anorexia, ophthalmological effects, skin hyperpigmentation and precipitation of incipient psychosis have been reported as side effects of nicotinic acid therapy. Vasodilatation 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 D2 release and a niacin flush test has been used as a method of investigating essential fatty acid metabolism. Although flushing is not general regarded as an adverse effect and single oral doses of 100 mg do not alter heart rate or blood pressure, some patients reported dizziness after oral nicotinic acid (doses not defined).

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.

Evaluation

Flushing is not considered a relevant adverse endpoint of concern in relation to FSMP, since the effect occur mainly when nicotinic acid is consumed without food. Furthermore, no effects on blood pressure and heart rate were reported after a single oral dose of 100 mg. Therefore, no upper limit for niacin is considered necessary for the purposes of developing a standard for FSMP.

Vitamin B_6 (pyridoxine)

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. 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.

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.

Vitamin B_6	**Upper limit mg/day**	**Total diet / Suppl**	**Critical effect**	**human /animal data**
US	100	Total diet	neuropathy	human
UK	10	Suppl	histological changes in nerves	dogs
EU	25	Total diet	neurological effects	human

Safety Data

No adverse effects have been associated with high intake of vitamin B_6 from food sources. 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 in volunteers and patients, and case reports of patients have shown that the effects can 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 US (United States Institute of Medicine, 2000a) has set the upper level 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 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 upper limit in the US is set at 100 mg/day.

The UK (Expert Group on Vitamins and Minerals, 2003) stated that the human data are inadequate to establish an upper level, 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 Upper level 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 (Scientific Committee on Food, 2003) derived the upper limit 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 is considered not to be necessary, because the data were for a sub-group with high plasma concentrations, and because the resulting upper level 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.

Evaluation

High doses of vitamin B_6 can result in peripheral neuropathy in humans. The effect is dependent on both the dose and the duration of exposure.

For FSMP products, long-term effects are considered to be more relevant than short-term effects. Based on a careful review of the evaluations of the US, EU and the UK, the neurotoxicity of pyridoxine is considered a relevant adverse effect for FSMP. As the upper limits of both the EU and US were based on human data, using total dietary intake, they are considered more relevant than the upper limit derived by the UK. The upper limit from the EU report is considered the most relevant, because it was derived from longer-term studies in humans as compared to the US upper limit.

A level of 25 mg/day, based on the EU upper limit, is considered appropriate as an upper limit for FSMP.

Vitamin B_{12}

Vitamin B_{12} (cobalamin) is a cofactor for two enzymes: methionine synthase and L-methylmalonyl-CoA mutase. An adequate supply of vitamin B_{12} is essential for normal blood formation and neurological function.

Vitamin B_{12}	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	no upper limit		-	
UK*	2.0		-	
EU	no upper limit		-	

* Guidance level

Safety Data

No adverse effects have been associated with excess vitamin B_{12} intake from food or supplements in healthy individuals. 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.

Evaluation

Based on the absence of adverse effects an upper limit for vitamin B_{12} does not need to be established for the purposes of developing a standard for FSMP.

Folate

The term folate is used generically to describe the various derivatives of pteroylglutamic acid (PGA, folic acid), the common pharmaceutical and most stable form of the folate vitamins group, which is composed of three major subunits – pteridine, ρ-aminobenzoic acid, and glutamic acid.

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.

Folate	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	1.0	Suppl	masking vitamin B_{12} deficiency	human
UK*	1.5	Total	masking vitamin B_{12} deficiency	human
EU	1.0	Total diet	masking vitamin B_{12} deficiency	human

* Guidance level

Safety data

From the available data it can be concluded that (synthetic) folic acid can cause adverse effects, while no adverse effects have been reported with the consumption of excess folate from foods.

Folic acid is generally considered as safe in therapeutic use. Adverse effects may, potentially occur in specific groups, such as individuals being treated with drugs that interact with folic acid metabolism. Women at risk of a neural-tube-defect-affected pregnancy appear to be able to take folate supplements at up to 4 mg/day, without adverse reproductive or developmental effects.

Folic acid may lead to reversal of the 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 modification of vitamin B_{12} neurological sequela in pernicious anaemia (PA) patients as a result of folic acid supplementation, such as masking of the haematological signs and the potential of progression of neurological symptoms. Masking of the haematological signs 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.

Evaluation

Since FSMP will have added vitamin B_{12}, the masking of vitamin B_{12} deficiency through high folate intake is not relevant as an adverse effect. An upper limit for folate does not need to be established for the purposes of developing a standard of FSMP.

Vitamin C

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.

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.

Vitamin C	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	2000	Suppl	osmotic diarrhoea and gastrointestinal	human
UK*	1000	Suppl.	gastrointestinal	human
EU	No evaluation available			

* Guidance level

Safety data

The available data suggest that vitamin C is not associated with significant adverse effects and there are no specific toxic endpoints for vitamin C given orally to healthy subjects. High oral doses of vitamin C are associated with osmotic diarrhoea and gastrointestinal disturbances, generally at doses of several grams but have also been reported at doses of 1000 mg.

There are few controlled studies specifically investigating this adverse effect. The effects are generally not serious and are self-limiting; individuals experiencing these effects may easily eliminate them by reducing supplemental vitamin C intakes.

The *in vivo* data do not clearly show a causal relationship between excess vitamin C intake by apparently healthy individuals and other adverse effects (i.e. kidney stone formation, excess iron absorption, reduced vitamin B_{12} and copper levels, increased oxygen demand, systemic conditioning, pro-oxidant effects, dental enamel erosion, or allergic response) in adults and children.

Evaluation

Since the adverse effects are mild and follow supplemental bolus doses, the effects are not considered relevant for FSMP. Therefore, no upper limit needs to be established for vitamin C for the purposes of developing a standard for FSMP.

Vitamin D

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.

Vitamin D is metabolised to the steroid hormone 1,25-dihydroxyvitamin D, a process which is promoted by parathyroid hormone (PTH). 1,25-Dihydroxyvitamin D regulates calcium and phosphate metabolism via three target tissues: kidney, small intestine and bone. In the kidney, 1,25-dihydroxyvitamin D regulates calcium transport in the proximal tubule; in the small intestine, it regulates calcium and phosphate uptake from the gut. 1,25-dihydroxyvitamin D is also involved in the maintenance of plasma calcium levels via bone resorption and formation. 1,25-dihydroxyvitamin D regulates the synthesis of PTH by a negative feedback mechanism.

Beside exposure through some foods (fatty fish and fish oils, liver, milk and eggs, fortified foods) and supplements, vitamin D_3 is also produced photochemically from 7-dehydrocholesterol in the skin by exposure to sunlight or ultraviolet light.

Vitamin D	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	0.050	total diet	serum calcium levels	human
UK*	0.025	supplemental	serum calcium levels	human
EU	0.050	total diet	serum calcium levels	human

* Guidance level

Safety data

The adverse effects of hypervitaminosis D are probably largely mediated via hypercalcaemia, but limited evidence 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 hypercalcaemia associated with hypervitaminosis D gives rise to multiple debilitation effects. Specifically, hypercalcaemia can result in a loss in urinary concentrating mechanism of the kidney tubule, resulting in polyuria and polydipsia.

A decrease in glomerular filtration rate also occurs. Hypercalciuria results from the hypercalcaemia and the disruption of normal reabsorption processes of the renal tubules. In addition, the prolonged ingestion of excessive amounts of vitamin D and the accompanying hypercalcaemia can cause metastatic calcification of soft tissues, prominently the kidney, blood vessels, heart, and lungs. Moderate levels of vitamin D intake may enhance renal stone formation in predisposed individuals. It has been suggested that excess vitamin D may be linked to heart disease, but there is limited evidence for this. Intakes of vitamin D between 1.25 mg/week and 1.25 mg/day for 6 weeks to 5 years were found to be associated with reduced renal function and hypercalcaemia (United States Institute of Medicine 2000c).

Evaluation

High vitamin D intake has been shown to be associated with reduced renal function and hypercalcaemia even when the exposure period was relatively short (6 weeks). Therefore, an upper limit for vitamin D is considered necessary.
An upper limit of 0.050 mg/day is considered appropriate for FSMP. This level is based on the upper limits of the US and EU (Scientific Committee on Food, 2003), since these values were based on total dietary intake.

Vitamin E

The term vitamin E is used as a generic designation for a group of eight lipid-soluble compounds synthesised by plants. These compounds fall into two classes, tocopherols and tocotrienols, which exhibit the biological antioxidant activity of vitamin E.

It is unclear whether vitamin E functions solely as a lipid antioxidant, or whether it might also be required for the function of some other critical, but unknown metabolic factor. Vitamin E is thought to have basic functional importance in the maintenance of membrane integrity in virtually all cells of the body. Non-antioxidant functions have also been proposed for α- but not β-tocopherol including modification of gene transcription and expression.

Vitamin E	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	1000	Suppl	haemorrhagic toxicity	animals
UK	540	Suppl	blood clotting	human
EU	300	Suppl	blood clotting	human

Safety data

There is no evidence of adverse effects from the consumption of vitamin E naturally occurring in foods. Therefore, the reviews of the EU (Scientific Committee on Food, 2003), US (United States Institute of Medicine, 2000b) and the UK (Expert Group on Vitamins and Minerals, 2003) were limited to evidence concerning intake of α-tocopherol as a supplement, food fortificant, or pharmacological agent.

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 adverse effect observed by high vitamin E intake 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. 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.

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 can be identified based on a critical evaluation by Wheldon et al (Wheldon, 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 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.

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. 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, attention was drawn to the observation that the tendency to haemorrhage in aspirin users is increased by vitamin E.

There are limited data relating to the effects of vitamin E on morbidity and mortality from chronic diseases.

A study in male smokers has suggested that 55 IU/day vitamin E (equivalent to 37 mg *d*-α-tocopherol equivalents/day) may increase the risk of mortality from haemorrhagic stroke in hypertensive subjects who smoked.

Although biologically plausible, the significance of this finding is uncertain. It has not been repeated in other studies in subjects at high risk of cardiovascular events treated with higher doses of vitamin E (up to 600 mg/day); however, if it is an effect related to smoking there may have been too few smokers in these studies for any effect to be apparent. In addition, a large observational study of male health professionals did not report this association.

Evaluation

Since FSMP will have added vitamin K, the adverse effects of vitamin E (e.g. effects on blood clotting), which occur only at a low vitamin K status, is not relevant to consideration of FSMP. Therefore, no upper limit for vitamin E needs to be established for the purposes of developing a standard of FSMP.

Vitamin K

Vitamin K is a group of homologous fat-soluble compounds derived from 2-methyl-1,4-naphthoquinone. Vitamin K_1 refers to phylloquinone, vitamin K_2 refers to menaquinones. Several synthetic water-soluble compounds exist; these include menadione (vitamin K_3) and menadiol (vitamin K_4).

Vitamin K catalyses the carboxylation of a number of protein factors involved in blood clotting including prothrombin, forming of calcium binding sites on glutamyl side chains in the protein. Once carboxylated, the glutamates are referred to as gamma-carboxyglutamic acid (GLA).

Vitamin K	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US **UK** **EU**	Insufficient data Insufficient data Insufficient data			

Safety data

The data are sparse but the different forms of vitamin K are associated with different adverse effects. There are relatively few reports of human toxicity for vitamin K_1 and it is stated to be well tolerated in animal studies. Although there are some reports of genotoxicity in vitro and in vivo, no effect was found in cells taken from babies given prophylactic intramuscular vitamin K_1. The significance of the positive genotoxicity findings is uncertain.

High doses of vitamin K_3 (menadione) may result in oxidative damage, red cell fragility and the formation of methaemoglobin. Hyperbilirubinaemia, resulting in kernicterus and toxicity to the neonatal brain occurred in premature infants given high doses of vitamin K_3.

Local hypersensitivity reactions to injections have been reported. In animal studies, vitamin K_3 administration has resulted in anaemia, haemoglobinaemia, urobilinuria and urobilinogenuria. High doses have also been reported to cause liver damage. Vitamin K_3 has demonstrated some mutagenic activity in the Ames test, possibly as a result of the structure of the side chain.

Evaluation

The only allowed form of vitamin K for FSMP is phylloquinone, which is not associated with adverse effects. Therefore, an upper limit for vitamin K is unnecessary for the purposes of developing a standard for FSMP.

Biotin

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.

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.

Biotin	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US **UK*** **EU**	Insufficient data 0.97 Insufficient data	total	-	

* Guidance level

Safety data

There are relatively few human data available on the oral toxicity of biotin. The data available are in the form of anecdotal case reports or from clinical trials or supplementation studies designed primarily to investigate beneficial effects of biotin. The latter rarely specifically report on the presence or absence of adverse effects.

The animal toxicity database for biotin is very limited, especially when given by the oral route.

Evaluation

No upper daily limit for biotin 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. An upper limit for biotin is therefore not considered necessary for the purposes of developing a standard for FSMP.

Pantothenic acid

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.

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.

Pantothenic acid	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US **UK*** **EU**	Insufficient data 210 Insufficient data	total	-	human

* Guidance level

Safety data

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

No upper daily limit 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. An upper limit for pantothenic acid is therefore not considered necessary for the purposes of developing a standard for FSMP.

Selenium

Selenium is a metallic group VI element that is abundant and which can exist in 4 oxidation states (-2, +1, +2 and +6).

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.

Selenium	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	0.40	Total	hair loss and changes in nail pathology	human
UK	0.45	Total	hair loss and changes in nail pathology	human
EU	0.30	Total	hair loss and changes in nail pathology	human
WHO/FAO#	0.40	Total	hair loss and changes in nail pathology	human

Provisional upper limit

Safety data

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 (clinical selenium poisoning, which includes the occurrence of nail, hair and skin lesions) 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 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 (1989a and b) 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.

The EU (Scientific Committee on Food, 2003) 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 (United States Institute of Medicine, 2000b) 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 upper limit of 0.40 mg/day was derived for adults.

The UK (Expert Group on Vitamins and Minerals, 2003) 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 (2001) for the upper limit of selenium was based on a risk assessment report from the International Programme on Chemical Safety (EHC 58, 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 (EHC58). 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.

Evaluation

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 for FSMP. The most sensitive indicators of selenium toxicity are changes in nails and hair, therefore these endpoints are used for establishing an upper limit. The level of 0.40 mg/day, established by both the WHO and the US, has been adopted as an upper limit for FSMP.

Iodine

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. The recommended daily intake for iodine varies but for adults ranges from 100-200 μg/day.

Although iodine is an essential component of the diet, intakes in excess of physiological requirements may produce adverse effects, particularly on the thyroid gland and the regulation of thyroid hormone production and secretion.

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.

Iodine	**Upper limit μg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	1100	total	elevated TSH	human
UK*	940	total	change in thyroid hormones	human
EU	600	total	TSH levels	human
WHO/FAO#	1000	total	elevated TSH	human

* Guidance level
# Provisional upper limit

Safety data

A Draft 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.

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.

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 (WHO, 1988) and the Agency for Toxic Substances and Disease Registry (ATSDR, 2001). 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. This report therefore focuses 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).

Intakes of approximately 1 mg iodine per day however 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. Individuals with thyroid disorders or a long history of iodine deficiency may respond adversely however at levels of intake below the PTDI.

Evaluation

Sub-clinical hypothyroidism is considered a relevant adverse effect for FSMP. A level of 1.0 mg/day has been adopted as an upper limit for iodine for the purposes of developing a standard for FSMP.

Zinc

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.

Zinc is an essential constituent of more than two hundred metalloenzymes. Zinc plays a key role in the synthesis and stabilisation of genetic material and is necessary for cell division and the synthesis and degradation of carbohydrates, lipids and proteins.

Zinc	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	40	Total	reduced copper status	human
UK	42	Total	reduced copper status	human
EU	25	Total	reduced copper status	human
WHO/FAO	45	Total	reduced copper status	human

Safety data

The available data clearly show that zinc can cause adverse effects in humans and in domestic and laboratory animals. In humans, the most prominent effects of acute zinc toxicity include abdominal pain, nausea and vomiting, and occur at doses of approximately 200 mg or more.

Excess levels of dietary zinc interfere with the gastrointestinal absorption of copper, potentially leading to secondary copper deficiency. Symptoms of this include hypocupraemia, impaired iron mobilization, anaemia, leucopoenia, neutropenia, decreased superoxide dismutase (SOD) (particularly erythrocyte SOD (ESOD)), decreased ceruloplasmin, decreased cytochrome c oxidase, increased plasma cholesterol, increased LDL:HDL cholesterol, decreased glucose clearance, decreased methionine and leucine enkephalins, abnormal cardiac function and impairment of pancreatic enzymes, amylase and lipase. It has also been suggested that excess zinc is atherogenic.

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.
Zinc has been found to give positive results in some in vitro and in vivo genotoxicity tests. No data have been identified on the carcinogenicity of zinc.

A small study suggests that zinc supplementation increases the levels of glycosylated haemoglobin in diabetics. Sufferers from haemochromatosis may absorb larger amounts of zinc indicating possible increased risk of zinc-induced copper deficiency.

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 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.

Evaluation

High doses of zinc can result in secondary copper deficiency. Based on the severity of the effect, and having regard to the most vulnerable population group (diabetics), an upper limit for zinc is considered necessary. A level of 40 mg/day, based on the US limit (United States Institute of Medicine, 2001a), which takes into account the total dietary intake of zinc, has been adopted as an upper limit for the purpose of developing a standard for FSMP.

Calcium

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.

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.

Calcium	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	2,500	Total	Milk-Alkali syndrome	human
UK*	1,500	Suppl	gastrointestinal	human
EU	2,500	Total	evidence from different interventional studies	human

* Guidance level

Safety data

Calcium levels in the body are under the 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. Currently, the available data on the adverse effects of excess calcium intake in humans primarily concerns calcium intake from nutrient supplements. Of the many possible adverse effects of excessive calcium intake, the three most widely studied and biologically important are: 1) kidney stone formation (nephrolithiasis), 2) the syndrome of hypercalcaemia and renal insufficiency with and without alkalosis (referred to historically as milk-alkali syndrome when associated with a constellation of peptic ulcer treatments), and 3) the interaction of calcium with the absorption of other essential minerals.

These are not the only adverse effects associated with excess calcium intake. However, the vast majority of reported effects are related to or result from one of these three conditions.

Kidney stone formation

Kidney stones affect a large population. About 80% of kidney stones are composed of calcium oxalate or a mixture of calcium phosphate and calcium oxalate. Stones form only in urine that is supersaturated. Dietary calcium is not the determining factor in kidney stone formation, but higher intakes of oxalate, protein and vegetable fibre may play a role.

Milk-Alkali syndrome

Excessive calcium intake may lead to hypercalcaemia (serum calcium levels in excess of 10.5 mg/dl). Features of hypercalcaemia are progressive lethargy, confusion and ultimately coma (at serum calcium concentrations above 14 mg/dL). These effects are reversible and are directly related to the degree of hypercalcaemia. Headache, elevated cerebrospinal fluid protein and, rarely, convulsions, may also occur in patients with hypercalcaemia. However, hypercalcaemia more commonly results from an excessive ingestion of both calcium and alkali, such as antacid tablets, calcium supplements and milk (providing vitamin D which promotes calcium absorption), a condition, which is known as milk-alkali syndrome (MAS). Clinical signs of MAS are hypercalcaemia, alkalosis and renal insufficiency. MAS can be acute, intermediate (Cope's syndrome) or chronic (Burnett's syndrome) depending on the duration of exposure and symptoms. Hypercalcaemia, hyperphosphatemia and renal insufficiency are reversible after acute or intermediate exposure. However, chronic MAS is associated with irreversible or only partially reversible renal insufficiency and metastatic calcinosis (deposition of calcium in soft tissue). Historically, the majority of patients developing MAS have been middle-aged males ingesting milk and absorbable alkali, but this has decreased with the use of modern medication for peptic ulcer disease. More recently, case reports have described the syndrome occurring in predominantly female patients taking calcium-containing drugs for conditions such as autoimmune disease, organ transplantation, chronic renal failure and osteoporosis. The syndrome has been reported to occur at calcium carbonate intakes of 4000 mg/day and above.

Hypercalcaemia commonly occurs as a result of hyperparathyroidism and malignancy. Breast cancer, lung cancer, and multiple myeloma are the neoplasias most commonly associated with hypercalcaemia, due either to osteolytic secondary deposits or to ectopic parathyroid-like hormone production, typically in lung cancer.

Interaction with other minerals

High calcium diets and supplements can affect the bioavailability of other essential minerals, iron, zinc, magnesium and phosphorus. Calcium-mineral interactions are more difficult to quantify than kidney stones and MAS, since in many cases the interaction of calcium with several other nutrients results in changes in the absorption and utilisation of each. Thus, it is virtually impossible to determine a dietary level at which calcium intake alone disturbs the absorption or metabolism of other minerals.

Mechanisms of toxicity

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.

Vulnerable groups

Patients with renal failure are particularly susceptible to developing hypercalcaemia when taking calcium supplements. Individuals without renal failure taking diuretics may also be at increased risk. Patients with absorptive or renal hypercalciuria, primary hyperparathyroidism and sarcoidosis may have a higher risk of renal stone formation following calcium supplementation.

Evaluation

High calcium intake has been shown to be associated with kidney stone formation, reduced renal function and hypercalcaemia even when the exposure period was relatively short. Therefore, an upper limit for calcium is appropriate for the purpose of developing a standard for FSMP.

An upper limit of 2500 mg/day for calcium has been established, based on the upper limits of the US (United States Institute of Medicine 2000c) and the EU (Scientific Committee on Food, 2003), since these values were based on total dietary intake.

Magnesium

Magnesium is a metallic element of group II of the periodic table and has an atomic weight of 24.3. 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.

Magnesium	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	350	non-food	diarrhoea	human
UK*	400	Suppl	diarrhoea	human
EU	250	Suppl	diarrhoea	human

Safety data

Magnesium, when ingested as a naturally occurring substance in foods, has not been demonstrated 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.

The common effect of excessive ingestion of magnesium is osmotic diarrhoea. Magnesium is used therapeutically for its laxative effect. This effect produced by pharmacological use of various magnesium salts is an osmotic effect and may be accompanied by other mild gastrointestinal effects such as nausea and abdominal cramping. Magnesium ingested as a component of food or food fortificants has not been reported to cause this mild, osmotic diarrhoea even when large amounts are ingested. Although magnesium supplements are used, comparatively few serious adverse reactions are reported until high doses are ingested. However, some individuals in the populations may be at risk of a mild, reversible adverse effect (diarrhoea) even at doses from non-food sources that are easily tolerated by others. Thus diarrhoea was chosen by the US (United States Institute of Medicine 2000c), UK (Expert Group on Vitamins and Minerals, 2003) and EU (Scientific Committee on Food, 2003) as the most sensitive toxic manifestation of excess magnesium intake from non-food sources.

At larger pharmacological doses (e.g. repeated daily ingestion of 30 g) of magnesium can clearly result in more serious adverse reactions, such as metabolic alkalosis, hyperkalaemia, paralytic ileus and cardio respiratory arrest.

Evaluation

Osmotic diarrhoea is considered a mild and reversible adverse effect and is quite apparent to the individual. Since FSMP products are prescribed under medical supervision, this adverse effect would be recognised and result in a change of treatment. An upper limit for magnesium is not considered necessary for the purpose of developing a standard for FSMP.

Iron

Iron 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 majority of functional iron within the body is present in haem proteins, such as haemoglobin, myoglobin and cytochromes, which are involved in oxygen transport or mitochondrial electron transfer. Many other enzymes also contain or require iron for their biological function.

Many of the key biological functions of iron in living systems rely on the high redox potential, enabling rapid conversion between the Fe^{2+} and Fe^{3+} forms. The redox potential is, however, also potentially harmful in terms of the capacity for oxidative damage to cellular components such as fatty acids, proteins and nucleic acids. However, iron within the body is normally bound to carrier proteins and/or molecules with antioxidant properties, which minimise the capacity of the free ion to cause oxidative stress.

Iron	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	45	Total	gastrointestinal	human
UK*	17	Suppl.	gastrointestinal	human
EU	no assessment available			

* Guidance level

The guidance value of the UK (Expert Group on Vitamins and Minerals, 2003) and the upper level of US (United States Institute of Medicine, 2001a) does not apply to the small proportion of the population who have increased susceptibility to iron overload, via a mechanism of unregulated (increased) absorption from the diet, associated with the homozygous haemochromatosis genotype (estimated prevalence, approximately 0.4% in Caucasian populations).

Safety data

In humans acute iron poisoning is associated with severe gastrointestinal damage which may include haemorrhagic gastroenteritis. Blood and other fluid loss may lead to shock and coma. In some cases, apparent recovery may take place, possibly due to a latency period during which the iron is distributed throughout the body. Systemic iron toxicity is characterised by multi-system damage, principally in the liver, metabolic acidosis, coagulopathies and cardiovascular collapse.

Acute poisoning is relatively unusual in adults, the lethal dose being approximately 100 g, but is more common in children. Iron overload as a result of dietary intake is unusual in the normal population and only a handful of case reports exist describing this phenomenon. This may be due to the reduction in iron absorption that occurs as exposure increases. Individuals with conditions such as hereditary haemochromatosis (HHC) are particularly vulnerable to iron overload, which occurs as a result of enhanced uptake. In subjects heterozygous for the condition, a small increase in iron storage may occur. It has been suggested that heterozygous subjects (up to 1% of the population) may have an increased risk of cardiovascular disease but this remains controversial. Similarly, the suggestion that high iron status may be associated with other chronic conditions remains unresolved.

Studies in rodents suggest a pattern of iron overload comparable with that seen in haemochromatosis, with cellular changes but not with fibrosis occurring. Reproductive studies in rodents have shown no significant evidence of iron transfer across the placenta. This is supported by a study in an ovine model where maternal iron poisoning did not result in increases in foetal serum iron levels. However one study reports that iron gluconate is teratogenic, causing exencephaly in mice following administration on the 8^{th} and 9^{th} days of gestation.

For iron-replete individuals in non-developing countries, the most common side effects reported are gastrointestinal in nature, usually constipation but nausea, vomiting and epigastric pain have also been reported. These effects are reported to follow supplement doses of between 50 and 220 mg iron/day, the frequency increasing at higher dose levels. The severity and occurrence of effects depends on the formulation of the supplement. A number of studies have examined the effects of different iron formulations.

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.

Evaluation

Diarrhoea is considered a mild and reversible adverse effect and is quite apparent to the individual. Since FSMP products are prescribed under medical supervision, this adverse effect would be recognised and result in a change of treatment. An upper limit for iron is not considered necessary for the purpose of developing a standard for FSMP.

Phosphorus

Phosphorus is a group 5 element of the periodic table and has an atomic weight of 30.97.

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.

Phosphorus	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	4,000	Total	serum inorganic phosphorus levels	human
UK	2,400	Total	gastrointestinal	human
EU	no assessment available			

Safety data

The majority of the published data relating to the toxicity of phosphorus in humans focus on accidental or intentional ingestion of the more toxic forms of phosphorus that are not found in food or food supplements (e.g. elemental yellow phosphorus).

Serum inorganic phosphorus intake (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.

The predominant adverse reaction to orally administered phosphorus (as various phosphate salts, including sodium, potassium, ammonium and glycerol) in human supplementation studies is osmotic diarrhoea, which has been reported at intakes of 750 mg/day and above. Other mild gastrointestinal effects, including nausea and vomiting have been noted in some studies.

The US (United States Institute of Medicine 2000c) 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.

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. Moreover, information is lacking concerning adverse effects in the zone between normal P_i and levels associated with ectopic mineralization. An uncertainty factor of 2.5 was used, since the relation between intake and blood level is known.

Evaluation

Osmotic diarrhoea is considered a mild and reversible adverse effect and is quite apparent to the individual. Since FSMP products are prescribed under medical supervision, this adverse effect would be recognised and result in a change of treatment. An upper limit for phosphorus is not considered necessary for the purpose of developing a standard for FSMP.

Manganese

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 risk assessment, the word manganese refers to ionic manganese, except when specific manganese compounds are mentioned.

Manganese is a component of a number of enzymes and activates a range of others. Glycosyl transferases are specifically activated by manganese.

Manganese	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	11	Total	neurotoxicity	human
UK	12.2	Total	neurotoxicity	human
EU*	not enough data available, but should be as low as possible			

* EU considered the available data not suitable for establishing an upper limit.

Safety data

Manganese has low acute toxicity. Occupational exposure, for example in manganese miners 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 of 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.

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.

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.

With the risk characterisation 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.

Evaluation

High doses of manganese can result in neurotoxicity. This is a serious adverse effect, with the elderly especially sensitive. The margin between the recommended daily intake and adverse effects levels is small, therefore, an upper limit is considered necessary. A level of 11.5 mg manganese/day (mean of UK (Expert Group on Vitamins and Minerals, 2003) and US (United States Institute of Medicine, 2001a)) has been established as an upper limit for the purpose of developing a standard for FSMP.

Copper

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.

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.

Copper	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	10	Total	hepatotoxicity	human
UK	10	Total	forestomach, kidney and liver damage	animal
EU	5	Total	hepatotoxicity	human
WHO/FAO	10 (f), 12 (m)	Total	hepatotoxicity	human

Safety data

Acute copper toxicity is rare, but can occur as a result of food or beverage contamination. However, the emetic properties and unpleasant taste of copper salts prevent their frequent accidental or deliberate ingestion. Signs of acute copper toxicity include salivation, epigastric pain, nausea, vomiting and diarrhoea. Individual susceptibility varies, but vomiting has been associated with consumption of beverages contaminated with copper ranging from 25 to 840 mg/L. Intakes of 25 – 75 mg copper have been quoted as emetic doses but lower intakes have resulted in the same symptoms when taken on an empty stomach. Ingestion of ≥100 g copper sulphate may produce intravascular haemolysis, acute hepatic failure, acute tubular renal failure, shock, coma or death. Haemodialysis patients and subjects with chronic liver disease are potentially sensitive to copper excess.

Children may be at increased risk of copper toxicity due to a combination of efficient uptake and immature biliary excretion. However, copper is accumulated in the third trimester of pregnancy without apparent adverse effect, suggesting that neonates may be resistant to high levels of hepatic copper. Subjects with Wilson's Disease and, possibly, Indian copper cirrhosis are sensitive to excess copper intake.

Copper is kept under tight homeostatic control to prevent the accumulation of excess amounts. Where dietary copper is high, absorption is reduced and, in particular, biliary excretion increased. Other mechanisms, which sequester excess copper within the cell, may also occur. Copper toxicity occurs when such defences are overwhelmed. Thus, in man, liver toxicity has only been seen in genetically determined conditions such as Wilson's disease and in Indian Childhood Cirrhosis where hepatic copper accumulation occurs. There is no evidence for copper carcinogenicity in the general population, although an elevated incidence of hepatoma has been suggested in untreated Wilson's disease patients or subjects recovering from Indian childhood cirrhosis.

In the general human population, the key adverse effects usually associated with excess copper intake are gastrointestinal, resulting from consumption of copper in water or beverages.

There are some animal data for copper, although few from adequate chronic studies. Forestomach lesions, liver and kidney toxicity and anaemia were reported in a sub-chronic toxicity study. Reproductive effects have been reported in laboratory animals, but these findings are not consistent.

Daily intakes of copper ranging from 2 to 32 mg in drinking water have been reported to cause symptoms of general gastric irritation (US EPA 1987). This low limit in water is of interest given that an intake of 2 mg/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 12 mg/day seem to have no detrimental effect on human health (WHO 1996). This will take account of the quantity likely to be consumed from the usual diet (<10 mg/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 (United States Institute of Medicine, 2001a) 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 (Scientific Committee on Food, 2003) 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.

Evaluation

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 upper limit for FSMP. A level of 10 mg copper/day, based on the US, and FAO/WHO evaluations, has been adopted as an upper limit.

Molybdenum

Molybdenum does not exist naturally in the metallic state, but occurs in association with other elements.

The basis of the importance of molybdenum is in its role in metalloenzymes. All of the molybdoenzymes are oxidoreductases, which exploit the variable valency states of molybdenum. The molybdenum in molybdoenzymes is inserted as part of a prosthetic group, known as the 'molybdenum cofactor'. In humans, xanthine oxidase and sulphite oxidase are important molybdoenzymes.

Molybdenum	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	2	total	reproductive effects	rat
UK*	0.23		insufficient data	
EU	0.6	total	reproductive effects	rat
WHO/FAO				

* Guidance level, the level is the current estimated maximum intake from the UK diet.

Safety data
It is recognised that molybdenum interacts with copper and sulphates in living organisms, but the mechanism of this interaction has not been elucidated. The presence of dietary copper and sulphate affects the amount of molybdenum absorbed and retained by the body.

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. Occupational exposure, by inhalation, to molybdenum containing dusts has been associated with pneumoconiosis.

Although non-ruminant animals will develop symptoms of toxicity when fed high molybdenum diets, ruminants are much more sensitive. Thus the toxicity seen in these species cannot be related to the effects that would be expected in man. The toxicity is primarily expressed as a copper deficiency and the ambient sulphate level has a marked effect on the interaction between copper and molybdenum.

Molybdenum toxicity in animals is commonly referred to as molybdenosis or teart. In appearance it is similar to the disease of copper deficiency. Signs of molybdenum toxicity in animals include anaemia, anorexia, profound diarrhoea, joint abnormalities, osteoporosis, hair discoloration, reduced sexual activity and death.

Few data are available concerning oral molybdenum toxicity in humans, but some data exist that suggest an increased incidence in gout-like symptoms (joint pains and increased serum uric acid) in populations with a high molybdenum intake (1 – 15 mg/person/day). The form of the molybdenum is uncertain. Few details of this study are available.

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.

Based on studies in rats and mice, the EU (Scientific Committee on Food, 2003) and US (United States Institute of Medicine, 2001a) established a NOAEL of 0.9 mg/kg/day. There do not appear to be sufficient data to justify lowering the degree of uncertainty from the usual uncertainty factor for extrapolating from experimental animals to humans. Thus, the usual value of 10 was selected. The US used a UF of 3 for intraspecies variation which was based on the expected similarity in pharmokinetics of molybdenum among humans, while EU used a UF of 10 for intraspecies variation.

Individuals who are deficient in dietary copper intake or have some dysfunction in copper metabolism that makes them copper-deficient could be at increased risk of molybdenum toxicity. However, the effect of molybdenum intake on copper status in humans remains to be clearly established.

Evaluation

Based on the lack of evidence of molybdenum toxicity in humans, an upper limit does not need to be established for the purpose of developing a standard for FSMP.

Sodium

Sodium chloride is the simple ionic salt of sodium and chlorine. It is an odourless clear or white soft crystal with a distinctive taste.

Sodium, together with potassium, is an essential mineral for regulating body fluid balance. Sodium is the most abundant cation in the extracellular fluid and sodium salts account for more than 90% of the osmotically active solute in the plasma and interstitial fluid. Consequently, sodium load is the major determinant of extracellular volume. Chloride is also important in maintaining the fluid balance and is an essential component of the gastric and intestinal secretions.

Sodium	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	5,800	total	blood pressure	humans
UK*	-	total	blood pressure	humans

* It is not possible to establish a safe upper level for sodium chloride because there appears to be a graded response across doses that include the current estimated intake in the UK. Sodium is not ordinarily suitable for use in supplements.

Safety data

Although rare, acute sodium chloride toxicity may be caused by ingestion of 500 – 1000 mg sodium chloride/kg bodyweight. Symptoms include vomiting, ulceration of the gastrointestinal tract, muscle weakness and renal damage, leading to dehydration, metabolic acidosis and severe peripheral and central neural effects. This is however, normally self-limiting. High sodium chloride intakes increase calcium excretion and may increase the risk of kidney stone formation. There is evidence for a causal relationship between the consumption of sodium (mainly from common salt) and both blood pressure and the age-related rise in blood pressure. Data suggest that 30% of a normotensive population may be salt sensitive.

In rodents, extremely high doses of sodium chloride during pregnancy caused musculoskeletal abnormalities, foetotoxicity and foetal death and post-implantation mortality and abortion. Administration to rats of diets containing high levels of sodium chloride throughout pregnancy and during the early life of offspring have been shown to permanently alter fluid retention and to increase blood pressure in the offspring.

Increased blood pressure is seen in susceptible sectors of the population (those who are ‘salt sensitive’), at intake levels that are not above average for the population as a whole. Results are available from numerous trials in hypertensive individuals, in which decreasing sodium chloride intake has been shown to have beneficial effects, by lowering blood pressure. However, the data from administration of increased levels of dietary sodium chloride are minimal. Opinion is divided concerning the long-term influence of dietary sodium chloride intakes greater then 6000 mg per day on the development of essential hypertension.

Increases in both systolic and diastolic blood pressures were observed in normotensive adults receiving 2200 mg/day supplementary sodium, with estimate total sodium chloride intake of 7500 mg/day. Two small trials in normotensive individuals have shown that intakes of sodium chloride of approximately 14,000 mg/day lead to increased blood pressures. The assumption is made that similar or greater effects might follow augmentation of sodium chloride intake in hypertensive individuals.

Evaluation

For the general population, the UK (Expert Group on Vitamins and Minerals, 2003) and US (United States Institute of Medicine, 2004) have recommended that the current salt intake should be reduced, due to the correlation between salt intake and hypertension. However, since FSMP products are prescribed under medical supervision, effects on blood pressure would be recognised and result in a change of treatment. An upper limit for sodium is not considered necessary for the purpose of developing a standard for FSMP.

Potassium

Potassium is an alkaline, metallic element. It is not found in the elemental form in nature and is always found combined with other substances, most commonly as the chloride salt (KCl). Potassium is widely distributed in silicate rocks, and occurs in salt beds and seawater.

Potassium, together with sodium, is essential for the maintenance of normal osmotic pressure within cells. About 98% of the total body potassium is located intracellularly where the concentration can be 30 times that of the extracellular concentration. The extracellular potassium concentration is a critical determinant of neuromuscular excitability. Potassium is also a cofactor for numerous enzymes and is required for secretion of insulin by the pancreas, for phosphorylation of creatine and for carbohydrate metabolism and protein synthesis.

Potassium	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US#	-	food		human
UK*	3,700			human

There is no evidence that in normal persons high levels of potassium from food would result in adverse effects. However, supplemental potassium could result in adverse effects and therefore should only be offered under medical supervision.
* Guidance level

Safety data

A number of case reports of accidental and deliberate poisoning with potassium have shown that large doses of potassium result in hyperkalaemia and hypernatraemia and lead to in changes in acid-base balance and respiratory and heart rates. However, the dose associated with the onset of hyperkalaemia and adverse effects varies depending on potassium status and clearance time. Supplementation studies have generally not reported side effects, although it is unclear whether side effects were specifically investigated in many of these studies. However, endoscopic investigation following periods of potassium supplementation has shown that potassium supplementation may cause local irritation in the gastrointestinal tract, leading to erosion and ulcerations.

The available animal data are not relevant to this risk assessment as the effects described are considered to be due to the anionic components, such as bromate and iodate.

Older people and infants may be more vulnerable to potassium toxicity due to lower renal function, as may patients with conditions such as pre-existing hyperkalaemia, renal disease, acidosis, insulin deficiency or digitalis intoxication.

Evaluation

No upper limit for potassium is proposed for the purpose of developing a standard for FSMP, however some groups might be more vulnerable to potassium toxicity and medical supervision is necessary.

Thiamin

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.

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.

Thiamin	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	no upper limit	food	no adverse effects	human
UK*	100	supplemental	no specific effect	human
EU	no upper limit	total diet	no adverse effect	human

* Guidance level, for water-soluble forms of thiamine only

Safety data

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.

It is generally accepted that ingested thiamin has a very low toxicity in humans. Most data are either in the form of case reports of possible thiamin-associated adverse effects or from thiamin supplementation studies designed primarily to investigate potential beneficial effects. The latter do not always specifically report an absence of adverse effect. The limited amount of human data indicates that adverse effects are generally CNS-related and occur only at very high doses. A small number of individuals may show an allergic response to lower doses, but reports of these lower dose-related events are rare. It is possible that this sub-population may be the same sub-group that is susceptible to adverse effects, e.g. anaphylaxis etc, following parenteral administration of thiamin.

The animal database is also very limited. 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.

Evaluation

Based on the low toxicity of thiamin, an upper level does not need to be established for the purpose of developing a standard of FSMP.

Riboflavin

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.

Clinically, riboflavin promotes normal growth and assists in the synthesis of steroids, red blood cells, and glycogen. 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.

Riboflavin	**Upper limit mg/day**	**Total diet / suppl**	**Critical effect**	**human /animal data**
US	no upper limit	food	no adverse effects	human
UK*	43	total	no specific effect	human
EU	no upper limit	total diet	no adverse effect	human

* Guidance level,

Safety data

In several human studies riboflavin was well tolerated with no reports of adverse events. Data on the toxicity of riboflavin in experimental animals are sparse. Acute oral administration of riboflavin to rats produced no adverse effects. Riboflavin has also been administered orally to rats, mice, rabbits and dogs for long periods without obvious toxicity. However, in none of these studies was a full evaluation performed, and in most cases only a very limited number of endpoints was investigated.

Evaluation

Based on the low toxicity of riboflavin, an upper level does not need to be established for the purpose of developing a standard for FSMP.

Chromium

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.

Trivalent chromium has been shown to potentiate insulin action and thereby influences carbohydrate, lipid and protein metabolism.

Chromium	Upper limit mg/day	Total diet / suppl	Critical effect	human /animal data
US	no upper limit	total diet	insufficient data	human
UK*	10	total diet	no adverse effect	animal
EU#	1	supplementation	no adverse effect	human
WHO	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.

Safety data

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 risk 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
Based on the low toxicity of chromium, an upper level does not need to be established for the purpose of developing a standard for FSMP.

NUTRITIVE SUBSTANCES

N-acetyl-methionine

N-acetyl-L-methionine is classified as a food additive by the USFDA (21CFR172.372), although in the USA it cannot be added to infant foods and foods containing added nitrites/nitrates in order to limit the possible formation of nitrosamines (SCF, 1999). Under US regulations, the amount of additive used for nutritive purposes should not exceed 3.1% w/w L and DL-methionine (USFDA, 2003). The purpose of the food additive is to enhance the biological quality of the total protein in a protein-containing food. The European Food Safety Authority (EFSA, 2003) recently assessed the safety of n-acetyl-L-methionine for use in FSMP.

Safety data

There is limited data available to assess the safety of N-acetyl-methionine, other than reviews by the FDA (1992), the United States Institute of Medicine (2001b) and the EU (EFSA, 2003).

Mammalian tissues contain acylase-I, which is one of the enzymes enabling utilisation of amino acids from exogenous and endogenous acyl derivates (including dipeptides and N-acetyl amino acids derived from protein hydrolysis). Deacetylation of N-acetylhistidine was inhibited in the mouse kidney after intraperitoneal injection of a mixture of N-acetylhistidine and N-acetyl-L-methionine. This suggests that the efficiency of deacetylation may be affected when specific mixtures of N-acetyl amino acids are ingested.

After loading with equimolar quantities of L-methionine and N-acetyl-L-methionine, *in vivo* studies in pigs and in humans demonstrated similar mean plasma methionine concentrations. However, plasma methionine concentrations peaked slightly later after administration of N-acetyl-L-methionine than after L-methionine. The observed delay and the fact that N-acetyl-L-methionine was not detected in portal or venal plasma indicate that N-acetyl-L-methionine is hydrolysed before the absorption in either the intestinal lumen and/or mucosal cells with the release of free methionine.

The delay in absorption does not affect the ability of N-acetyl-L-methionine to serve as a methionine source as demonstrated in animal feeding studies measuring growth rate and protein efficiency ratio. In these studies the bioavailability of L-methionine and N-acetyl-L-methionine was similar. Also a metabolic balance study in humans supports equivalent utilisation of N-acetyl-L-methionine and L-methionine in terms of nitrogen retention.

Data on genotoxicity, reproductive and developmental toxicity of N-acetyl-L-methionine are not available. Such toxicity studies are not needed in the light of the proposed levels of use and the hydrolysis of N-acetyl-L-methionine to physiological substrates (acetate and methionine).

Possible toxic effects of N-acetyl-L-methionine will be related to the toxicity of excessive L-methionine, which in animal manifests as depressed feed intake and body weight gain and tissue damage. As N-acetyl-L-methionine is intended to replace L-methionine in FSMPs, the exposure to N-acetyl- L-methionine is estimated to correspond to the current intake of L-methionine from these foods.

EFSA concluded that N-acetyl-L-methionine as a source of L-methionine for use in FSMP in children over one year of age and adults is not of concern from the safety point of view.

The US has not established an upper limit for L-methionine due to inadequate data (USA Institute of Medicine, 2001b).

Exposure data

The addition of N-acetyl-methionine to products is normally limited by the level required to meet requirements for methionine and levels of methionine used in existing FSMPs.

The mean intake of L-methionine from food and supplements in the USA is 1.8g/day with men aged 51 to 70 years the highest consumers (99th percentile) at 4.1g/day (USA Institute of Medicine, 2001b). In individuals consuming 100g protein/day, the daily methionine intake is 1.4g methionine/day (FDA, 1992).

For the application to approve the use of N-acetyl-L-methionine as a FSMP in the EU it was estimated that the typical daily intake of N-acetyl-L-methionine by patients with phenylketonuria would range from 0.86 g (providing 0.67 g of L-methionine) for a 1-2 years old child to 3 g (providing 2.34 g of L-methionine) for an adult in order to provide virtually all their daily intake of methionine.

Evaluation

The exposure to L-methionine from the addition of N-acetyl-L-methionine to FSMP will correspond to that of L-methionine if used as a source of L-methionine, and therefore is unlikely to give rise to adverse health effects based on the present knowledge on methionine toxicity.

L-asparagine monohydrate

Asparagine is considered a non-essential amino acid, although early studies in the scientific literature (1960-70's) have suggested that it may be required for maximal growth in infants. The industry has suggested that it is used in metabolic formulae for patients with particular metabolic disorders.

Safety data
There is limited data available to assess the safety of asparagine, other than reviews by the FDA (1992) and the United States Institute of Medicine (2001b). Therefore, there is insufficient data to determine the safe level of human intake of asparagine (FDA, 1992; USA Institute of Medicine, 2001b). However, as asparagine is rapidly converted to aspartate in the GI-tract, safety data on aspartate can be used to establish an upper safe level.

The use of 8.6g/day aspartate in food supplements has not been associated with adverse effects based on single oral dose studies, although no long-term studies are available (FDA, 1992). However, the potential for adverse effects on the foetus or in developing children has not been assessed and would suggest that use in these populations would need to be used under strict medical supervision.

Since the artificial sweetener aspartame contains about 40 per cent aspartic acid, studies on the effects of oral administration of this dipeptide provide useful information on the safety of aspartic acid. Aspartame is a dipeptide of two amino acids aspartame and phenylalanine with an additional methyl ester group. It has been the subject of over 100 scientific studies. Radio labeled studies in animals have revealed that aspartame is rapidly digested to three moieties, phenylalanine, aspartic acid, and the methyl ester, which are then absorbed, metabolised, and excreted by normal biochemical pathways.

A wide range of toxicological studies (acute, sub-chronic, chronic, teratology and genotoxicity) have been performed in various animal species. No significant toxicological or carcinogenic effect has been attributable to aspartame administration in doses up to 13g/kg in sub-chronic studies (mice, hamsters, rats, dogs and monkeys) and up to 8g/kg in chronic studies (mice and rats).

JECFA (WHO, 1980) allocated an ADI for aspartame as a food additive of 0-40 mg/kg of body weight. The allocation of an ADI to aspartame, was based on observations in a long term rat study and further biochemical studies in humans analyzing renal changes in both species, and brain tumours in rats.

There has been an unprecedented number of clinical studies to determine whether aspartame would be tolerated by normal adults and children, and with studies on special population groups such as the obese and diabetics, as these groups may be larger consumers due to their unique dietary and nutritional situations. To date, no adverse effects have been demonstrated.

Exposure data

Daily intakes of L-asparagine from 100g of dietary protein is about 7.4 g asparagine/day or 3.2 g aspartic acid (FDA, 1992).

Industry provided data that suggested this nutrient would be used at levels of up to 1.9 g/100 g powder in infants and adults with phenylketonuria, branched chain ketoaciduria and with intolerance to intact protein.

Evaluation

Daily intake through the diet in healthy subjects up to 7.4 g asparagine/day or 3.2 g aspartic acid/day does not result in adverse effects.

Asparagine is rapidly converted to aspartate, which has low toxicity. Therefore, for FSMP, an upper limit is not considered necessary.

Chromium acetate and chromium potassium sulfate dodecahydrate

Various forms exist for chromium (III) compounds, e.g. chromium potassium sulphate dodecahydrate; chromium chloride, chromium acetate, chromium picolinate and chromium sulfate.

Chromium is currently permitted in Code in infant formula as chromium sulphate (recommended maximum amount 2 μg/ 100 kJ, not legally binding) and in supplementary sports foods (100 mg-inorganic, permitted form chromium chloride; 50 mg organic, permitted forms high chromium yeast, chromium picolinate, chromium nicotinate, and chromium aspartate). At Draft Assessment of P242 – FSMP the following chromium forms were proposed to be permitted: chromium sulphate and chromium chloride. During consultation the Australian and New Zealand Enteral Nutrition Manufacturers Association (ANZENMA) requested chromium acetate and chromium potassium sulfate dodecahydrate to be accepted as other permitted forms of chromium.

No information is available regarding the approval of chromium acetate in other countries. Chromium potassium sulfate dodecahydrate is considered to be a potassium salt of chromium sulfate.

Safety data on chromium acetate

A general safety assessment of chromium III compounds was included in the mineral and vitamins part of this safety assessment. It was concluded that chromium III compounds are of low toxicity. Therefore an upper limit for chromium III is not necessary. The general safety assessment was for the purpose of setting an upper limit, not for specifying which chromium III compounds are considered safe. Therefore, more discussion of chromium acetate and chromium potassium sulfate dodecahydrate is necessary.

Trivalent chromium compounds, with the exception of acetate, hexahydrate of chloride, and nitrate salts, are generally insoluble in water (ATSDR, 2000). This could increase the absorption of chromium III in the intestines. There are no studies available, which could indicate that, the change in solubility would not alter absorption resulting similar effects as insoluble chromium III compounds. There is one old chronic study available where chromium acetate was administered in drinking water to rats for 2-3 years (Schroeder et al, 1965). No adverse effects were observed at the highest level (0.46 mg/kg bw/day), however this dose was ~5000 times lower than studies with chromium trichloride which were used to determine the safety of chromium III compounds.

Safety data on chromium potassium sulfate dodecahydrate

Chromium potassium sulfate dodecahydrate has similar features as chromium sulfate and is therefore not soluble in water. Therefore, it can be assumed that the toxicological profile of chromium potassium sulfate dodecahydrate is similar to the toxicological profile of chromium sulfate and that within the safety of chromium III compounds, chromium potassium sulfate dodecahydrate is included.

Evaluation

Based the different solubility of chromium acetate compared to other chromium III forms, its toxicological profile could not be determined. Therefore it is proposed that this form should not be permitted for FSMP.

Since the characteristics of chromium potassium sulfate dodecahydrate are similar to the already permitted form chromium sulfate, it is proposed that chromium potassium sulfate docecahydrate be permitted as a chromium compound. Therefore, the following chromium compounds are proposed to be permitted: chromium sulphate, chromium chloride and chromium potassium sulfate dodecahydrate.

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Attachment 4

Labelling Assessment

Proposal P242 – Food For Special Medical Purposes

The purpose of this assessment is to consider the labelling requirements for food for special medical purposes (FSMP).

Background

Labelling is one of a number of risk management tools used by Food Standards Australia New Zealand (FSANZ). FSANZ uses labelling in the development of food standards if there is –

- a demonstrated risk to public health and safety; and/or
- a need to ensure the adequacy of information for informed choice; and/or
- the potential for misleading and deceptive conduct.

Labelling of FSMP

The majority of FSMP (99%) in Australia and New Zealand are imported predominately from the United States of America (US) or Europe (EU) and are therefore, labelled according to the regulations of these regions. For the most part labelling features such as food identification including the food name, lot and batch number and manufacturer/supplier contact details, date marking, warning statements, directions for use and storage, ingredient listing and nutritional information are applied consistently across the majority of different FSMP products, and are often consistent with the Codex labelling standards.

Most manufacturers of FSMP customise labelling information for the domestic market by providing supporting product literature to health professionals. However, the information provided and that contained on the label do not always comply with the requirements of the Code.

Labelling Requirements in the Code

The Code does not explicitly recognise FSMP and therefore unlike other foods, FSMP do not have any specific labelling requirements. However, there are a number of generic labelling provisions in the Code that currently apply to FSMP. These include:

- food identification including the food name, lot and batch number and local manufacturer/supplier contact details (Standard 1.2.2);
- mandatory warning and advisory statements and declarations (Standard 1.2.3);
- ingredient labelling (Standard 1.2.4);
- date marking (Standard 1.2.5);
- directions for use and storage (Standard 1.2.6);
- nutrition information (Standard 1.2.8);
- legibility (Standard 1.2.9);
- percentage of characterising ingredients (Standard 1.2.10);
- health and related claims (Standard 1.1A.2); and
- country of origin labelling (Standard 1.1A.3).

Position at Draft Assessment

The application of generic labelling standards were assessed on a case-by-case basis according to the assessed risk to public health and safety, and the information needs of health professionals and consumers. For the most part, the application of generic labelling standards to FSMP labels was seen as necessary, although a number of modifications were made to adapt these requirements specifically to FSMP.

A summary of the labelling requirements proposed at Draft Assessment is provided in the box below.

Generic Labelling Requirements

- The majority of generic labelling requirements in the Code to apply to FSMP including: health and related claims (Standard 1.1A.2), country of origin (Standard 1.1A.3), food identification and local supplier details (Standard 1.2.2), mandatory warning and advisory statements and declaration (Standard 1.2.3), ingredient labelling (Standard 1.2.4), date marking (Standard 1.2.5), directions for use and storage (Standard 1.2.6), and legibility requirements (Standard 1.2.9).
- The requirements of Standard 1.2.8 – Nutrition Information Requirements to not apply to FSMP except for:
  - definitions; and
  - claims for lactose and gluten.
- Exemption from the provisions of Standard 1.2.10 – Percentage Labelling of Characterising Ingredients.

Specific Labelling Requirements

- Inclusion of a mandatory advisory statement that FSMP are to be used only under medical supervision, preceded by words to the effect of 'Important Notice'.
- Permission for the labelling of a statement on the condition, disease or disorder for which the FSMP has been specifically formulated.
- For nutrition information requirements:
  - the declaration of a nutrition information statement that may be in the form of a table with: the energy content, protein, fat, carbohydrate, vitamin, mineral and other nutritive substance quantity expressed per 100 g or 100 mL as prepared; and
  - the number of servings per package and serving size.

Additional Labelling Specific to FSMP other than VLED

- The labels of FSMP other than VLED to contain a statement:
  - that the product poses a health hazard when consumed by individuals who do not have the disease(s), disorder(s) or medical condition(s) for which the product is intended;
  - that the product is not for parenteral use;
  - that the product is or is not intended as the sole source of nutrition;
  - concerning the adequate precautions, known side effects, contraindications, and product-drug interactions;
  - specifying the nutrient(s) which have been modified relative to normal requirements; and
  - information, where appropriate, on the specific age group(s) for which a product is intended.

Additional Labelling Specific to VLED

- The labels of VLED to include:
  - the prescribed statement 'for the dietary management of obesity';
  - reference to the importance of maintaining an adequate daily fluid intake;
  - a statement that the product may be unsuitable for use by pregnant, nursing and lactating women or by infants, children, adolescents and elderly; and
  - a statement on the recommended daily quantity of the product to be consumed, with the quantity to be established by the manufacturer of the VLED.

Rationale for Change To Draft Assessment Position

Submitters from all sectors expressed concern that the proposed labelling requirements at Draft Assessment may have a negative impact on the currently available range and supply of FSMP (**Australian Food and Grocery Council** (AFGC), **Australia New Zealand Enteral Nutrition Manufacturers Association** (ANZENMA), **Australian Society of Inborn Errors of Metabolism** (ASIEM), **Australian Self Medication Industry** (ASMI), **Dietitians Association of Australia** (DAA), **Novartis Consumer Health Australasia** (NCHA), **New Zealand Dietetic Association** (NZDA), **New Zealand Food Safety Authority** (NZFSA). ASIEM and the DAA were concerned that manufacturers will need to make significant and onerous changes to the labels of imported FSMP to comply with the proposed draft standard.

Generic Labelling Information

The decision to apply the majority of generic labelling requirements to FSMP was to meet FSANZ's statutory objectives of protecting public health and safety, providing adequate information to enable consumers to make informed choices, and to prevent misleading and deceptive conduct.

Submitters (ANZENMA, ASIEM, DAA, **South Australian Department of Human Services** (SADHS)) indicated that a large proportion of FSMP are imported in small and infrequent quantities and therefore, proposed generic labelling will impact on the availability of FSMP. Availability would be affected by price increases or removal of products from the market due to the impact of re-labelling/reformulation.

The possible impacts of withdrawal of FSMP from domestic markets is likely to have a greater impact on public health and safety than withdrawing generic labelling requirements for the following reasons:

- a reduction in availability of certain FSMP may compromise patients' health;
- any reduction in the availability of FSMP for patients with inborn errors of metabolism would have serious medical consequences; and
- international labelling requirements don't differ significantly from the Code.

<u>Proposed Approach</u>

To assure current availability of products, FSMP will need an exemption from the provisions within Standard 1.2.1. This exemption will effectively result in FSMP being free from compliance with the remainder of generic labelling requirements in Part 1.2 of the Code. However, to ensure that information essential to the use of FSMP is available to health professionals and consumers, a specific set of labelling provisions will be applied to FSMP in place of Part 1.2. These labelling requirements will be contained within a specific FSMP standard, and will include generic labelling requirements wherever the current range of FSMP can accommodate them.

Assessment of Generic Labelling Requirements

Food identification labelling including local supplier details

Name of the Food

Assessment

In Australia and New Zealand the label on a package of food must have a name or description to describe its true nature to allow consumers to make informed choices and to prevent misleading and deceptive conduct. The naming requirements for imported products are virtually identical which means that most imported products will satisfy Australia and New Zealand requirements.

Lot Identification

Assessment

In Australia and New Zealand the lot identification is required on the package of a food in the rare event of a food recall. A lot mark clearly identifies the lot a food comes from as well as the premises where the food was packed and prepared. Most FSMP already carry lot identification. The date mark and supplier's address details can help to satisfy the requirements of a lot mark.

Name and Business Address of the Supplier

Assessment

In Australia and New Zealand, the name and business address of the supplier are primarily placed on the label of a package of a food in the rare event of a food recall. These can be used in the absence of a lot mark. As the requirements in the EU and the US are virtually identical to Australia and New Zealand requirements, this information will be available on nearly all imported products.

In some circumstances it is likely that imported products will not have the name and address of a local supplier. As most products are not sold as individual units it is proposed to allow the supplier details to be provided on an outer carton. This will ensure that most imported products will not have to be re-labelled but will still provide adequate information in the case of a food recall.

Conclusion

The 'name of the food', 'lot identification' and 'name and address of the supplier' are essential labelling elements on FSMP in case of a food recall. In most circumstances overseas labelling will comply with the requirements in the Code with the possible exception of local supplier details. It will be unduly onerous to expect manufacturers to re-label each individual product with local supplier details when most products are shipped in bulk packs. It is therefore, proposed to allow the provision of this information on a transportation outer. This will allow the supplier to be contacted in the case of a food recall but not place onerous labelling requirements on importers.

Recommendation

Include food identification requirements for FSMP in draft Standard 2.9.5 allowing the name of the local supplier to be included on transportation outers.

Mandatory Warning and Advisory Statements and Allergen Declarations

Assessment

The Code requires that certain information be provided to consumers on labels and packages of food. This information may be in the form of a prescribed statement (which includes warning statements), an advisory statement or a specific declaration, depending on the degree of risk to the health and safety of consumers. This information is considered necessary for all foods to ensure that certain consumer groups are adequately informed of any potential risks to themselves, if they consume the product.

In most circumstances the labelling of overseas products will comply with the allergen labelling requirements in the Code. However, it is likely that there would be some situations where imported products would not meet these requirements. While people with allergens need to be informed of their presence to protect public health and safety, there is an inherent level of protection associated with the use FSMP because they are intended for use under medical supervision. Medical staff would be able to assist in the identification of allergies through clinical assessment and choose the appropriate products for patients accordingly. However, there would still need to be adequate information on the label of the FSMP, such as an ingredient list, to enable health professionals to choose the appropriate product. To assist health professionals, manufacturers also usually provide product-supporting literature that contains information on the presence of allergens in FSMP products.

If importers have to re-label products to comply with the allergen labelling requirements in the Code it is likely that they may withdraw the products from the domestic market. Also, to date there is no evidence of public health and safety risks to consumers of FSMP as a result of inadequate allergen labelling.

Codex and the EU require a number of additional warning and advisory statements on FSMP to assist health professionals to use them correctly and advise of any public health and safety risks to certain individuals. However, many of these statements are not mandatory with the regulations indicting that they 'should be provided' or are to be provided 'where/as appropriate'. Specific advisory and warning statements have been proposed for FSMP and are discussed later in this assessment.

Conclusion

There will be a greater risk to public health and safety if manufacturers withdraw their products from the domestic market, than through inadequate allergen labelling. There is no evidence of market failure associated with current allergen labelling on FSMP and as there is an inherent level of protection through medical supervision it seems appropriate to exempt FSMP from mandatory allergen declaration requirements contained in Standard 1.2.3. However, some information such as an ingredient list will need to appear on the label so health professionals can choose appropriate products for their patients. In addition, specific advisory or warning statements for FSMP will be included in Standard 1.2.3.

Recommendation

To exempt FSMP from Standard 1.2.3 except for specific mandatory warning and advisory statements.

Ingredient Listing

Assessment

Ingredient listing is required so consumers are aware of any substance, including food additives, used in the preparation, manufacture or handling of food. Ingredient listing are used for two purposes:

1. To protect public health and safety. For example, ingredient listing can assist certain individuals in identifying things that may cause a reaction; or
2. To prevent misleading and deceptive conduct. For example, ingredient listing prevents manufacturers from misleading consumers about the make up of products.

Industry feedback has indicated that the current range of FSMP already provide ingredient lists. In many circumstances overseas products will comply with Australia and New Zealand requirements and where they don't there will be sufficient information for supervising medical professionals to be able to make informed decisions with regard to a patients health and safety. In this case, reference to ingredient labelling requirements in US[34] and EU[35] regulations provides additionally flexibility for imported products without jeopardising public health and safety.

Conclusion

If products have to be re-labelled the biggest risk to public health and safety will be the withdrawal of products from the local market. Most FSMP already have ingredient labelling so allowing flexibility in the way products are labelled with this information will ensure products are still imported to domestic markets. It will also enable health professionals to identify ingredients that their patients need to avoid.

Recommendation

Include flexible ingredient labelling requirements for FSMP, which cover the aspects from relevant countries, in draft Standard 2.9.5 of the Code.

Date Marking

Assessment

Date marking provides valuable information to consumers on the quality of the product they are purchasing. Specifically, it offers a practical guide to consumers on the estimated length of time during which a product will retain certain expected characteristics relating to quality. For some food the date mark will also indicate the period of time it will remain safe to eat.

[34] US Code of Federal Regulations 21CFR101.4
[35] EC Directive 2000/13/EC, Article 6

Standard 1.2.5 permits food manufacturers to choose whether to label with a 'best before' date if the product can be safely consumed beyond the date but is no longer suitable for sale, or with a 'use by' date if they determine that the product will be unsafe for human consumption beyond this point in time. The EU have similar requirements whereas Codex and the US don't have an overarching requirement for use-by date.

Comments from industry have indicated that consideration should be given for the use of statements other than 'best before' or 'use by' in the date marking of FSMP. For example, the US have date marking formats which are consistent with the intent of domestic date marking requirements but use different wording, like 'Exp' (i.e. Expiry) instead of 'Use By'. Therefore, to prevent importers withdrawing their products from sale it is necessary to allow flexibility in the format for date marking, in particular the format in the US.

Conclusion

Date marking is essential to protect against the consumption of FSMP that may pose a risk to health and safety if they are not consumed by a certain date. However, unless alternative formats are permitted for date marks products may be withdrawn from sale in the domestic markets, which would increase health and safety risks to consumers.

Recommendation

Include date marking for FSMP in Standard 2.9.5 and allow flexibility in the format.

Nutrition Information Panel

Assessment

The nutrition information panel provides valuable information for consumers and in the case of FSMP, health professionals, to enable them to make informed choices about the products they are choosing.

At Draft Assessment, nutrition information panels were considered to be a form of labelling where some flexibility could be provided to facilitate the compliance of FSMP. It was proposed that nutrition information panels would not apply to FSMP except for provisions relating to definitions, and claims on lactose and gluten content.

Instead, basic nutrition information requirements were to apply to FSMP that were seen to be consistent with Codex and the EU FSMP regulations and other nutrition information could be supplied in supporting product literature.

However, accurate nutrition information is an essential component of FSMP labels, as health professionals rely on this information to make decisions on the use of products in situations where supporting product literature cannot be readily accessed. Basic information on the energy, fat, protein, carbohydrate and micronutrient content are essential labelling components for these situations. However, prescribing the exact format of this information may not add any value, so long as the health professional can interpret it.

Some of the submitters at Draft Assessment supported allowing varying formats such as the Codex requirements or accepted global practice. Numerous submitters (AFGC, ANZENMA, DAA, NA) indicated that the use of the number of serves and serving size on FSMP was inappropriate because the information is not useful according to how FSMP are used. For example, some FSMP, such as enteral feeds, are delivered in continuous amounts over time, or are used in varying amounts to meet the different nutritional requirements of specific medical conditions.

Standard 1.2.8 contains provisions relating to nutrition claims, including claims for: polyunsaturated, monounsaturated, and omega fatty acids; energy ('low joule'); lactose; gluten; salt and potassium. These provisions contain specific criteria that prevent nutrition claims from being misleading, or to ensure that such claims are based on a consistent product composition. However, these provisions were developed to manage the risks for nutrition claims made to the general public, and not for nutrition claims made to health professionals or the supervised consumers of FSMP. Therefore, the criteria specified for nutrition claims in Standard 1.2.8 are not considered relevant to FSMP and therefore should not apply.

The proposal at Draft Assessment to require FSMP to comply with Standard 1.2.8 requirements for claims in relation to gluten and lactose content of foods was to protect the health and safety of patients. For example, there are circumstances where patients require foods that are 'lactose free' and health professionals need to be sure that the products claiming to be 'free' are in fact 'free'.

In addition, the proposal to require gluten and lactose free claims to be consistent with the requirements in Standard 1.2.8 was to ensure consistency throughout the Code and with fair trading legislation. Fair trading legislation, which overrides the Code, stipulates that the conduct of corporations cannot be misleading or deceptive. The Australian Competition and Consumer Commission (ACCC) and the New Zealand Commerce Commission who enforce fair trading legislation in Australia and New Zealand have indicated that a product that claims to be 'free' must be 'free' unless permitted for in legislation (i.e. the Code).

Submitters were not opposed to the requirement for gluten and lactose free claims to comply with the criteria outlined in Standard 1.2.8 of the Code.

Conclusion

Nutrition information is necessary on the label to assist health professionals with the use of the FSMP. However, nutrition information panels outlined in Standard 1.2.8 of the Code are not entirely useful, particularly when we consider how FSMP are used and administered. Therefore, to prevent importers withdrawing their products from local markets but still ensuring that health professionals have adequate information to make decisions about products for their patients it is necessary to allow more flexible nutrition information requirements.

Information on the number of serves and serving sizes is not useful for FSMP because they are used differently to general-purpose foods. However, lactose and gluten free claims need to be consistent with the criteria outlined in Standard 1.2.8 to ensure the health and safety of patients, consistency with the rest of the Code and fair trading legislation.

Recommendation

Include nutrition information requirements for FSMP in draft Standard 2.9.5 and allow more flexibility in the presentation of the information. Information on serving size and number of serves per package will not be required. Lactose and gluten free claims will be required to meet the criteria stipulated in Standard 1.2.8 of the Code.

Percentage Ingredient Labelling

Assessment

Percentage ingredient labelling is required to assist consumers to make informed choices about products and to prevent misleading and deceptive conduct among manufacturers.

The percentage labelling requirements are very similar between Australia/New Zealand, Codex and the EU. Whilst it is unlikely that imported products won't comply with the regulations in the Code it is believed it is not necessary to require percentage labelling on FSMP as they are specifically designed products for a medical purpose. Consumers and medical professionals are unlikely to require this information or use this information to choose products.

Conclusion

Percentage labelling information is not required on FSMP as it is unlikely that consumers or health professionals, in choosing the appropriate FSMP, will use this information.

Recommendation

That FSMP be exempted from percentage labelling requirements in Standard 1.2.10.

Directions for Use or Storage

Assessment

Directions for use and storage are required where, because of the nature of the food and reasons of public health and safety, consumers need directions about the use or storage of a food. It is likely that most imported FSMP, with the possible exception of products from the US, would comply with the requirements in the Code.

Directions for use and storage should be mandatory on FSMP because health professionals need to ensure they use products correctly to reduce the risks to their patients of inappropriate use. Feedback from industry has indicated that most FSMP currently provide directions for use and storage.

Conclusion

FSMP require directions for use and storage to enable medical professionals to use them correctly. While most products contain this information it is necessary to make the information mandatory. FSMP will be exempt from all the other generic labelling requirements in Part 1.2 of the Code.

To make it easier for manufacturers to find the regulations that relate to FSMP it makes sense to put this information in the one spot. For example, in draft Standard 2.9.5.

Recommendation

Exempt FSMP from the directions for use and storage in Standard 1.2.6 of the Code and ensure that these requirements are mandatory in draft Standard 2.9.5

Health Claims

Assessment

Health claims are currently prohibited on food by Transitional Standard 1.1A.2. If FSMP are to be used in their correct manner, then some recognition and identification of the purpose for their use must be provided, including the disease state(s) that they have been designed for. This identification of disease states has been recognised by other existing international regulations for FSMP, including Codex.

At Draft Assessment, permission for FSMP to make reference to disease states was provided, specifically overriding the prohibitions contained in clauses 3(c) and (d) of Standard 1.1A.2. However, the ASMI does not consider labelling of FSMP with disease states or conditions for nutritive purposes to be a contravention of the prohibition of health claims contained in the transitional Standard 1.1A.2. ASMI's position provides clear evidence that the health and related claims transitional Standard is open to interpretation, which is one of the reasons it is currently under review.

The Australia New Zealand Food Regulation Ministerial Council (ANZFRMC) recently passed policy guidelines onto FSANZ to guide a review of health and related claims. Whilst the policy guidelines will permit health claims in the future it will be at least 12 months before the review is complete and a new standard is in place. Until such time the transitional Standard will remain in place.

While stakeholders are generally in favour of permitting reference to disease states on FSMP they are opposed to claims of therapeutic or prophylactic action. They believe these claims are not associated with the effective use of FSMP and as such the prohibition should be maintained.

Conclusion

To prevent any confusion over the interpretation of whether reference to disease states are considered health claims or not, Transitional Standard 1.1A.2 will apply to FSMP as previously proposed at Draft Assessment, pending the development of the new standard for health claims, which is currently underway. The permission to label with the disease or disorder for which a FSMP is specifically formulated is to remain (see further discussion below).

Country of Origin Labelling

Assessment

Country of origin labelling (CoOL) facilitates consumer choice by providing information on where a food was made or produced. Country of origin is mandatory on all packaged foods in Australia and New Zealand and some unpackaged imported products such as fish, nuts, and fruit. However, it is not mandatory for imported products from the US and the EU. Codex, like the EU, only require CoOL if its omission could mislead or deceive the consumer.

Country of origin requirements are often satisfied by information on the label which indicates where it was packed for retail sale. In many cases this information will be present on FSMP.

FSMP are essential to the health and welfare of certain individuals. It is unlikely that consumers will choose products based on their country of origin for two reasons:

1. Often products will only be made and produced in one country; and
2. The products often need to be consumed by the patient, regardless of the country of origin or they risk their health and safety.

The Ministerial Council have passed on policy advice to FSANZ, which clearly indicates that CoOL is a consumer information issue and is not a public health and safety issue. Therefore, as the risk to public health and safety will be greater if overseas importers decide to withdraw their products from the domestic market because they don't comply with mandatory CoOL requirements it would be more beneficial to consumers of FSMP to exempt them from CoOL in the Code.

Conclusion

CoOL is a consumer information issue. There will be a greater risk to public health and safety if importers withdraw their products from the domestic market than not having information on country of origin.

Recommendation

It is recommended to exempt FSMP from country of origin labelling.

Labelling for all FSMP

Assessment

The requirement to label FSMP with a statement to the effect 'Important Notice: Foods for Special Medical Purposes are to be used only under medical supervision' was to prevent inappropriate use by consumers. The statement is a useful reminder to consumers that FSMP should be used under medical supervision.

This statement has been identified as a key feature of the proposed overarching risk management framework for FSMP (see Section 5.2.1 of the Preliminary Final Assessment Report), and is also required under Codex and EU requirements. No submitter expressed any concerns with the requirement to include this statement on the label.

At Draft Assessment it was proposed where FSMP have been specifically formulated for a condition, disease or disorder, the label on the package of the food must include a statement indicating the condition, disease or disorder, and any nutritional modifications for which the food has been specifically modified. This information was permitted at Draft Assessment to ensure health professionals have adequate information to ensure the correct use of FSMP, particularly those that have been designed specifically for patients with specific disease states.

Submitters (AFGC, ANZENMA, ASMI, SADHS) supported the permission to label with a reference to the condition or disorder for which a FSMP has been designed. This requirement is also consistent with Codex requirements.

Conclusion

The requirement to label FSMP with a statement to the effect 'Foods for Special Medical Purposes are to be used only under medical supervision' is a useful reminder to consumers of how FSMP are intended to be used and will assist in preventing inappropriate use.

The requirement to label FSMP that have been specifically formulated for a condition, disease or disorder, with a statement indicating the condition, disease or disorder, and any nutritional modifications for which the food has been specifically modified was supported by submitters. This information will assist health professionals to ensure correct use of FSMP.

Recommendation

It is recommended to include the following mandatory advisory statement and additional labelling for FSMP:

- Food for special medical purposes are to be used only under medical supervision.

- Where FSMP have been specifically formulated for a condition, disease or disorder, the label on the package of the food must include a statement indicating the condition, disease or disorder, and any nutritional modifications for which the food has been specifically modified.

Labelling Requirements Specific only to FSMP except for VLEDs

Advisory Statements

Assessment

At Draft Assessment three advisory statements were proposed for FSMP except for VLED to manage public health and safety risks associated with inappropriate use. The statements would also harmonise the labelling of FSMP in Australia and New Zealand with international FSMP requirements, namely Codex and the EU.

The mandatory advisory statement 'not for parenteral use' was supported by some submitters (DAA and the NZDA) on enteral and oral products to prevent inappropriate use. However, the ANZENMA does not support the statement because it is mandatory whereas in the EU the statement is voluntary. They suggested using the words 'where appropriate' in the Code.

The ‘not for parenteral use’ advisory statement is necessary to prevent inappropriate use of FSMP. There is potential for FSMP that are used in tube feeding (i.e. nutritionally complete FSMP) to be mistaken for total parenteral nutrition (TPN) formula, a concern expressed in submissions from both the DAA and the NZDA. With the potential for error in product administration, a warning against parenteral use is unlikely to be effective unless it is always visible at the site of tube feeding. Therefore, it will be necessary to mandate the display of this statement on the product label itself. The requirement to have this statement is consistent with Codex requirements and the EU have voluntary requirements.

The mandatory advisory statement ‘the product poses a health hazard when consumed by persons who do not have a disease, disorder or medical condition for which the product is intended’, was not supported by some submitters. Submitters commented that to label a FSMP as a ‘health hazard’ is inappropriate’. The DAA suggested that to label with a ‘health hazard’ is suitable to VLED only and that a statement regarding use in certain conditions was more suitable for FSMP.

The EU only requires this statement ‘as appropriate’ whereas Codex require it when it poses a health hazard when consumed by individuals who do not have the disease(s), disorder(s) or medical condition(s) for which the product was intended. To align more with the regulations in the EU and Codex it is proposed to label FSMP with the disease, disorder, or physiological condition for which the product has been formulated. This will protect against inappropriate use but prevent alarm amongst consumers that the product could be a ‘health hazard’.

The mandatory advisory statement ‘the product is intended/not intended (as the case may be) as the sole source of nutrition’ was proposed at Draft Assessment to enable health professionals to clearly identify what FSMP are nutritionally complete products and the ones that aren’t. This information was designed to protect against inappropriate use. Only one submitter opposed this approach on the basis that the EU only requires this information ‘as appropriate’. Codex does not require this information.

FSMP are to be used under the supervision of a medical professional. Therefore, it could be argued that the absence of information on nutritional adequacy is unlikely to increase risks to health and safety through inappropriate use. Also, as this statement is not a requirement under Codex and US regulations and only voluntary in the EU there could be a greater risk to public health and safety if manufacturers withdraw their products from domestic markets because of onerous labelling requirements. As a result it is proposed to not require this statement on FSMP.

Conclusion

Advisory statements are necessary on FSMP to protect against inappropriate use. Of the advisory statements proposed at Draft Assessment only the statement ‘not for parenteral use’ is considered appropriate to advise against inappropriate use without placing onerous labelling requirements on importers.

The advisory statement ‘the product poses a health hazard when consumed by persons who do not have a disease, disorder or medical condition for which the product is intended’ is not considered necessary as it is seen as more appropriate to label the product with the disease, disorder, or physiological condition for which the product has been formulated.

This will protect against inappropriate use but prevent alarm amongst consumers that the product could be a 'health hazard'. It will also align Australia and New Zealand regulations more with Codex and the EU.

The advisory statement ''the product is intended/not intended (as the case may be) as the sole source of nutrition' is not considered necessary because FSMP are used under the supervision of medical professionals and because only the EU require this statement as a voluntary requirement it may pose onerous labelling requirements on importers.

Recommendation

It is recommended to retain the following advisory statements for nutritionally complete FSMP other than VLED:

- not for parenteral use.

The following advisory statements will not be required:

- the product poses a health hazard when consumed by persons who do not have a disease, disorder or medical condition for which the product is intended.
- the product is intended/not intended (as the case may be) as the sole source of nutrition.

Additional Labelling requirements for FSMP other than VLED

Assessment

At Draft Assessment it was proposed that FSMP other than VLED would be required to include a statement 'advising of any precautions, side-effects, contraindications and potential interactions with drugs' in consuming the food. This statement was considered necessary so supervising medical professionals could prescribe appropriate products to patients without increasing the risk to their public health and safety.

Some submitters (ASIEM, DAA and NZDA) supported the inclusion of this statement where the risks and side effects were known. However, several industry submissions were not supportive of this requirement for the following reasons:

- the large volume of information required would be impractical to include on the label;
- It is the responsibility of the supervising health professionals and drug manufacturers to provide information on drug-nutrient interactions and contraindications;
- Labelling with the statement 'use under medical supervision' is sufficient to meet these risks; and
- This requirement is voluntary under Codex.

The requirement to include this information is voluntary under the EU regulations and there is no requirement in the US to include this information on FSMP. As FSMP are for use under 'medical supervision' it is likely that the supervising medical professionals will be aware of any necessary precautions, side-effects, contraindications and potential interactions with drugs in consuming the food.

At Draft Assessment it was proposed to include a statement on FSMP other than VLED 'advising where the product has been formulated for a specific age group'. This is a voluntary requirement under the EU regulations and mandatory under Codex requirements. It is likely that most imported products would comply with this requirement and the information would be useful for health professionals to protect the health and safety of their patients. Therefore, it is proposed to include a requirement to label if FSMP other than VLED are formulated for specific age groups.

Conclusion

The requirement to include information on the label on any precautions, side-effects, contraindications and potential interactions with drugs associated with consuming a FSMP appears onerous when FSMP are used under the supervision of a medical professional, this requirement is voluntary under Codex and EU regulations and is not required in the US.

The requirement to include information on the label that the product has been formulated for a specific age group is useful for health professionals to ensure correct use of FSMP. In addition, as most products would already comply with this requirement it is not going to be overly onerous on importers.

Recommendation

Retain the requirement to label with a statement 'advising where the product has been formulated for a specific age group' in draft Standard 2.9.5. The statement 'advising of any necessary precautions, side-effects, contraindications and potential interactions with drugs in consuming food' is no longer required.

Labelling Specific to VLED

Warning and Advisory Statements

Assessment

At Draft Assessment it was proposed to have one warning statement and two advisory statements on VLED to protect the health and safety of consumers. VLED are the FSMP product most likely to be misused by consumers because of their use in management of obesity, which could increase risks to health and safety. As the risk of misuse is high, the specific format of the information should be prescribed to achieve consistent and uniform disclosure by manufacturers and to prevent misleading and deceptive conduct. Uniform disclosure is necessary to enhance confidence among health professionals in locating and using products and to reinforce consumers about their appropriate use.

The warning statement 'this product is for the dietary management of obesity' is necessary for medical professionals and consumers to be able distinguish VLED from other FSMP. There is a small risk that VLED could be mistaken for other FSMP, if they do not have any information on the label that clearly distinguishes them from other products.

No submitters were opposed to the requirement for this warning statement. ORFAM did not object to this approach although they did not believe it was necessary. Codex has a mandatory requirement to include the warning statement 'for the dietary management of obesity' whereas the EU and the US don't require the statement.

The advisory statement 'it is important to maintain an adequate daily fluid intake while using the product' was proposed at Draft Assessment so medical professionals had adequate information to be able to advise their patients of how to correctly use products. Only one submitter did not support this statement because they believe VLED are used under medical supervision, and this advice should be routinely provided to the patient.

The EU and Codex have mandatory requirements to include a statement about the importance of maintaining adequate fluid intake. The US doesn't require this statement but the majority of VLED would have this information.

The advisory statement 'the product may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly' was proposed at Draft Assessment so health professionals were aware of who the product was suitable for. The NZDA supports this approach. However the ANZENMA and ORFAM did not support this approach because the labelling may create confusion among obese individuals and they are used under medical supervision so this advice shall be routinely provided.

The NHMRC clinical guidelines for children and adolescents[36] recommends that VLED therapy in adolescents should be undertaken only by specialist obesity-management teams and that VLED therapy is never indicated for children. Therefore, the proposed statement at the draft assessment would appear inconsistent with the NHMRC clinical practice guidelines[1].

Codex requires a similar mandatory statement except it is qualified with 'except where medically indicated'. The EU or the US has no requirement to include this statement. While it would appear that the statement is inconsistent with clinical practice guidelines, by making the statement consistent with Codex and adding a qualifier 'except where medically indicated' would clarify the inconsistency. It would also ensure the domestic regulations would align with Codex.

Conclusion

In most circumstances VLED would be easily identifiable and information on their use routinely provided by health professionals. However, the advisory statement and warning statements are a useful reminder to health professionals and consumers on what the products are intended for, so they can easily be distinguished from other FSMP.
This is important because VLED are the products, which are most likely to be misused by consumers because of their impact on weight reduction.

The proposed requirements at Draft Assessment are consistent with the Codex legislation and some EU legislation. Therefore, many VLED will already contain this information.

[36] National Health and Medical Research Council, Clinical Practice Guidelines for the Management of Overweight and Obesity in Children and Adolescents, Commonwealth of Australia, 2003.

While the advisory statement 'the product may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly' appears inconsistent with NHMRC clinical practice guidelines by adding a qualifier 'except when medically indicated' will ensure they are not inconsistent with the guidelines and ensure consistency with Codex legislation.

Recommendation

Retain the warning statement 'this product is for the dietary management of obesity' and the advisory statement 'it is important to maintain an adequate daily fluid intake while using this product'.

Insert the qualifier 'except where medically indicated' in the proposed advisory statement 'the product may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly'.

Additional Labelling Specific to VLED

In addition to the advisory and warning statements for VLED it was proposed at Draft Assessment to require the label for VLED to include a statement of the recommended daily consumption. This information was proposed to advise of appropriate use and to prevent inappropriate use.

The requirement to label with a recommended daily consumption amount has been reassessed as highly prescriptive, especially given that overseas VLED regulations do not prescribe this additional requirement. Several submitters indicated that the labelling of a recommended daily quantity for VLED established by the manufacturer is inappropriate because the dosage and concentration is the responsibility of the supervising health professional (NZDA, ORFAM). In addition, VLED can often be used in smaller quantities with food.

Conclusion

The requirement to label with a recommended daily consumption is not consistent with most international regulations and is onerous on manufacturers when FSMP are used under the supervision of a medical professional.

Recommendation

The requirement to label with a recommended daily consumption in Standard 2.9.5 is no longer required.

Summary of Recommendations

At Draft Assessment it was proposed that the majority of generic labelling requirements would apply to FSMP to meet FSANZ's statutory objectives of protecting public health and safety, providing adequate information to enable consumers to make informed choices and to prevent misleading and deceiving conduct.

However the possible impacts of withdrawal of FSMP from domestic markets, due to prescriptive labelling requirements, is likely to have a greater impact on public health and safety than withdrawing the application of generic labelling requirements to FSMP for the following reasons:

- A reduction in availability of certain FSMP may compromise patients health;
- Any reduction in the availability of FSMP for patients with inborn errors of metabolism will have serious medical consequences; and
- International labelling requirements don't differ significantly from the Code.

Therefore, FSANZ has reassessed the labelling requirements for FSMP and now proposes to ensure that information essential to the use of FSMP is available to consumers by applying a specific set of labelling provisions in place of Part 1.2 of the Code, which will include generic labelling requirements wherever the current range of FSMP can accommodate them.

Therefore, revised draft Standard 2.9.5 to include:

- the application of the following generic labelling requirements:

    - food identification requirements for FSMP allowing the name of the local supplier to be included on transportation outers or in accompanying documentation;
    - flexible ingredient labelling requirements for FSMP;
    - date marking for FSMP and allow flexibility in the format;
    - directions for use and storage of FSMP;
    - nutrition information requirements for FSMP and allow more flexibility in the presentation of this information; and
    - requirement to label FSMP with a condition, disease or disorder for which they have been specifically formulated.

- the following mandatory advisory statement and additional labelling:

    - that FSMP are to be used 'only under medical supervision'; and
    - with a statement 'advising where the product has been formulated for a specific age group'.

- for nutritionally complete FSMP (other than VLED) the mandatory advisory statement 'not for parenteral use'.

- for VLED:

    - a warning statement 'This product is for the dietary management of obesity'
    - the advisory statement 'it is important to maintain an adequate daily fluid intake while using this product'; and
    - Insert the qualifier 'except where medically indicated' in the proposed advisory statement 'the product may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly'.

- exemption from:

- mandatory allergen declaration;
- percentage labelling requirements;
- relevant aspects of the transitional standard on health claims; and
- country of origin labelling.

Attachment 5

Food Technology Report

Proposal P242 Food for Special Medical Purposes (FSMP)

Introduction

As part of the review of the *Food Standards Code* (the Code), Food Standards Australia New Zealand (FSANZ) is reviewing Australian and New Zealand regulations covering Food for Special Medical Purposes (FSMP) in Proposal P242. FSMP are used under the supervision of medical or other health professionals.

Background

The term to describe products used in the nutritional management (oral or tube fed) of patients is 'Food for Special Medical Purposes'(FSMP).

In the United States [1], the term 'medical food' is used and defined in the Orphan Drug Act Amendments of 1988 [21 USC 360ee (b)(3)]. The US definition for a medical food (MF) is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation. Generally, to be considered a MF, a product must at a minimum, meet the following criteria;

- the product is a food for oral or tube feeding;
- the product is labelled for the dietary management of a medical disorder, disease, or condition; and
- the product is labelled to be used under medical supervision, and is primarily obtained through hospitals, clinics, and other medical and long term care facilities.

FSMP are distinguished from the broader category of foods for special dietary use by the requirement that FSMP be used under medical, or another health professional's supervision.

FSMP are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in its natural state) for the patient who is seriously ill or who requires the product to meet their specific dietary requirements.

In general, FSMP are often analogous to infant formulas, in that the technology base is similar for the manufacture of both products.

Potential health hazards associated with FSMP include compositional errors and microbiological and/or environmental contamination. In 1986, four Peruvian infants died as a result of being fed oral rehydration solutions which, because of a manufacturing error by a New York firm, contained lethal concentrations of potassium.

Food Additive Permissions for Use in FSMP

A food additive is defined in the purpose clause to Standard 1.3.1 – Food Additives of the Code, as any substance not normally consumed as a food in itself and not normally used as an ingredient of food, but which is intentionally added to a food to achieve one or more technological functions specified in Schedule 5 to Standard 1.3.1. A food additive may only be added to food where expressly permitted in Standard 1.3.1 and in order to achieve an identified technological function according to Good Manufacturing Practice (GMP).

The Australia New Zealand Enteral Nutrition Manufacturers Association (ANZENMA), representing the majority of FSMP manufacturers, requested that FSANZ consider the provision of permission for all food additives listed in Schedule 2 of Standard 1.3.1 for use in FSMP with the exception of the following functional groups: flavour enhancers, foaming agents, glazing agents, humectants, preservatives, propellants and raising agents.

Note that most food additives that are usually considered as preservatives are listed for specified foods in Schedule 1 of Standard 1.3.1 and not in Schedule 2. Note also that all food additives listed in Schedule 2 are also generally permitted processing aids due to clause 3 (b) of Standard 1.3.3 – Processing Aids.

The additives currently listed in Schedule 2 may generally be added to processed foods to perform a technological function provided that the proportion of the additive does not exceed the maximum level necessary to achieve one or more technological functions under conditions of Good Manufacturing Practice (GMP).

Schedule 2 additives are permitted in accordance with GMP in processed foods specified in Schedule 1. As FSMP are processed, as opposed to fresh or raw foods, if they are listed as a category in Schedule 1, they will automatically gain approval for all food additives listed in Schedule 2, unless otherwise specified. This outcome is consistent with the review of food additives, as a general approach is recommended for the majority of food additives that have high or not specified Acceptable Daily Intakes (ADIs) and do not raise any safety concerns. Some of the functional groups of additives listed in Schedule 2 were not requested, however they would not have a reason or a permission to be added to FSMP if they did not serve a technological function in that food.

ANZENMA also requested that FSANZ consider the provision of permission for all colours and colour fixatives listed in Schedules 3 and 4 of Standard 1.3.1 for use in FSMP.

The colours listed in Schedule 3 are permitted in accordance with GMP in processed foods specified in Schedule 1. The colours listed in Schedule 4 are permitted to a maximum level of 70 mg/L in beverages and 290 mg/kg in other foods specified in Schedule 1.

If FSMP are listed as a category in Schedule 1, they will as processed foods, automatically gain permission for Schedule 3 colours, unless otherwise specified. Most processed foods also have the general permission for Schedule 4 colours, with the restricted levels of use.

ANZENMA further requested that FSANZ consider the provision of permission for the preservatives – methlyparaben, sorbic acid and its salts, benzoic acid and its salts and tertiary butylhydroquinone (TBHQ) for use in FSMP.

Note that TBHQ (319) is usually considered as an antioxidant rather than as a preservative.

Note also that the only direct permissions for methylparaben (methyl p-hydroxybenzoate) (218) and propylparaben (propyl p-hydroxybenzoate) (216) in Schedule 1 are for category 0.1- Preparations of food additives. Food additives are permitted to be carried-over into other foods by clause 7 of Standard 1.3.1. The parabens are only expected in flavoured or coloured processed foods as they are generally used to preserve flavours or colours that have neutral or high pH values, where the more commonly used preservatives are not effective.

Sorbic acid and sodium, potassium and calcium sorbates (200, 201, 202 and 203) are permitted in a number of food categories to specified maximum levels in Schedule 1.

Benzoic acid and sodium, potassium and calcium benzoates (210, 211, 212 and 213) are also permitted in a number of food categories to specified maximum levels in Schedule 1.

Processing Aids in FSMP

A processing aid is defined in Standard 1.3.3 as a substance, used in the processing of raw materials, foods or ingredients, to fulfil a technological purpose relating to treatment or processing, but does not perform a technological function in the final food and the substance is used in the course of manufacture of a food at the lowest level necessary to achieve a function in the processing of a food, irrespective of any maximum permitted level specified.

Processing aids are prohibited for use in foods unless the provisions in Standard 1.3.3 give explicit permission to do so. ANZENMA has not commented on the provisions for processing aids in the FSC. As mentioned above, all Schedule 2 additives are generally permitted processing aids. FSMP are composed of ingredients or raw materials that are foods. The FSMP industry should not have any technological need for the use of processing aids outside of the current permissions.

Conclusion

As FSMP represent processed foods which are a general class of specific foods that are composed of a number food ingredients, the use of all Schedule 2, 3 and 4 additives is technologically justified. This can be achieved by including an entry for FSMP into Schedule 1 of Standard 1.3.1, which provides Schedule 2, 3 and 4 permissions. As with all processed foods, the proportion of the additive used in any food must not exceed the maximum level necessary to achieve one or more technological functions under conditions of GMP. In simpler terms, additives that are not needed should not be added. An approval to use flavour enhancers does not mean they have to be used.

All additives permitted in category 0.1- Preparations of food additives will be permitted in FSMP by virtue of the carry-over clause (Clause 7, Standard 1.3.1), where the preparations are used in an individual FSMP. That is, a flavoured product will be permitted to contain flavours and the additives permitted in the category, provided that the levels in the final food are no greater than would be introduced by the use of the flavour ingredient under proper technological conditions and GMP. This situation would be similar for a coloured FSMP or a FSMP that contains baking compounds.

Similarly all additives permitted as antioxidants for edible oils will be permitted in individual FSMP by carry-over, if an edible oil which can contain the antioxidant is used as an ingredient. Foods that contain the preservatives, sorbates and benzoates can also be used as ingredients in FSMP, with similar carry-over permissions.

Reference:

1. U.S. Food Drug Administration, Center For Food Safety Applied Nutrition Medical Foods - Import And Domestic. Issued December 21, 1998 Chapter 21 - Food Composition, Standards, Labeling And Economics.

Attachment 6

Microbiological Evaluation

PROPOSAL P242 - FOODS FOR SPECIAL MEDICAL PURPOSES (FSMP)

Foods for special medical purposes (FSMP) are principally formulated food products for the dietary management of individuals (including children) with either ongoing chronic medical or disability conditions or during acute phases of illness, injury or disease states. FSMP are used under the supervision of medical or other health professionals. They include 'complete nutrition' formulas either consumed orally or through an enteral route (e.g. naso-gastric tube), as well as specialised dietary supplement formula or foods, and formula for very low energy diets (VLED) used for weight loss.

The microbiological risks associated with the use of these products may depend on several factors including the health status of the consumer (host susceptibility); the nature of the food and how it is processed, and how the food is prepared and handled.

FSMP include ready-to-use liquid products and powdered products, which are reconstituted with water before use. The ready-to-use liquid products are commercially sterile, shelf stable foods. Commercially sterile foods should be free of any viable pathogenic microorganisms or organisms (including spores), which could grow under normal storage and handling. However powdered products are not commercially sterile. Pathogenic microorganisms of concern in these products include *Bacillus cereus*, *Salmonella* spp. and *Enterobacter sakazakii*.

Incidence of Foodborne Illness

There is little data associating FSMP with food-borne illness except in the context of infant formula. While infant formula *per se* is outside the scope of Proposal P242, the association of food-borne illness with their use is applicable to FSMP (due to the similarities in production of powdered product, handling practices and a vulnerable population group) and is discussed below.

While a number of pathogenic microorganisms have been isolated from infant formula (including *Bacillus cereus*, *Clostridium perfringens*, *Staphylococcus aureus*), outbreaks of food-borne illness attributable to contaminated infant formula have largely been associated with *Salmonella* spp. and *Enterobacter sakazakii.* Outbreaks of *Salmonella* infections after consumption of contaminated infant formula were reported in the United Kingdom in 1985 (Committee on the Microbiological Safety of Food, 1990) and in Canada in 1992 from infant formula produced in the United States (ICMSF, 1998).

Another outbreak of Salmonellosis occurred in Spain in 1994 (Usera *et al*, 1996). These outbreaks were traced to contamination from processing equipment during manufacture.

Enterobacter sakazakii has been found in a number of infant formula products at low levels (Nazarowec-White & Farber, 1997). Over the past several years, clusters of *E. sakazakii* infections in neonates have been reported internationally (van Acker *et al*, 2001; Himelright *et al*, 2002; Weir, 2002). This organism causes sepsis, meningitis or necrotizing enterocolitis in infants, with a high fatality rate (as high as 33%). Most recently (March/April 2002), an

international recall of the product Portagen (a formulated product for infants and children under 2 years who do not efficiently digest or absorb conventional fat) was initiated following an outbreak of *E. sakazakii* infection in a neonatal intensive care unit in the United States, in which the Portagen product was used (CDC, 2002). The FDA has subsequently recommended that non-commercially sterile infant formula products should preferably not be used within neonatal intensive care units where commercially sterile liquid products are available.

Host Susceptibility

The susceptibility of populations to food-borne illness is influenced by many factors. There are sub-groups within the general population, which are at greater risk from food-borne infections, both in the development and severity of illness. These include the elderly, the immunocompromised (including the chronically ill), pregnant women and the very young. FSMP are specifically formulated for vulnerable sections of the population that have particular nutritional requirements because of medical conditions or disabilities.

The Elderly

Increased susceptibility to food borne infections in elderly populations (>65 years of age) is due to a number of factors including (Smith, 1998; Morris & Potter, 1997):

- a decrease in humoral and cellular immunity;
- changes in the gastrointestinal tract such as decreased production of gastric acid and decreased motility of the gastrointestinal tract;
- malnutrition; and
- the increased use of antacids and antibiotics.

In particular, the incidence and severity of salmonellosis and Campylobacteriosis seems to be higher among the elderly than the general population (Morris & Potter, 1997). The severity of infection is also likely to be more severe. *Salmonella* infections, for example, are more likely to cause bacteraemia in the elderly which increases the risk for death.

The Immunocompromised

Immunocompromised individuals include those on chemotherapy or radiation therapy; recipients of organ transplants taking immunocompromising drugs; persons with AIDS or with other chronic diseases. AIDS patients show a clear increase in susceptibility to *Salmonella* infections with a several fold increase in the risk of septicaemia (Morris & Potter, 1997). For those individuals that have undergone organ transplantation or cancer chemotherapy, the use of immunosuppressive drugs as well as antimicrobial drugs will increase susceptibility to food-borne infection. These patients are at significantly greater risk of dying from enteric viral infections than the general population (Gerba *et al*, 1996).

Pregnancy

The escalated production of progesterone during pregnancy leads to a decrease in cell-mediated immune function. This increases the susceptibility of pregnant women and the foetus to certain food-borne infections, particularly from intracellular pathogens such as *Listeria monocytogenes*, *Toxoplasma gondii*, Hepatitis E virus and *Coxiella burnetii* (Smith, 1999).

The Very Young

In young children, less than 5 years of age, the lack of a fully developed immune system and a smaller infective dose-by-weight required to cause illness increases their susceptibility to food-borne illness. Young children are particularly susceptible to the development of complications as a result of food-borne infection from enterohaemorrhagic strains of *Escherichia coli* (EHEC), which can lead to the development of haemolytic uraemic syndrome. Premature infants fed on formula have very little gut immunity and are very susceptible to food-borne infection.

Nutritional Status

Along with the age or health related factors that affect the host's ability to deal with food-borne pathogens, the nutritional status of the host can also play a role in the development and severity of food-borne infection. Studies suggest that clinical and subclinical nutritional deficiencies could lead to greater susceptibility to food-borne pathogens. It is recognised, for example, that nutritional deficiencies in vitamin A and zinc increase the risk of diarrhoeal diseases (King *et al*, 2000). While not fully understood, the nutritional status of the host may have an important impact on gut-mediated immunity.

Food Processing Considerations

Liquid products

Ready-to-use liquid FSMP products are commercially sterile, shelf stable foods. This means they have been thermally processed to be free of microorganisms capable of reproducing in the food under normal conditions of storage and distribution.

Powdered products

While powdered products undergo heat processing during their manufacture, they are not subjected to high temperatures for sufficient time to make the final packaged product commercially sterile. Post-processing recontamination may occur during cooling, storage, and packaging operations. While microorganisms may slowly die during storage of the dried product, many remain viable during prolonged storage. Spore forming organisms, being the most resistant, retain viability for long periods of time (ICMSF, 1998). Microorganisms that may be of greatest concern in these powdered products include *Bacillus cereus*, *Salmonella* and *Enterobacter sakazakii*.

Food Preparation and Handling Considerations

Liquid Products

As liquid products are processed to be commercially sterile, they should not pose a microbiological risk to a consumer unless they are administered under conditions of poor hygienic practice. This would be unlikely in a hospital or clinical environment. Liquid foods consumed at home would be provided as canned or UHT products and are either administered enterally (via tube feeding) or drunk directly from the package (via a straw or poured into a glass). These practices raise no particular microbiological concerns.

Once these products have been opened, however, they can no longer be considered to be commercially sterile and must be handled appropriately to avoid microbiological contamination and growth. Any opened product should be covered and refrigerated and used within 24 hours. Any leftover product should be discarded after this time. Products hung for enteral feeding should be replaced with new product once the recommended hang time has been reached.

Dry Products

Dry products require more handling and preparation than ready-to-use liquid products and this increases the risk of microbiological contamination. Food powders are generally reconstituted with water, which, for infant feeding, should be sterilised by boiling before use. The equipment used to prepare and administer the food may also be a source of contamination and so should be thoroughly cleaned and, if appropriate, sterilised (such as infant feeding bottles).

Microorganisms are unable to grow in dry food products however, once the powder has been reconstituted in water, any pathogens present may begin to grow if the product is not stored appropriately. Once the powdered food has been made up it should be used immediately or refrigerated and used within 24 hours (prolonged ambient storage of the reconstituted food could allow the growth of pathogens present). Any partially consumed product should be discarded and not kept to be re-used at a later feed. Powdered products made up for continuous enteral feeding should not have excessive hang times. The United States Food and Drug Administration (FDA) have recently recommended that hang times for powdered formula products should not exceed 4 hours (Weir, 2002).

Conclusions

Individuals consuming FSMP may be more susceptible to food-borne illness because of their health status and/or age (such as young infants). As these foods may be the sole source of nutrition for ‘at risk’ individuals, it is critical that these products are of a high microbiological quality.

Ready-to use liquid products are commercially sterile and if handled and prepared hygienically, pose no particular microbiological concern. Published data on food-borne illness associated with these products is not readily found in the literature.

Control over the microbiological quality and safety of these products is achieved primarily through strict adherence to good manufacturing and hygienic practices at the manufacturing facility. Guidance on the handling of these products after opening and subsequent use (such as storage instructions and keeping time) should be provided.

Powdered products to be fed to 'at risk' groups pose a higher microbiological risk than ready-to-use liquid products as they are not commercially sterile. Powdered products cannot be produced to be commercially sterile, but a high microbiological quality is achieved through adherence to good manufacturing and hygienic practices at the manufacturing facility. Indications of the risk of powdered products comes from food-borne illness data which indicates that powdered infant formula including specialised formula preparations pose a particular risk to neonates are from *E. sakazakii* contamination. Microorganisms are unable to grow in powdered products, however any pathogens present may grow once the product is reconstituted and if stored incorrectly. Extra care is required in the preparation and handling of powdered FSMP products to ensure the public health and safety of 'at risk' groups consuming these products.

RISK MANAGEMENT RECOMMENDATIONS

The majority of FSMP products are provided through healthcare settings (e.g. hospitals and nursing homes), and are prepared under the supervision of health professionals. Guidance on the handling of FSMP products used within a home/community setting, including handling after opening and subsequent use (such as storage instructions and keeping time), should be provided by health care professionals.

Microbiological standards/criteria require that commodities meet a specified level of safety at a given point in time after processing, such as the end of manufacture or at the retail level. They are commonly referred to as 'end-point specifications' because they do not require any preventive measures to be implemented during processing, but compel the manufacturer to achieve a prescribed level at the end of processing.

As FSMP are highly specialised products, and there are only four multi-national companies that almost exclusively supply the Australian and New Zealand market for FSMP-type products, microbiological standards/criteria are not the best approach to manage their safety.

In addition, in Australia 90% of FSMP products are provided through healthcare settings (e.g. public and private hospitals, nursing homes) and in New Zealand it is estimated 95%-99% of the FSMP market is distributed via prescription hence it would be difficult to enforce endpoint criteria.

Instead, microbiological guidelines for FSMP are proposed (see Table 1) to aid manufacturers in producing safe FSMP products. Such guidelines ensure preventive measures are implemented through the entire production and handling chain, and should be published in 'The User Guide - Microbiological Limits for Food'[37].

[37] http://www.foodstandards.gov.au/assistanceforindustry/userguides/microbiologicallimit1410.cfm

Table 1: Proposed microbiological guidelines* for powdered foods for special medical purposes

Food	Micro-organism	n	c	m	M
Foods for special medical purposes - powdered	*Bacillus cereus*/g	5	0	-	10^2
	Coagulase-positive staphylococci/g	5	1	0	10
	Coliforms/g	5	2	<3	10
	Salmonella/25 g	10	0	0	
	SPC/g	5	2	10^3	10^4
	Clostridium perfringens/g	5	2	<1	10
	Listeria monocytogenes /25g	5	0	0	
Foods for special medical purposes – (liquid) heat-treated/sterilised	Products should comply with a test for commercial sterility.				

*** Guideline criteria developed by FSANZ for various foods are not mandatory.** These guideline criteria act as an identification point for unacceptable levels of microbial contamination foods. When these levels are exceeded it generally indicates a failure in the food production process or hygiene procedures. It means that action should be taken to identify and remedy the problem. Standard 1.6.1 specifies microbiological standards for nominated foods or classes of foods. Foods listed in this standard must meet the prescribed microbiological limits at any state of their manufacture or sale.

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Attachment 7

Summary of Submissions

PROPOSAL P242 – FOODS FOR SPECIAL MEDICAL PURPOSES

List of Submitters

A public consultation period occurred from the 18 December 2002 to 24 March 2003 for the Draft Assessment of Proposal P242. During this period, 17 separate submissions were received by FSANZ. A list of the submitters that provided comment on the Draft Assessment Report is provided below.

- Australasian Society of Inborn Errors of Metabolism - Dietitians Group (ASIEM)
- Australian Food and Grocery Council (AFGC)
- Australia New Zealand Enteral Nutrition Manufacturers Association (two submissions provided) (ANZENMA)
- Australian Self-Medication Industry Inc. (late submission) (ASMI)
- BioActive Technologies (BT)
- Dietitians Association of Australia (DAA)
- Food Technology Association of Victoria Inc. (FTAV)
- European Commission, Enterprise Directorate-General (EC)
- Ms Kay Gibbons, Clinical Dietitian (KG)
- Nestlé Australia Ltd. (NA)
- New Zealand Dietetic Association (NZDA)
- New Zealand Food Safety Authority (NZFSA)
- Novartis Consumer Health Australasia Pty. Ltd. (NCHA)
- Nu Skin Enterprises Australia Inc. (NSEA)
- ORFAM Pty Ltd. (ORFAM)
- South Australian Department of Human Services (SADHS)

COMMENTS MADE ON THE DRAFT ASSESSMENT FOR PROPOSAL P242 - FOODS FOR SPECIAL MEDICAL PURPOSES (FSMP)

Preferred Regulatory Option

Option	Submitters Supporting Option	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text	
		Supported	**Not Supported**
1 – Maintain Status Quo	AFGC, ASMI, FTAV, KG	• FSANZ has not demonstrated any market failure with the currently unregulated usage of FSMP, or that FSMP are unsafe/inappropriate [AFGC, KG]. • The current labelling of FSMP is sufficient to meet the provision of adequate information to consumers without further regulation [AFGC]. • Products are not currently developed without regard to best practice and are utilised under the supervision of health professionals. This provides a level of nutritional 'insurance' [KG]. • If FSMP are to be regulated, then it should be as therapeutic goods and not as foods [FTAV].	• Option 1 is not an option as it leaves in place the delays and continuing negative impact on government and industry. [NSEA].
2 – Regulation by a discreet standard in the FSC	ANZENMA, NA, NZFSA, ORFAM, SADHS.	• A discreet standard should be placed in the FSC that only sanctions FSMP as foods, rather than the format proposed at Draft Assessment [ANZENMA]. • The **NZFSA** supports the development of a discreet standard in principle, but not one that is overly prescriptive. It is important that FSMP products are not withdrawn from the domestic market.	• In the absence of evidence for a safety risk with the current access to FSMP, there is no purpose in changing the regulatory requirements for FSMP in Australia or New Zealand [AFGC]. • Arguments raised in the impact analysis supporting Option 2 are largely hypothetical [KG]. • Option 2 may limit the product range available in Australia, or result in companies withdrawing from the market. This is of particular concern for items with a limited sale [KG, AFGC].

Other Comments on the Proposed Regulatory Options:

- **NSEA** states that FSMP should not be recognised as being available for general consumption. The application of general food standards is therefore inappropriate.
- **NSEA** supports a different option (named Option 3) that would amend relevant food standards to ensure that these standards do not apply to FSMP. This would eliminate the regulatory uncertainty surrounding the importation of FSMP.
- Although supportive of Option 2 in principle, the **NZDA** recommended that a further assessment should be made of the costs to industry and the consumer before any regulations are implemented.

Regulatory Considerations

Issue	**Comments** **Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text**
Costs and Benefits Associated with Option 2	In the impact analysis the AFGC considers that FSANZ overstates the benefits and understates the restriction associated with Option 2. <u>Costs:</u> • There will be a cost to industry to comply with Option 2 that will inevitably result in increased costs for consumers [AFGC, KG, NZDA, ORFAM]. • Although supportive of Option 2 in principle, the ANZENMA has indicated that 95% of FSMP will be non-compliant with the proposed standard. • It was estimated that the costs associated with Option 2 could result in a 20% price increase for products manufactured by ORFAM. • The compositional requirements would result in a business impact of $250000 for Nestlé, as its FSMP products would no longer be supplied to the Australian market. <u>Benefits:</u> • If Option 2 only sanctions FSMP as legitimate foods without other requirements, then it would remove importation concerns and contribute to the ongoing investment in local research and development [ANZENMA]. • Benefits for Option 2 include standardised labelling, and the potential for the adoption of an existing code in its entirety [KG].
The safety of FSMP	• Several industry and health professional submitters did not agree with the view that FSMP are unsafe and pose a risk to the general public [AFGC, ANZENMA, DAA, NA, NZDA]. - There has been no evidence demonstrating safety concerns with the current unregulated environment for FSMP [ANZENMA, DAA, NA], or of non-compliance with the basic requirement of a food being safe under the Food Acts of Australia and New Zealand [NA]. - FSMP are supervised by health professionals in their use and therefore pose a lesser risk to the public than other foods [AFGC, ANZENMA, NZDA]. - FSMP need to meet strict overseas regulations that contribute to the protection of public health and safety in domestic markets [AFGC, ANZENMA, NZDA]. - Consumers are unlikely to be aware that FSMP are unregulated, and would consider these products to be safe [NA].
Regulation of VLED	• The **SADHS** stated that there are different risks between FSMP and VLED. Therefore, it was recommended that VLED be included as a separate category in Part 2.9 of the *Food Standards Code*. • **NCHA** were concerned that regulations for VLED have evolved from one region of the world only, e.g. the European Union (EU); and may limit product innovation.

Objectives and Principles for Proposal P242

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
The Objectives of the Proposal	• **Ms Kay Gibbons** agreed with the objectives of P242 as provided at Draft Assessment. • The AFGC support the objectives of protecting public health and safety, and the use of adequate labelling information to permit informed choice by consumers and their carers. However, it states that: - no regard has been given to 'consistency between domestic and international food standards' and ' the need for a standard to be based on risk analysis using the best available scientific evidence' as stated in the FSANZ Act; and - supply issues for FSMP have not been fully considered, that is, the majority of FSMP are imported in small and infrequent quantities. It is therefore recommended that another objective should be provided - *'to not jeopardise supply of FSMP needed in small quantities on an infrequent basis'*. • The **NZDA** stated that the objectives of FSANZ in P242 are unclear when the current use of FSMP has not been established as unsafe or inappropriate.
Underlying Regulatory Principles	• The **AFGC** states that the underpinning regulatory principles for special-purpose foods are in effect policy principles, and therefore should be referred to the Australia New Zealand Food Regulation Ministerial Council.

Definitions Provided at Draft Assessment

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
The definition of special purpose foods	• The **AFGC** supports the categorisation of FSMP as special-purpose foods. However, it was suggested that the associated need *'to provide appropriate regulatory measures to mitigate the risk to the target group from inappropriate consumption'* should relate to 'inappropriate composition' instead of 'inappropriate consumption'. Support was also given for the proposed definition of 'special-purpose foods'.
The definition of protein	• **Nestlé** stated that the definition for protein, and the prescribed method of analysis for protein (Schedule 4) were inappropriate. • It is unclear whether this definition only applies to minimum protein levels in VLED [ANZENMA]
The definition of FSMP	• Support for the definition of FSMP was given by health professional and industry submitters [ANZENMA, DAA, NA, NZDA]. Although supported, several submitters proposed minor changes to the wording: - Expansion of 'medical supervision' to include supervision by dietitians [DAA, NZDA]. - 'for use solely under medical supervision' to 'should be used under medical supervision' [ANZENMA]. - 'impaired capacity to take, digest, absorb or metabolise' to 'impaired capacity to take, digest, absorb, metabolise or excrete' [ANZENMA] - 'cannot be achieved solely' to 'may not be achieved solely' [ANZENMA]. • The SADHS commented that the proposed definition of FSMP excludes patients who use VLED. These patients do not have a 'limited or impaired capacity to take absorb or metabolise ordinary foodstuffs', and obesity can be managed by modification of the normal diet.

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
The definition of VLED	• **ANZENMA** recommended that the definition of VLED be clarified further, as these products could be used as a supplement and thus result in a daily energy intake greater than 3350 kJ. It was suggested that the upper energy limit for VLED be removed from compositional provisions and placed into the definition of VLED.

Access and Availability of FSMP

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
The distribution and access of FSMP	• Several health professional / industry submitters supported the decision to maintain current distribution and access practices for FSMP [ANZENMA, KG, NA, NZDA, ORFAM]. - FSMP should be available for purchase from pharmacies and hospitals, through health professionals (including retail pharmacists) [DAA, NZDA], or direct from the manufacturer / medical distributor [DAA]. - The warning 'use under medical supervision' is an adequate risk management strategy [KG]. • **BioActive Technologies** stated that a proportion of food products that could be classified as FSMP are not provided through healthcare settings. Examples provided were low energy weight management products and formulated high fibre foods for bulk forming laxative applications. It was suggested that these products should be covered by formulated beverages regulations.
The availability of FSMP	• As a large proportion of the FSMP market is imported, the proposed labelling / compositional changes will impact on the availability of FSMP [ANZENMA, ASIEM, DAA, SADHS]. - Availability would be affected by price increases or removal of products from the market due to the impact of re-labelling / reformulation. This would restrict access to FSMP [AFGC, ANZENMA, SADHS]. - Any reduction in the availability of FSMP for patients with inborn errors of metabolism will have serious medical consequences [ASIEM].

Advertising

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Restriction on advertising	• Some submissions from the health professional sector supported a restriction on advertising [KG, NZDA]. - VLED should be treated separately for advertising [DAA, NZDA]. - Limited advertising of VLED may be applicable where a wide range of other similar foods exists on the market (e.g. meal replacements). The content of such advertising would need to be monitored [KG]. - Access to information on FSMP should be restricted to health professionals [NZDA]. • Comments against the restriction on advertising were received from industry submitters [AFGC, ANZENMA, BT, NA, ORFAM]. - The restriction is not warranted, as there is no evidence of market failure or

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
	public health and safety risks associated with the use of FSMP [AFGC, NA]. The AFGC considers that a restriction on advertising to health professionals only would not meet the needs of users of FSMP e.g. Self-help groups - The **AFGC** stated that no evidence was provided in support of the public health and safety risks or high rates of self-treatment for morbid obesity associated with VLED. It was further mentioned that what evidence exists indicates that the morbidly obese are not likely to undertake self-treatment. - Public health and safety may actually be adversely affected by preventing advertising to consumers, as consumer access to health professionals is decreasing [ANZENMA]. - Many weight loss products are more readily abused through self-treatment than VLED, yet are still permitted to advertise [ORFAM]. - There are various industry codes of practice that could apply to advertising of FSMP [ANZENMA] e.g. Medicines Australia, Australian Self-Medication Industry, and New Zealand Advertising Authority.
The term 'health professional publication'	• **Ms Kay Gibbons** provided support for the term 'health professional publications'. • Several submitters indicated that the expression 'health professional publications' was too narrow [AFGC, ANZENMA, ASMI, DAA, NA, NZDA, ORFAM]. It was recommended that this expression be expanded to include: - patient support groups, and disease specific consumer groups [AFGC, ANZENMA, ASMI, NA]; - conferences, educational forums and meetings, direct mail campaigns, emails and websites [ANZENMA, DAA, NZDA]; - trade exhibitions [ANZENMA, NZDA]; and - product information and leaflets [DAA]. • Clarification should be to be given to the disciplines covered by 'health professionals' [ASMI, NZDA, ORFAM]. Both **ANZENMA** and **ASMI** recommended the use of the definition for health professionals as stated under Part 2, Division 1(4) of the Australian *Therapeutic Goods Regulations 1990**.

**** - These regulations list health professionals as: medical practitioners, psychologists, dentists, veterinary surgeons, pharmacists, physiotherapists, dietitians, scientists working in medical laboratories, and nurses.***

Composition of FSMP

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Risk Assessment for proposed composition	• Nutrient ranges should be based on practice and the best available evidence [AFGC, KG]. • The mixture of EU and United States Institute of Medicine (IOM) values to set maximum limits is an ad hoc process to risk assessment and is therefore incorrect [AFGC]. • Two submitters questioned the compositional requirements when no safety issues had been identified [NZDA, NZFSA], although in principle, NZFSA supported the risk-based approach to composition.

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Impact of proposed composition	• Submissions from industry and health professional sectors indicated that the compositional requirements proposed at Draft Assessment would have adverse effects on the current range of FSMP [ANZENMA, ASMI, KG, NA, NCHA, NZDA, ORFAM]. - The proposed compositional requirements would increase the price of FSMP, limit product choice and result in a restriction / absence of supply of FSMP [ASMI, KG, NA, NZDA]. - The proposed composition would disrupt supply of current State and Federal Government Tenders [ANZENMA]. - The proposed compositional requirements would result in the two FSMP produced by Nestlé being withdrawn from the Australian and New Zealand markets. - Novartis indicated that its product range would be seriously affected if FSMP regulations do not allow both US and European compositions. - ORFAM indicated that the compositional requirements proposed at Draft Assessment would result in the reformulation of its VLED products. It was stated that this will pose no technical difficulty, however a cost will be incurred.
Minimum limits for vitamins and minerals	• Several submitters from across all sectors supported the minimum limits (that apply only to nutritionally complete FSMP) proposed at Draft Assessment [AFGC, ANZENMA, NZDA, NZFSA]. - Nutritionally complete FSMP need to be nutritionally adequate for use as the sole source of nutrition [DAA, NZDA]. Agreed that minimum quantities of micronutrients are required per daily quantity to meet recommended intakes [AFGC]. - Some of the minimums requirements are of concern to **ANZENMA**, and a further review of these provisions is required. - **Nestlé's** products will be non-compliant with the minimum levels for niacin, vitamin B_{12}, folate, and magnesium.

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Maximum limits for vitamins and minerals	• Concern was raised over the maximum limits provided at Draft Assessment by a number of submitters representing all sectors [AFGC, ANZENMA, ASMI, DAA, KG, NA, NZDA, NZFSA]. The following concerns were raised: - The majority of FSMP will be unable to comply with the proposed maximum limits [ANZENMA, DAA, KG, NZDA], resulting in reduced availability and/or increased prices [DAA]; - The maximum limits do not take into account the situation where a patient's health status may result in nutritional requirements exceeding normal limits [AFGC, ANZENMA]. - Maximum limits should be established only where a risk from daily intakes of FSMP has been identified [AFGC, NZFSA]; - No maximums should be prescribed as medical supervision is provided with the use of FSMP [AFGC]. - The **DAA** is unaware of clinical evidence indicating that excess intake beyond the proposed maximum limits has a deleterious effect on any patient group; - The composition of FSMP is constantly improving, and maximum limits will impede such progress [NZDA]; and - It is unclear as to how composition is to be harmonised with EC directives when the proposed maximums prevent this [NZDA]. - The adult intake of 8700 kJ / day used to calculate requirements is inappropriate, as patient requirements in some situations may be as low as 6000 kJ / day. Therefore, requirements should be expressed as a daily amount similar to VLED requirements [AFGC]. - Given medical supervision, there is no justification for maximum limits except where there is sufficient evidence of adverse health effects [ANZENMA]. • Of the submitters commenting on maximum limits, three indicated that they did not support any introduction of maximum limits for FSMP [AFGC, ANZENMA, NZDA]. - Comment received from **ANZENMA** questions the use given that the US upper limits have not been generated for application to FSMP. . • **Nestlé** indicated that its FSMP products would be non-compliant with the maximum limit for vitamin A, while **Ms Kay Gibbons** indicated that consideration of current products against the proposed maximums indicate that the amount by which a nutrient falls outside the range is minor, and does not generally constitute a variation of multiple times the acceptable limit.
Non - nutritionally complete FSMP	• Several health professional submitters indicated that nutritionally incomplete FSMP could experience problems with compositional requirements (maximum limits) expressed as a proportion of energy content. Where energy is not a major nutrient supplemented in a FSMP, then it is impossible to comply with the maximum limits [ASIEM, DAA, NSEA, NZDA]. This is of particular significance for low-volume FSMP for rare genetic disorders [ASIEM].

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
VLED	• Support was received for the additional compositional requirements for VLED from several industry and health professional submitters [ANZENMA, KG]. • Although supported, the composition of VLED should also include permissions for vitamin K, chromium, and fluoride additions as allowed for nutritionally complete non-VLED [ANZENMA]. Also questions the maximum limits for certain nutrients: - vitamin E, as it is eligible for listing in complementary medicines without a maximum; - niacin, as nicotinamide is not significantly toxic and the consequence of excess nicotinic acid intake is mild flushing; and - magnesium, as it is not restricted for complementary medicines or dietary supplements - VLED should be required to provide the recommended daily allowances of minerals, vitamins, trace elements, and fatty acids in a dose/serve [DAA]. - VLED should have a minimum daily amount set for micronutrients [AFGC]. • **Ms Kay Gibbons** considers that macronutrient requirements are important for VLED, but do not need to be mandated, as there is an inconsistency in prescribing macronutrient requirements for VLED and not for nutritionally complete non-VLED FSMP.
Certain medical conditions	• Two submissions were received recommending that the permission for FSMP to deviate from sodium and potassium levels be extended to all prescribed compositional requirements. Such deviations should only occur where they are necessary for the intended use of a FSMP, and can be justified through scientific evidence [ANZENMA, EC]. - The **ANZENMA** indicated that this permission would be consistent with European regulations. • **Ms Kay Gibbons** mentioned that it is unclear as to whether the permission to vary from sodium and potassium requirements for certain medical conditions applies to FSMP for non-specific use.
Schedule of permitted forms	• **Ms Kay Gibbons** supports the permitted forms of nutrients / additives proposed at Draft Assessment. • The **ANZENMA** requested consideration be given to permitting other forms of nutrients that are permitted elsewhere (e.g. Standard 1.1.1, Standard 2.9.1, Listable medicines) • Flexibility should be given in FSMP regulations to accommodate new ingredients or the extension of use for approved substances in response to scientific advances in the dietary management of medical conditions [DAA, NZDA].
Other general comments on composition	• **Ms Kay Gibbons** recommended the adoption of the EU minimum and maximum compositional requirements as an alternative to the proposed compositional requirements for FSMP. The rationale for a decision not to prescribe macronutrient content for nutritionally complete non-VLED but for micronutrients is unclear . • **ANZENMA** supports the use of the Codex general principle on the composition of FSMP. • **NSEA** stated that the expression of minimum and maximum micronutrient requirements per 100 kJ was unsuitable as the measure depends as much on the energy content of the product as the micronutrient content. Therefore it is recommended that Schedule 2 of draft Standard 2.9.5 be changed to use the RDIs / ESADDIs as the basis for establishing vitamin and mineral compositional requirements.

Labelling of FSMP

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Impact of proposed labelling	• Submitters from all sectors expressed concern that the proposed labelling requirements may have a negative impact on industry and consumers [AFGC, ANZENMA, ASIEM, ASMI, DAA, NCHA, NZDA, NZFSA]. - FSANZ should use performance-based principles to establish labelling requirements on FSMP suitable to the needs of health professionals and consumers [ASMI]. - Manufacturers will need to make significant and onerous changes to the labels of imported FSMP to comply with the proposed draft standard [ASIEM, DAA]. - Labelling requirements will increase the cost of 90% of FSMP for consumers due to the cost of compliance for industry, reduce the range of general and specialised FSMP in Australia and New Zealand, and impede product innovation [NZDA]. - Even though generic labelling requirements are important for general-purpose foods, **NZFSA** questions the impact of the proposed labelling requirements on a small and highly specialised market.
Provision of labelling information on supporting product literature	• Submissions from both industry and health professionals were received advocating the use of supporting product literature (e.g. pamphlets and brochures provided to health care professionals) as a means of providing domestic labelling information not mandated by overseas regulations [AFGC, ANZENMA, ASMI, DAA, NCHA]. - Reference was given to the provision of local supplier details on this material [AFGC, ANZENMA]. - **ASMI** stated that supporting literature is able to provide the risk management of a label, as similar distribution techniques for FSMP are used in Australia for pharmacist only and prescription only therapeutic goods.
Application of generic labelling requirements	• Industry cannot meet the labelling requirements proposed at Draft Assessment. If generic labelling statements are applied to FSMP, a large percentage of FSMP will fail to comply [ANZENMA]. Problems include local supplier details, allergy labelling, labelling of ingredients, characterising ingredients and directions for use and storage. • The provision of domestic supplier details is adequately met by product supporting literature [AFGC]. • The primary package 'case or carton' could display the local supplier details as very few products are sold as individual units [ANZENMA].
Date marking	• **ANZENMA** requested that consideration be given to the use of overseas date marking requirements such as 'EXP', 'best before', or words to the effect of 'use by'.
Declaration of nutrition information – general comments	• **ANZENMA** recommended that FSANZ accept global practice in respect to nutrition information statements. • **AFGC** supports the provision of nutrition information consistent with Codex requirements, even if it is in a non-domestic format. • **Nestlé** stated that expressing nutrition information as prepared for consumption (Clause 7(4)) may not be relevant for all products; e.g. thickeners.

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Declaration of nutrition information – number of serves and serving size	• Comments by health professional and industry submitters indicated that the requirement to label with the number of serves and the serving size was inappropriate [AFGC, ANZENMA, DAA, NA]. The following arguments were provided: - Inconsistent with EU and USA requirements where most products are sourced [ANZENMA]. - A number of FSMP – particularly enteral formula – need to be delivered in continuous amounts over time [AFGC, ANZENMA], or in volumes specific to certain medical conditions [ANZENMA, DAA]. - Codex STAN 180-1991 allows this requirement to be voluntary under Clause 4.5.6 (using the statement 'if applicable'), and infant formula regulations in the FSC set a precedent for not providing nutrition information per serve [NA]. - Comments by health professional and industry submitters indicated that the requirement to label with the number of serves and the serving size was inappropriate • **The ANZENMA requested**: - replacement of 'average' with 'average or minimum' in clause 7; and - use of other values besides per 100 g or 100 ml.
Mandatory advisory statement – *'use under medical supervision'*	• The wording of an advisory statement 'use under medical supervision' should include supervision by a dietitian [NZDA, SADHS]. - It was further stated by **SADHS** that if the inclusion of dietetic supervision would result in the removal of products from the market, then the use of a non-prescribed advisory statement would be supported. • Several industry submissions did not support the inclusion of 'important notice' before an advisory statement on medical supervision [AFGC, ANZENMA, NA]. Such a requirement: - is not provided in Codex, US or Canadian regulations [ANZENMA, NA]; - is unnecessary as generic legibility requirements in the FSC are sufficient, and industry would need to over-stick labels (at a cost) to meet this requirement [AFGC]; and - suggests that FSMP have a greater risk than actually exists [ANZENMA]. • The **AFGC** did not support regulation of labelling 'use under medical supervision', stating that it is an unnecessary as all products currently on the market label with this statement.
Mandatory warning and advisory statements for VLED	• The **NZDA** supports the labelling of 'may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly' on VLED. • **ANZENMA** and **ORFAM** did not support the statement 'may not be suitable for pregnant, nursing or lactating women or by infants, children, adolescents or the elderly' on VLED. It was mentioned that: - members of these population groups can be obese, and if a VLED were to be recommended by a health professional to these people, then labelling would create anxiety and confusion [ANZENMA]; and - VLED are used under medical supervision, and this advice should be routinely provided to the patient [ORFAM]. • ORFAM did not support the statements 'it is important to maintain an adequate daily fluid intake while using the product' as VLED are used under medical supervision, and this advice should be routinely provided to the patient. • ORFAM does not object to the requirement to label with the warning 'for the dietary management of obesity', although this requirement is considered unnecessary.

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Mandatory advisory statement – *'not for parenteral use'*	• Submissions from the **DAA** and the **NZDA** supported the labelling of 'not for parenteral use' for oral and enteral products to prevent inappropriate use. • The **ANZENMA** does not support the statement 'not for parenteral use', as the European Union provides voluntary regulation for this statement using the words 'where appropriate FSMP are to include…'. **ANZENMA** requests that 'where appropriate' be included in domestic regulations.
Mandatory advisory statement – *'intended / not intended as the sole source of nutrition'*	• The **ANZENMA** does not support the statement 'intended / not intended as the sole source of nutrition', as the European Union provides voluntary regulation for this statement using the words 'where appropriate FSMP are to include…'. ANZENMA requests that 'where appropriate' be included in domestic regulations.
Mandatory advisory statement – *'the product poses a health hazard when consumed by persons who do not have a disease, disorder or medical condition for which the product is intended'*	• Submitters from industry and health professional sectors commented that the requirement to label a FSMP as a 'health hazard' is inappropriate [AFGC, ANZENMA, DAA, NA]. - FSMP do not pose a health risk to healthy individuals, as they are composed of normal nutritional ingredients. Furthermore, the use of these products occurs under medical supervision [AFGC, ANZENMA]. - The requirement to label with a 'health hazard' statement is suited to VLED only. It was suggested that a statement regarding use in certain conditions was more suitable for FSMP [DAA]. - The labelling of a FSMP as a 'health hazard' may not always be a true statement, as all family members can use foods that are provided for people with medical conditions. Therefore, this statement would breach the Trade Practices Act [NA].
Additional labelling requirements – '*advising of any necessary precautions, side-effects, contraindications and potential interactions with drugs, in consuming the food'*	• Support was received from health professional submitters for the labelling of known side effects, contraindications, and product-drug interactions where known [ASIEM, DAA, NZDA]. - Information on the side effects for some ingredients / nutrients is necessary for certain health conditions. An example provided was the labelling of 'low lactose' products and the method of removing lactose – if lactose has been split into its glucose and galactose components, then patients with galactosaemia are at a health risk from consuming such a product [ASIEM, DAA]. - The **NZDA** stated that this information should not be a mandatory requirement as adverse effects are dependant on dietary patterns and associated use of medications. • Several industry submissions were not supportive of the requirement to label with known side effects, contraindications, and product-drug interactions [AFGC, ANZENMA, NA]. - The large volume of information required would be impractical to include on the label of FSMP [AFGC, ANZENMA, NA]. - It is the responsibility of the supervising medical professionals and drug manufacturers to provide information on drug-nutrient interactions and contraindications [ANZENMA, NA]. - Labelling with the statement 'use under medical supervision' is sufficient to meet these risks [AFGC]. - This requirement is voluntary under Codex STAN 180-1991 [NA].

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Additional labelling requirements – daily quantity for VLED	• Several submitters indicated that the labelling of a recommended daily quantity for VLED established by the manufacturer is inappropriate, as: - the dosage and concentration is the responsibility of the supervising health professional [NZDA, ORFAM]. - VLED can sometimes be used in smaller supplemental quantities. It was suggested that this requirement be related to 'when the product is intended as the sole source of nutrition' [ANZENMA].
Additional labelling requirements – reference to disease states	• Support was received for the ability to label with a reference to the condition disease or disorder for which a food for special medical purposes has been designed [AFGC, ANZENMA, ASMI, SADHS]. - The **ASMI** does not consider the context of labelling a FSMP with disease states or conditions for nutritive purposes to be a contravention of the prohibition on health claims. It was also stated that claiming on FSMP labels could be captured under a proposed Trans-Tasman arrangement for the pre-market clearance of advertisements containing therapeutic claims **. • The **SADHS** mentioned that it did not support the permission extending to VLED. It was stated that because VLED are available via pharmacies / supermarkets, such labelling would result in self-diagnosis.

** - This arrangement has been proposed for both foods and medicines under Recommendation 12 of the 'Report of a Review of Advertising Therapeutic Products in Australia and New Zealand', for which a copy can be obtained from http://www.tga.health.gov.au/docs/html/advrev.htm.

OTHER COMMENTS MADE IN SUBMISSIONS

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Transition and Stock-in-Trade Periods	• Several industry submitters recommended an extension to the transition period from 2 years to 4 years to accommodate current tenders which are in place, and any reformulation of FSMP; and an extension to the stock-in-trade period from 12 months to 2 years, as the majority of FSMP have a long shelf life [AFGC, ANZENMA, NA]. • **ORFAM** indicated that the two-year transition period was reasonable.
Micro-biological requirements	• The NZDA supported the proposed microbiological requirements provided at Draft Assessment given the higher at risk status of the target consumer.
Application of standards requiring pre-market clearance	• **BioActive Technologies** supports the application of pre-market clearance standards. • The **NZDA** commented that information on genetic modification and irradiation should be placed on the label of a FSMP.
Errors in draft variations	• Amendment [2](f) should refer to Clause 8 instead of Clause 9 [NA]. • Amendments [7] and [8] refer to Volume 2 when there is no longer a Volume 1 [NA].

COMMENTS MADE OUTSIDE THE SCOPE OF P242

Issue	Comments Names of submitters providing comments are abbreviated in square brackets [ ] unless stated in bolded text
Classification of FSMP as therapeutic goods	• The **FTVA** stated that if regulation of FSMP is required, then these products should be regulated under the Therapeutic Goods Act 1989. FSMP are aligned more closely with therapeutic purposes than food products.
Importation and re-exportation of foods	• NSEA commented that current food standards legislation precludes the importation into Australia for re-export of foods that are non-compliant with domestic food standards. Such foods are classified 'failing foods' as defined by Clause 3(1) of the Australian Imported Food Control Act 1992, even though such products are not distributed for sale in Australia. - It was suggested that the Imported Food Control Act should be amended, or alternatively, the FSC amended to reflect that standards apply to foods only consumed in the domestic market.
Over-the-counter products	• BioActive Technologies has submitted the following three comments: - Some foods sold over-the-counter could be classified as FSMP (examples given were the company's range of weight management foods and high-fibre foods for laxative purposes). It was recommended that these products be covered by Formulated Beverage regulations. - FSMP like products traditionally sold over the counter or by direct sales should remain free to advertise and promote directly to the public. - Over-the-counter products are not purchased by 'at risk' or vulnerable individuals, as apposed to FSMP used by patients under constant medical supervision. Therefore, the manufacture of over-the-counter FSMP should not be required at microbiological standards greater than those for Food-Type Dietary Supplements.
Definition of Novel Foods	• BioActive Technologies stated that the current definition of 'novel foods' was too restrictive and would require the evaluation of ingredients that would otherwise be accepted with the use of a broader definition.