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

SUPPORTING DOCUMENT 1

PROPOSAL P242 – FOOD FOR SPECIAL MEDICAL PURPOSES

Risk Assessment Report

Summary

There are inherent risks associated with the use of foods for special medical purposes (FSMPs) that primarily relate to their specialised nature and the special dietary circumstances associated with their use. These risks were previously investigated by FSANZ at its Preliminary Final Assessment (2004) for Proposal P242.

Since 2004, there have been further developments on the safety of substances added to FSMPs, and new issues have also emerged relating to the risks associated with the use of FSMPs. FSANZ has therefore reviewed the previous 2004 risk assessments conducted on FSMPs, and has further investigated the new scientific developments since 2004.

Review of previous 2004 risk assessments

In reviewing the previous 2004 risk assessments, FSANZ has identified the following:

1. There are eighteen new forms of nutrients/related substances that have been added to permitted forms lists in overseas regulations. Another form (lutein) has also been added to Standard 2.9.1 – Infant Formula Products since 2004. In 2004, the risk assessment determined that Australian and New Zealand FSMP permitted forms should harmonise where possible with overseas regulations, and should also include permitted forms that had been established as safe for use in infant formula. In accordance with these decisions, FSANZ has determined that the nineteen new forms can also be permitted for use in FSMPs. A list of these nineteen forms is located in Appendix 1.

2. At Preliminary Final Assessment (2004), FSANZ conducted two assessments that investigated the risks associated with micronutrient inadequacy and the safety of micronutrient levels from FSMPs represented as being nutritionally complete. From these assessments, FSANZ recommended twenty-six minimum and nine maximum micronutrient requirements for FSMPs represented as nutritionally complete.

   FSANZ reaffirms the outcomes of the micronutrient assessments undertaken at Preliminary Final Assessment, and recommends that the minimum and maximum requirements that were proposed in 2004 should be retained. There has been no new evidence provided in submissions to demonstrate that the minima and maxima levels proposed in 2004 are inappropriate for managing the risks of inadequate and/or excessive micronutrient intakes from those FSMPs represented as nutritionally complete. A full list of these minimum and maximum requirements can be found in Appendix 1.

In addition to point 1 above, FSANZ notes that one of the additional permitted forms (selenium enriched yeast) has no purity specification in Standard 1.3.4 – Identity and Purity of the *Australia New Zealand Food Standards Code* (the Code). This risk assessment has therefore identified a specification that can be included in Standard 1.3.4.

Assessments relating to new scientific developments

Food additives and processing aids

At Preliminary Final Assessment, FSANZ proposed to include an entry for FSMPs in Schedule 1 of Standard 1.3.1 – Food Additives. An entry for FSMPs in Schedule 1 provides a mechanism to permit the addition of food additives listed under Schedules 2, 3 and 4 of Standard 1.3.1 to FSMPs.

Since 2004, FSANZ has consulted with the FSMP industry and asked whether the approach proposed at Preliminary Final Assessment would reflect the use of food additives in existing FSMPs sold in Australia and New Zealand. FSANZ was subsequently advised by the FSMP industry of fourteen other food additives that should be specifically included in Schedule 1 of Standard 1.3.1 (eight preservatives, four intense sweeteners, and two antioxidants).

FSANZ has assessed all of the proposed additives and determined that they each have a technological function associated with their addition to FSMPs. All of these additives are familiar to FSANZ, have permissions within the Code, and have a history of safe use. Further assessment on whether maximum levels of use are required for these additives has identified that:

- 11 out of the 14 requested food additives (four sorbates, four benzoates, acesulphame potassium, aspartame-acesulphame salt, and saccharin) can be permitted for use in FSMPs under Schedule 1 of Standard 1.3.1. FSANZ has also identified maximum levels associated with use of these food additives in FSMPs. Submitters should note that the maximum level set for saccharin is lower than its interim level for beverage type special dietary foods in the United States (200 mg/kg versus 400 mg/kg).
- One food additive, aspartame, has permission in Schedule 2 of Standard 1.3.1 for general use in processed foods. This permission is considered to be satisfactory for the manufacture of FSMPs.
- Two of the fourteen requested food additives (butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)) do not require explicit FSMP permission in Schedule 1 of Standard 1.3.1. FSANZ has concluded that the carry-over provisions in clause 7 of Standard 1.3.1 are sufficient for the presence of these food additives in FSMPs.

Additionally, FSANZ has reassessed the Preliminary Final Assessment permission for Schedule 2, 3 and 4 additives. FSANZ has determined that Schedule 4 colour permissions should not apply to FSMPs. Schedule 2 and 3 additives can, however, be used for FSMPs.

On the basis of these outcomes, this risk assessment recommends the inclusion of 11 new permissions in Schedule 1 of Standard 1.3.1 for the use of food additives in the manufacture of FSMPs, and permission to use the additive permissions in Schedules 2 and 3 of Standard 1.3.1 for FSMPs. FSANZ has posed some questions in Section 4 of this risk assessment relating to these proposed changes.

A list of the 11 permitted additives food additives and their maximum levels of use are provided in Appendix 1 of this risk assessment.

Fermentable oligosaccharides, lactose, fructose, and polyols (FOLFAPs)

Fermentable oligosaccharides, lactose, fructose, and polyols (FOLFAPs) are widespread in the diet. FOLFAPs is an acronym developed by FSANZ since the more commonly used term *FODMAPS* (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) is trademarked. The two acronyms are essentially the same; however, FOLFAPS is more specific in that the literature identifies lactose as the only disaccharide of interest and fructose as the only monosaccharide of interest.

FOLFAPs are readily fermentable carbohydrates which can cause luminal distention of the distal small intestine and the proximal colon in some individuals. Recent scientific opinion considers luminal distention to be the physiological basis for the gastrointestinal symptoms associated with consumption of FOLFAPs. Dietary challenge studies using FOLFAPs have demonstrated that in some individuals, the intake of these substances can induce gastrointestinal symptoms and increase gas production (measured via methane and hydrogen breath testing), while dietary studies limiting FOLFAPs intake have shown symptom reduction.

The relationship between FOLFAPs intake and gastrointestinal symptoms has been demonstrated in both Inflammatory Bowel Disease (IBD) and functional bowel disorders (FBD), the former consisting of Crohn's disease, ulcerative colitis and indeterminate colitis, and the latter being a term that applies to conditions where signs of pathology associated with IBD are not found. It is likely that a number of individuals with these gastrointestinal conditions will use FSMPs, especially if they are admitted to hospitals or healthcare centres for management of their conditions, or for other non-related medical conditions.

Due to the emerging evidence of an association between FOLFAPs and the gastrointestinal conditions noted above, FSANZ has undertaken a review of the literature to determine the significance of the presence of FOLFAPs in FSMPs. The literature identified by FSANZ was not specifically focused on the health effects of FOLFAPs, rather the review was designed to observe the variance in symptoms in relation to exclusion and re-challenge of diets with FOLFAP substances. This material demonstrated the following:

- Seven studies that examined the health effects of increasing the FOLFAP content of the diet demonstrated an association between increasing FOLFAP intakes and increased gastrointestinal symptoms (diarrhoea, abdominal distention, abdominal pain and flatulence). Tolerance to different types and amounts of FOLFAPs varied among individuals which may be related to individually-determined non-dietary factors such as lactase and glucose transporter proteins. The balance of bowel biota was also identified as a potentially important influence on the tolerance to different FOLFAPs in individuals. Certain FOLFAPs have been shown to exert a laxative effect at high enough doses, and some (e.g. lactulose) are utilised medically for these effects.

- For those that consume FSMPs (specifically enteral nutrition products containing FOLFAPs), there is an increased risk of diarrhoea during or following enteral nutrition regardless of the principal underlying condition being treated. FSANZ notes, however, that the evidence of health effects related to FOLFAPs in FSMPs is very limited (one pilot retrospective case-control study on enteral nutrition products only).

On the basis of the available evidence, FSANZ considers that the presence of FOLFAPs in FSMPs may produce adverse health effects, especially for FSMP consumers with pre-existing gastrointestinal disorders. However, it is difficult to quantify the magnitude of this health risk given the limited available literature. As a result, FSANZ has posed several questions for submitter comment in Section 5 of this document, which relate to the magnitude of the risk.

Conclusions of the risk assessment

The risk assessment concludes the following:

- Nineteen new forms of nutrients /related substances have been determined as safe for addition to FSMPs.
- The minimum and maximum micronutrient requirements (for FSMPs represented as nutritionally complete) proposed in the 2004 drafting remain applicable.
- Eleven food additives are determined as safe and technologically justified for use in FSMP. These food additives are in addition to the food additive permissions in Schedules 2 and 3 of Standard 1.3.1, and the processing aid permissions in Standard 1.3.3, that were already recommended for FSMP. Schedule 4 food additives (colours) are not permitted for addition to FSMP.
- The available evidence indicates that there is a health risk for those with pre-existing IBD or FBD from the presence of FOLFAPs in FSMPs, however there is insufficient evidence to determine the magnitude of this risk.

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1. Introduction

There are inherent risks associated with the use of foods for special medical purposes (FSMPs) that primarily relate to their specialised nature and the special dietary circumstances associated with their use. These risks were previously investigated by FSANZ at its Preliminary Final Assessment (2004) for Proposal P242, specifically by the assessment of:

- the inadequate provision of nutrition when FSMPs do not contain sufficient quantities of vitamins and minerals;
- safety concerns from the excess intake of certain vitamins and minerals; and
- the safety of substances added to FSMPs, including nutrients, food additives, and processing aids.

Since 2004, there have been further developments on the third point above, and new issues have emerged relating to the risks associated with the use of FSMPs. These developments include:

- The European Food Safety Authority (EFSA) has undertaken further assessments on the safety of certain nutrient forms for addition to FSMPs;
- Further information has been provided by the FSMP industry regarding the food additives and processing aids that are used in FSMP manufacture; and
- Recent evidence has emerged regarding risks associated with the consumption of fermentable oligosaccharides, lactose, fructose, and polyols (FOLFAPS) by individuals with gastrointestinal disorders.

1.1 Purpose of this risk assessment

FSANZ is undertaking this assessment to review previous risk assessments conducted on FSMPs and to further investigate new scientific developments since 2004. Section 2 below outlines the decisions relating to previous risk assessments for Proposal P242, where only an update on this position is required. Sections 4 and 5 detail the new risk assessments that have been undertaken in regards to the emerging issues for food additives/processing aids and FOLFAPs.

The outcomes of the findings on these issues will be used to inform the risk management considerations of Proposal P242.

2. Updates and revisions since Preliminary Final Assessment

2.1 Chemical forms for nutrients/related substances

A list of permitted forms of nutrients and related substances was proposed as part of the 2004 draft Standard 2.9.5. There were two main principles that were utilised in developing this list:

1. The objective of harmonising Australian and New Zealand FSMP regulations where possible with overseas regulations.
2. FSANZ also considered that forms permitted for use in infant formula were also suitable for addition to FSMPs, by virtue of their safety for use by infants (another nutritionally vulnerable group).

To achieve the first principle, FSANZ referred to European legislation regarding forms permitted for addition to FSMPs. The European Union was (and still remains) the only major overseas region supplying FSMPs to the domestic market that has undertaken a safety and nutritional assessment on a wide range of substances appropriate for addition to FSMPs. In accordance with the second principle, the draft Standard 2.9.5 cross-references to the list of permitted forms in the Schedule to Standard 2.9.1 – Infant Formula Products, so that these forms can also be added to FSMPs. FSANZ also included additional forms permitted in the Codex Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Young Children (CAC/GL 10 1979).

At this stage of Proposal P242, FSANZ reaffirms the two principles above, and the three sources that were combined to produce the list of permitted forms that can be added to FSMPs. Since 2004, there have been nineteen new additional forms added to each of these three sources, and FSANZ has determined that these new additional forms should also be permitted for addition to FSMPs. The new forms that will be included in the list of permitted forms for FSMPs (Schedule 1 of draft Standard 2.9.5) are detailed in the sections below, and are summarised as a list in Appendix 1.

2.1.1 The Schedule to Standard 2.9.1

Since 2004, FSANZ has conducted a safety assessment on the addition of lutein to infant formula (as part of Application A594), and subsequently approved the inclusion of this substance in the Schedule to Standard 2.9.1.

2.1.2 European permissions for substances added to FSMPs

The European Commission has recently updated its list of permitted forms (EC regulation 953/2009) on the basis of scientific opinions from the European Food Safety Authority (EFSA) regarding additional forms that can be added to FSMPs (European Commission, 2009). The new forms approved for use in FSMPs by the European Commission (that are not already captured in the Schedule to Standard 2.9.1) are as follows:

Table 1: New forms added to EC regulation 953/2009 not previously captured by draft Standard 2.9.5

Substance	Permitted form
Vitamin E	D-alpha-tocopherol polyethylene glycol-1000 succinate (TPGS)
Calcium	Calcium bisglycinate
	Calcium citrate malate
	Calcium malate
	Calcium L-pidolate
Magnesium	Magnesium bisglycinate
	Magnesium L-pidolate
	Magnesium potassium citrate
Iron	Ferrous L-pidolate
Zinc	Zinc bisglycinate
Potassium	Potassium L-pidolate
Selenium	Selenium enriched yeast

When approving the addition of selenium enriched yeast to FSMPs, the European Commission included additional criteria relating to its purity (footnote 2 of EC regulation 953/2009). These criteria were developed originally by EFSA as part of its scientific

assessment (EFSA, 2008), which used data on samples with a limited specification. FSANZ will therefore apply these specifications to the permissions for selenium enriched yeast, by including a purity specification in Standard 1.3.4 – Identity and Purity. This specification will read as follows:

Specification for selenium enriched yeast

Selenium enriched yeasts are produced by culture in the presence of sodium selenite as a source of selenium. These yeasts contain selenium according to the following criteria.

1.	Total selenium content (mg/g of the dried form as marketed)		max. 2.5
2.	Levels of organic selenium species (% total extracted selenium)		
	Selenomethionine	min. 60	max. 85
	Other organic selenium compounds (including selenocysteine)		max. 10
3.	Levels of inorganic selenium (% total extracted selenium)		max. 1

2.1.3 Codex Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Young Children

These lists were revised by the Codex Alimentarius Commission in 2008, and expanded to include further permitted forms that could be used in infant formula products. The new forms (not already captured by the other two sources) are listed in Table 2.

Table 2: New forms added to CAC/GL 10-1979

Substance	Permitted form
Pantothenic acid	DL-panthenol
Fluoride	Calcium fluoride
Iron	Ferric orthophosphate
Magnesium	Magnesium hydroxide carbonate
Choline	Choline hydrogen tartrate

2.1.4 Other forms requested in submissions to Proposal P242

FSANZ has received submitter requests to consider permissions for other forms that are not listed in the three sources above. FSANZ has determined at this stage of Proposal P242 that these forms should not be permitted, as they have no comparable permissions either domestically or overseas. Permissions for these forms are best considered as part of a separate Application process that would occur after draft Standard 2.9.5 is gazetted.

2.2 Micronutrient composition of FSMPs represented as nutritionally complete

At Preliminary Final Assessment (2004), FSANZ conducted two assessments that investigated the risks associated with micronutrient inadequacy and the safety of excessive micronutrient levels from FSMPs represented as being nutritionally complete.

2.2.1 Minimum micronutrient requirements proposed at Preliminary Final Assessment

The 2004 assessment on micronutrient inadequacy determined that there is a significant risk of an insufficient micronutrient intake with the use of a product represented as nutritionally complete, should such a product contain inadequate amounts of micronutrients. Inadequate nutrition support was identified as prolonging a medical condition, with possible adverse consequences on morbidity and mortality for the patient.

The 2004 drafting therefore proposed minimum requirements for 26 vitamins, minerals and electrolytes. In the interests of harmonising domestic regulations with the most comprehensive and internationally applicable compositional requirements, the minimum requirements (and the range of nutrients) were adopted from the minimum values for vitamins, minerals and trace elements established in European FSMP regulations (European Commission Directive 1999/21/EC).

2.2.2 Maximum micronutrient requirements proposed at Preliminary Final Assessment

FSANZ provided a safety assessment at Preliminary Final Assessment that was used as the basis for setting maximum micronutrient limits for FSMPs that are represented as nutritionally complete.

The safety assessment identified that most vitamins and minerals did not have any established safety concerns associated with their addition to FSMPs. However, excessive intakes of vitamins A, B_6, D, selenium, iodine, zinc, calcium, manganese and copper were identified as having the potential to produce severe and chronic adverse health effects, which were considered to be significant hazards, given that FSMPs represented as nutritionally complete are often consumed as the sole source of nutrition over a long period of time.

FSANZ therefore proposed maximum content limits for vitamins A, B_6, D, selenium, iodine, zinc, calcium, manganese and copper. These limits were based on United States Upper Levels set by the U.S. Institute of Medicine. As shown in Table 3 below, with the exception of the limits for vitamin A, vitamin D and calcium, the limits are close to or exceed those limits within European FSMP regulations.

Table 3: Comparison of the maximum requirements proposed at Preliminary Final Assessment versus those in European FSMP regulations

Vitamin or Mineral	Maximum limit proposed at Preliminary Final Assessment (per MJ)	Maximum limit in European Commission Directive 1999/21/EC (per MJ)
Vitamin A (µg)	345	430
Vitamin B_6 (mg)	2.9	1.2
Vitamin D (µg)	5.7	6.5
Calcium (mg)	287	420
Copper (mg)	1.15	1.25
Iodine (µg)	115	84
Manganese (mg)	1.32	1.2
Selenium (µg)	46	25
Zinc (mg)	4.6	3.6

2.2.3 Revision of micronutrient requirements

FSANZ reaffirms the outcomes of the micronutrient assessments undertaken at Preliminary Final Assessment, and recommends that the minimum and maximum limits that were proposed in 2004 should be retained. There has been no new evidence provided in submissions to demonstrate that the minima and maxima proposed in 2004 are inappropriate for managing the risks of inadequate and/or excessive micronutrient intakes from those FSMPs represented as nutritionally complete. A full list of these minimum and maximum requirements can be found in Appendix 1.

3. Key risk assessment questions

1. The following questions apply to each additive / processing aid that requires a permission for use specifically in FSMPs:
    a) Has the technological function been articulated clearly for the requested food additives and processing aids?
    b) If a requested food additive or processing aid is not currently permitted in the Code, is its stated technological function supported by the available literature/data?
    c) Is there a need to establish maximum levels of use for the requested food additives and processing aids, in order to protect public health and safety? If so, what should they be?

2. For FOLFAPs the following questions have been applied:
    a) How prevalent in the community are:
        - Functional Bowel Disorders
        - Inflammatory Bowel Disease?
    b) What are the adverse health consequences from consumption of FOLFAPs from general dietary sources for those with:
        - Inflammatory Bowel Disease
        - Functional Bowel Disorders (including Irritable Bowel Syndrome)
        - Small Intestine Bacterial Overgrowth syndrome?
    c) What are the adverse health consequences from consumption of FOLFAPs by:
        - Consumers of FSMP as a partial dietary replacement
        - Those receiving total or near total nutrition through enteral feeding?

4. Assessment of food additives and processing aids

The use of food additives in foods in Australia and New Zealand is subject to the requirements of Standard 1.3.1 – Food Additives of the Code. Food additives are intentionally added to a food to achieve one or more technological functions (specified in Schedule 5 to Standard 1.3.1) in the final food. 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). Food additives are added to foods to assist in maintaining the quality, taste and safety of processed foods.

It is important to note that, in accordance with GMP, the proportion of a food 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 a food additive does not mean that food additive has to be used.

The use of processing aids in foods is subject to the requirements of Standard 1.3.3 – Processing Aids of the Code. Processing aids differ from food additives in so far as they perform a technological function during the processing of a food, but not in the final food. Processing aids are prohibited for use in foods unless there are explicit permissions in Standard 1.3.3.

There is currently no specific permission in Standard 1.3.1 for the addition of food additives to FSMPs. At Preliminary Final Assessment, FSANZ proposed an approach to permit the use of food additives in foods for special medical purposes. This approach is outlined in more detail below.

FSANZ has recently consulted with the FSMP industry and asked whether the approach proposed at Preliminary Final Assessment would satisfactorily reflect the use of food additives in existing FSMPs sold in Australia and New Zealand; the majority of which are sourced from overseas markets.

In this assessment, FSANZ has investigated the technological function or justification for the use of these food additives, safety of use and the potential for harmonisation with international regulations

4.1 Previous considerations at Preliminary Final Assessment

At Preliminary Final Assessment, FSANZ proposed to include an entry for FSMPs in Schedule 1 of Standard 1.3.1 – Food Additives. Where specified in Schedule 1 of Standard 1.3.1, food additives in Schedules 2, 3 and 4 may be added to processed foods in accordance with GMP. FSANZ concluded, that as FSMPs are processed foods containing a number of food ingredients, the use of all Schedule 2, 3 and 4 food additives was technologically justified. The proposed inclusion of an entry for FSMPs in Schedule 1 of Standard 1.3.1, specifying that Schedule 2, 3 and 4 food additives may be added reflected this conclusion. Please note that as part of this assessment, FSANZ has considered whether the inclusion of a permission to add Schedule 4 colours to FSMPs is warranted. This is discussed in more detail below.

FSANZ indicated that foods and ingredients used to prepare FSMPs may also contain food additives (provided the foods and ingredients themselves are permitted to contain food additives) and that these food additives may therefore be present in the final FSMPs. Clause 7 of Standard 1.3.1 – Carry-over of additives, provides for the presence of additives as a result of carry-over, provided that the level of the additive in the final food is no greater than would be introduced by the use of the ingredient under proper technological conditions and GMP.

For example, all additives permitted as antioxidants for edible oils will be permitted to be present in individual FSMPs by carry-over if edible oil (containing the antioxidants) is used as an ingredient. Similarly, foods that contain the preservatives sorbates and benzoates can also be used as ingredients in FSMPs, with similar carry-over permissions.

All Schedule 2 additives are generally permitted processing aids due to clause 3 (b) of Standard 1.3.3 – Processing Aids. The FSMP industry is not expected to have any technological need for the use of processing aids outside of the current permissions in Standard 1.3.3 – Processing Aids.

4.2 Food additives requested by industry for use in FSMPs

The FSMP industry has identified some food additives that may require specific inclusion in Schedule 1 of Standard 1.3.1 (in addition to the permissions proposed by FSANZ at PFAR). These food additives may be used in some FSMPs available on the Australian and New Zealand markets. The majority of these products are manufactured overseas in accordance with overseas regulatory requirements and are imported into Australia and New Zealand.

The FSMP industry has requested specific permission in Schedule 1 of Standard 1.3.1 for the additives listed in Table 1 below. This is in addition to the permission for the presence of these additives by carry-over in FSMPs proposed by FSANZ at PFAR. Table 1 also includes the maximum permitted levels of use of the additives in the European Union and United States of America.

Table 4: Schedule 1 food additives specifically requested by FSMP industry

Additive (INS)	**Maximum permitted level (mg/kg or mg/L)**	
	Europe	**United States of America**
Preservatives		
Sorbic acid (200)	1500*	GMP
Sodium sorbate (201)	NP	GMP
Potassium sorbate (202)	1500*	GMP
Calcium sorbate(203)	1500*	GMP
Benzoic acid (210)	1500*	1000 (GRAS)
Sodium benzoate (211)	1500*	1000 (GRAS)
Potassium benzoate (212)	1500*	NP
Calcium benzoate (213)	1500*	NP
Intense sweeteners		
Acesulfame K (950)	450	GMP
Aspartame (951)	1000	GMP
Saccharin (and its Na, K, Ca salts) (954)	200	400 mg/L (12 mg/fluid ounce) for beverages, fruit juice drinks and bases or mixes 30mg per serve in processed foods
Aspartame-Acesulfame salt (962)	450	NP
Antioxidants		
Butylated hydroxyanisole (320)	NP	GRAS: 0.02% of fat or oil content
Butylated hydroxytoluene (321)	NP	GRAS: 0.02% of fat or oil content

* Maximum level applies to each additive used singly or in combination. If used in combination, there may be no more than 1500 mg/kg total sorbates and benzoates combined[1].

NP – not permitted

FSANZ has proposed the following questions in relation to each food additive requested to have a specific permission of use in FSMPs in Standard 1.3.1:

[1] This concept is consistent with clause 6 of Standard 1.3.1 regarding maximum levels of additives performing the same technological functions in foods.

a) Has the technological function been articulated clearly for the requested food additives and processing aids?
b) If a requested food additive or processing aid is not currently permitted in the Code, is its stated technological function supported by the available literature/data?
c) Is there a need to establish maximum levels of use for the requested food additives and processing aids, in order to protect the health and safety of FSMPs consumers? If so, what should they be?

4.3 Determination of whether there is a technological function for the requested food additives

Each of the additives requested by the FSMP industry (listed in Table 1) are currently permitted in a range of foods in accordance with Schedule 1 of Standard 1.3.1. The technological functions of these food additives are well established for use in the foods in which they are permitted. Therefore, assessment questions (a) and (b) are satisfactorily addressed through the existing permissions for these food additives, in specific types of foods, in Standard 1.3.1.

FSANZ notes that the use of these food additives is subject to the principles of GMP described earlier in this assessment and that the additives would only be used in foods in which such use is technologically justified.

4.4 Identifying maximum levels of use for the requested food additives

FSANZ recognising the importance of FSMPs for the intended consumers in the Australian and New Zealand market, and that the majority of existing products are manufactured overseas in compliance with European and/or United States regulatory requirements. FSANZ therefore considers that it is appropriate to harmonise the requirements for food additive use in FSMPs as much as possible with these international requirements.

In considering whether to harmonise with these overseas maximum levels, FSANZ has compared them with the existing maximum levels for the requested food additives set out in Schedule 1 of Standard 1.3.1. This comparison provides an indication as to whether the overseas maximum levels are consistent with use levels already permitted in foods in Australia and New Zealand.

Note that where FSANZ has concluded that a specific permission (for the addition of a food additive to FSMPs) in Schedule 1 is justified, the principle of GMP applies. That is, FSANZ expects that these food additives would only be added to those FSMPs in which they are technologically justified, and at the minimum possible level to achieve that function (despite any maximum level that may be set).

4.4.1 Preservatives

4.4.1.1 Sorbates

Sorbic acid and sodium, potassium and calcium sorbates (referred to collectively as sorbates hereafter) are permitted, in Schedule 1 of Standard 1.3.1, in a wide variety of processed foods including cheese, dried fruits and vegetables, low joule jams and spreads, sugar confectionery, pasta, bread and baked products, dried meat, semi-preserved fish and fish products, liquid

tabletop sweeteners, fruit juice, water-based flavoured drinks, dairy- and fat-based desserts and sauces, mayonnaise and salad dressings.

The maximum permitted levels for sorbates in Standard 1.3.1 in commonly consumed foods are consistent with the maximum levels of use in FSMPs in the European Union regulations (1500 mg/kg). The United States permits sorbates at levels consistent with good manufacturing practice rather than setting a maximum level.

Conclusion
FSANZ concludes that a maximum permitted level in Schedule 1 of Standard 1.3.1 of 1500 mg/kg of sorbates is appropriate for FSMPs.

4.4.1.2 Benzoates

Benzoic acid and sodium, potassium and calcium benzoates (referred to collectively as benzoates hereafter) are permitted, in Schedule 1 of Standard 1.3.1, in a wide variety of processed foods including oil emulsions, liquid ice confection, low joule jams and spreads, icings and frostings, semi-preserved fish and fish products, liquid tabletop sweeteners, sports foods, fruit and vegetable juices, water-based flavoured drinks, dairy- and fat-based desserts and sauces, mayonnaise and salad dressings.

The maximum permitted levels for benzoates in Standard 1.3.1 in commonly consumed foods are consistent with the maximum levels of use in FSMPs in the European Union regulations (1500 mg/kg). Benzoic acid and sodium benzoate are generally recognised as safe (GRAS) in the United States at 0.1% (equivalent to 1000 mg/kg).

Conclusion
FSANZ concludes that a maximum permitted level in Schedule 1 of Standard 1.3.1 of 1500 mg/kg of benzoates is appropriate for FSMPs.

4.4.2 Intense sweeteners

4.4.2.1 Acesulfame-potassium

Acesulfame-potassium is permitted, in Standard 1.3.1, in a wide variety of foods including liquid milk products, ice creams, fruit and vegetable spreads, confectionery, flour products (including pasta), biscuits, cakes, pastries, tabletop sweeteners, sports foods, meal replacements and supplementary foods, water-based flavoured drinks and mixed foods such as desserts, sauces and toppings.

The maximum permitted levels for acesulfame-potassium in Standard 1.3.1 range from 150 mg/kg in electrolyte drink products and 500 mg/kg in liquid milk products and supplementary foods, to 2000 mg/kg in confectionery and 3000 mg/kg in water-based flavoured drinks and fruit juice products. Acesulfame-potassium is also permitted to be used at levels of GMP in tabletop sweeteners.

Acesulfame-potassium is permitted at 450 mg/kg in FSMPs in the European Union regulations and at GMP in the United States. To be consistent with other maximum levels set in Standard 1.3.1 for acesulfame-potassium, FSANZ considers it would be appropriate to set a maximum level of use, rather than a GMP permission for use in FSMPs.

Conclusion
FSANZ concludes that a maximum permitted level in Schedule 1 of Standard 1.3.1 of 450 mg/kg of acesulfame-potassium is appropriate for FSMPs, as this level is consistent with the maximum permitted level in the European Union regulations and similar food products included in Schedule 1 of Standard 1.3.1.

4.4.2.2 Aspartame

Aspartame is listed in Standard 1.3.1 as a Schedule 2 food additive. Schedule 2 food additives are permitted in processed foods as a result of use in accordance with GMP unless otherwise prohibited in Schedule 1 of Standard 1.3.1. Therefore, aspartame is permitted in processed foods as a result of use in accordance with GMP. Clause 4 of Standard 1.3.1 provides additional clarification regarding the requirements for the use of intense sweeteners in foods.

Aspartame is also specifically permitted in some foods in Schedule 1 of Standard 1.3.1, including confectionery (10000 mg/kg), brewed soft drink (1000 mg/kg), electrolyte drinks (150 mg/kg) and formulated beverages (GMP).

FSANZ has already indicated that Schedule 2 food additives are recommended to be permitted in FSMPs. As a schedule 2 food additive, aspartame will be permitted to be used in FSMPs if a separate category for FSMPs is included in Schedule 1 of Standard 1.3.1. This approach has already been proposed by FSANZ and FSANZ considers it unnecessary to have specific permission for the addition of aspartame to FSMPs in Schedule 1 in addition to the permission for the use of Schedule 2 food additives.

Conclusion
FSANZ concludes that given aspartame is a Schedule 2 food additive, it would be permitted to be added to FSMPs as a result the inclusion of a FSMP category in Schedule 1 of Standard 1.3.1. FSANZ does not consider a separate permission for aspartame in Schedule 1 of Standard 1.3.1 is required for FSMPs.

4.4.2.3 Saccharin

Saccharin (and its sodium, potassium and calcium salts) is permitted, in Standard 1.3.1 in a variety of foods including fruit and vegetable spreads, low joule chewing gum, liquid and tablet or powdered tabletop sweeteners, low joule fruit juice products, water based flavoured drinks, jelly, sauces and toppings.

The maximum permitted levels for saccharin in Standard 1.3.1 range from 50 mg/kg in brewed soft drinks, 80 mg/kg in low joule fruit and vegetable juice products and 150 mg/kg in water based flavoured drinks, up to 1500 mg/kg in fruit and vegetable spreads, low joule chewing gum, sauces and toppings. Saccharin is also permitted to be used at levels of GMP in liquid, tablet and powdered tabletop sweeteners.

Saccharin is permitted at 200 mg/kg in FSMPs in the European Union regulations. Saccharin is permitted in special dietary foods in the United States at approximately 400 mg/L for beverages (12 mg/fluid ounce), fruit juice drinks and bases or mixes and at 30 mg per serve in processed foods (on this basis, 30 mg in a 100 gram serving would equate to 300 mg/kg of

saccharin). However, the permitted levels in the United States are interim levels and are subject to review.

The maximum permitted levels of saccharin in Standard 1.3.1 are less than the European Union maximum permitted level for beverage products, but above this level for spreads, low joule chewing gum and sauces and toppings. The maximum permitted levels of saccharin in Standard 1.3.1 are also below the maximum permitted level for beverages in the United States, but likely greater than the levels of use permitted in processed special dietary foods.

Conclusion
FSANZ concludes that a maximum permitted level in Schedule 1 of Standard 1.3.1 of 200 mg/kg of saccharin is appropriate for FSMPs. This level is consistent with the maximum permitted level in the European regulations and more consistent with the existing permissions for beverages in Standard 1.3.1. However, this level is lower than the interim level for beverage type special dietary foods in the United States.

Question for submitters

Will the recommended level of 200 mg/kg of saccharin in FSMPs pose any problems for current formulations of FSMPs imported into Australia?

4.4.2.4 Aspartame-acesulphame salt

Aspartame-acesulphame salt is permitted in Standard 1.3.1 for use in a wide variety of foods including liquid milk products, ice creams, fruit and vegetable spreads, confectionery, flour products (including pasta), biscuits, cakes, pastries, tabletop sweeteners, sports foods, meal replacements and supplementary foods, fruit and vegetable juice products, water-based flavoured drinks and mixed foods such as desserts, sauces and toppings.

The maximum permitted levels for acesulfame-potassium in Standard 1.3.1 range from 230 mg/kg in electrolyte drink products and 450 mg/kg in flour products, and from 1100 mg/kg to 6800 mg/kg in the other food products in which it is permitted to be added. Aspartame-acesulphame salt is also permitted to be used at levels of GMP in tabletop sweeteners.

Aspartame-acesulphame salt is permitted at 450 mg/kg in FSMPs in the European Union regulations but is not permitted in the United States.

Conclusion
FSANZ concludes that a maximum permitted level in Schedule 1 of Standard 1.3.1 of 450 mg/kg of Aspartame-acesulphame salt is appropriate for FSMPs.

4.4.3 Antioxidants - butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)

BHA and BHT are permitted, in Schedule 1 of Standard 1.3.1, in a limited number of foods including dried milk powder, edible oils and oil emulsions, walnut and pecan nut kernels, bubble gum and chewing gum. The maximum permitted levels of BHA and BHT permitted in Standard 1.3.1 range from 70 mg/kg in walnut and pecan nut kernels, up to 200 mg/kg in edible oils and oil emulsions (100 mg/kg for BHT). BHA is also permitted in flavourings used in preparations of food additives at 1000 mg/kg. However, use at this level is expected

only where flavourings used in the preparation of food additives and would constitute only a very small proportion of a final food product.

There is no provision for the addition of BHA or BHT to FSMPs in the European regulations. However, BHA and BHT do have GRAS permission in the United States at up to 0.02% of fat or oil content of a food. BHA and BHT are antioxidants that can act to preserve fats and oils from oxidative damage. The 0.02% GRAS level is based on the fat or oil content of foods, rather than being permitted at 0.02% of the final food product. The 0.02% GRAS level corresponds to the level of 200 mg/kg of BHA, and is slightly higher than the 100 mg/kg of BHT, permitted in edible oils in Standard 1.3.1.

FSANZ considers that the existing permissions for BHA and BHT in Schedule 1 of Standard 1.3.1 are appropriate for use in ingredients that may be used to manufacture FSMPs. For example, an edible oil used as an ingredient in FSMPs may contain BHA at up to 200 mg/kg. BHA would be permitted to be present in the final FSMP product by virtue of the carry-over provisions outlined earlier in clause 7 of Standard 1.3.1. FSANZ does not expect that additional levels of BHA or BHT would be justified outside of the carry-over provisions for ingredients outlined in clause 7 of Standard 1.3.1.

Conclusion
Given the nature of BHA and BHT, and the permitted level of use in the United States, FSANZ considers that the carry-over provision of clause 7 of Standard 1.3.1 is satisfactory and appropriate for ingredients used in FSMPs. FSANZ considers that a separate permission for BHA and BHT in FSMPs is not required in Schedule 1 of Standard 1.3.1.

4.5 Other Schedule 1 food additives used in FSMPs

FSANZ notes some other Schedule 1 food additives may be present in FSMPs imported into Australia and New Zealand. However, the FSMP industry did not request specific permissions for these food additives in FSMPs in Schedule 1 of Standard 1.3.1. The food additives that FSANZ noted are ascorbyl palmitate (INS 304) and tocopherol, d-alpha-, concentrate (INS 307). Because both of these food additives are antioxidants and their regulation is considered to be similar to the FSANZ position on the antioxidants BHA and BHT (described above), FSANZ considers it likely that the presence of these food additives in FSMPs will be addressed by the carry-over provisions in clause 7 of Standard 1.3.1.

4.6 Re-assessment of allowing colours in Schedule 4 of Standard 1.3.1 to be used in FSMPs

At Preliminary Final Assessment, FSANZ proposed to include permission to add Schedule 4 food additives (artificial colours) to FSMPs (in addition to Schedule 2 and 3 food additives). However, the use of artificial colours in foods has come under increasing scrutiny in recent years. Internationally, food regulators and the food industry have investigated the technical merits of using alternative sources of colours to add to foods.

At Preliminary Final Assessment, the FSMP industry did not specifically request the addition of Schedule 4 colours to FSMPs.

Conclusion

Given the lack of a specific request from the FSMP industry and the potential for alternative colours to be utilised in foods, FSANZ considers that permission to add Schedule 4 food additives to FSMPs is not required in Schedule 1 of Standard 1.3.1. This is different from the approach taken at Preliminary Final Assessment for Schedule 4 food additives.

Question for submitters

Is there a justified technological need for the addition of Schedule 4 colours to FSMPs?

4.7 Response to Risk Assessment Question 1

1. The following questions have been applied to each additive / processing aid that requires a permission for use specifically in FSMPs:
   a) Has the technological function been articulated clearly for the requested food additives and processing aids?
   b) If a requested food additive or processing aid is not currently permitted in the Code, is its stated technological function supported by the available literature/data?
   c) Is there a need to establish maximum levels of use for the requested food additives and processing aids, in order to protect public health and safety? If so, what should these maximum levels be?

FSANZ consulted with the FSMP industry and received requests to include specific permissions for a number of food additives in FSMPs under Schedule 1 of Standard 1.3.1. Each of the requested food additives is currently permitted in Standard 1.3.1 to be added to a variety of processed foods. These existing permissions by Standard 1.3.1 mean that the technological function for each requested food additive has previously been articulated and supported in a range of processed food products; and therefore provide satisfactory answers to questions a) and b) above.
With respect to question c), FSANZ considered that the establishment of maximum levels was justified for the food additives listed in Table 5, at the levels indicated in the Table.

Table 5: Proposed maximum permitted levels of food additives in FSMPs in Schedule 1 of Standard 1.3.1

INS Number	Additive Name	Max Permitted Level
200 201 202 203	Sorbic acid and sodium, potassium and calcium sorbates	1500 mg/kg
210 211 212 213	Benzoic acid and sodium, potassium and calcium benzoates	1500 mg/kg
950	Acesulphame potassium	450 mg/kg
954	Saccharin	200 mg/kg
962	Aspartame-acesulphame salt	450 mg/kg

FSANZ did not consider it necessary to set a maximum permitted level for aspartame, as it is listed as a Schedule 2 food additive in Standard 1.3.1 and Schedule 2 food additives are permitted in Schedule 1 of Standard 1.3.1 in accordance with use levels associated with GMP.

FSANZ also considered that separate permissions for BHA and BHT in FSMPs in Schedule 1 of Standard 1.3.1 were not justified. FSANZ concluded that the carry-over provisions provided for in clause 7 of Standard 1.3.1 were sufficient for the presence of these food additives in FSMPs.

FSANZ also considered that permission to add Schedule 4 food additives (artificial colours) to FSMPs is not required in Schedule 1 of Standard 1.3.1.

5. Assessment of Fermentable Oligosaccharides, Lactose, Fructose and Polyols (FOLFAPs)

FOLFAPS comprise fructose (monosaccharide); lactose (disaccharide); fructans and galactans (oligosaccharides); and polyols (Muir *et al*., 2009) (Gibson and Shepherd, 2009) and are widespread in the diet. FOLFAPs is an acronym coined by FSANZ since the more commonly used term *FODMAPS (*i.e. fermentable oligosaccharides, disaccharides, monosaccharides and polyols) is trademarked. The two acronyms are essentially the same; however, FOLFAPS is more specific in that the literature identifies lactose as the only disaccharide of interest and fructose as the only monosaccharide of interest.

FOLFAPs occur naturally in some foods and their ingredients may be added to foods for technological reasons (e.g. to emulsify or thicken food) and for nutritional reasons (e.g. as a dietary fibre or for their prebiotic effect).

FOLFAPs are readily fermentable carbohydrates which, while not hydrolysed in the small intestine, are efficiently hydrolysed and fermented in the large intestine (Teuri *et al*., 1999) causing luminal distention of the distal small intestine and the proximal colon. The luminal distention can be caused by solids (undigested carbohydrates), liquids (water drawn in due to increased osmotic potential) and gas (from bacterial fermentation) and is considered to be the physiological basis for gastrointestinal symptoms associated with consumption of FOLFAPS (Gibson and Shepherd, 2009; Rangnekar and Chey, 2009). Although all FOLFAPs share the effects of increased osmosis and rapid fermentability, it is likely that the effects will be additive when delivered in combination to the colon (Gibson *et al*., 2007).

5.1 Functional Bowel Disorders (FBD) and Inflammatory Bowel Diseases (IBD) and their relationship to FOLFAPs consumption

5.1.1 Characterisation of Functional Bowel Disorders and Inflammatory Bowel Diseases

Symptoms of intolerance to FOLFAPS in the community are observed in many conditions ranging from functional bowel disorders (FBD) through to Inflammatory Bowel Disease (IBD).

A functional bowel disorder (FBD) is a functional gastrointestinal disorder with symptoms attributable to the mid or lower gastrointestinal tract, including irritable bowel syndrome, functional abdominal bloating, functional constipation, functional diarrhoea, and unspecified functional bowel disorder (Thompson *et al*., 1999).

Table 5 provides schema of the various classifications of diseases within IBD and disorders within FBD. Crohn's disease ulcerative colitis and indeterminate colitis are subsets of IBD, and irritable bowel syndrome is a subset of functional bowel disorders, of which lactose intolerance, fructose absorption and small intestine bacterial overgrowth are further subsets.

Although IBD and FBD qualitatively overlap in terms of the symptoms experienced, and may be present simultaneously, they are diagnostically distinct and one is not a subset of the other. IBD is identifiable by histological, endoscopic or radiographic investigation (Yap *et al*., 2008), whereas FBDs are diagnosed where symptoms persists despite no identifiable pathology (Thompson *et al*., 1999).

Table 5: Schema of Inflammatory Bowel Disease, Functional Bowel Disorders and their diagnostic subsets

<table>
<tr><th>Inflammatory bowel disease</th><th colspan="3">Functional bowel disorders</th></tr>
<tr><td>Crohn's disease</td><td colspan="3" rowspan="2">Irritable bowel syndrome</td></tr>
<tr><td>Ulcerative colitis</td></tr>
<tr><td>Indeterminate colitis</td><td>Lactose intolerance</td><td>Fructose Malabsorption</td><td>Small Intestine Bacterial Overgrowth</td></tr>
</table>

IBD predominantly manifests as Crohn's disease & ulcerative colitis and indeterminate colitis, however FOLFAPs intolerance and FBD symptoms have been observed in these populations concurrent with pre-existing pathologic evidence of disease (Gibson and Shepherd, 2005).

Irritable Bowel Syndrome (IBS) is the FBD most commonly associated with FOLFAPs consumption and has a range of diagnostic criteria and several classifications – characterised as diarrhoea predominant, constipation predominant or diarrhoea and constipation together (ROME II criteria) (Primavera *et al*., 2010). The most common non-invasive diagnostic tests (i.e. other than a biopsy) for IBS are hydrogen and methane breath tests, specifically those showing bacterial fermentation of unhydrolysed carbohydrates following challenges with isolated carbohydrate solutions (Fernandez-Banares *et al*., 1993; Johlin *et al*., 2004).

Fructose Malabsorption (FM) and Lactose Intolerance (LI) are commonly considered to be subsets of IBS, however trial evidence suggests that FM and LI can exist concurrently (Teuri *et al*., 1999).

Fructose is a key constituent of FOLFAPs and is common in the western diet. It is consumed as a free monosaccharide or constituent of sucrose, or as fructans (oligosaccharides) (Gibson *et al*., 2007). The human intestine does not have a specific mucosal enzyme for digestion or transport of fructose. Instead, absorption of fructose primarily relies on facilitation by glucose transporters (GLUT 5 and GLUT 2) which can be overwhelmed after the ingestion of large amounts of fructose (Rangnekar and Chey, 2009). As a result, fructose is absorbed more efficiently in the presence of glucose. This outcome seems to account for the symptom-inducing effect of fructose *in excess* of glucose rather than fructose alone (Gibson and Shepherd, 2009).

Lactose Intolerance (LI) causes symptoms similar to IBS; consequently most investigations show increased LI among IBS sufferers. Symptoms are caused by unhydrolysed lactose, which draws water by osmosis into the small intestine (Gudman-Hoyer, 1994). Individual sensitivity to lactose varies, with some people having LI being able to tolerate small amounts of lactose (Vesa *et al*., 1996). LI has been recognised for some time whereas the literature on fructose malabsorption and other FOLFAPs is more recent. The literature indicates genetic differences in prevalence rates of LI such that LI is lowest in Scandinavia and Northwest Europe (areas with high historical intake of lactose) and highest (up to 100%) in Southeast Asia and parts of Africa with low historical intake of lactose (Gudman-Hoyer, 1994). Such

genetic variations have not been identified in relation to sensitivity to other FOLFAPs possibly due to the emerging nature of the research.

Small Intestine Bacterial Overgrowth (SIBO) is a subset of IBS although there is also some evidence of bacterial overgrowth in those with IBD. Symptoms appear to be analogous to other forms of IBS, and separate classification is possible via bacterial count from a small bowel aspirate/biopsy. FOLFAPs are implicated in one potential pathway encouraging the growth of colonic bacteria in the small intestine (which are free bacteria in the healthy individual) (Bures J *et al*., 2010).

5.1.2 Irritable Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS) incidence in Australia and New Zealand

As yet, there have been no national epidemiological studies published in Australia of the number of new cases of IBD. Recently however, a prospective incidence study carried out in Greater Geelong, Victoria suggested a crude annual incidence rate of 29.3 per 100,000 for IBD, comprising Crohn's disease (CD), 17.4 per 100,000; ulcerative colitis (UC), 11.2 per 100,000; and indeterminate colitis, 0.8 per 100,000. Although no ethnic differences were reported, these incidence rates are among the highest in the literature (Wilson *et al*., 2010).

The incidence of IBD in New Zealand has risen dramatically over the past 50 years. Data show a clear geographical variation reflecting differing regional ethnic distributions; IBD is less common in Maori than Caucasian people with almost no incidence in Pacific Islanders (Gearry and Day, 2008). A recent prospective study of paediatric IBD in New Zealand reported an estimated incidence of paediatric onset IBD of 2.9 cases per 100,000, including 1.9 cases per 100,000 per year of CD and 0.5 cases per 100,000 per year of UC: 94% of the CD cohort was from Europe. A recent report from a Canterbury IBD project, with adult and paediatric data, estimated a crude incidence of 25.2 per 100,000 per year IBD, including 16.5 per 100,000 per year of CD and 7.6 per 100,000 per year of UC (Yap *et al*., 2008).

IBS has been reported to affect up to 15% of the general population globally with up to 17% of those affected requiring hospitalisation due to this condition (Barrett and Gibson, 2007); (Gibson and Shepherd, 2009). However national estimates for Australia and New Zealand are only beginning to emerge. The BEACH program (a continuous national study of general practice (GP) activity in Australia), indicated an average of approximately 285,000 GP visits annually related to IBS management, three quarters of which were for females, and 31% for patients aged 25-44 years (Charles and Harrison, 2006). Most estimates of population prevalence in New Zealand have been extrapolated from data centred on the US and Europe, on the assumption that IBS symptoms are as common in New Zealand as in those countries. In 2002, a validated Bowel Disease questionnaire administered to 980 participants of the Dunedin Multidisciplinary Health and Development Study showed 64% of respondents reported at least one of the measured symptoms associated with IBS, with females exhibiting symptoms more than twice as often as males: 4.5% reported abdominal pain, 9.1% chronic constipation, and 17.1% chronic diarrhoea. These results verify that the prevalence of IBS related symptoms in New Zealand is very similar to that recorded in Europe and the US (Barbeztt *et al*., 2002).

IBD is emerging as a significant health problem among non-Caucasian populations in Asia, (Yap *et al*., 2008). With continued migration to New Zealand, more IBD among New Zealanders of Asian origin might be expected.

5.2 Adverse health effects from FOLFAPS consumption and dietary management

Seven studies were identified that addressed the gastrointestinal health effects from consumption of FOLFAPs substances (Croagh *et al*., 2007; Fernandez-Banares *et al*., 1993; Gearry *et al*., 2009; Halmos *et al*., 2010; Ledochowski *et al*., 2000; Shepherd *et al*., 2008; Teuri *et al*., 1999). Collectively, these studies indicate that FOLFAPs may be poorly absorbed by some individuals such as those with functional bowel disorders, particularly IBS. The low absorptive nature and high osmotic potential of FOLFAPs has been implicated in both the prebiotic and putative effects of these substances (increased frequency of bowel movements, greater fluidity or softness of bowel movements and diarrhoea (Gibson and Shepherd, 2009))

FOLFAPs provocation tests have been demonstrated to induce symptoms and increase gas production associated with bacterial fermentation and dietary studies limit FOLFAPs intake have shown improvement in symptoms (Gearry *et al*., 2009).

The tolerance to different classes of FOLFAPS in IBD and IBS varies from individual to individual. The bowel biota may be implicated in the tolerance levels of individuals to different FOLFAPs but other factors which vary from individual to individual, such as presence of lactase and glucose transporter proteins, are also important in the overall tolerance of FOLFAPs by individuals (Bures J *et al*., 2010; Gibson and Shepherd, 2009).

In sufficiently high doses, FOLFAPs exert a laxative effect in most people and sorbitol provides an example of a polyol FOLFAP that has a known laxative[2] effect which, together with lactulose, may be used clinically for its laxative inducing effects.

The management of IBD in the community is directed towards reducing gastrointestinal inflammation, however concurrent functional gut disturbance may be unresponsive to pharmacotherapy and thus dietary management analogous to that for IBS (Gearry *et al*., 2009) could be required. Dietary management of IBS/IBD depends on recognition of symptom-inducing foods and involves removal of these foods and gradual reintroduction until acceptable symptomatic relief/ management is achieved. Dietary education is generally undertaken in one-on-one consultations with registered dietitians so that it can be tailored to the specific sensitivities of the individual and suitable foods and potential triggers can be identified (Barrett and Gibson, 2007).

Reduction of all FOLFAPs in the diet (rather than a single group as in fructose or lactose malabsorption) has been found to be effective in managing symptoms of up to 72% of individuals with FBD, and the low FOLFAPs approach also provides effective relief of non-pathologic gastrointestinal symptoms in those with IBD, (Barrett and Gibson, 2007; Gibson and Shepherd, 2005; Gibson and Shepherd, 2009; Shepherd *et al*., 2008).

Gibson and Shepherd note that the total dose of FOLFAPs in the diet will dictate the severity of symptoms experienced by an individual. Therefore assessment of the total dietary intake of FOLFAPs is critical to defining the degree of FOLFAPs restriction recommended for each individual (Gibson and Shepherd, 2009).

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[2] Standard 1.2.3 requires foods containing sorbitol above a threshold of 25g/100g be labelled with an advisory statement to the effect that excess consumption of the food may have a laxative effect

In the case of SIBO, it appears that symptoms resulting from FOLFAPs intake are not only dependent on the prebiotic present, but are also due to the balance of biota that the prebiotics promote in the gut, which has a high degree of inter-individual variability (Barrett and Gibson, 2007; Bures J *et al*., 2010).

These observations may be of relevance to symptom development in those individuals who are long term or lifetime users of FSMPs.

5.3 Risk from FOLFAPS consumption specific to FSMP users

While there are a range of studies addressing the effects of FOLFAPS *per se*, there is a paucity of data about the health effects of FOLFAPs consumed in FSMPs. This is problematic as FSMP consumers are more vulnerable than the general population.

A review of the literature to assess the risks to health from consumption of FOLFAPS in clinical settings identified just one retrospective study of diarrhoea in patients receiving FSMPs in the form of enteral nutrition (EN) (Halmos *et al*., 2010). Halmos and colleagues (2010) consider that most patients without gastrointestinal functional disorders or disease who receive EN would not require as stringent a restriction of FOLFAPs as in the IBS population. Only higher doses of FOLFAPs (as in most of the formulas used in this study), would be expected to trigger diarrhoea in those ordinarily asymptomatic (Halmos *et al*., 2010)

Halmos *et al*. (2010) studied the FOLFAP content of enteral feeds and concluded that length of hospital stay and enteral nutrition duration independently predicted diarrhoea development. These findings suggest that FBD sufferers may use FSMPs while under medical supervision *and* that those on enteral feeds may be particularly susceptible to the symptoms of FBD (Halmos *et al*., 2010).

5.4 Response to Risk Assessment Question 2

For FOLFAPs the following questions have been posed:

a) How prevalent in the community are:
- Functional Bowel Disorders
- Inflammatory Bowel Disease?

b) What are the adverse health consequences from consumption of FOLFAPs from general dietary sources for those with:
- Inflammatory Bowel Disease
- Functional Bowel Disorders (including Irritable Bowel Syndrome)
- Small Intestine Bacterial Overgrowth syndrome?

c) What are the adverse health consequences from consumption of FOLFAPs by:
- Consumers of FSMP as a partial dietary replacement
- Those receiving total or near total nutrition through enteral feeding?

Although there are no national epidemiological studies of the prevalence of FBD (including IBS) and/or IBD in Australia and New Zealand, regionally collected incidence data along with GP reporting, indicate that FBD (in the form of IBS) and IBD are prevalent in both countries. There is also some evidence that prevalence is increasing. New Zealand data show those of European descent are at higher risk than those of Māori or Pacific Island descent, while differences in incidence by ethnicity have not been reported in Australia.

Recent data have demonstrated consumption of FOLFAPs (from general dietary sources) by those with pre-existing FBD and/or IBD may exacerbate gastrointestinal symptoms, and that the reduction of dietary FOLFAPs may provide symptomatic relief. However it is not clear if consumption of FOLFAPs is causal in FBD. There is some evidence that SIBO is associated with the consumption of FOLFAPs (Barrett and Gibson, 2007) and SIBO is implicated in the pathophysiology of IBS (Reddymasu *et al*., 2010).

In the community, dietary management of IBS/IBD relies on the recognition of symptom-inducing foods and one-on-one dietetic education to control FOLFAP levels and sources until acceptable symptomatic relief for the individual is achieved. However, it is also likely that a number of individuals with IBS/IBD will be prescribed or recommended to use FSMPs containing FOLFAPs. This likelihood increases if affected individuals are admitted to hospital or a healthcare centre for management of their conditions, or for other non-related medical conditions.

For those on FSMPs containing FOLFAPs (specifically enteral nutrition products), there is an increased risk of diarrhoea during or following enteral nutrition regardless of the underlying principal condition being treated. FSANZ notes, however, that the evidence is limited on the contribution of FOLFAPs in FSMPs to increased episodes of diarrhoea (one pilot retrospective case-control study on enteral nutrition products only).

In addition, no information was identified in regard to:

- the size of the population at risk from consumption of FOLFAPs from FSMPs;
- the proportion of those FBD (including IBS) and/or IBD patients receiving FSMPs, either during their hospital stay or while under medical supervision; or
- the prevalence of FBD (including IBS) in FSMP users.

5.5 Questions to submitters

As a result of the uncertainties about the potential risk that FOLFAPs in FSMPs might pose, FSANZ is interested in any additional information relating to FSMP users of any age group, particularly those chronically dependent on these products, and the use of these products in the management of IBD and IBS.

Questions to Submitters

- Are FSMPs used in the management of FGD and/or IBD (including during hospitalisation)?
- What is the prevalence of FBD and /or IBD in consumers of FSMPs?
- Do FOLFAPs exacerbate FBD and/or IBD in consumers of FSMPs that are used in the management of these conditions?
- Do FOLFAP ingredients in FSMPs promote the development of FBD and /or IBD in patients with no earlier signs of these conditions?

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Appendix 1

Summary of substance additions to FSMPs and the limits on these additions

Permitted forms

Substance	Permitted form
Calcium	Calcium bisglycinate
	Calcium citrate malate
	Calcium malate
	Calcium L-pidolate
Choline	Choline hydrogen tartrate
Fluoride	Calcium fluoride
Iron	Ferric orthophosphate
	Ferrous L-pidolate
Lutein	Lutein
Magnesium	Magnesium bisglycinate
	Magnesium hydroxide carbonate
	Magnesium L-pidolate
	Magnesium potassium citrate
Pantothenic acid	DL-panthenol
Potassium	Potassium L-pidolate
Selenium	Selenium enriched yeast
Vitamin E	D-alpha-tocopherol polyethylene glycol-1000 succinate (TPGS)
Zinc	Zinc bisglycinate

Minimum and maximum micronutrient requirements for FSMPs represented as nutritionally complete

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
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 1 mg alpha-tocopherol equivalents per MJ	No maximum set
Biotin	1.8 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

Food Additives

INS Number	Additive Name	Max Permitted Level
200 201 202 203	Sorbic acid and sodium, potassium and calcium sorbates	1500 mg/kg
210 211 212 213	Benzoic acid and sodium, potassium and calcium benzoates	1500 mg/kg
950	Acesulphame potassium	450 mg/kg
954	Saccharin	200
962	Aspartame-acesulphame salt	450 mg/kg