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

Supporting document 1

Composition Assessment – Proposal P242 (Final Assessment)

Food for Special Medical Purposes

Table of Contents

1 Introduction

FSANZ has conducted two prior assessments of the composition and safety of foods for special medical purposes (FSMP); firstly, at Preliminary Final Assessment (2004) and in a Consultation paper (December 2010) for Proposal P242. This latest assessment extends the assessment on the nutrient composition requirements of FSMP, considers chromium picolinate as a form of chromium suitable for use in FSMP, and includes a revision to the consideration of fermentable oligosaccharides, lactose, fructose, and polyols in FSMP.

FSMP are primarily imported into Australia and New Zealand. As such, the need for international harmonisation has determined the scope of the various assessment components.

2 Findings from Previous FSANZ Risk Assessments

2.1 Preliminary final assessment report – 2004

FSANZ completed a risk assessment of FSMPs in 2004. The findings from this risk assessment can be found at http://www.foodstandards.gov.au/_srcfiles/P242_FSMP_PFAR.pdf . The findings are not reproduced in detail in this document, but a summary is provided below.

1. When an FSMP is the sole source of nutrition, there is a potential risk of insufficient micronutrient intake if the FSMP is nutritionally inadequate for an individual. Inadequate nutritional support can prolong a medical condition with possible adverse consequences on morbidity and mortality for the patient. This risk diminishes substantially when FSMPs are consumed along with other foods in the diet.

2. Some vitamins and minerals were identified as having potential safety concerns within the context of their use in FSMPs; therefore an upper limit for their use in FSMP was considered necessary. These micronutrients are vitamins A, B6 and D, selenium, iodine, zinc, calcium, manganese and copper.

3. For certain a medical conditions, there is a need to reduce the amount of some micronutrients below the levels required for the maintenance of adequate nutrition in healthy people. In these circumstances, the recommended upper levels of intake for the condition could be below normal minimum requirements. For example, low intakes of sodium, potassium and phosphorus are required for the management of certain medical conditions e.g. renal disease. Thus, if medically indicated, a decrease in the minimum requirement for sodium, potassium and phosphorus content of FSMP is appropriate.

4. The following forms of nutritive substances were considered to be safe for use in FSMP:

    - **permitted forms listed in Standard 2.9.1** – Infant formula products
    - **L-serine**, and the double amino acid salts **L-arginine-L-aspartate**, **L-lysine-L-aspartate**, and **L-lysine-L-glutamate dihydride** (as assessed by the then European Scientific Committee on Food, now EFSA)
    - **N-acetyl-L-methionine** and **L-asparagine** monohydrate in FSMP were unlikely to be associated with adverse health effects (as assessed by FSANZ)
    - **chromium potassium sulfate dodecahydrate** because it is similar to the already permitted form chromium sulfate.

The following forms of nutritive substances were **not** considered to be safe for use in FSMP:

- **permitted forms listed in Standard 1.1.1** – Preliminary Provisions – Application, Interpretation and General Prohibitions, cannot be guaranteed as safe for use in FSMPs, as these provisions are intended to apply to a normal healthy population
- **chromium acetate** because its toxicological profile could not be determined as the solubility of this form is different to other chromium III forms.

5. 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.

2.2 Consultation paper – 2010

FSANZ also completed an assessment of FSMPs in 2010. The findings from this risk assessment can be found at http://www.foodstandards.gov.au/_srcfiles/P242%20FSMPs%20Cons%20Paper%20SD1.pdf The findings from this report are summarised in the following section.

1. The minimum and maximum micronutrient composition requirements (for FSMPs represented as a sole source of nutrition) proposed in the 2004 drafting were retained.

2. An assessment of the potential risk of adverse health effects from fermentable oligosaccharides, lactose, fructose, and polyols (FOLFAPs) in FSMP was undertaken in response to stakeholder concerns. This has been updated at Final Assessment.

3. An additional nineteen permitted forms of nutrients and nutritive substances were determined as safe to be added to FSMP. These were obtained from Schedule 1 of Standard 2.9.1, the European Commission, and the Codex Advisory List CAC/GL 10-1979.

3 Updates to the Assessment since 2010

3.1 Micronutrient composition of FSMPs

3.1.1 Minimum micronutrient content requirements for products represented as a sole source of nutrition

In the December 2010 consultation paper, FSANZ proposed to retain the 26 minimum micronutrient levels proposed in 2004. In the interests of harmonising domestic regulations with the most comprehensive and internationally applicable compositional requirements, the minimum requirements were adopted from the minimum values for vitamins, minerals and trace elements established in European FSMP regulations (European Commission Directive 1999/21/EC). Industry advised FSANZ that these levels were already being met for most FSMP products.

Pre-consultation in 2010, FSANZ compared the EU minimum levels against the current Australian and New Zealand NRVs. This comparison concluded that adoption of the estimated average requirement (EAR) values as the minimum composition requirements for FSMPs would require an increase in the minimum values for approximately half of the

micronutrients and a decrease for the remainder. At the time, no further action was considered necessary because the primary driver for micronutrient composition was international harmonisation. The minimum composition requirements also ensure a basic and consistent level of nutritional quality for FSMP used as a sole source of nutrition.

However, in submissions to the December 2010 consultation paper, several stakeholders commented that the minimum composition requirements in the EU regulations were lower than the 2006 EAR. In response, FSANZ considered the potential risks associated with this further in 2011.

3.1.1.1 Estimate of intakes

The potential risks of inadequate micronutrient intakes were assessed in two ways. Firstly, the European minimum composition values were used to model daily nutrient intakes for the lower and upper end of the estimated energy requirement (EER) range for each age and gender group (in children and adults as outlined in the 2006 Australia and New Zealand NRVs). These estimates of minimum level intakes were then compared to the Australian and New Zealand 2006 EARs.

Based on the assumption that products would only contain micronutrients at the minimum composition value (i.e. a 'worst case' scenario), the comparison identified potential for nutrient intakes below EARs. It should be noted that no comparisons were made with adequate intake values (AIs). Tables of these results can be found in Attachment 2 and are summarised below.

For most age groups in female children, levels of folate, vitamin B12, pantothenic acid, biotin, calcium, phosphorus, and magnesium have potential for intakes to be just below the EAR. In male children, pantothenic acid, biotin, phosphorus, magnesium and chromium have potential for intakes to be just below the EARs for most age groups. In adult females, levels of selenium, magnesium, calcium, iron, and phosphorus are potentially just below EARs, as well as folate and vitamin A for the older age groups. In adult males, magnesium is the only nutrient with potentially low intake in the under 50 age groups. In the over 50 age groups, there is potential for magnesium, phosphorus and vitamin A intakes to fall just below the EAR.

Second, for adults only, FSANZ modelled potential daily nutrient intakes using the product composition information from nutrition information panels on a small sample of FSMP products. This analysis was based on the theoretical models of daily intake discussed above. Daily nutrient intakes were estimated for each age and gender group for a range of FSMP with different product composition. The theoretical daily intakes were calculated based on the bed rest physical activity level for the range of adult EERs (listed in the 2006 Australia and New Zealand NRVs). The bed rest activity level equates to approximately two-thirds of the energy requirements of an active person.

The second analysis showed variation in the potential nutrient intakes across the different products although most products supplied nutrients at levels that would meet the EAR for all nutrients. In general, in younger adults a greater number of products provided nutrient intakes above the EAR for various energy intakes. As would be expected, increased age and subsequent decreases in energy intakes result in a higher potential for daily nutrient intakes below the EAR. Tables of these results can be found in Attachment 2.

A review of nutrition information panels on a range of FSMP packages showed that most products contain nutrients at levels above the EU minimum level requirements. Information supplied during targeted consultation in late 2011, advised that FSMP products manufactured in Europe list the average quantity of a nutrient across the shelf life of the

product. For labels of USA origin, the nutrient information panel reflects the minimum quantity of a nutrient across the entire shelf life of the product; thus most products will have nutrient levels above the minimum composition levels specified in the regulations.

3.1.1.2 Characterisation of the risk

For the nutrients where EARs were found to have potential not to be met, the difference of intakes below the EAR was low. Given EARs are only estimates of the prevalence of inadequate nutrient intakes, the prevalence of impaired nutritional status in the population would require further investigation using biological measures, such as blood levels. It is also useful to note that whilst the various NRVs are expressed on a per day basis, they should apply to intakes assessed over a period of about 3 to 4 days (NHMRC & NZ MoH, 2006).

It must be recognised that there is wide variation in energy and nutrient requirements for various life stage groups in the population. Also, NRVs are healthy population recommendations and individual requirements can vary from these population recommendations particularly in unwell or vulnerable groups. These factors are taken into consideration on an individual case by case basis when FSMP are being supplied to patients. The manufacturer provides information regarding the total volume of their product that is required for nutritional adequacy when used as a sole source of nutrition (e.g. nutritionally complete in 1.5 litres) as well as the nutrient composition of a product. These are used to assess the nutritional adequacy of a product against disease specific requirements where known, or at least against cautious application of a specific NRV. Particular micronutrients may be monitored for specific medical conditions e.g. copper for Wilson's Disease; zinc, vitamins A and C for wound healing; sodium, potassium, phosphate and magnesium for renal disease etc. If it is known that any nutrients are not complete in a given volume over a long period of time, this would be monitored by the health professional or medical practitioner. Micronutrient supplements or multivitamin preparations can also be used where required to make-up any nutrient deficit and ensure nutritional adequacy.

In summary, several factors mediate the potential risk of inadequate micronutrient intakes when FSMP are used as the sole source of nutrition:

- The levels proposed in the draft standard (as already used in the FSMP industry) are minimum composition values and FSMP products on the market generally contain micronutrients at levels above these requirements

- FSMP are used under the supervision of a medical practioner or health professional, and use is monitored. This could result in a range of products being used over time (particularly if the timespan was considerable), coupled with supplement use.

- While the nutrient requirements of severely ill people can be considerably higher than for healthy people, there are a variety of products within the FSMP category for use in different disease states.

3.1.2 Maximum micronutrient content requirements for products represented as a sole source of nutrition

Previous safety assessments conducted in 2004 and 2010 identified the potential for a safety risk in nine micronutrients if FSMP represented as a sole source of nutrition contained excessive levels. In response, maximum composition limits were set for vitamins A, B6 and D, selenium, iodine, zinc, calcium, manganese and copper in these products.

The maximum limits for composition proposed in 2004 and 2010 were determined from a FSANZ assessment of the US IOM Dietary Reference Intakes, the European Union

(Scientific Committee for Food), FAO/WHO and the Nutrient Reference Values for Australia and New Zealand (NHMRC & NZ MoH, 2006); the reference level used from these sources were selected based on an evaluation of age and quality of the scientific evidence base. These proposed maximum limits were intended to relate solely to the use of the substances in FSMP, and not intended to be used as general upper limits.

Submitter feedback to the December 2010 Consultation paper lead FSANZ to consider harmonising maximum composition limits with the European FSMP regulations. The European limits were developed with the intention of providing a vitamin or mineral intake above which there are no further identified nutritional benefits; and to minimise the risk of toxicity associated with the vitamin/mineral. Industry submitters advised that products from European markets already met the European limits.

A comparison of the European limits against the 2010 limits proposed by FSANZ was undertaken. This showed an increase in the maximum composition limit for vitamins A and D, calcium and copper and a decrease in vitamin B6, zinc, iodine, selenium and manganese (Table 1).

Table 1: Comparison of changes to the proposed maximum composition levels for vitamins and minerals in FSMP suitable for use as a sole source of nutrition between 2010 and 2011

Nutrient	Maximum composition limit (per MJ) proposed in 2010	Maximum composition limit (per MJ) proposed in 2011 (Current EU regulations)	Increased amount or decreased amount
Vitamins			
Vitamin A	345 µg	430 µg retinol equivalents	↑
Vitamin B_6	2.9 mg	1.2 mg	↓
Vitamin D	5.7 µg	6.5 µg or 7.5 µg*	↑
Minerals			
Calcium	287 mg	420 mg or 600 mg*	↑
Zinc	4.6 mg	3.6 mg	↓
Iodine	115 µg	84 µg	↓
Selenium	46 µg	25 µg	↓
Manganese	1.32 mg	1.2 mg	↓
Copper	1.15 mg	1.25 mg	↑

Notes:
* The higher amount applies only to products intended for children aged one to ten years.

3.1.2.1 Estimate of intakes

FSANZ also modelled intakes of micronutrients to assess whether daily intakes for nutrients with a maximum composition limit would be likely to exceed the 2006 Australia and New Zealand upper levels of intake (ULs).

For children, intakes were estimated using the PAL of 1.2 for each gender and age group from 3 to 18 years. These intakes were then compared to the relevant UL for each nutrient (where a UL was set). Results of these intake estimates and comparisons are shown in Tables A2.1-A2.2 in Attachment 1.

For adults, two models were constructed. One model used an average energy intake of 8700 kJ per day and the European maximum limits to estimate daily intakes. This estimates higher

micronutrient intakes than those needed in bed rest i.e. a worst case scenario. Comparison of this intake model to the ULs, identified potential exceedances of the UL for calcium and copper.

The second model used the minimum and maximum EER at the PAL of 1.2 for each adult age and gender group and the European maximum limits to estimate daily intakes. The results of these models compared against the 2006 UL (where they exist) are shown in Tables A4.1-A4.3 in Attachment 1. In women intakes of calcium had potential for intakes above the UL for two age groups. Several age groups for males had estimated intakes above the UL for vitamin A, calcium and copper.

3.1.2.2 Characterisation of the risk

Although usual intakes above the UL have potential risk of adverse effects from excessive nutrient intake; there are several factors which potentially mediate the risk of excess micronutrient intakes when FSMP are used as the sole source of nutrition:

- These limits are maximum composition limits and may not reflect the actual levels of addition to FSMP products. FSANZ collected a sample of different product labels. Of the products sampled, the majority have levels of micronutrients well below the European maximum composition limits (on per mega joule of energy basis). Noting that the draft Standard 2.9.5 is proposing to permit variations from the composition requirements for specific medical conditions, a range of nutrient levels is expected across different products.

- The requirement to use FSMP under medical supervision means that the overall health and safety risks associated with the consumption of these products is minimal, or can be sufficiently managed.

3.2 Safety of chromium picolinate as a form of chromium for use in FSMPs

In submissions in 2010 FSANZ was asked to consider extending the current permission for chromium picolinate in Standard 2.9.4 – Formulated Supplementary Sports Foods to FSMP. It was requested that no maximum amount be set for the addition of chromium picolinate in FSMP.

In Australia and New Zealand, inorganic or organic trivalent chromium is permitted to be added to a number of special purpose foods in Part 2.9 of the Code, including:

- infant formula products (Schedule 1 of Standard 2.9.1)
  - chromium sulphate

- formulated meal replacements (Standard 2.9.3, cross-references to Standard 2.9.4) and formulated supplementary sports foods (Schedule 1 of Standard 2.9.4)
  - chromium chloride
  - high chromium yeast
  - chromium picolinate
  - chromium nicotinate
  - chromium aspartate.

In the December 2010 Consultation Paper, permissions to add trivalent chromium were proposed in the forms of chromium chloride and chromium potassium sulphate, as well as chromium sulphate by virtue of cross-referencing to Schedule 1 of Standard 2.9.1.

FSANZ considers that there are no safety issues associated with the use of chromium picolinate as a form of trivalent chromium in FSMP, on the basis of the following considerations:

- FSANZ has previously assessed chromium picolinate as a safe and suitable form of trivalent chromium to be added to another special-purpose food (formulated supplementary sports foods). The safety of this form was assessed as part of the toxicology assessment for Proposal P92 – Sports Foods.

- As part of the 2004 safety assessment for Proposal P242, it was concluded that there is a low toxicity of trivalent chromium; therefore a restriction on the maximum amount that is present in FSMP would not be required and addition to FSMP poses a low risk to the health of FSMP consumers.

- There is no Australian and New Zealand UL for chromium.

3.3 Assessment of Fermentable Oligosaccharides, Lactose, Fructose and Polyols (FOLFAPs) – Revised since 2010

The term FOLFAPs refers to the following carbohydrates: fermentable oligosaccharides, lactose, fructose and polyols (FOLFAPs). FOLFAPs is an acronym developed by FSANZ for the purpose of this proposal because the more commonly used term FODMAPS (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) is trademarked (Gibson and Shepherd, 2010). 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 all small molecular weight carbohydrates, grouped together because of their similar physiochemical properties. This group is characterised by their tendency to be poorly digested and absorbed in the small intestine thus they undergo fermentation in the large intestine.

FOLFAPs occur naturally in some foods and may be added as ingredients to foods for technological reasons (e.g. to emulsify or thicken food) and for nutritional reasons (e.g. as fibre or for their prebiotic effect).
FOLFAP substances can be added to a range of FSMP products including oral nutrition, enteral formulas and nutrition supplements for the purpose of fibre supplementation.

The emerging evidence of an association between FOLFAPs and adverse gastrointestinal effects for a proportion of the Australian and New Zealand population raised a question for FSANZ regarding the potential risk of the presence of FOLFAPs in FSMP. Some submitters considered that consumers of FSMP as a sole source of nutrition may be exposed to concentrated amounts of FOLFAPs, given that these products were used as complete dietary replacements. They stated that this could result in adverse health outcomes for individuals intolerant to FOLFAPs, such as those with irritable bowel syndrome (IBS).

In order to assess this, FSANZ has investigated the normal physiological effects of dietary FOLFAPs and their potential adverse effects in healthy individuals, individuals with gastrointestinal disorders and, where possible, in consumers of FSMP. There are a range of studies addressing the consumption of FOLFAPs by healthy individuals and their effects on functional bowel disorders; however there are limited clinical trial data about adverse health effects of FOLFAPs when consumed in FSMP. Thus the literature considered in this assessment includes the emerging evidence base on FODMAPs as well as literature on individual fermentable carbohydrates.

Assessment questions

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?

3.3.1 Chemistry and characterisation of FOLFAPs

Carbohydrates can be classified using a combination of their chemical (degrees of polymerisation and type of chemical bond) and their physiological (digestible or fermentable) properties (as shown in Table 2). Carbohydrates have varied rates of digestion and absorption in the small intestine, as well as varied fermentability and fermentation end product profiles in the large intestine depending on their physiochemical properties (Englyst, Liu and Englyst, 2007). The physiological effects of carbohydrates depend on the site, rate and extent of digestion or fermentation in the gastrointestinal tract (Cummings and Englyst, 1995).

Table 2: Classification of principal dietary carbohydrates

Major class of carbohydrate	DP	Sub group and examples	Site of digestion and absorption
Sugars	1-2	(i) Monosaccharides: glucose, fructose, galactose (ii) Disaccharides: sucrose, maltose, trehalose, lactose (iii) Sugar alcohols (Polyols): sorbitol, maltitol, lactitol	Absorbed in small intestine, with exceptions for free fructose (refer to section 3.1.1.1) Mainly hydrolysed and absorbed in small intestine Lactose and some trehalose partly fermented. Poorly absorbed in small intestine and partly fermented (varies relative to molecular weight)
Oligosaccharides	3-10	(i) Malto-oligosaccharides (from starch breakdown)	a) 'Digestible': digested and absorbed from the small intestine. b) 'Resistant': pass into the large intestine and may be partially or completely fermented
		(ii) Other oligosaccharides (non-digestible oligosaccharides) fructo-oligosaccharides galacto-oligosaccharides	Fermented: some selectively stimulate Bifido bacteria in the colon
Polysaccharides	>10	(i) starch	a) 'Digestible' b) 'Resistant' – not absorbed in small intestine but fermented in the colon

Major class of carbohydrate	DP	Sub group and examples	Site of digestion and absorption
		(ii) non-starch polysaccharides	a) Derived from plant cell walls – regulates carbohydrate digestion in small intestine, mostly fermented and may affect laxation. b) Non-cell wall derived – variously affects lipid and carbohydrate absorption and mostly fermented

Source: Modified from Cummings and Stephen (2007) and Jones (2002).

3.3.1.1 Absorption and digestion of carbohydrates

Carbohydrates are either absorbed in the upper gastrointestinal tract (small intestine) or fermented providing short chain fatty acids (SCFA) in the lower gastrointestinal tract. Carbohydrate type, origin and food processing all contribute to the food properties that can influence the rate of carbohydrate release from food (Englyst, Liu and Englyst, 2007). Carbohydrate digestion rate is also influenced by, how it is consumed (i.e. alone or with other foods) and whether it has been cooked (Cummings and Stephen 2007).

The physiochemical properties of carbohydrates also influence their rates of digestion and absorption in the small intestine or fermentability and profile of fermentation products in the large intestine (Livesey 2001; Englyst et al. 2007). The main factors limiting carbohydrate absorption are passive absorption of the small molecules and the enzymatic digestion of chemical bonds (Marteau and Flourié 2001). As shown in Table 2 and discussed below, FOLFAPs have some differences in absorption and digestion mechanisms.

- Lactose absorption depends on the activity of lactase in the epithelial brush border to split lactose into glucose and galactose; malabsorption (either temporary or permanently) is common in individuals, and is known to be prevalent in some populations (Shepherd and Gibson 2006; Shepherd et al. 2009).

- There is no specific mucosal enzyme for the digestion and transport of fructose (Rumessen and Gudmand-Hoyer, 1986). Fructose absorption in the small intestine primarily relies on facilitation by glucose transporters (GLUT 5 and GLUT 2) (Johlin et al. 2004; Rangnekar and Chey 2009). Fructose released from the hydrolysis of sucrose is generally completely absorbed as the process is facilitated by presence of glucose in the gut (Shepard and Gibson, 2006). Thus free fructose present in the gut without glucose (i.e. as the monosaccharide, not having been released from hydrolysis of sucrose) has a limited absorptive capacity. Studies in healthy individuals have shown that free fructose has a limited absorptive capacity although there is a wide inter-individual range. Factors which affect the proportion of fructose absorbed include: the amount of glucose consumed at the same time, the capacity of epithelial transporters and the speed of transit through the small bowel (Shepard and Gibson 2006).

- Polyols are generally not readily absorbed due to their chemical structure (the presence of an alcohol group and saccharide linkages). Although most polyols are fermented, the proportion absorbed and fermented varies in different polyols and in individuals (Gibson 2011). Polyols are often utilised for their known laxative effects.

- Oligosaccharides[1] including fructo-oligosaccharides, short chain fructo-oligosaccharides (scFOS) and galacto-oligosaccharides (GOS) are not absorbed because the small intestine lacks enzymes to hydrolyse fructose–fructose bonds (Gibson and Newham 2007).

Despite these difference in absorption mechanisms, FOLFAPs are all small molecules characterised by their osmotic effects (related to their molecular weight) in the colon and rapid fermentability (Gibson and Newham 2007).

3.3.2 Physiological effect of FOLFAPs in healthy individuals

3.3.2.1 Effects on the gastrointestinal system

FOLFAPs are poorly absorbed in the small intestine, thus they enter the bowel where they are subject to anaerobic fermentation. The speed of bacterial fermentation in the bowel is influenced by the chain length of the carbohydrate; thus oligosaccharides and sugars are fermented more rapidly than polysaccharides such as soluble dietary fibre (Gibson and Shepherd 2009). The end products of carbohydrate fermentation in the gastrointestinal tract are SCFA, mainly acetic, propionic and butyric acids. Small quantities of gases are also produced in the gastrointestinal tract. Hydrogen constitutes the bulk of gas produced, although some individuals also produce methane and carbon dioxide (Livesey 2001).

During carbohydrate digestion most of the gas produced in the bowel is reabsorbed. Studies have calculated (stoichiometrically) that 30 g of carbohydrate (estimated to be a standard daily amount fermented in the human gastrointestinal system) releases gas at about 4 mL/hour over 24 hours (Livesey 2001). However, when carbohydrates reach the bowel rapidly and are easily fermented production of SCFA as well as hydrogen and methane increases. This is demonstrated in studies where FOLFAP carbohydrates can be completely fermented within about six hours (Livesey 2001).
This can also result in a rapid gas release rate; a single dose of 30 g of fermentable carbohydrates (FOLFAPs) is estimated to average about 15 mL/min. This rapid increase in SCFA and gas can exceed the rate of absorption and cause measurable luminal distension.

In some individuals this luminal distention is considered to be the physiological basis for abdominal discomfort and gastrointestinal symptoms such as pressure/bloating, or cramp/colic and sharp/stinging pain (Serra et al. 1998). This can also lead to changes in bowel function and transit time (Gibson and Shepherd 2009; Ong et al. 2010; Lomer 2011).

Water is actively secreted into the upper gastrointestinal tract after a meal. The presence of FOLFAPs in the small intestine can draw additional water in to maintain osmolality, which can eventually result in an elevated water load entering the colon (Livesey 2001; Rangnekar and Chey 2009). Increasing the luminal water content subsequently affects gut motility and has potential to temporarily promote diarrhoea (Gibson and Shepherd 2009).
The physiological effects of increased water and fermentation in the bowel after consumption of individual FOLFAPs have been well validated with lactose, polyol and free fructose consumption, and can occur in susceptible individuals regardless of health status (Ledochowski et al. 2000; Marteau and Flourié 2001).

The effects of increased fermentation and increased water flow into the bowel post-consumption of fermentable carbohydrates (as described above) are normal and measurable physiological responses. However in some individuals these effects can result in a range of

[1] Throughout the scientific literature, the terms scFOS, FOS and oligofructose are used interchangeably. In this report, scFOS refers specifically to sucrose-derived oligofructose with a degree of polymerisation (DP) ranging from 2 to 4 and an average DP = 3.5.

functional gastrointestinal and intolerance symptoms including altered motility, bloating, abdominal pain and diarrhoea (Teuri et al. 1999; Marteau and Flourié 2001; Bouhnik et al. 2007; Paineau et al. 2008; Majid et al. 2011). These symptoms and tolerance are reported with varying severity, due to inter-individual differences in factors such as absorption capacities, motility patterns, colonic responses, and intestinal sensitivity (Marteau and Flourie 2001; Livesey 2001; Cummings and Stephen 2007).

3.3.2.2 Tolerance levels of FOLFAPs

Evidence on the tolerance of total FOLFAP content of the diet in healthy individuals is still an evolving area of research. However, there is a large evidence base on the tolerance of lactose, free fructose and polyols; related to adverse gastrointestinal effects including abdominal discomfort, bloating, cramps, flatulence, stomach rumbling, and diarrhoea. This evidence base is discussed in this section.

Many studies have demonstrated large variation in absorption of and response (tolerance) to the individual FOLFAPs. Factors such as carbohydrate digestion rate, an individual's bowel microbiota composition and current health status are considered to influence an individual's tolerance to individual FOLFAPs (Cummings et al. 2001; Marteau and Flourié 2001). While healthy individuals vary in their gastrointestinal response to individual FOLFAPs, evidence demonstrates that there appears to be 'threshold levels' for many of them (Marteau and Flourié 2001; Skoog and Bharucha 2004).

Fructose can be consumed in the diet as the monosaccharide (free fructose) and as a component of the disaccharide sucrose. As discussed in section 3.3.1.1, there is a limited absorptive capacity for **free fructose** (without glucose present in the lumen) due to the limitations of the facilitated glucose transport mechanism. Incomplete fructose absorption in small intestine results in fructose entering the bowel. This can induce luminal distension and lead to subsequent intolerance symptoms in some individuals (Barrett and Gibson 2007). The absorptive capacity of free fructose appears to be dose dependent; however there appears to be wide variation among individuals.
Provocation studies investigating fructose absorption in healthy individuals suggest that the absorption threshold ranges between 25-50 g after single doses of free fructose (Truswell et al. 1988; Beyer et al. 2005; Gibson et al. 2007; Barrett et al. 2010).

Lactose absorption depends on activity of lactase in the epithelial brush border to split lactose into glucose and galactose. In lactose malabsorption, reduced lactase activity means lactose passes into the large intestine without hydrolysis and is fermented there by the bacterial flora drawing water by osmosis into the small intestine (Gudman-Hoyer 1994; Teuri et al. 1999). Reduced lactase activity is present in a large proportion of some populations, depending on ethnicity and environmental factors, and can also occur on a temporary basis with illness and some medication use (Barret and Gibson 2007). Individual sensitivity to lactose varies; symptoms depend on how severe the hypolactasia is and, as for fructose malabsorption, the response of the bowel to the luminal distension and increased osmotic load. Many people with reduced lactase activity are able to tolerate small amounts of lactose in foods (Vesa et al. 1996).

Factors affecting **polyol** tolerance include the dose of polyol ingested, the type of polyol (monosaccharide, disaccharide or polysaccharide), the form of the food ingested and consumption pattern (Storey et al. 2006).

Intervention studies have shown a consistent tolerance dose-dependent effect in healthy populations and **scFOS** consumption. Several studies report that doses of 10-20g/day and above result in increases in abdominal bloating, discomfort and flatus compared to controls (Bouhnik et al. 2007; Marteau and Flourié 2001; Paineau et al. 2008). Oku and Nakamura

(2003) found that the consumption of 10 g of scFOS in healthy participants resulted in abdominal symptoms 30-60 minutes after administration.

3.3.2.3 Functional bowel disorders

Functional bowel disorders (FBDs) are gastrointestinal disorders characterised by symptoms of abdominal bloating, constipation, diarrhoea, visceral hypersensitivity and abnormal gastrointestinal motility (Thompson et al. 1999). These symptoms are often described as 'functional' gut symptoms as they are related to alterations in the function of the gastrointestinal and enteric nervous system rather than being structural abnormalities (Barrett and Gibson 2007). FBDs tend to be diagnosed where signs of pathology associated with inflammatory bowel disease (IBD) are not found and mechanisms of visceral hypersensitivity and disorders of the gut-brain axis are involved (Barrett and Gibson 2007). 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.

Irritable Bowel Syndrome (IBS) is characterised by abnormalities in motility and visceral sensation (Rangnekar and Chey 2009). It is the most commonly diagnosed FBD and has a range of diagnostic criteria and several classifications – characterised as diarrhoea predominant, constipation predominant or diarrhoea and constipation together (Primavera et al. 2010). In IBS, the structure of the intestine is not affected and instead symptoms are a result of intestine muscular dysfunction, or hypersensitivity of the intestine to stretching or movement. IBS can be diagnosed through non-invasive hydrogen and methane breath tests, specifically those showing bacterial fermentation of un-hydrolysed carbohydrates following challenges with isolated carbohydrate solutions (Fernandez-Banares et al. 1993; Johlin et al. 2004). Historically, lactose intolerance and fructose malabsorption have been considered as subsets of IBS as they both induce symptoms seen in IBS, and most investigations show increased lactose intolerance among IBS sufferers. More recent research has suggested that sensitivity to the effects of fructose malabsorption in patients with FBD or IBS is heightened.

Small Intestinal Bacterial Overgrowth (SIBO) involves abnormal growth (i.e. >105 colony forming units/mL) in the small intestine of endogenous bacteria, resembling those usually found in the large intestine (Reddymasu et al. 2010). Early research in this area suggested that SIBO was a cause of FBD; more recent research suggests SIBO is a subset of IBS. It is suggested that SIBO contributes to the pathophysiology of IBS, although there is also some evidence of bacterial overgrowth in those with IBD particularly Crohn's disease (Barrett and Gibson 2005). 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 et al. 2010).

Incidence and prevalence of FBD in Australia and New Zealand

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 are only beginning to emerge.

The BEACH program (a continuous national study of general practice (GP) activity in Australia) reported that an average of approximately 285,000 GP visits annually were related to IBS management. Of these, three quarters 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 U.S.A and European data 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. Females exhibited 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 U.S.A (Barbeztt et al. 2002).

The role of diet and FOLFAPs in functional bowel disorders

Patients with FBD commonly relate their symptoms to specific foods. There is a large, well established evidence base demonstrating that consumption of individual FOLFAPs induces functional bowel symptoms in individuals with FBD. Studies of patients with FBD have showed that consumption of amounts of fructose, sorbitol, and fructose-sorbitol mixtures ranging from 5-30 g/day result in aggravation of gastrointestinal symptoms (Rumessen and Gudmand-Hoyer 1988; Fernadez-Barnares et al. 1993; Ledochowski et al. 2000).

Dietary management of FBD has not been a common recommendation by medical practitioners until recent years. Historically, when dietary changes in FBD were recommended by health professionals they focused on removing lactose from the diet and modifying fibre intakes (Gibson 2011). Recognition of the physiological effects of fermentable carbohydrates in both healthy populations and those with FBD has led to consideration of these as dietary triggers in FBD symptoms. These observations have led to the suggestion that removal of all FOLFAPs from the diet might lead to improvement in symptoms (Shepherd and Gibson 2006). Hence, more recent dietary management of FBD is based on recognition of symptom-inducing foods and removal of these foods with gradual reintroduction until acceptable symptomatic relief/management is achieved. Research in this area is still growing.

Studies have examined the relationship between consumption of FOLFAPs, colonic gas production, increased delivery of water to the colon and subsequent IBS symptoms to support this theory. In a randomized, single-blinded, crossover intervention trial, Ong et al. (2010), compared the patterns of breath hydrogen and methane as well as reported symptoms in response to high (50 g/day) and low (9 g/day) FOLFAP diets in IBS patients. The study demonstrated colonic gas production is reduced with a low FOLFAP diet (in both healthy people and subjects with IBS) when compared to a high FOLFAP diet. In conjunction with the difference in physiological effects, all symptoms were significantly worse in patients with IBS when on the high FOLFAP diet (Ong et al. 2010). Provocation studies have shown fructose loads given to individuals induce symptoms of bloating, abdominal discomfort, nausea, and disturbed bowel motility much more readily in subjects with IBS than in those without it (Barrett et al. 2010).

Evidence from observational studies indicates that patients with FBD experience a reduction in symptoms from a restriction of dietary FOLFAPs, similar to the improvement reported by patients with fructose malabsorption. Re-introduction of dietary FOLFAPs also results in patients reporting reoccurrence of symptoms (Shepard et al. 2008).

A small body of evidence also suggests that reduction of all FOLFAPs in the diet (rather than a single group such as fructose or lactose) has been found to be effective in managing symptoms of up to 72% of individuals with FBD (Gibson and Shepherd 2005; Barrett and Gibson 2007; Shepherd et al. 2008; Gibson and Shepherd 2009). These findings are further supported by a recent controlled trial comparing a low FOLFAP diet with other common dietary approaches in IBS symptom management, which found that a low FOLFAP diet

accompanied by dietary advice was more successful in improving multiple symptoms than standard United Kingdom dietary advice (Stuadacher et al. 2011). However, there is a limited amount of well powered, double blind, randomised control trials to demonstrate that withdrawal of total FOLFAPs from the diet will specifically reduce symptoms in patients with IBS (Gibson and Newham 2007).

3.3.3 Inflammatory bowel diseases (IBD) and functional bowel disorders (FBD) and their relationship to FOLFAPs consumption

Gastrointestinal symptoms such as bloating, abdominal pain and diarrhoea are commonly experienced by individuals with Inflammatory Bowel Disease (IBD) and Functional Bowel Disorders (FBD) as well as in patients consuming FSMP. Given that FOLFAPs can already induce these physiological effects in healthy individuals, the following sections investigate whether FOLFAPs will exacerbate the presentation of gastrointestinal symptoms in individuals with IBD or FBD.

3.3.3.1 Inflammatory bowel disease

IBD encompasses Crohn's disease and ulcerative colitis. It is characterised by inflammation and ulceration of the gastrointestinal tract with symptoms of abdominal pain, diarrhoea and gastrointestinal bleeding (Leenen and Dieleman 2007; Barrett et al. 2009; Lomer 2011). IBD can lead to irreversible damage of the intestinal structure and function, and is identifiable by histological, endoscopic or radiographic investigation (Yap et al. 2008).

Crohn's disease is a chronic and relapsing inflammatory disorder that can affect any part of the gastrointestinal tract, although it is most common in the large and small intestine and rarely seen in the duodenum. The main pathological features of Crohn's disease are ulcers in the intestine wall (both shallow and deep), connection of the intestinal lumen with surrounding structures (fistulae) and scar tissue leading to narrowing of the small and large intestine lumen (strictures causing lumen obstruction). The disease is episodic, with alternating periods of active inflammation and remission periods.

Ulcerative colitis shares some similar clinical and pathological features with Crohn's disease. However, ulcerative colitis only affects the large intestine, mainly the rectum. The inflammation tends to be continuous and extend distally, only occurring in the mucosa (inner lining).

Incidence and prevalence of IBD in Australia and New Zealand

In Australia, there have been no national epidemiological studies published on IBD incidence and prevalence. One prospective incidence study was carried out in Greater Geelong, Victoria, between April 2007 and March 2008. The annual incidence rate in the Geelong region was 29.3 per 100,000 for IBD overall, comprising 17.4 per 100,000 for Crohn's disease; 11.2 per 100,000 for ulcerative colitis; and 0.8 per 100,000 for indeterminate colitis (Wilson et al. 2010).

Data from three hospital-based studies and one population-based study indicated that, the incidence of IBD in New Zealand has risen dramatically over the past 50 years (Gearry and Day 2008). The 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 prospective paediatric IBD study in New Zealand estimated the incidence of paediatric onset IBD for New Zealand in 2002-03 of 2.9 cases per 100,000 per year (95% CI: 1.79–4.03) including 1.9 cases per 100,000 per year (95% CI: 0.82–3.0) of Crohn's disease and 0.5 cases per 100,000 per year (95% CI: 0.4–0.6) of ulcerative colitis (Yap et al. 2008). Based on a prospective incidence of IBD in Canterbury

for 2004, Gearry et al. (2006) estimated age-standardised (using World Health Organization World Standard Population) crude incidence of IBD of 25.2 per 100,000 per year (95% CI: 20.8-30.2), including 16.5 per 100,000 per year (95% CI: 13.0-20.4) of Crohn's disease and 7.6 per 100,000 per year (95% CI: 5.3-10.6) of ulcerative colitis.

No data were identified on the incidence or prevalence of IBD in populations consuming FSMP. Anecdotal evidence suggests that the prevalence of IBD in FSMP consumers would be similar to the general population.

Diet and FOLFAPs in inflammatory bowel disease (IBD)

The exact pathogenesis of IBD is still unknown, although current research on the aetiology suggests IBD is caused by a combination of genetic, environmental and immunological factors.

As would be expected, dietary management and treatment of the two phases of IBD (active and remission) differ greatly. In adults, enteral feeding is used in conjunction with corticosteroids to reduce inflammation. Exclusive enteral feeding is now commonly used in active disease periods of Crohn's disease to manage inflammation, particularly in children and adolescents (Day et al. 2008; Lomer 2011). This practice is based on evidence which suggests that enteral feeding and bowel rest can help to reduce inflammation and improve mucosal healing (Leach et al 2008; Lomer 2011). The mechanism behind this is uncertain, but observations of key changes observed in microbiota following enteral feeding support a link with the intestinal microbiota (Schneider et al. 2006; Wierdsma et al. 2009; Otley, Russell and Day 2010; Majid et al. 2011). Several studies investigating the role of diet in active stages of IBD have concluded that the diet (particularly fat and fibre composition of enteral formula) can alter the intestinal and faecal microbiota, potentially influencing inflammation via changes in the mucosal immune system (Lindsay et al. 2006; Lomer 2011).

Functional gastrointestinal symptoms are commonly experienced by patients with IBD during both active and remission phases of the disease (Leenen and Dieleman 2007; Barrett et al. 2009; Lomer 2011). Understanding of physiological effects of FOLFAPs has led to consideration of the role of FOLFAPs in functional gastrointestinal symptoms in patients with IBD. Common reports in the literature of concurrent fructose and lactose malabsorption in patients with Crohn's disease and ulcerative colitis, suggests that FOLFAP carbohydrates have a tendency to be poorly absorbed by individuals with IBD; although there is little evidence that FOLFAPs are responsible for functional symptoms in these patients (Barrett et al. 2009). One retrospective pilot study in patients (n=72) with Crohn's disease and ulcerative colitis during remission phases, reported that reduction of FOLFAPs in the diet reduced abdominal pain, bloating, wind and diarrhoea improved (Gearry et al. 2009).

3.3.3.2 Tolerance of FOLFAPs by individuals with IBD

As with healthy populations, tolerance of the effects of FOLFAPS varies from individual to individual in patients with FBD and IBD, for the same reasons discussed in section 3.2.2.

Initial studies in ileal pouch patients have indicated that reduction of dietary FOLFAPs can reduce the osmotic load on the pouch reducing the frequency of stools per day (Croagh et al. 2007). Barrett et al. (2010) conducted a study investigating the effect of dietary FOLFAPs on the content and of water and fermentable substrates of ileal effluent in ileostomy patients. The study found that high FOLFAP intake increased delivery of water and fermentable substrates to the proximal colon compared to a low FOLFAP intake. This suggests that FOLFAPs in the diet may be more clinically significant (i.e. likely to induce to adverse

symptoms) for the IBD population than a healthy population due to a lower FOLFAPs tolerance (Teuri et al. 1999; Barrett et al. 2009; Benjamen et al. 2010).

3.3.4 The use of FOLFAP-containing FSMP

While knowledge of the FOLFAP content of foods in the general diet is growing in Australia, few studies have specifically investigated the total FOLFAP content of any FSMP. As discussed in previous sections, FSMP are often used in the management of both IBD and FBD in hospitalised and non-hospitalised patients, and can be consumed orally or through an enteral route. Enteral feeding is used for nutritional support in a wide range of other disease states, and in both the short and long term.

Temporary bowel disorders, particularly diarrhoea are commonly reported to occur in enteral tube feeding (Whelan 2007). Adverse abdominal symptoms are also commonly reported in patients using FSMP as a sole of nutrition, who have not previously reported functional bowel symptoms (Wierdsma et al. 2009). Several causes of enteral feeding associated diarrhoea have been identified, and it is often thought to be multi-factorial. Mechanisms proposed include antibiotic use, the composition of the gastrointestinal microbiota, and the composition of enteral formulas (Elia et al. 2008; Wierdsma et al. 2009; Majid et al. 2011). The well-established physiological effects of lactose and polyol in adverse gastrointestinal effects has resulted in these substances being restricted or routinely omitted from all enteral formulas for several years (Halmos et al. 2009).

Recent research has considered a functional role for some FOLFAP ingredients in enteral formulas. There is an emerging body of research which has investigated the addition of different types of carbohydrates (as fibre or prebiotics) to enteral formulas for the maintenance of intestinal microflora and prevention of diarrhoea associated with enteral formula use. FOLFAP content of enteral formula has been considered in relation to the potential prebiotic action of some osmotically active carbohydrates.

Many studies investigating prevention of diarrhoea associated with enteral tube feeding have focused on enteral formula composition, adding fibre blends with inulin, oligosaccharides and scFOS for a functional purpose. The purpose of this addition is to reduce the rate of gastric emptying and increase SCFA concentrations where these have been reduced as a result of total enteral nutrition. Research suggests that their addition may alter gastrointestinal microbiota composition and SCFA production, which in turn may reduce gastrointestinal inflammation in remission phases of IBD (Whelan et al. 2005; Lindsay et al. 2006; Whelan 2007; Leenan & Dieleman 2007; Wierdsma et al. 2009; Majid et al. 2011).

3.3.5 Tolerance of FOLFAPs present in FSMP

Patients on total enteral tube feeding or long term enteral feeding are the most vulnerable population in relation to nutritional issues, including potential risk of adverse gastrointestinal effects from FOLFAPs. As the effect of FODMAPs on gastrointestinal symptoms is an emerging area, there is little direct evidence focusing on the tolerance of FOLFAPs in FSMP. One retrospective study examined a range of factors associated with the development of diarrhoea in patients being tube-fed. Using case notes of patients a univariate analysis was conducted to investigate associations between diarrhoea and factors such as: the number of days on tube feeding; whether patients were receiving antibiotics or proton pump inhibitors; mode of delivery of enteral feeding; and enteral formula composition (including the total FOLFAP content of the enteral formulas). The univariate analysis identified the following predictors of diarrhoea: hospital stay greater than 11 days (OR 4.2); duration of enteral nutrition greater than 11 days (Odds Ratio 4.0) and antibiotic use (OR 2.1). A second analysis was conducted to adjust for influencing variables using a logistic regression model. This showed there was a five-fold reduction in the risk of developing diarrhoea seen in

patients initiated on a particular enteral formula, *Isosource 1.5* (OR 0.18). The study had focused on the total FOLFAP content of enteral formulas and the seven most commonly used enteral formulas were analysed for FOLFAP content. The analysis found FOLFAP content of the formula ranged from 10.6 to 36.5 g/day. *Isosource 1.5* had the lowest FOLFAP content of the enteral formulas analysed. The study concluded that that the enteral formula FOLFAP content was the one factor independently associated with the development of diarrhoea (Halmos et al. 2009). These results suggest that the FOLFAP content of FSMP may play a role in diarrhoea associated with enteral feeding however further evidence is required.

Tolerance to fibre (including some FOLFAPs) in enteral formulas has been reported across a range of patient groups in studies investigating prevention of enteral formula related diarrhoea (as discussed above). These studies have shown mixed results, with wide variation in the tolerance to fibre reported in these studies. For example, Elia et al. (2008) conducted a systematic review and meta-analysis on the clinical and physiological effects of fibre-containing enteral formula. Overall, twenty-six of the fifty-one studies in the review reported intolerance symptoms (defined as the incidence of abdominal cramps, bloating, flatulence, nausea and vomiting) with use of enteral formula; this included five studies in healthy people and twenty one studies in patients (both in hospital and community settings). The patient groups received enteral formula through several different routes (i.e. oral, naso-gastric tube) and a range of 'fibre' types and amounts were added to the enteral formulas. Mean fibre intakes across the studies ranged from 7 to 33 g/day. The specific FOLFAP amount was not reported in any of the studies, although several listed inulin, oligofructose and scFOS/FOS as part of the fibre blends. One aspect of the review was a meta-analysis of RCTs of hospitalised patients and the incidence of diarrhoea with fibre administration. This found a reduction in diarrhoea incidence with fibre administration (OR).68: 95%CI: 0.48-0.96). This reduction of diarrhoea with fibre supplementation was more likely to occur when the incidence of diarrhoea in the group was high.

Elia et al (2009) also found a difference in reporting of adverse effects between studies which added individual dietary fibre isolates (reported to be highly fermentable) and studies that added blends of fibre. These studies reported that when high doses (approximately 26 g) of highly fermentable fibres such as FOS, inulin and hydrolysed guar gum were added alone to enteral formula, the increased gaseous production caused increased flatulence and other adverse symptoms. These symptoms were not seen when similar amounts of fibre blend were added to enteral formula (Elia et al. 2008). These findings have been supported by further studies of fibre supplemented enteral formula. For example, a recent placebo-controlled trial of FOS supplementation (comprised fructose polymers of differing chain lengths (70% oligofructose with a degree of polymerisation (DP) <10 and 30% inulin with a DP >10) in patients with active/acute Crohn's disease, found that consumption of 15 g per day of FOS (alone as a supplement) aggravated abdominal symptoms in active Crohn's disease, with more patients in the FOS group withdrawing from the study than the control group (Benjamin et al. 2011).

In contrast, Wierdsma et al. (2009) compared the effect of a fibre free enteral formula with a fibre and FOS (composition of FOS not defined) supplemented enteral formula. The fibre blend contained 10.6 g fibre (comprised of 4.5 g oats, 3.6 g soy polysaccharide, 1.7 g gum arabic and 0.8 g carboxymethylcellulose) and 7 g FOS per litre. The study population consisted of hospitalised and non-hospitalised, long-term enterally-fed head and neck cancer patients. The study found consumption of an average 11 g/day scFOS (when combined with fibre) was well tolerated, with no difference in reported abdominal complaints between the test and control groups.

The differences reported in tolerance to fibre and FOLFAPs in enteral formula is a result of normal physiological processes and differences in carbohydrate digestion and absorption.

There are also several limitations of this group of studies. As discussed above definitions of fibre and substances such as inulin, oligosaccharides and short-chain fructo-oligosaccharides differ across the literature, as does reporting of methodology thus it is often difficult to determine the type and of amount of FOLFAPs used in the study.

3.3.6 Response to assessment questions

a) *How prevalent in the community are:*
   - *functional bowel disorders*
   - *Inflammatory bowel disease?*

Data on the prevalence of inflammatory bowel disease and functional bowel disorders in the Australian and New Zealand populations is limited, although estimates for IBD in the New Zealand population suggest its prevalence may be increasing. The limited availability of data means there is uncertainty in determining what proportion of the Australian and New Zealand population is affected.

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?*

There is evidence demonstrating that FOLFAP consumption can induce adverse gastrointestinal effects including abdominal discomfort, bloating, cramps, flatulence, stomach rumbling, and diarrhoea. The evidence for these effects is well demonstrated in functional bowel disorders particularly irritable bowel syndrome (which is thought to incorporate small intestine bacterial overgrowth syndrome).
The evidence for a role of FOLFAPs in adverse gastrointestinal effects in inflammatory bowel disease is limited. There is some evidence suggesting FOLFAPs may be involved in functional gastrointestinal symptoms; however there is also evidence supporting the use of some FOLFAPs in prevention of diarrhoea.

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?*

There is limited evidence demonstrating adverse gastrointestinal effects or adverse health effect from consumption of FOLFAPs in FSMP when used as partial dietary replacement. Evidence of the effects of FOLFAPS in enteral formula is mainly based on addition of fibres which incorporate FOLFAPs. Results from these are mixed, thus it is difficult to confirm the effects of FOLFAPs alone.

3.3.7 Summary of the FOLFAP assessment/characterisation

There is normal physiological response in the gastrointestinal tract from the digestion and absorption of FOLFAPs. In some healthy individuals, this response can induce functional gastrointestinal symptoms such as bloating, flatulence, abdominal discomfort, and diarrhoea.

There is currently little evidence to demonstrate a link between the total FOLFAP content of FSMPs and the development of functional bowel disorders and symptoms. FSANZ concludes that there is potential for FSMP containing FOLFAPs to be associated with functional gastrointestinal symptoms whether consumed in the general diet or FSMP.

Individuals with FBD appear, in general, to be more susceptible to these symptoms and have a much lower tolerance to FOLFAPs than healthy controls. The limited evidence for IBD suggests these individuals are likely to be susceptible to FOLFAPs, however studies report mixed results. The evidence does suggest that individuals with pre-existing gastrointestinal disorders may be susceptible to the FOLFAP content of FSMPs; however there are several factors which influence an individual's digestion and absorption of fermentable carbohydrates. Thus there is a large amount of variation in individual tolerance of FOLFAPs regardless of the individual's health status and use of FSMP. In addition, some studies indicate that FOLFAPs used in fibre supplements, when used in FSMPs to help treat symptoms in IBD, are well tolerated at low levels (Welters et al. 2002; Furrie et al. 2005; Lindsay et al. 2006; Hedin et al. 2006; Leenan and Dieleman 2007). Based on the available evidence FSANZ is unable to identify a common tolerance level for total FOLFAP content of FSMP.

3.4 Composition Assessment Summary

In summary the conclusions of this composition assessment are as follows:

1. *New permitted substances or permitted forms*
   - In 2010, an additional nineteen permitted forms of micronutrients and nutritive substances were determined as safe to be added to FSMP.
     - These were obtained from Schedule 1 of Standard 2.9.1, the European Commission, and the Codex Advisory List CAC/GL 10-1979.

   - In 2011, chromium picolinate is considered safe and technologically suitable for use in FSMP.

2. *Micronutrient minimum composition values in FSMP*
   Aligning the minimum micronutrient composition values for FSMP with the European minimum micronutrient values poses no risk to public health and safety.

3. *Micronutrient maximum composition limits in FSMP*
   Adopting the European maximum composition limits for vitamin A, vitamin B6, vitamin D, selenium, iodine, zinc, calcium, manganese and copper poses no risk to public health and safety.

4. *FOLFAPs in FSMP*
   - Data on the prevalence of inflammatory bowel disease and functional bowel disorders in the Australian and New Zealand populations is limited, although estimates for IBD in the New Zealand population suggest its prevalence may be increasing. The limited availability of data means there is uncertainty in determining what proportion of the Australian and New Zealand population is affected.

   - There is evidence demonstrating that general dietary consumption of FOLFAPs can induce adverse gastrointestinal effects including abdominal discomfort, bloating, cramps, flatulence, stomach rumbling, and diarrhoea functional bowel disorders particularly irritable bowel syndrome (which is thought to incorporate small intestine bacterial overgrowth syndrome).

   - The evidence for these effects is well demonstrated in functional bowel disorders particularly irritable bowel syndrome (which is thought to incorporate small intestine bacterial overgrowth syndrome). Given the individual differences in carbohydrate digestion and tolerance to FOLFAPs it is not possible to quantify a relationship between the FOLFAPs and adverse gastrointestinal symptoms.

- The evidence for a role of FOLFAPs in adverse gastrointestinal effects in inflammatory bowel disease is limited. The use of FSMP in this patient group varies depending on the phase of disease (i.e. active or remission), with FSMP occasionally being used as a sole source of nutrition in active phases of the disease.

- Evidence of the effects of FOLFAPS in enteral feeding (as a total source of nutrition) is mainly based on addition of fibres which incorporate FOLFAPs. Results from these are mixed, thus it is difficult to confirm the effects of FOLFAPs alone.

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Attachment 1: Micronutrient intake estimate data tables

The following tables show the modelling of nutrient intakes for each age-gender group when products with minimum composition are consumed as a sole source of nutrition. The model used the 2006 NHMRC estimated energy requirements (EER) for each group based on the physical activity level (PAL) of 1.2. For each energy intake, potential nutrient intakes were calculated on the assumption that FSMP products will contain nutrients at the minimum level required. These calculations provide a 'worst-case' scenario. These figures were then compared to the relevant EAR. The shaded cells indicate that the potential intake would not meet the EAR for that age and gender group.

Table A1.1: Female children nutrient intake modelling and comparison against EAR

Nutrient	Unit	3 yr old	4 yr old	5yr old	6 yr old	7 yr old	8 yr old	9 yr old	10 yr old	11 yr old	12 yr old	13 yr old	14 yr old	15 yr old	16 yr old	17 yr ol	18 yr old
Vitamin A	µg RE	352.8	369.6	394.8	420	436.8	462	495.6	529.2	554.4	588	630	672	714	747.6	772.8	789.6
Vitamin C	mg	22.7	23.7	25.4	27	28.1	29.7	31.9	34.0	35.6	37.8	40.5	43.2	45.9	48.0	49.7	50.76
Thiamin	mg	0.63	0.66	0.71	0.75	0.8	0.8	0.9	0.9	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.4
Riboflavin	mg	0.8	0.8	0.9	1.0	1.0	1.1	1.2	1.2	1.32	1.4	1.5	1.6	1.7	1.8	1.9	1.9
Vitamin B6	mg	0.8	0.8	0.9	1.0	1.0	1.1	1.18	1.26	1.32	1.4	1.5	1.6	1.7	1.8	1.9	1.9
Niacin EN	mgNE	9.2	9.6	10.3	11.0	11.4	12.1	13.0	13.9	14.5	15.4	16.5	17.6	18.7	19.6	20.2	20.7
Folate as DFE for EAR/RDI	µg	105.0	110.0	117.5	125.0	130.0	137.5	147.5	157.5	165.0	175.0	187.5	200.0	212.5	222.5	230.0	235.0
Vitamin B12	µg	0.7	0.7	0.8	0.8	0.9	0.9	1.0	1. 1	1.1	1.2	1.3	1.4	1.4	1.5	1.5	1.6
Pantothenic acid	mg	1.4	1.5	1.6	1.7	1.8	1.9	2.1	2.2	2.3	2.5	2.6	2.8	2.9	3.1	3.2	3.3
Biotin	µg	7.6	7.9	8.5	9	9.3	9.9	10.6	11.3	11.9	12.6	13.5	14.4	15.3	16.0	16.5	16.9
Calcium	mg	504.0	528.0	564.0	600.0	624.0	660.0	708.0	756.0	792.0	840.0	900.0	960.0	1020.0	1068.0	1104.0	1128.0
Phosphorus	mg	302.4	316.8	338.4	360.0	374.4	396	424.8	453.6	475.2	504.0	540.0	576.0	612.0	640.8	662.4	676.8
Magnesium	mg	75.6	79.2	84.6	90.0	93.6	99	106.2	113.4	118.8	126.0	135.0	144.0	153.0	160.2	165.6	169.2
Iron		5.0	5.3	5.6	6.0	6.2	6.6	7.1	7.6	7.9	8.4	9.0	9.6	10.2	10.7	11.0	11.3
Zinc		5.0	5.3	5.6	6.0	6.2	6.6	7.1	7.6	7.9	8.4	9.0	9.6	10.2	10.7	11.0	11.3

Nutrient	Unit	3 yr old	4 yr old	5yr old	6 yr old	7 yr old	8 yr old	9 yr old	10 yr old	11 yr old	12 yr old	13 yr old	14 yr old	15 yr old	16 yr old	17 yr ol	18 yr old
Iodine	µg	65.1	68.2	72.8	77.5	80.6	85.3	91.5	97.7	102.3	108.5	116.3	124.0	131.8	138.0	142.6	145.7
Selenium	µg	25.2	26.4	28.2	30.0	31.2	33.0	35.4	37.8	39.6	42.0	45.0	48.0	51.0	53.4	55.2	56.4
Chromium	µg	12.6	13.2	14.1	15.0	15.6	16.5	17.7	18.9	19.8	21.0	22.5	24	25.5	26.7	27.6	28.2
Molybdenum	µg	29.4	30.8	32.9	35.0	36.4	38.5	38.5	44.1	46.2	49.0	52.5	56	59.5	62.3	64.4	65.8

Table A1.2: Male children nutrient intake modelling and comparison against EAR

Nutrient	Unit	3 yr old	4 yr old	5yr old	6 yr old	7 yr old	8 yr old	9 yr old	10 yr old	11 yr old	12 yr old	13 yr old	14 yr old	15 yr old	16 yr old	17 yr old	18 yr old
Vitamin A	ug RE	352.8	369.6	394.8	420.0	436.8	462.0	495.6	529.2	554.4	588.0	630.0	672.0	714.0	747.6	772.8	789.6
Vitamin C	mg	22.7	23.7	25.4	27.0	28.1	29.7	31.9	34.0	35.6	37.8	40.5	43.2	45.9	48.1	49.7	50.76
Thiamin	mg	0.6	0.7	0.7	0.7	0.8	0.8	0.9	0.9	1.0	1.1	1.125	1.2	1.275	1.335	1.38	1.41
Riboflavin	mg	0.8	0.9	0.9	1.0	1.0	1.1	1.18	1.3	1.3	1.4	1.5	1.6	1.7	1.78	1.84	1.8
Vitamin B6	mg	0.8	0.9	0.9	1.0	1.0	1.1	1.18	1.3	1.3	1.4	1.5	1.6	1.7	1.78	1.84	1.8
Niacin EN	mgNE	9.2	9.7	10.3	11.0	11.4	12.1	13	13.9	14.5	15.4	16.5	17.6	18.7	19.6	20.2	20.7
Folate	µg	105	110	117.5	125	130	137.5	147.5	157.5	165	175	187.5	200	212.5	222.5	230.0	235.0
Vitamin B12	µg	0.7	0.7	0.8	0.85	0.9	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.5	1.5	1.6
Pantothenic acid	mg	1.5	1.5	1.6	1.7	1.8	1.9	2.1	2.2	2.3	2.5	2.6	2.8	2.9	3.1	3.2	3.3
Biotin	µg	7.6	7.92	8.5	9.0	9.4	9.9	10.6	11.3	11.9	12.6	13.5	14.4	15.3	16.0	16.5	16.92
Calcium	mg	504	528	564	600.0	624	660.0	708.0	756.0	792.0	840.0	900.0	960.0	1020.0	1068.0	1104.0	1128.0
Phosphorus	mg	302.4	316.8	338.4	360.0	374.4	396.0	424.8	453.6	475.2	504.0	540.0	576.0	612.0	640.8	662.4	676.8
Magnesium	mg	75.6	79.2	84.6	90.0	93.6	99.0	106.2	113.4	118.8	126.0	135.0	144	153.0	160.2	165.6	169.2
Iron	mg	5.0	5.3	5.6	6.0	6.2	6.6	7.1	7.6	7.9	8.4	9.0	9.6	10.2	10.7	11.0	11.3
Zinc	mg	5.0	5.3	5.6	6.0	6.2	6.6	7.1	7.6	7.9	8.4	9.0	9.6	10.2	10.7	11.0	11.3
Iodine	µg	65.1	68.2	72.9	77.5	80.6	85.3	91.5	97.7	102.3	108.5	116.3	124.0	131.7	138.0	142.6	145.7

Selenium	µg	25.2	26.4	28.2	30.0	31.2	33.0	35.4	37.8	39.6	42.0	45.0	48.0	51.0	53.4	55.2	56.4
Chromium	µg	12.6	13.2	14.1	15.0	15.6	16.5	17.7	18.9	19.8	21.0	22.5	24.0	25.5	26.7	27.6	28.2
Molybdenum	µg	29.4	30.8	32.9	35.0	36.4	38.5	38.5	44.1	46.2	49.0	52.5	56.0	59.5	62.3	64.4	65.8

Table A2.1 Comparison against 2006 Upper Levels of intake – female children

Nutrient	3 yr old	4 yr old	5yr old	6 yr old	7 yr old	8 yr old	9 yr old	10 yr old	11 yr ol d	12 yr old	13 yr old	14 yr old	15 yr old	16 yr old	17 yr old	18 yr old
Vitamin A	596.4	630	663.6	705.6	747.6	789.6	840	873.6	924	974.4	1024.8	1058.4	1083.6	1100.4	1108.8	1117.2
Vitamin D	8.52	9	9.5	10.08	10.68	11.28	12	12.48	13.2	13.92	14.64	15.12	15.48	15.72	15.84	15.96
Vitamin B6	1.42	1.5	1.6	1.7	1.78	1.88	2	2.08	2.2	2.32	2.44	2.52	2.58	2.62	2.64	2.66
Niacin	15.62	16.5	17.4	18.48	19.58	20.68	22	22.88	24.2	25.52	26.84	27.72	28.38	28.82	29.04	29.26
Folate as DFE	177.5	187.5	197.5	210	222.5	235	250	260	275	290	305	315	322.5	327.5	330	332.5
Vitamin E	7.1	7.5	7.9	8.4	8.9	9.4	10	10.4	11	11.6	12.2	12.6	12.9	13.1	13.2	13.3
Sodium	852	900	948	1008	1068	1128	1200	1248	1320	1392	1464	1512	1548	1572	1584	1596
Calcium	511.2	540	568.8	604.8	640.8	676.8	720	748.8	792	835.2	878.4	907.2	928.8	943.2	950.4	957.6
Phosphorus	127.8	135	142.2	151.2	160.2	169.2	180	187.2	198	208.8	219.6	226.8	232.2	235.8	237.6	239.4
Magnesium	8.52	9	9.48	10.08	10.68	11.28	12	12.48	13.2	13.92	14.64	15.12	15.48	15.72	15.84	15.96
Iron	8.52	9	9.48	10.08	10.68	11.28	12	12.48	13.2	13.92	14.64	15.12	15.48	15.72	15.84	15.96
Zinc	1.065	1.125	1.19	1.26	1.335	1.41	1.5	1.56	1.65	1.74	1.83	1.89	1.935	1.965	1.98	1.995
Copper	110.0	116.3	122.5	130.2	137.95	145.7	155	161.2	170.5	179.8	189.1	195.3	199.95	203.05	204.6	206.15
Iodine	42.6	45	47.4	50.4	53.4	56.4	60	62.4	66	69.6	73.2	75.6	77.4	78.6	79.2	79.8
Selenium	49.7	52.5	55.3	58.8	62.3	65.8	70	72.8	77	81.2	85.4	88.2	90.3	91.7	92.4	93.1

Notes:
1. Micronutrients in bold indicate a maximum composition limit is proposed in the Standard
2. All figures are rounded to one decimal place

Table A2.2 Comparison against 2006 Upper Levels of intake – male children

Nutrient	3 yr old	4 yr old	5yr old	6 yr old	7 yr old	8 yr old	9 yr old	10 yr old	11 yr old	12 yr old	13 yr old	14 yr old	15 yr old	16 yr old	17 yr old	18 yr old
Vitamin A	638.4	680.4	714.0	756.0	798.0	848.4	898.8	957.6	1008	1075.2	1142.4	1226.4	1293.6	1360.8	1402.8	1436.4
Vitamin D	9.1	9.7	10.2	10.8	11.4	12.1	12.8	13.7	14.4	15.3	16.3	17.5	18.5	19.4	20.0	20.5
Vitamin B6	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.3	2.4	2.6	2.7	2.9	3.1	3.2	3.3	3.4
Niacin	16.7	17.8	18.7	19.8	20.9	22.2	23.5	25.1	26.4	28.1	29.9	32.1	33.9	35.6	36.7	37.6
Folate	190.0	202.5	212.5	225.0	237.5	252.5	267.5	285.0	300.0	320.0	340.0	365.0	385.0	405.0	417.5	427.5
Vitamin E	7.6	8.1	8.5	9.0	9.5	10.1	10.7	11.4	12.0	12.8	13.6	14.6	15.4	16.2	16.7	17.1
Sodium	547.2	583.2	612.0	648.0	684.0	727.2	770.4	820.8	864.0	921.6	979.2	1051.2	1108.8	1166.4	1202.4	1231.2
Calcium	912.0	972.0	1020.0	1080.0	1140.0	1212.0	1284.0	1368.0	1440.0	1536.0	1632.0	1752.0	1848.0	1944	2004.0	2052.0
Phosphorus	547.2	583.2	612.0	648.0	684.0	727.2	770.4	820.8	864.0	921.6	979.2	1051.2	1108.8	1166.4	1202.4	1231.2
Magnesium	136.8	145.8	153.0	162.0	171.0	181.8	192.6	205.2	216.0	230.4	244.8	262.8	277.2	291.6	300.6	307.8
Iron	9.12	9.7	10.2	10.8	11.4	12.1	12.8	13.7	14.4	15.4	16.3	17.5	18.5	19.4	20.0	20.5
Zinc	9.12	9.72	10.2	10.8	11.4	12.12	12.84	13.68	14.4	15.3	16.3	17.5	18.5	19.4	20.0	20.5
Copper (mg)	1.14	1.2	1.3	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.2	2.3	2.4	2.5	2.6
Iodine	117.8	125.5	131.7	139.5	147.2	156.5	165.8	176.7	186.0	198.4	210.8	226.3	238.7	251.1	258.8	265.1
Selenium	45.6	48.6	51.0	54.0	57.0	60.6	64.2	68.4	72.0	76.8	81.6	87.6	92.4	97.2	100.2	102.6
Molybdenum	53.2	56.7	59.5	63.0	66.5	70.7	74.9	79.8	84.0	89.6	95.2	102.2	107.8	113.4	116.9	119.7

Notes:

1. Micronutrients in bold indicate a maximum composition limit is proposed in the Standard
2. All figures are rounded to one decimal place

Table A3.1 Comparison against 2006 EAR – female adults

Nutrient	Women 19-30		Women 31 -50		Women 51 -70		Women >70	
	min daily 6.1 MJ	max daily 8.4 MJ	min daily 6.3 MJ	max daily 7.5 MJ	min daily 6 MJ	max daily 7.2 MJ	min daily 5.6 MJ	max daily 6.9 MJ
Vitamin A (ug RE)	521.4	705.6	529.2	630.0	504.0	604.8	470.4	579.6
Vitamin C (mg)	32.9	45.4	34.0	40.5	32.4	38.9	30.2	37.3
Thiamin (mg)	0.9	1.3	0.9	1.1	0.9	1.1	0.8	1.0
Riboflavin (mg)	1.2	1.7	1.3	1.5	1.2	1.4	1.1	1.4
Vitamin B6 (mg)	1.2	1.7	1.3	1.5	1.2	1.4	1.1	1.4
Niacin (mg)	13.4	18.5	13.9	16.5	13.2	15.8	12.3	15.2
Folate (ug	152.5	210.0	157.5	187.5	150.0	180.0	140.0	172.5
Vitamin B12 (ug)	1.0	1.4	1.1	1.3	1.0	1.2	1.0	1.2
Calcium (mg)	512	705.6	529.2	630.0	504.0	604.8	470.4	579.6
Phosphorus (mg)	439.2	604.8	453.6	540.0	432.0	518.4	403.2	496.8
Magnesium (mg)	109.8	151.2	113.4	135.0	108.0	129.6	100.8	124.2
Iron	7.3	10.1	7.6	9.0	7.2	8.6	6.7	8.3
Zinc	7.3	10.1	7.6	9.0	7.2	8.6	6.7	8.3
Iodine (ug)	94.6	130.2	97.7	116.3	93.0	111.6	86.8	107.0
Selenium (ug)	36.6	50.4	37.8	45.0	36.0	43.2	33.6	41.4
Molybdenum (ug)	42.7	58.8	44.1	52.5	42.0	50.4	39.2	48.3

Notes:

1. All figures are rounded to one decimal place

Table A3.1 Comparison against 2006 EAR –male adults

	Men 19-30		Men 31 -51		Men 51-70		Men >70	
	Min daily 7.7 MJ	Max daily MJ 10.1	Min daily 7.6 MJ	Max daily 9.5 MJ	Min daily 7 MJ	Max daily 8.8 MJ	Min daily 6.3 MJ	Max daily 8.1 MJ
Vitamin A	646.8	848.4	638.4	798.0	588.0	739.2	529.2	680.4
Vitamin C	41.6	54.5	41.0	51.3	37.8	47.5	34.0	43.7
Thiamin	1.2	1.5	1.1	1.4	1.1	1.3	0.9	1.2
Riboflavin	1.5	2.0	1.5	1.9	1.4	1.8	1.3	1.6
Vitamin B6	1.5	2.0	1.5	1.9	1.4	1.8	1.3	1.6
Niacin EN	16.9	22.2	16.7	20.9	15.4	19.4	13.9	17.8
Folate	192.5	252.5	190.0	237.5	175.0	220.0	157.5	202.5
Vitamin B12	1.3	1.7	1.3	1.6	1.2	1.5	1.1	1.4
Calcium	646.8	848.4	638.4	798.0	588.0	739.2	529.2	680.4
Phosphorus	554.4	727.2	547.2	684.0	504.0	633.6	453.6	583.2
Magnesium	138.6	181.8	136.8	171.0	126.0	158.4	113.4	145.8
Iron	9.2	12.1	9.1	11.4	8.4	10.6	7.6	9.7
Zinc	9.2	12.1	9.1	11.4	8.4	10.6	7.6	9.7
Iodine	119.4	156.6	117.8	147.3	108.5	136.4	97.7	125.6
Selenium	46.2	60.6	45.6	57.0	42.0	52.8	37.8	48.6
Molybdenum	53.9	70.7	53.2	66.5	49.0	61.6	44.1	56.7

Notes:

1. All figures are rounded to one decimal place

Table A4.1: Comparison of the European maximum composition limits (proposed for use in Australia & NZ in 2011) with the 2006 ULs

Micronutrient	Unit	Maximum composition limit proposed in 2011 (based on EU regulations)		UL (NHMRC & NZMoH, 2006)	Maximum composition limit (proposed in 2011 draft Standard 2.9.5) as a per cent of the 2006 UL±
		Amount per MJ	Amount per day^		
Vitamin A+	µg RE	345	3000	3000	0
Vitamin B_6	mg	1.2	11	50	22
Vitamin D	µg	6.5 7.5*	57 65	80 80	30 81
Calcium	mg	420 600*	3654 5220	2500 2500	146 209
Zinc	mg	3.6	31	40	23
Iodine	µg	84	731	1100	34
Selenium	µg	25	218	400	46
Manganese	mg	1.2	10	Not provided	-
Copper	mg	1.25	11	10	110

Notes to table:

+ The maximum composition level applies to retinol forms of vitamin A only

^ Based on energy intake of 8700 kJ per day for both adults and children, rounded to nearest whole number

*Maximum composition level for children aged 1 -10 years

± rounded to whole numbers

Table A4.2: Comparison of intake estimates against 2006 Upper Levels of intake – female adults

Nutrient with maximum permitted level for products as sole source of nutrition	Women 19-30		Women 31 -50		Women 51 -70		Women >70	
	Min daily 6.1 MJ	max daily 8.4 MJ	min daily 6.3 MJ	max daily 7.5 MJ	min daily 6 MJ	max daily 7.2 MJ	min daily 5.6 MJ	max daily 6.9 MJ
Vitamin A (ug RE)	2623.0	3612.0	2709.0	3225.0	2580.0	3096.0	2408.0	2967.0
Vitamin D	7.3	10.1	7.6	9.0	7.2	8.6	6.7	8.3
Vitamin B6 (mg)	39.6	54.6	41.0	48.7	39.0	46.8	36.4	44.9
Calcium (mg)	2562	3528.0	2646.0	3150.0	2520.0	3024.0	2352.0	2898.0
Zinc	21.9	30.2	22.7	27.0	21.6	25.9	20.1	24.8
Iodine (ug)	512.4	705.6	529.2	630.0	604.8	8.6	470.4	579.6
Selenium (ug)	152.5	210.0	157.5	187.5.4	150.0	9.0	140.0	172.5
Copper	7.6	10.5	7.9	9.8	9.0	180.0	7.0	8.6

Notes:

1. Only micronutrients with a UL are included in the table
2. All figures are rounded to one decimal place

Table A4.3: Comparison of intake estimates against 2006 Upper Levels of intake – male adults

Nutrient with maximum permitted level for products as sole source of nutrition	Men 19-30		Men 31 -51		Men 51-70		Men >70	
	min daily 7.7 MJ	max daily MJ 10.1	min daily 7.6 MJ	max daily 9.5 MJ	min daily 7 MJ	max daily 8.8 MJ	min daily 6.3 MJ	max daily 8.1 MJ
Vitamin A	3311.0	4343.0	3268	4085	3010.0	3784.0	2709.0	3483.0
Vitamin D	9.2	12.1	9.12	11.4	1.2	10.5	7.6	9.7
Vitamin B6	50.1	65.7	49.4	61.75	45.5	57.2	41.0	52.6
Calcium	3234.0	4242.0	3192	3990	2940.0	3696.0	2646.0	3402.0
Zinc	27.7	36.4	27.36	34.2	25.2	31.7	22.7	29.1
Iodine	646.8	848.4	638.4	798	588.0	739.2	529.2	680.4
Selenium	192.5	252.5	190	237.5	175.0	220.0	157.5	202.5
Copper	9.6	12.6	9.5	11.875	8.7	11.0	7.9	10.1

Notes:

1. Only micronutrients with a UL are included in the table
2. All figures are rounded to one decimal place

Attachment 2: Glossary

Degree of polymerisation	The degree of polymerisation (DP) refers to the number of monomeric units in a macromolecule or polymer. For the purposes of this risk assessment, this term refers to carbohydrate polymers.
Enteral formula	A formula that is delivered into the gastrointestinal system, but also bypasses the oral cavity and oesophagus.
Enteral feeding	Feeding directly into the gastrointestinal system by bypassing the oral cavity and oesophagus. A common approach for this feeding is to use a tube that is delivered via the nose and into the stomach (naso-gastric) or small intestine (naso-jejunal, naso-duodenal).
FOLFAPS	FOLFAPS is an acronym coined by FSANZ to describe a group of fermentable carbohydrates comprised of: fructose (monosaccharide); lactose (disaccharide); fructans and galactans (oligosaccharides); and polyols. It refers to the same substances as the more commonly used term FODMAPS (i.e. fermentable oligosaccharides, disaccharides, monosaccharides and polyols) which is trademarked by Australian researchers Shepherd and Gibson.
Functional bowel disorder (FBD)	Functional bowel disorder (FBD) refers to gastrointestinal disorder with functional symptoms attributable to the mid or lower gastrointestinal tract, including irritable bowel syndrome.
Fructose	Fructose is a simple sugar or monosaccharide. It can be found in foods as a free monosaccharide, as a constituent of the disaccharide sucrose, or as fructans (oligosaccharides).
Fructose Malabsorption	Fructose malabsorption refers to a failure to completely absorb fructose in the small intestine. It is linked to gastro-intestinal symptoms as described in IBS.
Fructan	Polymers of fructose.
Irritable Bowel Syndrome (IBS)	Irritable Bowel Syndrome (IBS) has a range of diagnostic criteria and several classifications – characterised as diarrhoea predominant, constipation predominant or diarrhoea and constipation together (ROME II criteria).
Lactose Intolerance	Lactose intolerance causes symptoms similar to IBS. Symptoms are caused by unhydrolysed lactose, which draws water by osmosis into the small intestine. Individual sensitivity to lactose varies for those with lactose intolerance.
Polyols	A polyol is an alcohol containing multiple hydroxyl groups. For the purposes of this assessment, the term polyol refers of sugar alcohols only.
Oligosaccharide	A carbohydrate polymer with a DP of 3-10.
Fructo-oligosaccharides	Fructo-oligosaccharides is used to describe those fructose polymers with β (2→1) fructosyl-fructose linkages, where the average DP is less than four and is typically produced from enzymic condensation of sucrose.
Short chain fructo-oligosaccharide (scFOS)	scFOS refers specifically to sucrose-derived oligofructose with a degree of polymerisation (DP) ranging from 2 to 4 and an average DP = 3.5.
Inulin	Inulin is used to describe those fructans' with β (2→1) fructosyl-fructose linkages, where the average DP is equal to or greater than ten.

Long chain inulin	Long-chain inulin is used to describe those fructans with β (2→1) fructosyl-fructose linkages, where the average DP is equal to or greater than 23.
Oligofructose	Oligofructose is used to describe those fructans, with β (2→1) fructosyl-fructose linkages, where the average DP is less than ten but greater than or equal to four. Oligofructose is derived from inulin.