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

EXPLANATORY STATEMENT

PROPOSAL P306

ADDITION OF INULIN/FOS & GOS TO FOOD

For Information on matters relating to this Assessment Report or the assessment process generally, please refer to http://www.foodstandards.gov.au/standardsdevelopment/

Executive Summary

Food Standards Australia New Zealand (FSANZ) has prepared this Proposal to consider the regulatory status of inulin and fructo-oligosaccharide (FOS) added to general foods[1] and inulin, FOS and galacto-oligosaccharide (GOS) added to special purpose foods for infants and young children in the *Australia New Zealand Food Standards Code* (the Code).

For the purposes of this Proposal, special purpose foods for infants and young children (SPFYC) comprise: infant and follow-on formula, infant foods and formulated supplementary foods for young children, such as toddler formula.

Inulin is a naturally occurring carbohydrate belonging to a class of compounds known as fructans or fructose polymers. Scientists and food manufacturers use a range of terms to describe inulin, FOS and GOS. In this Report, FSANZ describes the substances of interest with the terms inulin, long-chain inulin, oligofructose, FOS and GOS. The term 'inulin-derived substances' is used to collectively refer to: inulin, long-chain inulin and oligofructose. It does not include FOS which in this report is defined as short chain fructans derived from sucrose.

Food manufacturers have added inulin-derived substances to the general food supply in Australia and New Zealand since the mid 1990s. Manufacturers do this for technological reasons, because these substances emulsify or thicken food, or for nutritional reasons, such as for their prebiotic[2] effect or as dietary fibre. Since 2001, inulin has appeared in a wide range of foods and is predominantly labelled as dietary fibre.

Manufacturers seek to add prebiotics to infant and follow-on formula to mimic the effects of oligosaccharides[3] that occur naturally in breast milk. These substances are not absorbed in the small intestine and reach the large intestine essentially intact. Breastfed infants generally have softer stools compared with formula-fed infants and this difference may be due in part to the presence of oligosaccharides in breast milk.

Purpose of the Proposal

The purpose of the Proposal is to confirm the regulatory position for the food industry of inulin-derived substances when added to the general food supply (and some special purpose foods), and to consider permissions for the addition of inulin-derived substances, FOS and GOS to infant formula products, infant foods and formulated supplementary foods for young children.

This matter arose as an unintended consequence of enforcement action in 2007 against a manufacturer that was adding long-chain inulin and GOS to infant formula sold in Australia and New Zealand. This action subsequently led to confusion among the broader food industry about the regulatory status of inulin when added to general foods. This confusion has a negative effect on the efficiency and international competitiveness of the food industry.

[1] General foods includes some special purpose foods regulated in Standards 2.9.3 and 2.9.4

[2] Prebiotics are defined as 'non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon' (adapted from Gibson and Roberfroid, 1995).

[3] In general terms an 'oligosaccharide' is a carbohydrate that consists of a relatively small number of linked monosaccharide units, typically between three and ten units (adapted from JCBN, 1980).

As a result of the confusion three applications were submitted to FSANZ that raise issues regarding the permissions and the status of these substances. The proposal is intended to meet the needs of these Applications.

Regulatory Approach

Approach to the Proposal

To provide regulatory assurance to the food industry in a timely and efficient manner, FSANZ decided, pursuant to section 36 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act) (as was in force prior to 1 July 2007), to omit one round of public consultation on this Proposal prior to making a Draft Assessment. In making this decision, FSANZ was satisfied that the issues raised by this Proposal would not have a significant adverse effect on the interests of anyone.

Consistent with section 36, this Proposal adopted a focused approach, by restricting consideration to resolving the current uncertainty surrounding the addition of inulin-derived substances to general foods and inulin-derived substances/FOS and GOS to special purpose foods for infants and young children. Therefore, **the approach taken is considered an interim regulatory response.** FSANZ has taken this interim approach as it plans to consider issues more broadly through a future review of the definition of 'nutritive substance' and its application in the Code, and to a future review of Standard 2.9.1 – Infant Formula Products.

The Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) recently agreed to develop policy guidance on the intent of Part 2.9 – Special Purpose Foods of the Code and on infant formula. The timing of the development of this policy guidance is not yet known.

Approach to risk assessment

General foods

As inulin-derived substances have been added to the general food supply for over a decade, the risk assessment has been confined to a description of the reasons for their addition to general foods and a description of their history of safe use in general foods.

FOS (as defined in this Report) and GOS are not widely added to the general food supply in Australia and New Zealand at this point in time, thus the addition of FOS and GOS to general foods has not been considered.

Special purpose foods for infants and young children

There are currently no Ministerial Policy Guidelines on the addition of substances to special purpose foods for infants and young children. As a result, FSANZ, in accordance with its statutory objectives, has confined the risk assessment to considering safety. This also included comparison of the amount of these or similar substances in breast milk, and whether they result in similar physiological and microbiological effects to breastfed infants.

Rationale for drafting approach

FSANZ considers the amendments proposed at Final Assessment have been drafted to provide regulatory clarity at this time, while not pre-empting the outcome of the Ministerial Council policy development and the future reviews of the definition of 'nutritive substances' and the infant formula products standard.

As an interim approach, in relation to the proposed draft variation to Standard 1.1.1, inulin-derived substances are taken not to be nutritive substances (and therefore require no pre-market approval) when added to general foods (see the new clause 9A in Standard 1.1.1). This approach recognises the status of inulin-derived substances as fulfilling both a technological and nutritional purpose in general foods.

FSANZ has, within the context of the Code, previously considered that inulin-derived substances, FOS and GOS when used in foods for infants and young children as regulated under Part 2.9, are 'nutritive substances' within the definition of that term in Standard 1.1.1 as a means of requiring pre-market assessment of foods for these vulnerable population groups. However, for the purposes of this section 36 Proposal, FSANZ has drafted the variations to the respective standards in Part 2.9, in a manner that ensures safety of permitting the addition of inulin-derived substances and GOS to infant formula products, infant foods and formulated supplementary foods for young children (toddler formula) but does not at this time adopt a position either way on the status of inulin-derived substances and GOS when added to these special purpose foods.

The approach to drafting proposed by FSANZ also ensures that reference to inulin-derived substances in Standard 1.1.1 and in Standards 2.9.1, 2.9.2 and 2.9.3 are not being treated differently in the Code, at this point in time.

No permission has been included for the addition of FOS (as defined in the Report) to infant formula products, infant foods or toddler formula because of insufficient evidence to assess its effects.

Additionally, in response to submitter concerns raised at Draft Assessment, FSANZ has taken the opportunity to amend Standard 2.9.1 to clarify that nutrition claims are not permitted on infant formula products.

Decision

At Final Assessment, FSANZ approves the following variations to the Code:

- to amend Standard 1.1.1 to state that inulin-derived substances are taken not to be nutritive substances;
- to amend Standard 2.9.1 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant formula products to a total maximum of 290 mg/100 kJ (0.8 g/100 mL);
- to amend Standards 2.9.2 and 2.9.3 Division 4 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant foods and formulated supplementary foods for young children up to a total maximum of 0.8 g/100 g and 1.6 g/serve (0.8 g/100 mL), respectively; and

- additional consequential amendments to Standard 2.9.1 to clarify intent on the prohibition of nutrition claims on infant formula products.

Changes to drafting since Draft Assessment

In response to comments received, FSANZ has made the following changes to the draft variations since Draft Assessment:

- The proposed definitions of inulin-derived substances and GOS have been reconsidered and consolidated.

- At Draft Assessment, FSANZ included FOS in the proposed variation to Standard 1.1.1. However, information provided to FSANZ indicates that FOS (as defined in this report) is not used in the Australian and New Zealand food supply; thus it has been excluded from the proposed draft variation to clause 9 of Standard 1.1.1.

- The specification for GOS has been removed because it was considered unnecessarily restrictive.

- Reference to Standard 1.2.8 has been removed because measurement methods for fructans are being dealt with in a separate Proposal

Conclusion

FSANZ concludes that the recommended approach provides a net benefit to affected parties at this time because:

General food supply

- There is a history of safe use of inulin-derived substances in food in Australia and New Zealand, so food manufacturers do not need express permission to add these substances to the general food supply.

- The proposed variations to the Code confirm the regulatory position for the food industry by clarifying the status of inulin-derived substances in the general food supply. This approach means the manufacture of food products currently containing inulin-derived substances can continue for both the domestic and overseas market, thus reducing potential barriers to trade. This will also avoid the financial implications for food manufacturers and suppliers of having to reformulate and re-label products.

Special purpose foods for infants and young children

- Based on the available evidence, FSANZ concludes that infant and follow-on formula containing up to 8 g/ L[4] of inulin-derived substances and/or GOS, singularly or combined, in any ratio, are unlikely to pose a risk to infants.

[4] 8 g/L is equivalent 0.8 g/100 mL used in the drafting.

- For older young children, infant foods and toddler formula and infant foods do not represent the sole source of nutrition. Based on the available evidence, FSANZ concludes that infant foods and/or toddler formula containing up to 8 g/ L inulin-derived substances and/or GOS, singularly or combined, in any ratio are unlikely to pose a risk to older infants and toddlers.

- There is insufficient evidence to assess the effects of adding FOS (as defined in this Report) to infant formula products, thus the permission for the addition of FOS to special purpose foods for infants and young children is not included in this Proposal.

- The recommended maximum levels of inulin-derived substances and/or GOS permitted to be added to infant formula products are consistent with those evaluated in clinical trials and are less than the levels of human milk oligosaccharides found in breast milk (up to 25 g/L).

- There is evidence that addition of inulin-derived substances and GOS and inulin-derived substances alone up to 10 g/L, added to infant formula products result in similar physiological i.e. softer consistency and lower pH of stools; and microbiological effects i.e. selective growth stimulation of intestinal Bifidobacterium to that of breastfed infants. There is insufficient evidence on the addition of GOS alone to draw conclusions.

- Providing express permissions for the addition of inulin-derived substances and GOS provides consumer choice and will likely maintain confidence in the safety of infant formula products, infant foods and toddler formula.

- The proposed approach also confirms the regulatory position for the food industry, thereby reducing potential trade barriers, supporting cost-effective production through harmonisation with overseas regulations, and supporting innovation.

- Furthermore, the proposed approach provides certainty for enforcement agencies in Australia and New Zealand by:

  - providing explicit permissions for the addition of inulin-derived substances and GOS (excluding FOS) to special purpose foods for infants and young children; and
  - clarifying the intent of Standard 2.9.1 in prohibiting nutrition claims on infant formula products.

FSANZ therefore approves the draft variations to the Code as provided at Attachment 1.

Consultation

This Proposal involved only one round of public consultation, pursuant to section 36 of the FSANZ Act. However, FSANZ undertook early targeted consultation prior to the Draft Assessment and again during development of this Final Assessment Report.

In response to the Draft Assessment Report, FSANZ received 30 submissions during the public consultation period of 21 December 2007 until 22 February 2008.

Twenty-two submissions were received from industry, six from government, one from a health professional organisation and one from a consumer group.

The general food supply and proposed amendments to Standard 1.1.1

In general submitters, including a majority of industry submitters, favoured amending Standard 1.1.1 to provide certainty on the use of inulin-derived substances in general foods. However, nearly half of these recommended FSANZ reconsider aspects of the amendment as proposed. The remaining submitters presented a divergent view, with several not indicating a preferred regulatory option.

Special purpose foods for infants and young children

Twenty-three of the total submissions received provided comment relating to special purpose foods for infants and young children (SPFYC).

Submitters' views were mixed in relation to the regulatory options proposed at Draft Assessment.

Just over half of those commenting on SPFYC supported amending the Code to permit the addition of inulin-derived substances and GOS to SPFYC. However of these, half recommended modifications to the amendments as proposed at Draft Assessment e.g. alternative definitions, reconsideration of levels and modifications to the proposed variation to the Code.

Several submitters preferred to maintain the *status quo*. Two submitters did not support either option as presented at Draft Assessment, and several raised issues with regard to SPFYC but did not state a preferred option.

Summary of FSANZ's response to Key Issues

Key issues identified in submissions included the differing regulatory approach proposed for general foods and SPFYC, the need to demonstrate benefit/efficacy of substances added to SPFYC, evidence for the safe addition of these substances when added singularly or in a range of ratios, the extrapolation of data from infant formula to infant foods, the range of definitions used, and the need for clarity in Standard 2.9.1 with regard to labelling and possible nutrition claims.

A full summary of the submissions received is at Attachment 2. Issues raised in submissions have been addressed in the main body of the Report and/or in Attachment 3.

Approach to the Proposal

FSANZ is aware that there is a polarity of views amongst enforcement agencies and food manufacturers in regards to the regulatory status of inulin-derived substances and GOS in foods.

For this reason and for the purpose of providing regulatory certainty at this time FSANZ has taken the recommended approach as an interim regulatory measure. It is outside the scope of this section 36 Proposal to give broader consideration to the issues.

Therefore as indicated FSANZ will undertake a review of the definition of 'nutritive substance' and its application in the Code at a later date.

Health benefit and efficacy in infants

At Draft Assessment, concern was expressed that there was insufficient evidence to demonstrate benefit/efficacy in infant formula products, infant foods and formulated supplementary foods for young children.

As noted above, FSANZ has, in the absence of ministerial policy guidance, confined the risk assessment to consider safety. This also included comparison of the amount of these or similar substances in breast milk, and whether they result in similar physiological and microbiological effects to breastfed infants. FSANZ's assessment found that at levels up to 10 g/L there is evidence of similar physiological i.e. softer stools and increased stool frequency; and microbiological effects i.e. increased growth of colonic *Bifidobacteria*, in some studies comparing breastfed and formula fed infants.

Safety and levels of addition

At Draft Assessment, FSANZ proposed a maximum level of 0.3 g/100 mL for inulin-derived substances for infant formula products. On the basis of new information, FSANZ has subsequently revised the drafting to permit a maximum level of up of 0.8 g/100 mL inulin-derived substances and GOS singularly or in combination, at any ratio. Issues were also raised at Draft Assessment in relation to the evidence for the singular addition of inulin-derived substances and GOS as well as the use of ratios other than 9:1, and the extrapolation of data to infant foods and toddler formula.

At Final Assessment, FSANZ has clarified that the risk assessment was informed by studies involving the addition of GOS and inulin-derived substances alone or in combination, to infant formula products, infant food, and toddler formula, and includes studies using concentrations of 4, 8 and 10 g/L. The assessment does not rely on any single study in order to make the stated recommendations. In addition to considering the evidence from clinical trials, FSANZ has also taken the levels of human milk oligosaccharides in breast milk into consideration, as well as relevant data. However, the proposed maximum permitted level of addition is based primarily on the evidence of safety of GOS and inulin-derived substances as assessed by clinical trials.

FSANZ sought additional expert opinion on the revised upper level for inulin-derived substances from the Infant and Child Health Scientific Advisory Group (ICSAG)[5] and also from an international peer reviewer Emeritus Professor John Cummings[6]. ICSAG members were generally supportive of the revised upper maximum limit based on the evidence. One member was not supportive of the increase on the basis of study methodology concerns. Professor Cummings considered that the evidence did provide reassurance of the safety of 0.8 g/100 mL of inulin-derived substances in infant formula.

[5] ICSAG is a scientific advisory group established by FSANZ and comprises experts in gastroenterology, paediatrics and child health.
[6] Professor John Cummings is Emeritus Professor of Experimental Gastroenterology, University of Dundee, Scotland.

As limited information is available on the safety of FOS (as defined in this Report) in foods for infants and young children, FSANZ could not assess FOS as part of the safety assessment.

Definitions and descriptions

At Draft Assessment, a number of definitions were proposed for inclusion in the draft variation. A number of submitters provided comment on these definitions including that: the substances as defined were difficult to characterise chemically; the source of inulin-derived substances may vary; there is inconsistency in the use of definitions; and there was a need for clarification of use of the separate terms defined in the Draft Assessment and how these could be used interchangeably within the permissions in the Code.

At Final Assessment, FSANZ has reconsidered and consolidated the definitions. The draft variation now includes definitions for 'inulin-derived substances' (excluding FOS) and 'GOS' only. FSANZ has consolidated the definitions in response to the issues raised in submissions. The consolidation: avoids the need for a range of terms to be defined, which is not practical or necessary given the varying nature of fructose polymers; avoids confusion with the existing common names used to describe fructose polymers, including inulin-derived substances; and is likely to be more practical from a compliance perspective.

Nutrition claims and Labelling

A number of submitters raised concern in relation to labelling and the potential for making nutrition claims on infant formula products.

To address this concern, FSANZ is proposing amendments to the infant formula products standard as part of this Proposal. These amendments aim to clarify the intent that nutrition claims are not permitted on infant formula products. Specifically, that a nutrition information statement is a single statement that is to contain all the nutrition information requirements as specified in Standard 2.9.1 clauses 16(1) and (2) and that any further reference (except in the statement of ingredients) to inulin-derived substances or GOS on the label of an infant formula product is not permitted.

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GLOSSARY

AFGC	Australian Food and Grocery Council
AI	adequate intake
AOAC	Association of Official Analytical Chemists
CoPoNC	Code of Practice on Nutrient Claims
DP	degree of polymerisation
EFSA	European Food Safety Authority
FOS	fructo-oligosaccharides
FOSHU	foods of specified health use
FSANZ	Food Standards Australia New Zealand
FSFYC	formulated supplementary foods for young children
GOS	galacto-oligosaccharides
GRAS	generally recognized as safe
HMOs	human milk oligosaccharides
ICSAG	Infant and Young Child Scientific Advisory Group
IFMAA	Infant Formula Manufacturers' Association of Australia
NFA	National Food Authority
NHMRC	National Health and Medical Research Council
NNS	national nutrition survey
NZFGC	New Zealand Food and Grocery Council
NZIFMA	New Zealand Infant Formula Marketers' Association
NZMoH	New Zealand Ministry of Health
SCFA	short chain fatty acid
SPFYC	special purpose foods for infants and young children
UL	upper level of intake
WTO	World Trade Organization

INTRODUCTION

Food Standards Australia New Zealand (FSANZ) has prepared this Proposal to consider the status of inulin/fructo-oligosaccharide (FOS) added to general foods[7] and the addition of inulin/FOS and galacto-oligosaccharide (GOS) added to special purpose foods for infants and young children in the *Australia New Zealand Food Standards Code* (the Code).

Inulin/FOS and GOS are often used generically to refer to a range of substances and there is no widely agreed set of definitions. Therefore, in this Report, the terms inulin, long-chain inulin, oligofructose, FOS and GOS are used to clarify the substances of interest; the term '**inulin-derived substances'** is used to collectively refer to inulin, long-chain inulin and oligofructose – it does not include FOS (see Section 1.4 for definitions of these and other terms used throughout this Report).

This Final Assessment Report discusses the background and approach to the assessment of this Proposal, the issues involved in the addition of inulin/FOS and GOS to food and makes recommendations for variations to the Code.

1. Background

In early 2007, one brand of infant formula products with added long-chain inulin[8] and GOS was launched on the Australian and New Zealand market. Long-chain inulin and GOS are added to infant formula to mimic the effects of oligosaccharides in breast milk. However, the addition of long-chain inulin and GOS to infant formula products is considered to require a pre-market safety assessment and an explicit permission in the Code. As no expressed permissions exist in the Code the relevant enforcement agencies subsequently took enforcement action against the manufacturer of these infant formula products.

An unintended consequence of this enforcement action was confusion among the broader food industry as to the regulatory status of inulin-derived substances when added to general foods. Food manufacturers were concerned about potential implications for their food products. In response to this concern, FSANZ initiated this Proposal to remove this confusion for the food industry regarding the addition of inulin-derived substances to the general food supply, and to specifically consider permissions for the addition of inulin-derived substances/FOS and GOS to infant formula products, infant foods and formulated supplementary foods for young children (FSFYC).

1.1 Section 36 Consideration

In the interest of dealing with this regulatory matter in a timely and responsive manner, FSANZ decided, pursuant to section 36 of the FSANZ Act (as was in force prior to 1 July 2007), to omit to invite public submissions in relation to this Proposal prior to making a Draft Assessment. FSANZ was satisfied that omitting one round of public consultation prior to making a Draft Assessment would not have significant adverse effects on the interests of anyone. To assist with facilitating consultation, advanced notification of this Proposal and the expected consultation period was publicly announced on 8 August 2007.

[7] General foods includes some special purpose foods regulated in Standards 2.9.3 and 2.9.4

[8] Long-chain inulin has been referred to by some manufacturers as long-chain FOS or high molecular weight FOS.

1.2 Nutritive substances

In the case of the recent enforcement action, the main regulatory issue is that inulin-derived substances/FOS and GOS are not listed as permitted 'nutritive substances' in the Table to clause 7 of Standard 2.9.1 – Infant Formula Products. As a result, there has been considerable discussion among the food industry, industry groups and food regulatory agencies as to whether these substances are 'nutritive substances' in the Code. The then National Food Authority (NFA) (a predecessor of FSANZ) stated in writing in the early 1990s that inulin did not require an explicit permission before it could be added to foods. However, in the mid-1990s, an Expert Panel on Infant Formula advised the NFA, as part of the revision of the infant formula standard (Proposal P93), that oligosaccharides should not be permitted to be added to infant formula because there was no demonstration of efficacy and some concerns about safety. This advice was tabled at the 33rd meeting of the NFA in August 1995.

Since that time, the current joint Code was introduced and contains a general prohibition on the addition of 'nutritive substances' to foods unless expressly permitted. This prohibition did not exist before 2002 as the concept of a 'nutritive substance' was introduced for the first time through its inclusion in the new joint Code. A 'nutritive substance' is defined in Standard 1.1.1, clause 2 as:

> *a substance not normally consumed as a food in itself and not normally used as an ingredient, but which, after extraction and/or refinement, or synthesis is intentionally added to a food to achieve a nutritional purpose, and includes vitamins, minerals, amino acids, electrolytes and nucleotides.*

Clause 9 of Standard 1.1.1 states that 'nutritive substances' must not be added to food unless expressly permitted in the Code.

It is outside the scope of this Proposal to review the definition of 'nutritive substance' in the Code to accommodate these and other substances not currently listed in the definition. Therefore, this Proposal has adopted a focused approach, consistent with a section 36 proposal, to resolve the current uncertainty surrounding the addition of inulin-derived substances/FOS to food and inulin-derived substances/FOS and GOS to special purpose foods for infants and young children. FSANZ plans to undertake a review of the definition of 'nutritive substance' and its application in the Code in the context of commencement of future work to consider what amendments to the Code are required in response to the policy guideline on Addition to Food of Substances other than Vitamins and Minerals. This consideration of the definition of nutritive substances will seek to ensure that further polarity of views and attendant confusion do not arise in the future.

1.3 Other related FSANZ work

FSANZ has received three Applications that relate to this Proposal.

An unpaid Application (A598) was received from Heinz Wattie's Limited[9] in December 2006 requesting amendments to the Code to allow the addition of FOS and GOS as 'nutritive substances' to infant formula products. The Applicant agreed to defer the Initial Assessment Report to await the outcome of this Proposal, on the basis that it will meet the needs of A598.

Nutricia Australia Pty Limited[10] submitted a paid Application (Application A609) in July 2007 requesting amendments to the Code to allow the addition of long-chain inulin and GOS as 'ingredients' to infant formula products and infant foods. An Initial Assessment Report for this Application was released for public comment in December 2007 concurrently with the Draft Assessment of this Proposal.

Orafti, a manufacturer of inulin and oligofructose, also submitted an unpaid Application (Application A613) in August 2007 seeking to clarify the status of these substances in the general food supply, and to consider a mechanism for control on the addition of nutritive-type substances to foods for infants and young children.

This Proposal does, however deal with aspects of each Application and may therefore satisfy in part, or whole, each of these respective Applications.

1.4 Terminology

1.4.1 Inulin-derived substances and fructo-oligosaccharides

Given the differences in the terminology currently in use, FSANZ developed terminology for fructose polymers to ensure there was clarity about these terms in assessing or considering the assessments for this Proposal and the related Applications. FSANZ acknowledges that there are diverse opinions regarding the description of inulin-derived substances and that a number of different terms and expressions are used to describe these substances. To ensure that there is clarity in this Report about the terminology and identity of these substances, the following terms are used:

- The term '**inulin-derived substances**' is used to collectively describe inulin, long-chain inulin and oligofructose. This term does not include those fructose polymers derived from sucrose;

- the term '**inulin**' is used to describe those fructans[11], with β (2→1) fructosyl-fructose linkages, where the average degree of polymerisation[12] (DP) is equal to or greater than ten:

  - the term '**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;

[9] Heinz Wattie's Application is seeking to add GOS at a maximum of 290 mg/100 kJ or FOS at a maximum of 110 mg/100 kJ or total oligosaccharides of 290 mg/100 kJ to infant formula products. No specifications were provided for these substances, hence until processing of the Application begins, FSANZ is uncertain of the specific substances being requested.

[10] Nutricia's Application is seeking to add GOS and long-chain inulin in the ratio 9:1 and at a level of 0.8 g/100 mL to infant formula products and infant foods.

[11] Polymers of fructose.

[12] Degree of polymerisation is the number of fructose or saccharide units.

- the term '**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. Chicory inulin, for example, contains about 30% oligofructose; and

- the term '**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.

FSANZ also acknowledges that sometimes oligofructose and inulin are referred to as 'FOS' and FOS is sometimes referred to as 'oligofructosyl-saccharose'. In addition, the terms oligofructose and FOS are sometimes used interchangeably. Given the differences in the terminology currently in use, this Report uses the terms described above to ensure clarity in the FSANZ assessment process and related consultations. More detail about the basis for these terms is in Attachment 4.

Fructans are characterised by the range of the DP, including the average DP. The DP is a measure of the number of fructose molecules or saccharide units in the substance. The DP ranges can vary for the different fructans with these ranges overlapping for the different substances. For this reason, the terms used above have been described on the basis of the average DP (see Attachment 4 for more information on the DP ranges for particular substances).

Throughout this Report the term '**long-chain inulin'** is used to describe the processed inulin fraction that is currently added to infant formula, follow-on formula, infant foods and FSFYC internationally. The terms **inulin**, **oligofructose** and **FOS** will be used where appropriate.

1.4.2 Galacto-oligosaccharides

The term '**galacto-oligosaccharides'** (sometimes referred to as oligogalactosyl-lactose) is used consistently to describe those substances comprised of between two and eight saccharide units with one of these units being a terminal glucose and the remaining saccharide units being galactose and disaccharides comprised of two molecules of galactose. While disaccharide lactose is present in GOS mixtures, it is not regarded as a galacto-oligosaccharide. GOS is produced from lactose by enzymatic action and is also referred to as 'trans-GOS'.

1.4.3 Oligosaccharides and polysaccharides

The terms oligosaccharides and polysaccharides are used throughout this Report.

Oligosaccharides refer to component sugars with a DP range 3-10.

Polysaccharides contain several simple sugars (DP > 10) linked together and are often referred to as complex carbohydrates.

Human milk oligosaccharides (HMOs) is a collective term used throughout this Report to refer to the oligosaccharide and polysaccharide content of human breast milk (see Section 7.1.1 and Attachment 5).

1.4.4 Prebiotics

Prebiotics is a term used in literature and by industry. Although it is not defined in the drafting, for the purposes of this Report, **prebiotics** are defined as *non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon* (adapted from Gibson and Roberfroid, 1995).

1.4.5 Formulated supplementary foods for young children

Formulated supplementary food is defined in Standard 2.9.3 as *a food specifically designed as a supplement to a normal diet to address situations where intakes of energy and nutrients may not be adequate to meet an individual's requirements.*

Formulated supplementary foods for young children (FSFYC) is defined in Standard 2.9.3 as *a formulated supplementary food for children aged one to three years.*

Toddler formula is the main type of formulated supplementary foods for young children currently available.

1.4.6 Special purpose foods for infants and young children

Special purpose foods for infants and young children is a collective term used throughout this Report to refer to; infant and follow-on formula, infant foods and formulated supplementary foods for young children, such as toddler formula.

1.5 Ministerial Policy Guidelines

When developing and varying food standards, FSANZ must have regard to any written policy guidelines formulated by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council). The Ministerial Council recently endorsed[13] a Policy Guideline on the *Addition to Food of Substances other than Vitamins and Minerals*. It does not however apply to special purpose foods, such as infant formula products, infant foods and FSFYC.

The Ministerial Council agreed in March 2008 to develop policy guidance on the intent of Part 2.9 – Special Purpose Foods and on infant formula. The timing of the development of this policy guidance is not yet known. In the absence of policy guidance, FSANZ has considered only the safety aspects of the addition of inulin derived substances and GOS to infant formula products, infant foods and FSFYC; potential benefits are not assessed in this Report (see section 5.2 for the assessment approach).

1.6 Domestic and international regulations

1.6.1 Domestic Regulations

The addition of inulin-derived substances to general foods is not regulated domestically unless it is added for a nutritional purpose; in which case it is captured by the operation of Standard 1.1.1 (see below). There are, however, domestic regulations specifically relating to the addition of substances to infant formula products, infant foods and FSFYC.

[13] On 2 May 2008

The Standards in the Code relevant to this Proposal are:

- **Standard 1.1.1 – Preliminary Provisions**, clause 2 defines and clarifies the use of a 'nutritive substance' (also see Section 1.2 of this Report).

- **Standard 2.9.1 – Infant Formula Products** regulates the compositional and labelling requirements for infant formula products. Clause 6 of Standard 2.9.1 prohibits the addition of 'nutritive substances' to infant formula products unless specifically permitted. Clause 7 lists the permitted 'nutritive substances' that may be voluntarily added to infant formula products, the form(s) in which they may be added, the minimum amount per 100 kJ for their declaration, and the maximum amount permitted per 100 kJ when the substance is added. The maximum permitted amount applies to the sum of the naturally occurring and added 'nutritive substance'.

Relevant definitions from Standard 2.9.1 are:

> ***infant*** *means a person under the age of 12 months.*
>
> ***infant formula product*** *means a product based on milk or other edible food constituents of animal or plant origin which is nutritionally adequate to serve as the principal liquid source of nourishment for infants.*
>
> ***infant formula*** *means an infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months.*
>
> ***follow-on formula*** *means an infant formula product represented as either a breast milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months.*

Standard 2.9.2 – Foods for Infants regulates the compositional and labelling requirements of foods intended and/or represented for use as food for infants. Foods in this Standard are intended to be fed to infants in addition to human milk and/or infant formula products. Clause 2 states that *food for infants must not contain a food additive or nutritive substance unless expressly permitted by this Code.*

Relevant definitions from Standard 2.9.2 are:

> ***food for infants*** *means a food that is intended and/or represented for use as a source of nourishment for infants, but does not include –*
>
> *(a) infant formula products; and*
> *(b) formulated meal replacements; and*
> *(c) formulated supplementary foods; and*
> *(d) unprocessed fruit and vegetables.*

Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods regulates the compositional and labelling requirements of these foods.

Division 4 – Formulated Supplementary Foods for Young Children, specifies the required macronutrient composition of these foods and also the addition of at least one ore more permitted vitamins and minerals.

> ***Formulated Supplementary Foods for Young Children*** *means a formulated supplementary for children aged one to three years.*

1.6.2 International regulations

Specific international regulations relating to the addition of inulin/FOS to general food do not appear to exist. The Applicant for A613 reported that in most other countries, the status of inulin and FOS as dietary fibre (and therefore as a macronutrient) has been confirmed[14].

There are, however, international regulations relating to the addition of inulin-derived substances/FOS and GOS to infant formula products and foods for infants. The relevant international regulations of which FSANZ is aware of are outlined below.

1.6.2.1 Codex Alimentarius

The recently adopted revised Codex Standard for Infant Formula[15] allows the addition of *optional ingredients* to infant formula. Optional ingredients, in addition to the essential compositional requirements, may be added *in order to provide substances ordinarily found in human milk and to ensure that the formulation is suitable as the sole source of nutrition for the infant or to provide other benefits that are similar to outcomes of populations of breast-fed babies*. The revised Standard also states that *the suitability for the particular nutritional uses of infants and the safety of these substances shall be scientifically demonstrated* and that *the formula shall contain sufficient amounts of these substances to achieve the intended effect, taking into account levels in human milk.*

The Codex Standards for Canned Baby Foods[16] states that *baby foods may* be *prepared from any suitable nutritive material that is used, recognized or commonly sold as an article or ingredient of food, including spices.* Similarly, the Codex Standard for Processed Cereal-based Foods for Infants and Young Children[17] allows the addition of *other ingredients suitable for infants who are more than six months of age and for young children*.

1.6.2.2 United States of America (U.S.)

Inulin from the root of the chicory plant (*Cichorium intybus*) is 'generally recognized as safe' (GRAS) for use in food as a bulking agent[18]. Of the 43 food categories that are permitted to contain added inulin in varying levels, baby foods and beverages are included, but infant formula is excluded.

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[14] ORAFTI. Application to amend the *Australia New Zealand Food Standards Code:* Application A613 – Definitions for Nutritive Substance and Nutritive Ingredient.

[15] Codex Alimentarius Commission. Alinorm 07/30/26 – Report of the 28th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses. Appendix II – Draft revised standard for infant formula and formulas for special medical purposes intended for infants.

[16] Codex Standards for Canned Baby Foods. Codex Stan 71-1981.

[17] Codex Standard for Processed Cereal-based Foods for Infants and Young Children. Codex Stan 074-1981, Rev 1-2006.

[18] US Food and Drug Administration. Agency Response Letter GRAS Notice No. GRN 000118, 5 May 2003. Available at: http://www.cfsan.fda.gov/~rdb/opa-g118.html

Based on these food categories, dietary intakes of inulin in the USA at the 90th percentile level are estimated to be approximately 6 grams per day for infants less than one year of age, approximately 15 grams per day for infants older than one year of age, and approximately 20 grams per day for the general population (i.e. two years of age and older).

FOS is GRAS for use as a bulking agent in specific foods[19,20]. Infant foods (0-12 months) and toddler foods (12-24 months) are included in the permitted range of foods but infant formula is explicitly excluded.

Also, the expert panel consensus statement concerning the GRAS status of a GOS mixture (BI^2MUNO, a low molecular weight GOS) for use in foods, dated 29 July 2007, concludes the proposed uses of BI^2MUNO (in specified general purpose foods) are GRAS based on scientific procedures[21]. The US Food and Drug Administration decision and response letter is not available at the time of Final Assessment of P306.

1.6.2.3 European Union

In December 2006, the European Commission published Commission Directive 2006/141/EC on infant formula and follow-on formula[22]. The previous directive, Commission Directive 91/321/EEC[23], was repealed on 1 January 2008.

Infant formula products and follow-on formula products containing added oligosaccharides have been marketed in the European Union for several years. Commission Directive 91/321/EEC provides a general provision for the addition of *other food ingredients* to infant formula and follow-on formula; this includes oligosaccharides[24].

However, at the request of Member States, the European Commission asked the Scientific Committee on Food[25] (SCF) to comment on *the suitability and safety of the resistant short chain carbohydrates, FOS and GOS, in infant formula and follow-on formula*. The SCF released two statements on the above matter in 2001[26,27]. The statements concluded that there were no major concerns about the combination of 90% GOS and 10% *high molecular weight oligofructosyl-saccharose*[28] in infant formula and follow-on formula in total concentrations up to 0.8 g/ 100 mL in the product ready for consumption.

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[19] US Food and Drug Administration. Agency Response Letter GRAS Notice No. GRN 000044, 22 November 2000. Available at: http://www.cfsan.fda.gov/~rdb/opa-g044.html

[20] US Food and Drug Administration. Agency Additional Correspondence Letter GRAS Notice No. GRN 000044, 1 June 2007. Available at: http://www.cfsan.fda.gov/~rdb/opag044a.html

[21] Clasado Ltd, Attachment 1, submission to Draft Assessment P306 Addition of Inulin/FOS and GOS to food, , 22 February 2008

[22] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. *Official Journal of the European Union, L 401/1, 30/12/2006.*

[23] Commission Directive 91/321/EEC of 14 May 1991 on infant formulae and follow-on formulae. *Official Journal of the European Union, L 175, 04/07/1991.*

[24] Personal communication – Health and Consumer Protection Directorate-General, European Commission, June 2007.

[25] Scientific Committee on Food is now known as the European Food Safety Authority (EFSA).

[26] Scientific Committee on Food. Statement on the use of resistant short chain carbohydrates (oligofructose and oligogalactose) in infant formulae and in follow-on formulae, expressed on 26 September 2001.

[27] Scientific Committee on Food. Additional statement on the use of resistant short chain carbohydrates (oligofructosyl-saccharose and oligogalactosyl-lactose) in infant formulae and in follow-on formulae, expressed on 13 December 2001.

[28] *High molecular weight oligofructosyl-saccharose* is referred to as 'long-chain inulin' in this report.

Subsequently, as part of a review of the essential requirements of infant formula and follow-on formula, the SCF was requested to address the content of FOS and GOS in these products. In April 2003, the SCF released a report[29] that reaffirmed its previous statement of December 2001. In addition, the SCF concluded that *fructans other than* [high molecular weight] *oligofructosyl-saccharose should not be included in infant formula and follow-on formula*, based on available data at that time.

In 2003, the European Commission requested the European Food Safety Authority (EFSA) to provide a scientific opinion on the safety and suitability for particular nutritional use by infants of oligofructose (referred to as fructo-oligosaccharides by EFSA) at conditions specified by a manufacturer of infant formula and follow-on formula. The conditions specified by the manufacturer were an infant formula supplemented with 1.5 or 3 g/L of oligofructose.

On 19 February 2004, the Scientific Panel on Dietetic Products, Nutrition and Allergies of EFSA concluded that *there is no evidence of benefits to infants from the addition of fructo-oligosaccharides to infant formula at the conditions specified by the manufacturer while there are reasons for safety concerns.*

This conclusion was based on *an increased prevalence of adverse effects, including loose stools, in infants fed formula with added fructooligosaccharides. As no measures were made to demonstrate satisfactory water balance, the possibility of increased risk of dehydration can not be excluded, raising concerns with respect to the safety of such formula*.

On 22 December 2006, the European Commission issued a revised Directive on infant formula and follow-on formula (Commission Directive 2006/141/EC). In relation to infant formula, this Directive states that:

Fructo-oligosaccharides and galacto-oligosaccharides may be added to infant formula. In that case their content shall not exceed: 0.8 g/100 mL in a combination of 90% oligogalactosyl-lactose and 10% high molecular weight oligofructosyl-saccharose.

Other combinations and maximum levels of fructo-oligosaccharides and galacto-oligosaccharides may be used in accordance with Article 5.

Article 5 states that:

Infant formula shall be manufactured from protein sources defined in point 2 of Annex I and other food ingredients, as the case may be, whose suitability for particular nutritional use by infants from birth has been established by generally accepted scientific data.

Such suitability shall be demonstrated through a systematic review of the available data relating to the expected benefits and to safety considerations as well as, where necessary, appropriate studies, performed following generally accepted expert guidance on the design and conduct of such studies.

The Directive also states that similar amounts and ratios may be voluntarily added to follow-on formula. This Directive was adopted by Member States on 31 December 2007.

[29] Scientific Committee on Food. Report of the Scientific Committee on Food on the revision of essential requirements of infant formulae and follow-on formulae, adopted on 4 April 2003.

1.6.2.4 United Kingdom

England, Wales, Scotland and Northern Ireland are required to implement the European Commission Directive 2006/141/EC by respective regulation in their own countries. For example, in England the *Infant Formula and Follow-on Formula (England) Regulations 2007* which came into force on 11 January 2008 give effect to the European Commission Directive 2006/141/ EC and also revoke and replace, in England, the existing *Infant Formula and Follow-on Formula Regulations 1995*.

The Food Standards Agency has prepared Guidance Notes to assist stakeholders in interpreting the provisions of the new Regulations.

1.6.2.5 Asian countries

Infant formula products with added inulin, oligofructose and GOS have been marketed in many Asian countries for a number of years. It appears that these countries do not prohibit the addition of these substances to infant formula. However, many Asian countries require products to be registered before they are permitted to be imported into the respective country. In some instances, product registration requires the product to be compliant with the food regulations of the country of origin.

In Japan, oligosaccharides have 'foods of specified health use' (FOSHU) status, relating to a *health function* as a food to *modify gastrointestinal conditions*[30].

Because of the permitted use of these substances in some Asian countries, in August 2007, the New Zealand Food Safety Authority published an exemption from the requirements of the Code, in relation to the use of oligosaccharides in the manufacture of dairy based infant formula products for export to specified countries, including China, Malaysia, Indonesia and Republic of Korea[31].

1.6.2.6 Canada

Health Canada Food and Drug Regulations, Part B Division 25 Infant Foods, Infant Formula include requirements pertaining to Human Milk Substitutes and Foods Containing Human Milk Substitutes.

Although the regulations do not refer specifically to inulin-derived substances and GOS, the regulatory approach (Divisions B.25.056 and B.25.046/048) limits the addition of 'nutritive substances' to those found in human milk and to levels equal to those found in human milk. The regulations also require evidence that the product is 'nutritionally adequate to promote acceptable growth and development in infants when consumed in accordance with directions for use'.

Guidelines for pre-market assessment of notified human milk substitutes (1990) rely on standards of evidence using breastfed infants or those fed standard formula as controls.

[30] Ministry of Health, Labour and Welfare. Available at: http://www.mhlw.go.jp/english/topics/foodsafety/fhc/02.html

[31] New Zealand Food Safety Authority. Animal Products (Exemption from New Zealand Standards – Oligosaccharides in Infant Formula Products) Notice 2007 (3 August 2007). Available at: http://www.nzfsa.govt.nz/dairy/publications/specifications/fos-gos-60b-exemption-notice-2007.pdf

1.7 Current use

1.7.1 Presence in food

Inulin/FOS occur naturally in many plant foods including wheat, bananas, onions, garlic, Jerusalem artichoke, chicory, soy beans and soy products. GOS is found in some dairy products, such as lactose-reduced milk and yoghurt.

1.7.2 Added to the general food supply in Australia and New Zealand

Inulin-derived substances have been used in the general food supply, and some special purpose foods, in Australia and in many other countries for almost 15 years. They are added to a range of foods in Australia and New Zealand including: bread, fruit juice, milk, breakfast bars, biscuits, chocolate, soup, custard, and ice cream. The purpose for their inclusion varies and can include functions such as promoting healthy gut bacteria or technical functions, for example, as a bulking agent (see Section 6.1). As far as FSANZ is aware, FOS (as defined in this Report) and GOS are not widely used in the general food supply in Australia and New Zealand.

1.7.3 Added to infant formula and to foods for infants and young children - internationally

Infant formula containing long-chain inulin and GOS has been available in the United Kingdom and Ireland for several years. However, similar products are not available for sale in Canada or the USA.

As mentioned previously, infant formula and follow-on formula containing added oligosaccharides have been marketed in the European Union for several years (see Section 1.6.2.3).

Many Asian and Middle Eastern countries also sell infant formula, toddler formula and infant cereal products containing inulin, oligofructose and GOS.

2. The Problem

In response to the advice from the then NFA in the early 1990s that explicit permission was not required to add inulin to foods, inulin-derived substances have been added to a wide range of foods in Australia and New Zealand. They are added for technological or nutritional reasons (see Section 6.1).

However, FSANZ is aware of growing confusion within elements of the food industry concerning the status of added inulin-derived substances and FOS, specifically whether these substances fall within the definition of a ‘nutritive substance’ and therefore require expressed permission for addition to food. This confusion stems from an apparent polarity of views as to the status of inulin-derived substances and FOS.

First, within the food industry some sectors consider the substances to be ‘nutritive substances’ while others consider them to be ‘ingredients’.

Second, some food regulatory agencies believe that the substances are ‘nutritive substances’, whereas some sectors of the food industry remain of the view that they are not of a nutritive nature.

This apparent confusion undermines an efficient and internationally competitive food industry (clause 18(2)(c) of the FSANZ Act).

3. Objectives

The specific objective of this Proposal is to confirm the regulatory position for the food industry of inulin-derived substances and FOS when added to the general food supply, and to consider permissions for the addition of inulin-derived substances, FOS and GOS when added to infant formula products, infant foods and FSFYC.

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in section 18 of the FSANZ Act. These are:

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

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

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

4. Key risk assessment questions

To assist in meeting the objectives of this Proposal, several key risk assessment questions have been addressed. Responses to these questions are provided in Sections 6 and 7.

General food supply

1. Why are inulin-derived substances added to the general food supply?
2. Is there evidence of the safe use of inulin-derived substances in the general food supply?

Special purpose foods for infants and young children

3. Are inulin-derived substances/FOS and GOS *present in breast milk?* If so:

- at what levels; and
- how do these compare with the levels proposed for infant formula products?

4. What are the *physiological effects* in infants and young children of consuming inulin-derived substances/FOS and GOS?

5. How do the identified physiological effects compare with those in similarly aged breastfed infants?

6. Do all *forms* of inulin-derived substances/FOS and GOS produce the same identified physiological effects?

7. What are the *potential risks* to infants and young children consuming formula containing added inulin-derived substances/FOS and GOS alone or in combination? If in combination, are there any *safety issues with different proportions*?

8. Is there a *maximum safe intake* above which *adverse effects* may occur?

9. How much inulin-derived substances/FOS and GOS do infants and young children already consume and how much additional inulin-derived substances/FOS and GOS would this age group consume if these substances were added to special purpose foods for infants and young children?

5. Approach to the Risk Assessment

5.1 General foods

Although the Ministerial Council has recently endorsed a Policy Guideline on the *Addition to Food of Substances other than Vitamins and Minerals*, the Ministers agreed that the Policy Guideline should apply only to new applications or proposals, thus it does not apply to this Proposal.

As inulin-derived substances have been added to the general food supply for over a decade, the risk assessment has been confined to a description of the reasons for their addition to general foods and a description of their history of safe use in general foods.

FOS (as defined in this Report) and GOS are not widely used in to the general food supply in Australia and New Zealand currently. As such, and in keeping with the restricted scope of the Proposal, the addition of FOS and GOS to general foods has not been considered.

5.2 Special purpose foods for infants and young children

There are currently no Ministerial Policy Guidelines on the addition of substances to SPFYC. As a result, FSANZ, in accordance with its statutory objectives, has confined the risk assessment to considering safety as well as nutritional equivalence with breast milk as assessed by comparable physiological and microbiological effects. The risk assessment and comparison of nutritional equivalence with breast milk included:

- estimated daily intake of human milk oligosaccharides among breastfed infants;

- estimated daily intake of inulin-derived substances, FOS and GOS among formula-fed infants and young children consuming foods with these substances added; and

- a safety assessment of inulin-derived substances, FOS and GOS when added in any combination or alone.

5.2.1 Expert advice and peer review of the risk assessment

To further enhance the scientific rigour of the risk assessment, FSANZ discussed the risk assessment at Draft and Final Assessment with the recently established Infant and Young Child Scientific Advisory Group (ICSAG)[32]. FSANZ convened this group to provide scientific advice on risk assessment issues relating to infants and young children. Their input relates to the health, nutritional status and safety of infants and young children consuming food products with added inulin/FOS and GOS. At Draft Assessment, a member of this Group, an expert in paediatric nutrition[33], peer reviewed the risk assessment relating to infants and young children (Section 6).

RISK ASSESSMENT

The risk assessment addresses the key risk assessment questions (refer Section 4) and is in two parts. The first part discusses the technological and nutritional reasons for adding inulin-derived substances to general foods including evidence for their safe use.

The second part compares the microbiological and physiological effects of adding inulin-derived substances/FOS and GOS to SPFYC with the effects of human milk oligosaccharides in breastfed infants. The details of each assessment are contained in Attachments 5 to 9.

Current intakes and additional intakes in infants and young children from added inulin-derived substances and GOS in general and special purpose foods have been estimated as a guide only; there is no upper reference value with which to compare these.

6. Inulin-derived substances added to the general food supply

6.1 Why are inulin-derived substances added to the general food supply?

Inulin-derived substances are added to the general food supply for technological (see Section 6.1.1) and nutritional reasons (see Section 6.1.2).

Based on the advice provided to FSANZ, FOS (as defined in this Report) and GOS are not added to the general food supply in Australia and New Zealand, hence they are not considered further in this Section.

The chemical structure of these substances, and their stability, method of analysis and mode of action is described in greater detail in Attachment 4.

[32] ICSAG is an scientific advisory group comprised of experts in gastroenterology, pediatrics and child health.
[33] Dr Clare Wall, Senior Lecturer, Human Nutrition, Auckland University, New Zealand.

6.1.1 Technological reasons

The technological reasons for adding inulin-derived substances to foods relate to their capacity to act as fat and sugar replacers as well as emulsifiers, thickeners and stabilisers. These functions vary with the nature of the inulin-derived substance (e.g. chain length), its concentration in a food and the food itself. The technological reasons relate to the dispersing properties of inulin, in particular its ability to mimic fat droplets dispersed in water. These dispersions can then be used in foods to replace fat or to impart textural qualities in foods.

The amount of inulin-derived substance used for these purposes will vary depending on the technological purpose to be fulfilled.

It has been reported that specific applications for inulin-derived substances include:

- beverages (to improve mouth feel or creaminess, but mostly for nutritional reasons (see Section 6.1.2));
- bread or cereal products (for fat or sugar replacement, processing benefits, or for nutritional reasons (see Section 6.1.2)); and
- dairy products (for fat or sugar replacement or texture improvement).

Some inulin-derived substances (e.g. oligofructose) are also used as sweeteners with the relative sweetness being dependent on the degree of polymerisation and the proportion of the monosaccharide and disaccharide content in these products.

Inulin-derived substances are generally stable in most food matrices but under acid conditions (e.g. certain beverages when not refrigerated) hydrolysis may occur. FSANZ considers that these substances are likely to have acceptable stability in most dry foods but that inulin type fructose polymers may not be suitable in unrefrigerated low pH liquid foods, as inulin potentially might be hydrolysed to fructose.

6.1.2 Nutritional reasons

In Australia and New Zealand, inulin-derived substances can be added to the general food supply as dietary fibre (see Section 6.2). Dietary fibre is defined in Standard 1.2.8 as:

…that fraction of the edible parts of plants or their extracts, or synthetic analogues, that are resistant to the digestion and absorption in the small intestine, usually with complete or partial fermentation in the large intestine. Dietary fibre includes polysaccharides, oligosaccharides (degree of polymerisation > 2) and lignins, and promotes one or more of the following beneficial physiological effects:

(i) laxation
(ii) reduction in blood cholesterol
(iii) modulation of glucose.

For the purposes of making a nutrition claim, inulin-derived substances may also be added to general foods as a biologically active substance.

A biologically active substance is defined in Standard 1.2.8 to *mean a substance, other than a nutrient, with which health effects are associated*.

6.2 Is there evidence of the safe use of inulin-derived substances in the general food supply?

Inulin-derived substances have been added to the general food supply since the mid 1990s. FSANZ considered the safety of inulin as part of Application A277 – Inulin & Fructo-oligosaccharides as Dietary Fibre. Since completion of the Application in 2001, added inulin-derived substances may be labelled as dietary fibre. Inulin has been added to a wide range of foods with the aim of increasing the fibre content. As described in Section 6.1.1, inulin-derived substances are also added to foods for technological reasons.

In humans, inulin-derived substances and FOS are resistant to digestion in the small intestine and pass largely intact into the colon, where they are subject to fermentation by the resident microflora. This fermentation results in the production of gases and short chain fatty acids (SCFAs). The SCFAs are utilised locally as an energy source by the resident microflora, taken up systemically for use as an energy source by the host, or excreted in the faeces.

Up to 20-30 g/day of inulin-derived substances can be tolerated by most adults, although some individuals may experience increased flatulence at levels of intake around 10 g/day. A high level of consumption of these substances e.g. over 30 g/day, may result in increased flatulence, and may cause more severe side effects such as stomach cramps and diarrhoea. However, these are common effects of over consumption of any dietary fibre. In addition, excessive consumption is likely to be self-limiting due to the unpleasant side effects.

The Adequate Intake (AI) of dietary fibre, from all sources, is 30 g/day among adult males aged 19 years and over, and 25 g/day among adult females aged 19 years and over (NHMRC and NZMoH, 2006). The AI is based on the median dietary fibre intake in the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS. Intakes of inulin-derived substances would have been fairly small at this time because these substances were only beginning to be added to the food supply. There is no UL set for dietary fibre, although there is a Suggested Dietary Target (SDT[34]) of 38 g for man and 28 g for women (NHMRC and NZMoH, 2006).

There are two published reports from Europe of allergic reactions to inulin-containing food (Gay-Crosier *et al*., 2000; Franck *et al*., 2005). Both individuals had a history of allergy to artichoke suggesting possible cross-reactivity between artichoke and inulin. The cross-reactivity appears to require an inulin protein compound. As inulin itself is not allergenic and artichoke allergy is rare even in Europe, FSANZ considers that inulin-containing food does not present a significant allergy concern from a public health and safety perspective.

In terms of nutrient interactions, data indicate that inulin-derived substances or FOS added to diets in the range of 8-20 g/day does not inhibit the absorption of magnesium, iron, zinc, copper, selenium or calcium along the small intestine. There is some indication that calcium, copper and magnesium absorption is enhanced in the large intestine when inulin-derived substances are included in the diet.

[34] SDT is *a daily average intake from food and beverages for certain nutrients that may help in prevention of chronic diseases.*

Otherwise, no adverse effects have been reported due to the consumption of foods containing inulin-derived substances. Thus, FSANZ considers these substances to have a history of safe use in the general food supply.

7. Inulin-derived substances/FOS and GOS added to special purpose foods for infants and young children

7.1 Composition of breast milk compared to infant formula with added inulin-derived substances/FOS and GOS

7.1.1 Are inulin-derived substances/FOS and GOS present in breast milk? If so, at what levels; and how do these compare with the levels proposed for infant formula?

FSANZ describes the carbohydrate composition of human breast milk in Attachment 5. The carbohydrates in greatest abundance in breast milk are lactose at approximately 7% of the milk. Approximately 1-2% of human milk is made up of oligo- and polysaccharides collectively referred to as human milk oligosaccharides (HMOs). To date over 200 HMOs have been identified in breast milk, but it is thought that the total number may be in the thousands. The total HMO content of breast milk may be up to 25 g/L during the first few weeks following birth; declining thereafter. From one to four months the concentration is likely to be around two-thirds of the concentration in early lactation. There is a large variation in the breast milk concentration of HMOs among individual women, as much as a four-fold difference; due in part to genetic variations. The effect of maternal diet on the carbohydrate content of breast milk has not been extensively studied.

Inulin-derived substances/FOS are not present in breast milk and GOS is found only in trace amounts. Cow's milk, the standard base of infant formula, contains only trace amounts of indigestible oligosaccharides and polysaccharides. Goat's milk contains a low concentration of oligosaccharides, reported to be in the order of 0.25-0.3 g/L (Martinez-Ferez *et al.* 2006). Although soy beans contain indigestible oligosaccharides, infant formula based on soy appears to contain soy protein isolate that is free from oligosaccharides.

The oligosaccharide and polysaccharide concentration of breast milk is higher (up to 15 g/L in mature breast milk) than the levels of long-chain inulin and GOS proposed to be added to infant formula in the two applications received from Heinz Wattie's (A598) and Nutricia (A609); both are seeking to add up to a maximum of 8 g/L of total oligosaccharides.

7.2 Physiological effects of inulin-derived substances/FOS and GOS in infants and young children

7.2.1 What are the physiological effects in infants and young children of consuming inulin-derived substances/FOS and GOS?

Similar to HMOs, inulin-derived substances/FOS and GOS are undigested in the small intestine. However, they influence the ecology of the infant's large intestine including the composition of the intestinal microflora (see Section 7.2.2.1), stool consistency and frequency, stool pH, and faecal SCFA profile (see Section 7.2.2.2).

7.2.2 How do the identified physiological effects compare with those in similarly aged breastfed infants?

7.2.2.1 Microbiological function

FSANZ has assessed the evidence on the effect of inulin-derived substances/FOS and GOS in combination or alone as a component in infant formula products on gut microflora (see Attachment 6).

Microbial colonisation of the gastrointestinal tract starts immediately after birth. The initial microorganisms are acquired from the mother through contamination during the birth, breastfeeding and caring, and from the environment. Because of the differences in exposure to the initial bacterial species and population from one individual to another, the exact pattern/distribution of the intestinal microflora in each individual is unique. Approximately 90% of the intestinal microflora of breastfed infants is *Bifidobacterium* and *Lactobacillus* species. This has been attributed to the preferential metabolism of HMOs by these bacterial species, as well as to the influence of lactoferrin, lactose, nucleotides and low concentration of proteins and phosphates in human breast milk

Increased dominance of *Bifidobacterium* and *Lactobacillus* species leading to a reduced colonic pH has been claimed to restrict the proliferation of other intestinal microorganisms in the colon. The competition for nutrients available in the colon by *Bifidobacterium* and *Lactobacillus* species has also been claimed to lead to an exclusion effect on other intestinal microorganisms. These suppressive effects on other intestinal microorganisms, particularly those that are pathogenic to the host are generally regarded as beneficial. Although direct and convincing evidence to support these claims is lacking.

In comparison to observations in breastfed infants, the proportion of *Bifidobacterium* and *Lactobacillus* species present in the gastrointestinal tract of formula-fed infants is relatively small, approximately 40-60% of the overall intestinal microflora; with the rest consisting of *Streptococcus*, *Bacteroids*, *Clostridium*, *Staphylococcus* and a few genera belonging to the family of Enterobacteriaceae.

There is some evidence to suggest that supplementation of infant formula with GOS and inulin-derived substances in a ratio of 9:1, or inulin-derived substances alone at intakes ranging from 4-10 g/L may selectively stimulate the growth of intestinal *Bifidobacterium* populations in infants. There is a lack of persuasive evidence to support the suggestion that supplementation by GOS in isolation, in infant or toddler formula selectively stimulates the growth of intestinal *Bifidobacterium* and *Lactobacillus* in infants. There is also insufficient evidence to allow any conclusions to be made about the effects of FOS on gut microflora in infants.

7.2.2.2 Stool consistency and frequency, stool pH and faecal SCFA profile

FSANZ has assessed the evidence on the physiological effect of added inulin-derived substances/FOS and GOS in infant formula products and infant foods, in particular, the effect on stool consistency and frequency, stool pH and faecal SCFA profile compared with breastfed infants and/or infants fed unsupplemented formula or foods (see Attachment 7).

Breastfed and formula-fed infants appear to have similar capability to digest complex oligosaccharides into SCFAs in the large intestine. SCFAs are easily absorbed thus preventing the occurrence of osmotic diarrhoea which can be caused by the presence of undigested carbohydrates in the gut. However, breastfed infants generally have softer and more frequent stools than formula-fed infants. This is at least partly due to the oligo- and polysaccharides that are unique to breast milk.

The bulk of the research has been done comparing standard infant formula to formula supplemented with GOS and long-chain inulin at a ratio of 9:1 at concentrations of 4-8 g/L of formula, with one study involving formula containing 10 g/L. The majority of studies testing supplemented formula reported softer stools, with a lower pH. The one study that examined faecal SCFA also reported that supplemented formula resulted in a SCFA profile similar to that reported for breastfed infants. The ability of GOS and inulin-derived substances to increase stool frequency is less well established, possibly because this effect gets smaller with age.

The study that examined the addition of GOS to infant formula in isolation, reported higher stool frequency in those infants receiving the GOS supplemented formula. The frequency was similar to that of a breastfed reference group however more data are needed to draw a firm conclusion. Data on the effect of formula supplemented with GOS alone on stool pH and faecal SCFAs is limited and contradictory, thus no conclusion can be made.

The addition of GOS and inulin-derived substances to infant foods did not influence stool frequency or softness, nor did it significantly lower stool pH. The sole addition of inulin-derived substances to infant formula products or infant foods may increase stool frequency or stool weight in infants less than 12 months of age. The limited data available suggests they have little effect on stool pH. There appears to be little impact on stool frequency or consistency in young children over 12 months of age.

FOS has not been sufficiently studied in infants and young children to allow any conclusions about their physiological effects to be made.

7.2.3 Do all forms of inulin-derived substances/FOS and GOS produce the same identified physiological effects?

The majority of the evidence is based on infants. Hence the ability to compare physiological effects is restricted to this age group.

A number of submitters to the Draft Assessment expressed concern over the lack of studies involving ratios of GOS to inulin-derived substances other than the 9:1 ratio. This included concern about the single addition of either GOS or inulin-derived substances. Fewer studies looking at the effects of GOS and inulin-derived substances have looked at ratios that differ from the commonly assessed ratio of 9:1. However, the available evidence indicates that the addition of GOS and inulin-derived substances at a ratio of 9:1, with a dose not exceeding 10 g/L, or inulin-derived substances alone, at a level up to 8 g/L, in infant formula products have comparable physiological and microbiological effects. In the absence of sufficient evidence on FOS no conclusions can be made.

7.3 Safety of inulin-derived substances/FOS and GOS in infants and young children

7.3.1 What are the potential risks to infants and young children consuming formula containing added inulin-derived substances/FOS and GOS alone or in combination? If in combination, are there any safety issues with different proportions?

FSANZ has assessed the available evidence on the potential for inulin-derived substances and GOS to cause adverse effects in infants and young children (see Attachment 8). The assessment was informed by studies involving the addition of GOS and inulin-derived substances, alone or in combination, at any ratio to infant formula products, infant food, and FSFYC. In addition to considering the evidence from clinical trials, FSANZ has also taken the levels of HMOs in breast milk into consideration, as well as relevant *in vitro* data. However, the suggested permitted level of addition is based primarily on the evidence of safety of GOS and inulin-derived substances as assessed by clinical trials. Limited information is available on the safety of FOS in infant formula and foods for infants and young children, therefore FSANZ could not assess FOS in infant formula and foods as part of the safety assessment.

Inulin-derived substances and GOS, like HMOs, are not digested to any great extent in the small intestine. As there is virtually no systemic exposure to these intact oligosaccharides, the only possible adverse effect identified was an increased osmotic potential within the colon, potentially leading to increased water loss and dehydration. FSANZ has considered this potential risk. This possibility had also previously been considered by the European Scientific Committee on Food. The potential risk is of greater concern in very young infants (newborns), who lack a fully developed renal system and may not have full colonisation of the colon with bacteria capable of breaking down added oligosaccharides. This potential hazard has been addressed in a range of studies in very young infants, and is discussed in Attachment 8, Safety Assessment Report, which concluded that the addition of inulin and GOS at the proposed levels is unlikely to pose any risk to very young infants.

Although fewer direct studies have been examined older infants (aged 4-6 months and above) and young children (aged 1-3 years) who might be consuming infant foods and FSFYC, these infants and young children are much less sensitive to potential dehydration as their kidneys are more developed, and have the ability to concentrate urine. The data from studies reviewed in older infants and young children have supported the view that the addition of inulin-derived substances and GOS are unlikely to pose a risk.

Since Draft Assessment FSANZ has concluded that inulin-derived substances and GOS, either alone or in any combination, at concentrations up to 8 g/L will beneficially contribute to increased osmotic potential in the colon of formula-fed infants; the increase is considered to be no greater than in breastfed infants where undigested HMOs also enter the colon. To reach this conclusion FSANZ has considered the following evidence:

- HMOs are present in colostrum and mature breast milk at levels up to 25 g/L and 15 g/L respectively; these levels are safe for newborn and older infants;
- GOS and long-chain inulin preparations at 8 g/L are safe for formula-fed infants;
- Inulin-derived substance preparations at 8 g/L are safe for formula-fed infants; and

- *In vitro* evidence that inulin-derived substances and GOS are fermented by colonic microflora to a similar or greater extent than HMOs.

Evidence from adult studies suggests that intakes of inulin-derived substances may lead to gastrointestinal signs, such as flatulence and bloating, in some individuals. However, no such adverse effects were reported in a recent infant study in which newborns up to the age of four days were fed infant formula containing up to 8 g/L of inulin-derived substances (Orafti, Synergy 1®) for four weeks. This direct evidence, in combination with the evidence described above, was considered sufficient to support the recommendation of a maximum permitted level of 8 g/L.

Some gastrointestinal discomfort may initially be experienced by young infants changing from breast milk or conventional formula to oligosaccharide-supplemented formula. The phenomenon of changed gastrointestinal effects is not uncommon for infants when their formula is changed. It is anticipated that this effect will be less evident in older infants (e.g. 6 months and over) as their gastrointestinal system is more mature. Unlike infant formula products, toddler formula and infant foods do not represent the sole source of nutrition for older infants and young children. It follows that if GOS, oligofructose and inulin pose no risk for newborns and infants, they will also pose no risk for older infants and young children.

The recommendations made in this Proposal aim to restrict the addition of very short chain fructose polymers, i.e. FOS, however inulin is generally made up of a distribution of fructans of different lengths, and it is impossible to draw a line at which point the fructose polymers become too short, nor would it be possible to enforce such a recommendation. Even long-chain inulin preparations will have some proportion of short chain fructose polymers. FSANZ is of the opinion, supported by the external reviewers (see Section 7.3.3.1), that the recommendations put forward are unlikely to pose any risk to young infants.

7.3.2 Is there a maximum safe intake above which adverse effects may occur?

Clinical trials in infants have provided formulas supplemented with up to 10 g/L of GOS and inulin-derived substances without evidence of harm. However, the majority of studies have assessed formula supplemented GOS and inulin-derived substances at 4-8 g/L. These studies support the conclusion that 8 g/L of GOS and inulin-derived substances, alone or in combination, are unlikely to pose a risk to infants including newborns.

7.3.3 External advice on safety issues

7.3.3.1 Responses from peer reviewers on the safety assessment

At Draft Assessment, two international experts in the fields of prebiotics[35], and dietary fibre and carbohydrates[36], respectively, peer reviewed the safety assessment.

Professor Gibson concurred with FSANZ's recommendation that 8 g/L in any combination of GOS, oligofructose and inulin, either alone or combined was safe. Professor Cummings was more circumspect.

[35] Professor Glenn Gibson, Head of Food Microbial Sciences, University of Reading, England
[36] Professor John Cummings, Emeritus Professor of Experimental Gastroenterology, University of Dundee, Scotland

He considered that these substances when added to infant formula would be safe for infants of all ages, however, he highlighted that inulin may cause gastrointestinal discomfort based on studies in adults where some individuals experienced increased flatulence at supplementary intakes of 10 g inulin/day. Professor Cummings suggested that in the absence of appropriate studies with inulin-derived substances at higher levels it would be justified to limit the addition of these to the levels that have been directly studied in infants (3 g/L) at that time. Professor Gibson had no similar concern about gastrointestinal symptoms.

This recommendation was considered by the ICSAG in early December 2007. Members agreed with the recommended upper levels for GOS, oligofructose and inulin; no significant issues were raised. Members also agreed to support Professor Cummings's suggestion to restrict the upper level of inulin-derived substances to 3 g/L. This was based on the absence at the time of clinical trial data to support a higher level.

At Final Assessment, however, FSANZ has amended the Safety Assessment Report to recommend that the maximum permitted amount of inulin-derived substances alone at any ratio to infant formula products be 8 g/L. This amendment was made on the basis of the study from Beneo/Orafti and referred to in Section 7.3.1. FSANZ did, however, seek additional expert opinion on the revised upper level for inulin-derived substances from ICSAG members and also from Professor Cummings.

Responses were received from three of the six external members of ICSAG. Of these, two members were generally supportive of increasing the maximum amount of inulin-derived substances added to infant formula products from 0.3 g/100 mL to 0.8 g/100 mL based on the evidence in the Beneo report. The third member was not supportive of the increase on the basis that the study was not large enough to identify statistically significant differences (there were 20 infants in each treatment group), the short duration of the study (28 days post birth and up to five days old) and the categories of crying behaviour, vomiting and regurgitation were not sufficiently sensitive to detect differences.

Professor Cummings considered that the evidence did provide reassurance of the safety of 0.8 g/100 mL of inulin-derived substances in infant formula. His conclusion was based on no significant differences in terms of growth, weight gain and food intake between infants fed either 0.8 g/100 mL of inulin-derived substances or those fed 0.8 g/100 mL of GOS and inulin-derived substances in a ratio of 9:1. He also noted that stool frequency was well below that of the breastfed infants indicating that infants fed this formula were not at risk of dehydration.

FSANZ considered these responses and in keeping with the majority of reviewers maintained its conclusion that a maximum of 0.8 g/100 mL of inulin-derived substances added to infant formula products is unlikely to pose a risk to infants fed this formula from birth onwards.

7.3.3.2 Anecdotal evidence regarding safety concerns of oligosaccharide supplemented infant formulas

The New Zealand Food Safety Authority provided anecdotal evidence (reports by parents) to FSANZ of a small number of adverse events including diarrhoea, blood and mucous in stools that may be associated with infant formula containing added long chain inulin and GOS.

FSANZ sought additional advice from an expert in paediatric nutrition who considered that although the information was suggestive of an adverse effect, the same effects could be due to other causes, such as rotavirus, which is common in infants.

7.4 Current and estimated additional consumption of inulin-derived substances/FOS and GOS in infants and young children

7.4.1 How much inulin-derived substances/FOS and GOS do infants and young children already consume and how much additional inulin-derived substances/FOS and GOS would this age group consume if these substances were added to special purpose foods for infants and young children?

A dietary intake assessment was undertaken to estimate:

- intakes of oligo-and polysaccharides from breast milk in three month olds;
- potential intakes from naturally-occurring inulin: and
- potential intakes from inulin-derived substances and GOS added to special purpose foods for infants and young children (see Attachment 9).

Current dietary intakes of inulin-derived substances and GOS were estimated based on natural sources and added sources according to the current market uptake of these substances in processed food products. An additional intake estimate was then calculated to account for potential intakes from infant formula products, infant foods and FSFYC supplemented with inulin-derived substances and GOS.

7.4.1.1 Breast milk assessment

Inulin-derived substances are not present in breast milk and the concentration of GOS in breast milk is negligible, therefore a 'breast milk' assessment was calculated for both Australia and New Zealand using the intakes of oligo- and polysaccharides for infants at three months of age.

For breastfed infants, it was assumed that breastmilk was the only food consumed by infants at three months and that one gram of breast milk is equal to one mL of breast milk.

7.4.1.2 Special purpose foods assessment

Applications (A609 and A598) and the literature reviewed by FSANZ were used as the basis for assigning concentrations for the addition of inulin-derived substances and GOS in infant formula products, infant foods and FSFYC.

Dietary intakes of inulin-derived substances and GOS were estimated in two ways:

- 'Combined' assessment – based on a combined concentration of inulin-derived substances and GOS in special purpose foods for infants and young children of 0.8 g/100 mL; and

- ‘Separate’ assessment – based on separate concentrations of inulin-derived substances and GOS, respectively at 0.8 g/100 mL in special purpose foods for infants and young children.

7.4.1.3 Theoretical diets

As food consumption data were not available for children less than two years of age in Australia, model diets were constructed for infants aged three, nine and 12 months. In New Zealand, food consumption data were not available for children less then five years of age, so a model diet was constructed for infants aged three months and toddlers aged 1-3 years. These diets included an estimated intake of 800 mL/day of infant formula for three month olds, of 545 mL/day of follow-on formula for nine month olds, of 425 mL/day of toddler formula for 12 month olds, and of 280 mL/day of toddler formula for 1-3 year olds plus intakes from infant foods and other foods. For infants aged three months two diets were estimated, the first assumed infants were exclusively fed infant formula, the second assumed infants were exclusively breastfed.

7.4.1.4 Results of dietary intake assessment

The estimated intake of oligo- and polysaccharides from breast milk for 3 month old infants is 12.0 g/day (i.e. 796 g/d x 15 g/L).

The estimated mean dietary intakes (g/day) from the addition of inulin-derived substances and GOS to special purpose foods for infants and young children are given in Table 1. More detailed results and additional assumptions underpinning the dietary intake assessment are described in Attachment 9.

Table 1: Estimated mean dietary intake (g/day) of inulin-derived substances/FOS and GOS among infants and toddlers for the combined and separate intake assessments, Australia and New Zealand

	Combined assessment intakes (g/day)			Separate assessment intakes (g/day)					
	Inulin-derived substances and GOS			Inulin-derived substances alone			GOS alone		
Age	Current intakes	Projected intake	Inc-rease	Current intakes	Projected intake	Inc-rease	Current intakes	Projected intake	Inc-rease
Australia									
3 months	**0**	**6**	**6**	**0**	**6**	**6**	**0**	**6**	**6**
9 months	**5**	**9**	**4**	**4**	**8**	**4**	**1**	**5**	**4**
1 year	**7**	**10**	**3**	**5**	**9**	**4**	**1**	**5**	**4**
New Zealand									
3 months	**0**	**6**	**6**	**0**	**6**	**6**	**0**	**6**	**6**
1-3 years	**17**	**19**	**2**	**12**	**15**	**3**	**5**	**7**	**2**

Source: FSANZ estimates based on model diets for each age group.

Australia

The estimates indicate that following the addition of inulin-derived substances and GOS to infant formula products, three month old infants are likely to have the highest increase in mean intakes for all three intake assessments. These levels are still well below the estimated daily intake of 12 g/day of oligosaccharides in breastfed infants. While the increases for older infants and children are not as great they are still considerable; with up to a 100% increase in mean intakes.

The main source of inulin-derived substances and GOS among Australian and New Zealand infants aged 9 months and 1 year were from supplemented follow-on formula, infant foods and FSFYC; intakes from naturally-occurring food sources and added to other foods did not make a large contribution to the estimated intakes in this age group.

New Zealand

The main source of inulin-derived substances and GOS intakes for New Zealand children (aged 1-3 years) were from yoghurts. Toddler formula was also a major contributor but was lower than yoghurts.

8. Summary of risk assessment

8.1 Inulin-derived substances added to the general food supply

There is a history of safe use of inulin-derived substances added to the general food supply. In Australia and New Zealand, the substances have been used since the mid-1990s. Since 2001, inulin could be labelled as dietary fibre in a wide range of foods. FSANZ understands that FOS (as defined in this Report) and GOS are not widely used in the food supply in Australia or New Zealand.

Although there have been reports from Europe of two individual patients with an allergy to inulin, these appear to be related to cross-reactivity between artichoke and inulin. The cross-reactivity appears to require an inulin-protein compound. As inulin itself is not allergenic and artichoke allergy is rare even in Europe, FSANZ considers that inulin-containing food does not present a significant allergy concern from a public health and safety perspective.

8.2 Inulin-derived substances/FOS and GOS added to special purpose foods for infants and young children

FSANZ has assessed the available evidence on the potential of inulin-derived substances and GOS to cause adverse effects in infants and young children. There was insufficient evidence to assess either the safety or physiological effects of FOS.

The evidence indicates that inulin-derived substances and GOS, like naturally occurring HMOs, are not digested to any great extent in the small intestine. When they reach the large intestine, mostly intact, there is a small beneficial increase in osmotic potential in the colon. This increase in osmotic potential from inulin-derived substances and GOS is similar that observed from HMOs and therefore no more likely to cause dehydration.

FSANZ has concluded, based on the available evidence that addition of a total level of 8 g/L of inulin-derived substances and GOS, alone or combined, at any ratio in infant formula products is unlikely to pose a risk to young infants. This conclusion is based on data from clinical trials which have provided formulas supplemented with up to 10 g/L of inulin-derived substances and GOS to infants without evidence of harm. Data also indicated that these oligosaccharides are fermented to a similar or greater extent than HMOs. The safety of this level (8 g/L) is further supported by the presence of higher levels of HMOs, up to 25 g/L in breast milk.

There is evidence that addition of inulin-derived substances and GOS and inulin-derived substances alone up to 10 g/L, added to infant formula result in similar physiological i.e. softer consistency and lower pH of stools; and microbiological effects i.e. selective growth stimulation of intestinal *Bifobacterium* to that of breastfed infants. There is insufficient evidence on the addition of GOS alone to draw conclusions.

Fewer direct studies have examined older infants and young children consuming infant foods and FSFYC. However, those available indicated that addition of a total level of 8 g/L of inulin-derived substances and GOS, alone or combined, at any ratio are unlikely to pose a risk. Further, older infants and young children are much less sensitive to potential dehydration as their kidneys are more developed, and have the ability to concentrate urine.

RISK MANAGEMENT

9. Identification of risk management issues

The risk assessment aimed to determine the safety of inulin-derived substances and GOS when added to special purpose foods for infants and young children, also comparing their microbiological and physiological effects with that of breastfed infants. The use of inulin-derived substances and FOS in the general food supply has also been considered.

FSANZ has considered the management of any risks identified through the risk assessment and from information provided through consultation with key stakeholders. Issues raised in submissions have been addressed throughout this Report where possible and have been summarised at Attachment 2. Also, FSANZ's response to the key issues raised are summarised at Attachment 3.

9.1 Inulin-derived substances, FOS and GOS added to general foods

9.1.1 History of safe use

FSANZ's risk assessment indicates that inulin-derived substances added to food have a history of safe use in the general food supply.

Therefore it is proposed at Final Assessment that the Code be amended to the effect that inulin-derived substances are taken **not** to be nutritive substances and therefore do not require express permission for addition to food. This is considered **an interim regulatory response to resolve the current uncertainty** surrounding the addition of inulin-derived substances to general purpose foods.

At Draft Assessment, it was proposed that FOS, along with inulin-derived substances would be taken **not** to be a nutritive substance, and therefore would not require express permission for addition to food. However, based on further information provided FSANZ understands that FOS as defined in this Report (i.e. fructose polymers derived from sucrose – see Section 1.4) is not used in the food supply in Australia or New Zealand. Therefore, at Final Assessment, FSANZ considers that it is not necessary to specifically include FOS (as defined in this Report) in the proposed amendments to the Code. Also, due to insufficient evidence FOS was not able to be considered in the risk assessment.

Also, FSANZ is not aware of the wide use of GOS added to food (other than to infant formula products, infant foods and FSFYC) and intakes from the general food supply from naturally-occurring GOS are likely to be negligible. Thus FSANZ considers it is not necessary to specifically include GOS in the Code, other than for their use in infant formula products, infant foods and FSFYC.

9.2 Inulin-derived substances and GOS added to special purpose foods for infants and young children

FSANZ has assessed the safety of inulin-derived substances and GOS and their potential to cause adverse effects in infants and young children, in particular, the effect on water balance and potential dehydration in infants fed solely on infant formula products containing inulin-derived substances and/or GOS.

9.2.1 Safety, levels of addition, permitted form and ratio of GOS and inulin-derived substances

At Final Assessment, the risk assessment concludes that a total level up to 8 g/L of inulin-derived substances and GOS added singularly or in combination in any ratio to infant formula products, infant foods and FSFYC is unlikely to pose a health and safety risk to infants and young children up to three years of age.

At Draft Assessment, the safety assessment noted that inulin may cause increased flatulence and bloating at supplementary intakes of 10 g inulin/day in adults. However, it was not clear if this would occur in infants due to differences in colonic microflora and overall diet. Therefore, at Draft Assessment FSANZ considered it prudent to limit the addition of inulin-derived substances to levels which have been shown to be well tolerated in infants i.e. 3 g/L (refer to Section 7.5.1).

At Draft Assessment, industry submitters were asked to provide comment on the addition of inulin-derived substances to infant formula products at more than the proposed levels of 110 mg/100 kJ (3 g/L).

Several industry submitters considered that the relatively low levels proposed for the addition of inulin-derived substances at Draft Assessment differed from the levels shown to be safe by suppliers of these products, and infant formula manufacturers. It was also noted that the relatively low level proposed was based on anecdotal evidence in infants of transient gastrointestinal effects. One industry submitter made available a more recent study on infants, that concluded that infant formula supplementation containing 8 g/L of inulin-derived substances was well tolerated and was unlikely to pose a risk to infants (refer to section 7.3.1).

Another submitter noted support for the higher level of 8 g/L if appropriate evidence was available.

In response to the totality of available evidence, at Final Assessment FSANZ is proposing the following levels[37] of inulin-derived substances and GOS:

- for infant formula products a permitted maximum level of 290 mg/100 kJ (8 g/L) for the total combined inulin-derived substances and GOS, or for the singular addition of either inulin-derived substances or GOS; and

- for infant foods a permitted maximum level of 0.8 g/100 g, as consumed for total combined inulin-derived substances and GOS, or for the singular addition of either inulin-derived substances or GOS; and

- for FSFYC a permitted maximum level of 1.6 g/serve[38] (8 g/L) for total combined inulin-derived substances and GOS, or for the singular addition of either inulin-derived substances or GOS.

FSANZ's assessment found very little evidence to support the safe addition of FOS (as defined in the Report) to infant formula products, infant foods and FSFYC. Therefore FOS has been excluded in this proposal from the substances permitted for addition to SPFYC. Also, on the basis of information provided to FSANZ it appears that manufacturers who are seeking to add these substances to SPFYC are adding inulin-derived substances, rather than FOS, as defined in this Report.

9.2.1.1 Units in draft Standard for concentration of inulin-derived substances and GOS

In the draft Standard, for infant formula products the maximum concentrations of inulin-derived substances and GOS are expressed per 100 kJ (of reconstituted or 'ready to drink formula), consistent with permissions for other voluntary substances in Standard 2.9.1. Specifically, 8 g/L equates to 290 mg/100 kJ.

For infant foods, in Standard 2.9.2 permissions for the maximum concentrations of inulin-derived substances and GOS are expressed per 100 g (as consumed), specifically 0.8 g/100 g.

For FSFYC, in Standard 2.9.3 Division 4 permissions for the maximum concentrations of inulin-derived substances and GOS are expressed per serve. Therefore 8 g/L equates to 1.6 g/serve.

9.2.1.2 Ratio of GOS to inulin-derived substances

The majority of studies considered in the risk assessment used a 9:1 GOS:inulin preparation, added to infant formula at a level of 8 g/L. However, studies using concentrations of 4, 6 and 10 g/L were also included, as were studies of GOS and inulin-derived substances alone.

FSANZ considers total added GOS and inulin-derived substances, in any ratio up to the proposed maximum level (refer to 9.2.2.1) is unlikely to pose a health and safety risk.

[37] The maximum permitted amounts only apply when the substance is added and then apply to the total of the naturally occurring and added substances.
[38] The level of 1.6 g per serve is based on a serving of 200 mL of toddler formula.

Therefore at Final Assessment, FSANZ does not consider it necessary to prescribe a ratio requirement in the Code.

FSANZ notes however, that Nutricia[39] in its Application A609, states that *Numico[40] presently holds an intellectual property position, including patents, in relation to the use of prebiotics GOS and long-chain FOS (high molecular weight) in a ratio of 9:1*. Consequently, other manufacturers will need to consider this position, including the patents, and make their own enquiries to inform the formulation of their infant formula products.

9.2.1.3 Changes to infant feeding regimes and potential gastrointestinal discomfort

FSANZ has also considered potential initial gastrointestinal discomfort that may be experienced by some young infants changing from breast milk or conventional formula to oligosaccharide-supplemented formula.

FSANZ considers changed gastrointestinal effects are not uncommon for infants when their formula is changed and that this effect is likely to be less evident in older infants (e.g. 6 months and over).

One submitter expressed concerns about the potential effects on very young infants. Section 7.3.1 notes this potential hazard has been addressed in a range of studies in very young infants. The Safety Assessment Report (Attachment 8) concludes that the addition of inulin-derived substances and GOS at the proposed levels is unlikely to pose a risk to very young infants. Section 7.3.1 also refers to an additional more recent study which included very young infants.

FSANZ acknowledges that heath professionals are the most appropriate source of information in guiding parents/carers in infant feeding. Health professionals who are advising those caring for formula-fed infants are likely to include information regarding potential gastrointestinal effects and the management of these, when changes are made to an infant's feeding regime.

9.2.1.5 Specifications for inulin-derived substances and GOS for addition

At Draft Assessment, it was considered necessary to include specifications for GOS. However, based on information provided to FSANZ the inclusion of specifications for GOS is considered to be unnecessarily restrictive and is no longer proposed at Final Assessment. GOS added to SPFYC would still need to comply with the general requirements in Standard 1.3.4 – Identity and Purity.

Specifications for inulin, long-chain inulin and oligofructose will vary in accordance with the wide variety of mixtures available. Therefore, it is not considered practical to develop specific specifications for these substances. However, there is a need to define these substances in the Code to ensure regulatory clarity. FSANZ is proposing that the definitions as described in the draft variations (see Attachment 1) be included into the Code to provide clarity on the identity of those substances which are permitted to be added to SPFYC.

[39] Nutricia's Application is seeking to add GOS and long-chain FOS in the ratio 9:1 and at a level of 0.8 g/100 mL to infant formula and infant foods.

[40] Numico is an international food manufacturer of specialised food products including the Nutricia brand of infant formula products and infant food.

9.3 Labelling requirements

9.3.1 Foods in the general food supply

Current labelling requirements for inulin-derived substances to food reside in Part 1.2 of the Code. Where no nutrition claim is made, added substances that are not already prescribed must be declared in the ingredient list and meet any relevant labelling requirements for the nutrition information panel (NIP).

9.3.1.1 Ingredient labelling

Submitters to the Draft Assessment Report have commented that the proposed definitions for inulin-derived substances, FOS, oligofructose and GOS in the drafting for Proposal P306 are inconsistent with internationally accepted definitions in the scientific literature. This inconsistency could impede attempts to provide uniformity on product labels, such as in ingredient lists. Particular concern was expressed over the interchangeablility of FOS and 'oligofructose' within the scientific literature.

The definitions of 'inulin-derived substances' and 'galacto-oligosaccharides' in the drafting (see Attachment 1) are not intended to act as prescriptive names for labelling purposes. Clause 4 of Standard 1.2.4 – Labelling of Ingredients allows for the declaration of ingredients in the statement of ingredients using either the common name of the ingredient or a name that describes the true nature of the ingredient. The current Editorial note to this clause provides further clarification by stating that the names of ingredients should be sufficiently detailed and accurate to ensure that that they are not false, misleading or deceptive, or likely to mislead or deceive.

FSANZ considers that the use of common terms for inulin-derived substances and GOS in ingredient lists will be sufficient to alert consumers to the presence of these substances in a food. For example, the generic term 'inulin' might be used in the ingredient list where inulin or long-chain inulin has been added to the food. Oligofructose or fructo-oligosaccharides could be used interchangeably. In both these instances, a consumer reading the ingredient list would be aware that an inulin-derived substance is present in the food, even if the common name term is not technically representative of the substance.

The limited variety of ingredient names for inulin-derived substances and GOS also ensures that there will be a degree of uniformity to the terminology used within ingredient lists.

Allowing the use of common names for inulin-derived substances and GOS is an approach that is consistent with the ingredient labelling practices of other countries. In a review of the international legal status of inulin and oligofructose[41] it was stated that 'inulin' is the generally accepted term in order to denote the presence of chicory inulin. It was also noted that the term 'fructo-oligosaccharides' was considered a synonym for oligofructose.

The review of the international legal status of inulin and oligofructose also states that where *…commercial products contain fractions of mono- and disaccharides, these sugars may need separate labelling. Native inulin and standard oligofructose products always contain some sugars, which can be considered as a normal part of the inulin or oligofructose.*

[41] Coussement, P. A. A., (1999). Inulin and Oligofructose: Safe Intakes and Legal Status. J. Nutr. 129: 1412S-1417S

Therefore, it has been legally accepted that these sugars do not have to be labelled specifically in most practical cases.

FSANZ supports this approach to ingredient labelling as it is consistent with current requirements in the Code. However, if mono- and di-saccharides were added to commercial preparations of inulin-derived substances prior to their use in a food, then these sugars will need to be declared separately in the statement of ingredients.

9.3.1.2 Nutrition information labelling and claims

Under the current Proposal, requirements for nutrition information labelling on general foods remain essentially unchanged.

Clause 5 of Standard 1.2.8 – Nutrition Information Requirements states that where a nutrition content claim is made for any other nutrient not already mandated, or a biologically active substance, the name and average quantity must be declared in the NIP in accordance with the prescribed format. Health claims about inulin-derived substances and GOS are not currently permitted under Standard 1.1A.2 – Transitional Standard for Health Claims.

If the food manufacturer makes a nutrition claim related to the presence of inulin-derived substances, then the content of these substances would need to be declared in the NIP. Subclause 5(5) of Standard 1.2.8 requires that where a nutrition claim is made about fibre, any specifically named fibre, sugars, or any other type of carbohydrate, a fibre declaration is then required in the NIP. Where a dietary fibre nutrition claim is made for an inulin-derived substance, the substance must be declared as a sub-sub-group nutrient, indented and nested under 'total dietary fibre'. Where a biologically active substance nutrition claim is made for an inulin-derived substance, the declaration of the claimed substance would appear in the NIP in accordance with format prescribed for biologically active substances in Standard 1.2.8.

Other nutrition labelling requirements in relation to the NIP, small packages and the form of the food, are covered in Division 2 of Standard 1.2.8 and apply to the substances being considered in this Proposal.

Clause 18 of Standard 1.2.8 notes that a declaration of dietary fibre in the NIP must be determined in accordance with the prescribed methods of analysis to determine total dietary fibre and specifically named fibre content of food. Established methods for the food components 'inulin and fructo-oligosaccharide', and 'inulin', are listed in the Table to clause 18(1). Clause 18 of Standard 1.2.8 notes that a declaration of dietary fibre in the NIP must be determined in accordance with the prescribed methods of analysis to determine total dietary fibre and specifically named fibre content of food. Established methods for the food components 'inulin and fructo-oligosaccharide', and 'inulin', are listed in the Table to clause 18(1). At Draft Assessment, FSANZ proposed changes to the terminology in this table. However at Final Assessment this change is no longer being recommended and has been removed from the draft variation.

FSANZ has recently recommended new regulations for nutrition, health and related claims, including a draft Standard 1.2.7, as part of Proposal P293 – Nutrition, Health & Related Claims. Within this context, general level health claims would be permitted for general foods containing inulin-derived substances subject to meeting substantiation requirements, the nutrient profiling scoring criteria and other requirements as detailed in draft Standard 1.2.7.

9.3.2 Infant-formula products

9.3.2.1 General labelling and packaging requirements

Specific labelling and packaging requirements for infant formula products are prescribed in Standard 2.9.1. In addition, the general labelling requirements under Part 1.2 of the Code, including Standard 1.2.4 also apply to these products, subject to any specified exemptions.

Under the current Proposal, permissions for the addition of inulin-derived substances and GOS to infant formula products will require specific declarations in the statement of ingredients.

9.3.2.2 Warning Statements

Clause 14 of Standard 2.9.1 prescribes specific warning statements that must be included in the label on a package of infant formula product. These statements refer to the importance of correctly following instructions for preparation, and for parents to seek advice from an appropriate health professional on a decision to use the product.

FSANZ has considered the need for a specific warning statement on infant formula products regarding the presence of inulin-derived substances and/or GOS and the possibility of any potential discomfort in some infants.

There is limited evidence that inulin-derived substances and/or GOS contribute to gastrointestinal discomfort during adaptation to a new formula, however this is not uncommon for infants who change formulations, and health professionals are likely to provide guidance on the management of any such effects (see section 8.2.4).

Also FSANZ's safety assessment (see Section 7.3 and Attachment 8) has concluded that the proposed amounts of inulin-derived substances and GOS are unlikely to pose a health and safety risk and that these amounts are less than the amounts found in breast milk.

Therefore, FSANZ considers mandating a specific warning statement regarding the presence of inulin-derived substances and/or GOS to be unnecessary. This approach was supported by those submitters who provided comment in relation to the need for a warning statement.

9.3.2.3 Nutrition information labelling

The intent of Standard 2.9.1 is to prohibit nutrition claims on infant formula products (with the exception of claims permitted under clauses 28 and 30). The rationale for this approach was provided in Proposal P93 – Review of Infant Formula, which resulted in Standard 2.9.1 of the joint Code. In the Supplementary Final Assessment Report for Proposal P93 (March 2002), FSANZ (formerly ANZFA) considered that:

> *The only reason for manufacturers to want to include any of these representations or declarations of nutrients in the label of an infant formula product is as a marketing tool. ANZFA does not consider it appropriate to use such information to market infant formula.*

The prohibition of representations of infant formula products is consistent with the requirements of the WHO International Code of Marketing of Breast Milk Substitutes and with the requirements of the MAIF agreement[42]. Inclusion of these provisions in the Food Standards Code makes them mandatory requirements and enforceable by law.

In addition, Transitional Standard 1.1A.2 specifically prohibits health claims from being made on infant formula products.

Several submitters expressed concern that the drafting of Standard 2.9.1 lacks clarity and that there is potential for infant formula products to make claims on the presence of inulin-derived substances and GOS in infant formula products. FSANZ has addressed these concerns as detailed below.

Clause 16 of Standard 2.9.1 regulates the declaration of nutrition information in the label on an infant formula product. FSANZ recommends that where inulin-derived substances and GOS are added voluntarily to infant formula products, a mandatory declaration of these substances will be required. This 'nutrition information statement' is intended to be a single statement which , together with the information required for energy, protein, fat, carbohydrate, and permitted vitamins and minerals and other nutritive substances, must contain the average amount of inulin-derived substances and/or GOS expressed as weight per 100 mL, and may be in the form of a table. As guidance, the Nutrition Information Table as provided in the 'Guidelines for Infant Formula Products' of Standard 2.9.1 has been amended to reflect how the presence of inulin-derived substances and GOS may be declared in accordance with the nutrition information statement requirements in clause 16.

Clause 20 of Standard 2.9.1 provides for claim prohibitions relevant to all infant formula products. Subclause 20(1)(f) prohibits a reference to the presence of a nutrient or nutritive substance except where it relates to the name of a low lactose or lactose free infant formula, or is in the ingredient list or the nutrition information statement. Clause 28 regulates claims on infant formula products formulated for metabolic, immunological, renal, hepatic or malabsorptive conditions. FSANZ recommends the insertion of a new subclause to clause 20 that will permit a reference to the presence of inulin-derived substances and GOS *only* in the statement of ingredients and the nutrition information statement.

Clause 20 will also be amended so that the reference to 'nutrition information statement' links back to Clause 16, where the provisions require the statement to contain specified nutrition information (see Attachment 1). This amendment prevents the term 'nutrition information statement' from being interpreted as referring to a claim.

The existing prohibition on nutrition claims would therefore extend to inulin-derived substances and GOS. Under Proposal P293, FSANZ is proposing to retain the prohibition of nutrition and health claims on infant formula products. Furthermore, the revised approach under draft Standard 1.2.7 is that the provisions for claims will not apply to Standard 2.9.1.

[42] The MAIF agreement is the Marketing in Australia of Infant Formulas: Manufacturers and Importers Agreement (May, 1992). Adopted as its Code of Conduct, the MAIF Agreement sets out the obligations of infant formula manufacturers and importers and it gives effect to the principles of the WHO Code.

Unless already permitted under Part 2.9 of the Code i.e. Standard 2.9.1, draft Standard 1.2.7 expressly prohibits nutrition content claims, general level and high level health claims, endorsements, dietary information and cause-related marketing statements for food on a label or in an advertisement for food. This means that the labelling provisions contained within Standard 2.9.1 will stand alone.

The majority of submitters who provided comment on FSANZ's proposed approach to the declaration of the presence if inulin-derived substances and/or GOS in infant formula products, supported this approach.

9.3.3 Infant foods

9.3.3.1 Ingredient labelling

Under existing Code requirements, Standard 1.2.4 applies to foods for infants as regulated in Standard 2.9.2 – Foods for Infants, with the exception of the requirement to declare compound ingredients.

FSANZ recommends that the addition of inulin-derived substances and GOS to foods for infants be permitted, where they must be declared in the ingredient list in accordance with the requirements in Standard 1.2.4.

9.3.3.2 Nutrition information labelling

At present, general requirements for nutrition information labelling under Standard 1.2.8 apply to food for infants, notwithstanding the exemptions from Standard 1.2.8 that are listed in clause 9 of Standard 2.9.2. Subclause 9(2) prescribes the format for the NIP, and overrides the provisions of Standard 1.2.8. General requirements for nutrition claims are prescribed under Standard 1.2.8; however, specific conditions in clauses 8 and 9 in Standard 2.9.2 will override these general requirements.

In response to the Draft Assessment Report, several submitters commented that claims relating to inulin-derived substances and GOS should not be made on the labels of foods regulated by Standard 2.9.2.

FSANZ, whilst acknowledging these comments, reaffirms the position that was taken in the Draft Assessment Report. As the current Proposal permits the addition of inulin-derived substances and GOS, existing labelling requirements under Standard 1.2.8 and Standard 2.9.2 will apply.

Draft Standard 1.2.7 will regulate permissions for nutrition content claims to be made for these substances on infant foods, as for general purpose foods. Where there is a direct inconsistency between requirements in draft Standard 1.2.7 and Standard 2.9.2, the latter would prevail to the extent of the inconsistency. General labelling provisions for nutrition claims in Standard 1.2.8 would also apply. Conditions for making a claim will depend on how inulin-derived substances are declared in the claim, that is, whether the property of the food is dietary fibre or an inulin-derived substance. Specific conditions apply for claims relating to dietary fibre and biologically active substances.

Infant foods are prohibited from carrying health claims under the existing requirements in the Code according to Standard 1.1A.2. However, under the draft Standard 1.2.7, health claims on infant foods will be permitted as for general purpose foods except that infant foods are to be exempted from having to meet the nutrient profiling scoring criteria. FSANZ considers that this exemption is appropriate because of the very specific compositional requirements of Standard 2.9.2.

9.3.4 Formulated supplementary foods for young children

9.3.4.1 Ingredient labelling

Under existing requirements, general labelling provisions contained within Standard 1.2.4 would apply to FSFYC, as regulated in Division 4 of Standard 2.9.3 – Formulated Meal Replacements and Formulated Supplementary Foods.

FSANZ recommends that the addition of inulin-derived substances and GOS to FSFYC be permitted, where they must be declared in the ingredient list in accordance with the requirements in Standard 1.2.4.

9.3.4.2 Nutrition information labelling

Current provisions in Division 4 of Standard 2.9.3 clause 7 regulate nutrition claims for vitamins and minerals in FSFYC. General labelling provisions for nutrition claims in Standard 1.2.8 would also apply. Where there is a direct inconsistency between nutrition labelling requirements in Standard 1.2.8 and in Standard 2.9.3, the latter would prevail to the extent of the inconsistency.

In response to the Draft Assessment Report, several submitters commented that claims relating to inulin-derived substances and GOS should not be made on the labels of FSFYC. Other comments indicated that if general level health claims were permitted, then the nutrient profile scoring criteria that have been proposed as part of Proposal P293 should not apply to these foods.

FSANZ acknowledges these comments and reaffirms the position that was taken in the Draft Assessment Report. FSANZ recommends the same approach to claims on FSFYC as for infant foods, whereby nutrition content claims about inulin-derived substances and GOS will be regulated under draft Standard 1.2.7, noting that where there is a direct inconsistency between requirements in draft Standard 1.2.7 and Standard 2.9.3, the latter would prevail to the extent of the inconsistency. General labelling provisions for nutrition claims in Standard 1.2.8 also apply where no conflict exists with Standard 2.9.3 (the provisions of Standard 2.9.3 override those of Standard 1.2.8). As for infant foods, conditions for making a claim will depend on how inulin-derived substances are declared in the claim. Specific conditions apply for claims relating to dietary fibre and biologically active substances.

FSFYC are not currently permitted to carry health claims according to Standard 1.1A.2. However, the introduction of draft Standard 1.2.7 will allow health claims on FSFYC in the same manner as for infant foods, and FSFYC to be exempt from the nutrient profiling scoring criteria because these foods have been specially formulated for specific purposes. FSFYC carrying health claims will be required to meet all other relevant requirements specified in draft Standard 1.2.7.

As noted for nutrition content claims, where there is a direct inconsistency between draft Standard 1.2.7 and Standard 2.9.3, the latter prevails to the extent of the inconsistency.

9.4 Enforcement

9.4.1 Regulatory Approach

Some submitters considered the different approach proposed for Standards 1.1.1 and for Standards 2.9.1, 2.9.2 and 2.9.3 with regard to the status of inulin-derived status and GOS, may not resolve the current uncertainty, and that the interim approach proposed at Draft Assessment would not provide clarity for enforcement.

Section 15 outlines FSANZ's rationale for the drafting approach at Final Assessment. Consistent with a section 36 proposal, this Proposal confines its consideration to resolving the current uncertainty surrounding the addition of inulin-derived substances to the general food supply (and some special purpose foods) and inulin-derived substances/FOS and GOS to special purpose foods for infants and young children. In this way, **the approach taken is considered an interim regulatory response.** FSANZ has taken an interim approach as it plans a future review of the definition of 'nutritive substances' and its application in the Code, in addition to a future review of Standard 2.9.1.

Therefore, for the purposes of this s36 proposal FSANZ has proposed:

- to amend Standard 1.1.1 to state that inulin-derived substances are taken not to be nutritive substances[43], and therefore do not need pre-market approval for addition to foods; and

- to amend Standards 2.9.1, 2.9.2 and 2.9.3 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, with maximum limits (refer to Section 9.2.2.1).

FSANZ considers these amendments will provide clarity for enforcement purposes at this time, as an interim regulatory measure, while not pre-empting the wider consideration of issues and outcome of the planned review of the definition of a nutritive substance and of Standard 2.9.1.

Further clarity which will assist enforcement has been provided through:

- consolidation of the definitions proposed at Draft Assessment (see Section 1.4 and Attachment 1); and

- amendments to Standard 2.9.1 to clarify the intent that a nutrition information statement means a single statement and that a reference to inulin-derived substances and GOS can only be made in this statement or in the list of ingredients (refer to Attachment 1).

[43] At Draft Assessment, FSANZ also included FOS in the proposed variation to Standard 1.1.1. However, recent information provided to FSANZ indicates that FOS is not widely used in the food supply; thus it has been excluded from the proposed draft variation to clause 9 of Standard 1.1.1.

9.4.2 Monitoring for compliance

Several submitters considered that suitable methods are not available for the measurement of inulin-derived substances in general foods. This issue is discussed further in the Chemical and Technical Assessment (Attachment 4).

FSANZ understands that methods have been published for determining the amount of inulin-derived substances in food. Ordinarily this would mean that compliance agencies and their appointed analysts could consider developing and validating their own methods that are suitable for monitoring compliance. FSANZ is not able to develop and validate methods for compliance agencies or their appointed analysts. In addition, methods have not been prescribed for the analysis of inulin-derived substances or galacto-oligosaccharides in infant foods and so compliance agencies could consider developing their own methods that are suitable for these matrices.

One point of potential confusion at Draft Assessment was the inclusion in the draft variation of an editorial change to the currently prescribed methods for determining fructose polymers in foods. This change was proposed to ensure that the terminology used in clause 18 of Standard 1.2.8 was the same as the terminology used in the AOAC method. It was not intended to indicate that this method would be prescribed for generally measuring fructose polymers in food and no change is now proposed to the terminology for the methods stated in clause 18 of Standard 1.2.8. In summary, compliance agencies and their appointed analysts can use any appropriate method for monitoring compliance with any requirements for fructose polymers in foods, except where it relates to nutrition labelling. In this case the methods prescribed in clause 18 of Standard 1.2.8 are to be used.

Given the uncertainty in relation to galacto-oligosaccharides in some milk-based foods, FSANZ considers that it is not appropriate to prescribe the Association of Official Analytical Chemists method for determining galacto-oligosaccharides. This approach will enable industry, compliance agencies and appointed analysts to continue to develop the methods to address any concerns with determining these substances in milk-based foods.

FSANZ has not sought expert analytical advice on the methods of analysis because methods are not prescribed for determining fructose polymers or galacto-oligosaccharides in food as part of this Proposal, and because the appropriateness of any method used for compliance purposes is not subject to any expert analytical advice obtained by FSANZ. In terms of methods of analysis, FSANZ acknowledges that compliance agencies may need time to develop compliance strategies, including validated methods with their appointed analysts.

9.5 Potential addition of FOS to SPFYC

Some submitters considered the proposed drafting could potentially result in the addition of FOS to SPFYC, as FOS is not specifically prohibited in SPFYC.

At Final Assessment, definitions as proposed at Draft Assessment have been consolidated (refer to Section 1.4). FOS (as defined in this Report) is excluded from the definition of inulin-derived substances. Therefore, at Final Assessment the proposed amendments to the Code that would permit the addition of inulin-derived substances to SPFYC exclude permission for the addition of FOS.

9.6 Pending reviews of Standard 2.9.1 and the definition of a nutritive substance.

Some submitters considered P306 should be deferred until the reviews of Standard 2.9.1 and the definition of a nutritive substance are completed.

As noted in Section 1.5 when developing and varying food standards, FSANZ must have regard to any written policy guidelines formulated by the Ministerial Council. The Ministerial Council recently agreed to develop policy guidance on the intent of Part 2.9 and on infant formula products. Once completed, these guidelines will inform the review of Standard 2.9.1.

The timing of the development of this policy guidance, or of the review of the definition of a nutritive substance is not yet known. Therefore, in the interest of responding to this regulatory matter in a timely manner, Proposal P306 was raised as an interim approach to address the current uncertainty.

9.7 Progression of Related Applications

Some submitters considered the progression of Application A609 – Addition of GOS, Long-chain Inulin to Infant Formula Products & Infant Food, at the same time as P306 to be confusing as they offer a significantly different option, and queried which will take precedence. FSANZ acknowledges the potential to create confusion but is bound by statutory timeframes on progressing Application A609.

FSANZ prepared Proposal P306 in response to regularity uncertainty amongst industry, manufacturers and the general public. Proposal P306 intends to clarify the current situation for both general purpose foods and SPFYC. Application A609 is a paid application, lodged after work on the Proposal had commenced. FSANZ has a statutory obligation to progress A609 within the legislated timelines. In accordance with the FSANZ Act and the direction of the FSANZ Board, the Proposal will take precedence.

9.8 Alignment with the Codex Alimentarius Standard for Infant Formula

Some submitters considered that Proposal P306 does not align with the Codex approach, specifically that the suitability for particular nutritional uses for infants should be scientifically demonstrated, that infant formula should mimic the levels in and effects of breast milk, provide sufficient amounts to achieve the intended effect, or provide other benefits similar to the outcome of breastfed infants. One submitter also referred to the EU Directive 2006/141/EC noting Article 5 refers to a systematic review of expected benefits in the assessment process.

FSANZ seeks to harmonise with international regulations whenever possible. However, as there are currently no Ministerial Policy Guidelines in place on the addition of substances to SPFYC, FSANZ has, in accordance with its statutory objectives, confined the risk assessment to considering safety as well as nutritional equivalence with breast milk as assessed by comparable physiological and microbiological effects.

FSANZ's assessment of nutritional equivalence to breast milk estimated that exclusively breastfed three month old infants would consume 12 g/day of 'human milk oligosaccharides' and infants consuming formula containing up to 8 g/L of inulin-derived substances and GOS would consume an estimated 6 g/day.

FSANZ's assessment found that at levels up to 10 g/L there is evidence of similar physiological (softer stools and increased stool frequency) and microbiological effects (increased growth of colonic bifidobacteria) in some studies comparing breastfed and formula fed infants.

Further information is provided in Sections – 7.2, 7.2.2 and 7.3.2

10. Regulatory options

10.1 Inulin-derived substances added to the general food supply

Two regulatory options have been identified at Final Assessment.

Option 1 – the *status quo* – reject the proposal, thus maintaining whereby there would be no explicit permissions for the addition of inulin-derived substances in food.

Option 2 – amend the Code to insert a clause in Standard 1.1.1 to the effect that inulin-derived substances are taken not to be nutritive substances, and therefore do not need explicit permissions for addition to food.

10.2 Inulin-derived substances and GOS added to special purpose foods for infants and young children

Two regulatory options have been identified at Final Assessment.

Option 1 – the *status quo* – reject the proposal, thus maintaining whereby there would be no explicit permissions for the addition of inulin-derived substances and GOS to infant formula products, infant foods and FSFYC.

Option 2 – amend Standard 2.9.1 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant formula products to a total maximum of 290 mg/100 kJ (8 g/L); and amend Standards 2.9.2 and 2.9.3 Division 4 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant foods and FSFYC to a total maximum of 0.8 g/100 g and 1.6 g/serve (8 g/L), respectively.

11. Impact Analysis

11.1 Affected Parties

The parties likely to be affected by the Application are:

- consumers of foods with added inulin-derived substances and GOS, including infants and young children who consume infant formula products, infant foods and FSFYC;
- carers of infants and toddlers consuming infant formula products, infant foods and FSFYC;

- manufacturers and / or marketers of specialty ingredients for application in foods (with added inulin-derived substances) and/or infant formula products, infant foods and FSFYC (industry);

- manufacturers, importers and exporters of foods with added inulin-derived substances, and infant formula products, infant foods and FSFYC with added inulin-derived substances and GOS (industry); and

- the Governments of the Australian States and Territories and New Zealand.

11.2 Benefit Cost Analysis

11.2.1 Foods in the general food supply

11.2.1.1 Consumers

Status Quo: maintaining the *status quo* for the general food supply is unlikely to have any significant impact on consumers. Based on their history of safe use, foods with added inulin-derived substances currently available on the market will not present a safety concern for consumers. Any potential advantage consumers may receive from the addition of inulin-derived substances will continue to be provided. However, if consumers are aware of the current uncertainty regarding the status of these substances, any uncertainty or confusion they may have regarding their use in foods could remain. Also, if the regulatory uncertainty causes manufacturers to reformulate or remove products that currently contain inulin-derived substances from the market, product choice and any potential benefits to consumers may decrease.

Option 2 would enable foods with added inulin-derived substances to continue to be manufactured and be available to consumers and, based on their history of safe use, will not present safety concerns for consumers. Any potential benefits consumers may receive from the addition of inulin-derived substances to foods will continue to be provided.

11.2.1.2 Industry

Status Quo: Maintaining the *status quo* for the general food supply would not confirm the regulatory position for the food industry around the use of inulin-derived substances in general foods. The current uncertainty amongst food manufacturers and suppliers of inulin-derived substances would continue. Manufacturers adding inulin-derived substances to foods would continue to be unsure if their products comply with the Code and potential enforcement action could remain a concern. The potential need to make compositional and labelling changes to products, with associated costs would also remain a concern for manufacturers.

Suppliers of inulin-derived substances would also remain uncertain as to the status of these substances with negative financial impact should manufacturers decide to reformulate their products without adding these substances.

A lack of clarity regarding the status of inulin-derived substances in general foods and uncertainty regarding compliance with the Code may also result in trade difficulties and create barriers to export in some instances.

Option 2 would confirm the regulatory position for food manufacturers and suppliers of inulin-derived substances. The manufacture of food products currently containing inulin-derived substances could continue for both the domestic and overseas market, thus reducing potential barriers to trade. This would also avoid the financial implications of having to reformulate and re-label products, for food manufacturers and suppliers of inulin-derived substances. Option 2 would also support product innovation for manufacturers.

11.2.1.3 Government

Maintaining the ***status quo*** may require enforcement agencies to determine whether they consider manufacturers of foods with added inulin-derived substances to be in breach of the Code. Option 2 provides clarity at this time that inulin-derived substances do not need express permission for addition to foods in the general food supply.

11.2.2 Special purpose foods for infants and young children

11.2.2.1 Consumers / carers

Maintaining the ***status quo*** for special purpose foods for infants and young children would not have a significant impact on consumers and their carers as suitable foods for this age group would continue to be available. However, any potential benefit provided by the addition of inulin-derived substances and GOS to these products would not be available to formula-fed infants, and toddlers. Also, carers of infants and toddlers may be confused as to the safety of these substances which could affect confidence and trust in infant formula products, infant foods and FSFYC, and therefore the industry as a whole.

Option 2 would provide consumers and their carers with an additional choice of special purpose foods for infants and young children and enable them to receive any potential advantages from the addition of inulin-derived substances and GOS. Option 2 would also clarify the safety of these products and maintain consumer confidence in infant formula products, infant foods and FSFYC.

These products with added inulin-derived substances and GOS may incur additional costs for consumers as any extra manufacturing costs may be passed on to consumers who purchase the products.

11.2.2.2 Industry

Maintaining the ***status quo*** would not confirm the regulatory position for the food industry around the status of inulin-derived substances and GOS in infant formula products, infant foods and FSFYC and uncertainty amongst manufacturers would remain.

Maintaining the *status quo* could limit the options to manufacture products which are suitable for both the local and overseas market as regulations would not harmonise with some countries, such as European Union countries.

Manufacturers may need to manufacture separate products for internal and external markets affecting economies of scale and therefore manufacturing costs.

In some instances, the status quo could impact on trade opportunities by restricting the ability to export products to countries that permit the addition of inulin-derived substances and GOS. Industry has noted that some countries will not accept/register products that do not comply with local regulations, for example some Asian countries. This would result in lost markets for those manufacturers with financial implications. Some manufacturers may need to reformulate products to meet overseas requirements causing additional costs.

Also, the *status quo* would not encourage innovation in product development.

Option 2 would confirm the regulatory position for manufacturers, and for suppliers of inulin-derived substances and GOS, by providing explicit permission (with limits) for the addition of these substances to infant formula products, infant foods and FSFYC.

Alignment with international regulations would allow for the single formulation and manufacture of products for both local and overseas markets maximising production costs and reducing barriers to trade.

In addition, **Option 2** is likely to maintain the trust of consumers in the infant formula and infant food industry.

Option 2 would potentially support product innovation for manufacturers of infant formula products. However, the intellectual property position held by Numico (see Section 9.2.2.2, including patents in relation to a specified ratio, may limit product innovation. Manufacturers would need to make their own enquiries and consider this in the development of new products.

11.2.2.3 Government

Maintaining the ***status quo*** may require enforcement agencies to determine whether manufacturers of special purpose foods for infants and young children are in breach of the Code should they add inulin-derived substances or GOS to these products.

Option 2 by providing explicit permissions for the addition of inulin-derived substances and GOS (with limits) to special purpose foods for infants and young children, will confirm the regulatory position for enforcement agencies at this time.

11.3 Comparison of Options

11.3.1 Foods in the general food supply

A comparison of the Options presented at Final Assessment indicates that maintaining the ***status quo*** (Option 1) would present no safety concerns for consumers as inulin-derived substances have a history of safe use in the general food supply.

However, maintaining the *status quo* would not provide certainty for manufacturers of foods, suppliers of inulin-derived substances and enforcement agencies. Potential enforcement action, reformulation and re-labelling of products and possible trade barriers could result in additional costs for food manufacturers and suppliers.

In comparison, **Option 2** also presents no safety concerns for consumers as inulin-derived substances have a history of safe use in the general food supply.

In addition, Option 2 would confirm the regulatory position for the food industry by clarifying the status of inulin-derived substances in foods and would avoid any negative financial impacts for both manufacturers and suppliers, and reduce any trade barriers.

The analysis of potential impacts, in conjunction with the history of safe use in the general food supply indicates that an overall net-benefit is achieved through **Option 2**.

11.3.2 Special purpose foods for infants and young children

A comparison of the Options presented at Draft Assessment indicates that maintaining the ***status quo*** (Option 1) would present no safety concerns for consumers as infant formula products, infant foods and FSFYC will remain available for infants and toddlers.

However, maintaining the *status quo* would not clarify the situation for consumers and their carers, or confirm the regulatory position for manufacturers and suppliers of inulin-derived substances and GOS, or enforcement agencies. Uncertainty would remain with negative financial, trade and potential enforcement implications for industry, lack of regulatory clarity regarding enforcement, and reduced choice for consumers. Also there may be a loss of consumer confidence in manufacturers of infant formula products, infant foods and FSFYC.

In comparison, **Option 2** also presents no safety concerns for infants or toddlers.

In addition, Option 2 would provide consumers with choice and is likely to maintain confidence in the safety of infant formula products, infant foods and FSFYC. Option 2 would reduce potential trade barriers, support cost-effective production through harmonisation with overseas regulations, support product innovation and avoid potential enforcement action. Also, the regulatory position would be confirmed for enforcement agencies regarding the need for any enforcement action in the future.

The analysis of potential impacts, in conjunction with the safety assessment indicates that an overall net-benefit is achieved through Option 2.

COMMUNICATION AND CONSULTATION STRATEGY

12. Communication

The issue of substances added to infant formula products is of public interest. The communication strategy for Proposal P306 aims to ensure relevant industry stakeholders, consumers, health professionals and jurisdictions are aware of any changes to the Code which may result from this Proposal. A range of communication channels and activities are available to provide appropriate information.

FSANZ undertook targeted communication on the proposed variation to the Code with key stakeholders.

Information regarding the changes to the Code will be provided on the FSANZ website and for the FSANZ Code Inquiry Line, particularly regarding the proposed permissions for addition of inulin-derived substances and GOS to special purpose foods for infants and young children. This will ensure consumers and health professionals have access to appropriate information.

FSANZ has reviewed the nature of the feedback received from submitters at Draft Assessment, and determined no additional communication strategies are required for the Final Assessment.

13. Consultation

FSANZ decided, pursuant to section 36 of the FSANZ Act (as was in force prior to 1 July 2007) to omit one round of public submissions prior to making a Draft Assessment of this Proposal. FSANZ made its decision under section 36 because it was satisfied that the Proposal raised issues that will not have a significant adverse effect on the interests of anyone. However, FSANZ undertook early targeted consultation with key stakeholders to assist in preparing the Draft Assessment.

The Draft Assessment Report was released for a public consultation period of approximately eight weeks from 21 December 2007 until 22 February 2008. In response to the Draft Assessment Report FSANZ received a total of 30 submissions.

Twenty-two submissions were received from the food industry, six from government agencies, one from a health professional organisation and one from a consumer group.

Submitters tended to provide separate comments in relation to the general food supply and SPFYC.

13.1 The general food supply and proposed amendments to Standard 1.1.1

In general, for the approach taken to the general food supply, submitters, including a majority of industry submitters, favoured amending Standard 1.1.1 to permit the addition of inulin-derived substances and FOS. However, nearly half of these recommended FSANZ reconsider aspects of the amendment as proposed.

Government submitters presented mixed views regarding their preferred approach including one with no stated preference.

The remaining submitters presented a divergent view, and of the total submitters overall, several did not indicate a preferred regulatory Option.

13.2 SPFYC and proposed amendments to Standards 2.9.1, 2.9.2 and 2.9.3

Twenty three of the total submissions received provided comment on the proposed amendments to the standards relating to SPFYC.

Submitters views were mixed in relation to the regulatory options proposed at Draft Assessment. Just over half of those commenting on SPFYC supported amending the Code to permit inulin-derived substances and GOS to SPFYC.

However of these, half recommended modifications to the amendments as proposed at Draft Assessment e.g. alternative definitions, reconsideration of levels and modifications to the proposed variation to the Code.

Several submitters preferred to maintain the status quo. Two submitters did not support either Option as presented at Draft Assessment, and several raised issues with regard to SPFYC but did not state a preferred Option.

Key issues raised in submissions have been addressed in this Final Assessment Report where possible, or in Attachment 3, and include:

- the need for clarification and consistency of definitions;
- the differing regulatory approaches proposed for general foods (Standard 1.1.1) and SPFYC (Standards 2.9.1, 2.9.2 and 2.9.3):
- the potential for FOS to be added to SPFYC;
- insufficient evidence to demonstrate benefit / efficacy in SPFYC;
- lack of alignment with the Codex Alimentarius Standard for Infant Feeding, and the EU Directive i.e. in relation to mimicking the effect of breast milk, providing sufficient amounts to achieve the intended effect, or providing benefits similar to the outcome of breastfed infants, and the assessment of benefit;
- the need for safety evidence in relation to the singular addition of these substances or the addition in a range of ratios;
- the extrapolation of data from infant formula to infant foods and formulated supplementary foods for children;
- a recommendation to include GOS in the amendment to Standard 1.1.1;
- the need for clarity in Standard 2.9.1 in relation to labelling and the potential for claims on infant formula products;
- the lack of suitable analytical methods of measurement for compliance and enforcement purposes;
- the need for an education / communication strategy;
- the lack of Ministerial policy guidance on the addition of substances to SPFYC; and
- the pending reviews of Standard 2.9.1 and the definition of a nutritive substance.

13.3 Targeted consultation

At Final Assessment, additional targeted consultation has been undertaken with representatives from the Australian (State and Territory) and New Zealand Governments and key manufacturers of infant formula products.

Specifically, Jurisdictional meetings were held to discuss the regulatory approach to the assessment of substances in infant formula products. In addition, one-to-one meetings with representatives from each jurisdiction were undertaken to discuss the regulatory approach taken at Final Assessment for this Proposal, and also to discuss FSANZ's consideration of issues raised at Draft Assessment.

13.4 World Trade Organization

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

As the proposed amendments to the Code would be voluntary permissions, it is expected they will harmonise Australian and New Zealand regulations with relevant current international practices, and therefore will not result in a potential barrier to trade. As such, it was decided that it was not necessary to notify the proposed amendments under either the Technical Barriers to Trade or Sanitary and Phytosanitary Agreements.

CONCLUSION AND DECISION

14. Conclusion and Decision

Decision

At Final Assessment, FSANZ approves the following variations to the Code:

- to amend Standard 1.1.1 to state that inulin-derived substances are taken not to be nutritive substances;
- to amend Standard 2.9.1 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant formula products to a total maximum of 290 mg/100 kJ (0.8 g/100 mL);
- to amend Standards 2.9.2 and 2.9.3 Division 4 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant foods and formulated supplementary foods for young children up to a total maximum of 0.8 g/100 g and 1.6 g/serve (0.8 g/100 mL), respectively; and
- additional consequential amendments to Standard 2.9.1 to clarify intent on the prohibition of nutrition claims on infant formula products.

FSANZ concludes that the preferred approach provides a net benefit to affected parties because:

14.1 General food supply

- There is a history of safe use of inulin-derived substances in food in Australia and New Zealand, so food manufacturers do not need express permission to add these substances to the general food supply.

- The proposed variations to the Code confirm the regulatory position for the food industry by clarifying the status of inulin-derived substances in the general food supply. This approach means the manufacture of food products currently containing inulin-derived substances can continue for both the domestic and overseas market, thus reducing potential barriers to trade. This will also avoid the financial implications for food manufacturers and suppliers of having to reformulate and re-label products.

14.2 Special purpose foods for infants and young children

- Based on the available evidence, FSANZ concludes that infant and follow-on formula containing up to 8 g/ L of inulin-derived substances and/or GOS, singularly or combined, in any ratio, are unlikely to pose a risk to infants.

- For older young children, infant foods and toddler formula and infant foods do not represent the sole source of nutrition. Based on the available evidence, FSANZ concludes that infant foods and/or toddler formula containing up to 8 g/ L inulin-derived substances and/or GOS, singularly or combined, in any ratio are unlikely to pose a risk to older infants and toddlers.

- There is insufficient evidence to assess the effects of adding FOS (as defined in this Report) to infant formula products, thus the permission for the addition of FOS to special purpose foods for infants and young children is not included in this Proposal.

- The recommended maximum levels of inulin-derived substances and/or GOS permitted to be added to infant formula products are consistent with those evaluated in clinical trials and are less than the levels of human milk oligosaccharides found in breast milk (up to 25 g/L).

- There is evidence that addition of inulin-derived substances and GOS and inulin-derived substances alone up to 10 g/L, added to infant formula products result in similar physiological i.e. softer consistency and lower pH of stools; and microbiological effects i.e. selective growth stimulation of intestinal Bifidobacterium to that of breastfed infants. There is insufficient evidence on the addition of GOS alone to draw conclusions.

- Providing express permissions for the addition of inulin-derived substances and GOS provides consumer choice and will likely maintain confidence in the safety of infant formula products, infant foods and toddler formula.

- The proposed approach also confirms the regulatory position for the food industry, thereby reducing potential trade barriers, supporting cost-effective production through harmonisation with overseas regulations, and supporting innovation.

- Furthermore, the proposed approach provides certainty for enforcement agencies in Australia and New Zealand by:

  - providing explicit permissions for the addition of inulin-derived substances and GOS (excluding FOS) to special purpose foods for infants and young children; and
  - clarifying the intent of Standard 2.9.1 in prohibiting nutrition claims on infant formula products.

FSANZ therefore approves the draft variations to the Code as provided at Attachment 1.

15. Rationale for preferred drafting approach

FSANZ has, within the context of the Code, previously considered that inulin-derived substances, FOS and GOS when used in foods for infants and young children as regulated under Part 2.9 – Special Purpose Foods, are 'nutritive substances' within the definition of that term in Standard 1.1.1 as a means of requiring pre-market assessment of foods for these vulnerable population groups.

However, for the purposes of this s36 Proposal, FSANZ has drafted the variations to the respective standards in Part 2.9, in a manner that ensures safety of permitting the addition of inulin-derived substances and GOS to infant formula products, infant foods and FSFYC but does not at this time adopt a position either way on the status of inulin-derived substances and GOS when added to SPFYC.

Therefore, for the draft variation to Standard 2.9.1, FSANZ has placed the reference to inulin-derived substances and GOS, with corresponding permissions, in a stand-alone provision (new clause 9A) rather than in the Table to clause 7 (which lists a number of permitted nutritive substances). **This drafting approach should not be taken to mean that inulin-derived substances and GOS in infant formula products under Standard 2.9.1 are not 'nutritive substances'**.

This interim approach has been taken because FSANZ plans to consider the issues more broadly by undertaking a review of the definition of 'nutritive substances' and its application to the Code, and a review of Standard 2.9.1 – Infant Formula Products. As noted in Section 1.5 the Ministerial Council recently agreed to develop policy guidance on the intent of Part 2.9. The timing of the development of this policy guidance is not yet known. Therefore, FSANZ considers the amendments proposed at Final Assessment have been drafted to provide regulatory clarity at this time, while not pre-empting the outcome of the Ministerial Council policy development and the future reviews of the definition of 'nutritive substances' and the infant formula products standard.

Furthermore, in relation to the proposed draft variation to Standard 1.1.1, **inulin-derived substances are taken not to be nutritive substances** and therefore requiring no pre-market approval when added to general foods. This is based on a history of safe use in Australia and New Zealand over many years and recognises the status of inulin-derived substances as fulfilling both a technological and nutritional purpose in general foods.

Standard 1.1.1 sets out the general application and interpretation provisions which apply to the Code. Each standard then contains provisions specific to that individual standard. As a general rule, direct inconsistency between Standard 1.1.1 and a specific clause in another standard would see the requirements of the specific standard override Standard 1.1.1 to the extent of the inconsistency.

Thus, the approach to drafting proposed by FSANZ also ensures that reference to inulin-derived substances in Standard 1.1.1 and in Standards 2.9.1, 2.9.2 and 2.9.3 are not being treated differently in the Code, at this point in time.

FOS (as defined in the Report) and GOS are not widely added to the general food supply in Australia and New Zealand at this point in time. As such, and in keeping with minimal effective regulation and the restricted approach to this section 36 Proposal, FSANZ has not proposed the regulation of FOS in food at this time.

In addition, in the drafting at Draft Assessment, the new subclause 2(3) was added to Standard 2.9.2. For clarity in the Final Assessment this has been renumbered to subclause 2(4), there has been subsequent re-numbering of clause 2 in Standard 2.9.2.

16. Implementation and Review

Following consideration and approval of the draft variations to the Code by the FSANZ Board, notification of the Boards' decision will be made to the Ministerial Council. Subject to any request from the Ministerial Council for a review of the decision, the amendments to the Code with respect to Standards 1.1.1, 2.9.1, 2.9.2 and 2.9.3 Division 4 will come into effect upon gazettal.

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ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Summary of Submissions
3. Response to Key Issues Raised
4. Chemical and Technological Uses Assessment
5. Human Milk Carbohydrates
6. Microbiological Assessment
7. Nutrition Assessment
8. Safety Assessment
9. Dietary Intake Assessment

Attachment 1

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

Standards or variations to standards are considered to be legislative instruments for the purposes of the Legislative Instruments Act (2003) and are not subject to disallowance or sunsetting.

To commence: on gazettal

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

[1.1] *inserting in clause 2 –*

galacto-oligosaccharides means a mixture of those substances produced from lactose by enzymatic action, comprised of between two and eight saccharide units, with one of these units being a terminal glucose and the remaining saccharide units being galactose, and disaccharides comprised of two units of galactose.

inulin-derived substances means mixtures of polymers of fructose with predominantly β (2→1) fructosyl-fructose linkages, with or without a terminal glucose molecule and includes inulin, but does not include those polymers of fructose produced from sucrose by enzymatic action.

[1.2] *inserting after clause 9 –*

9A Certain substances not nutritive substances

Inulin-derived substances are taken not to be nutritive substances.

[2] ***Standard 2.9.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting after clause 9 –*

9A Permitted inulin-derived substances and galacto-oligosaccharides

(1) Infant formula product may contain no more than –

(a) 290 mg per 100 kJ of inulin-derived substances; or
(b) 290 mg per 100 kJ of galacto-oligosaccharides; or
(c) 290 mg per 100 kJ of combined inulin-derived substances and galacto-oligosaccharides.

(2) For subclause (1) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally occurring and the added substances.

[2.2] *omitting paragraph 16(1)(c), substituting –*

(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL; and

(d) when added, the average amount of –

(i) a combination of inulin-derived substances and galacto-oligosaccharides; or
(ii) inulin-derived substances; or
(iii) galacto-oligosaccharides

expressed in weight per 100 mL.

[2.3] *omitting paragraph 16(2)(d), substituting –*

(d) a declaration –

(i) of the weight of one scoop in the case of powdered infant formula; and
(ii) of the proportion of powder or concentrate required to reconstitute the formula according to directions; and

(e) when added, the average amount of –

(i) a combination of inulin-derived substances and galacto-oligosaccharides; or
(ii) inulin-derived substances; or
(iii) galacto-oligosaccharides

expressed in weight per 100 mL.

[2.4] *omitting clause 20, substituting –*

(1) The label on a package of infant formula product must not contain -

(a) a picture of an infant; or
(b) a picture that idealises the use of infant formula product; or
(c) the word 'humanised' or 'maternalised' or any word or words having the same or similar effect; or
(d) words claiming that the formula is suitable for all infants; or
(e) information relating to the nutritional content of human milk; or
(f) subject to clause 28, a reference to the presence of any nutrient or nutritive substance, except for a reference to a nutrient or nutritive substance in –

(i) clause 30 – claims relating to lactose free formula or low lactose formula; or
(ii) Standard 1.2.4 – labelling of ingredients; or
(iii) clause 16-declaration of nutrition information; or

(g) subject to Division 3, a representation that the food is suitable for a particular condition, disease or disorder.

(2) Subject to clause 28, the label on a package of infant formula product must not contain a reference to inulin-derived substances or galacto-oligosaccharides except for a reference to either substances in –

(a) a statement of ingredients; or
(b) the nutrition information statement.

[2.5] *omitting the* Nutrition Information *table in the* Guidelines for Infant Formula Products, *substituting* –

NUTRITION INFORMATION

	Average amount per 100 mL made up formula *1	**Average amount per 100 g of powder (or per 100 mL for liquid concentrate)** *2
Energy	kJ	kJ
Protein	g	g
Fat	g	g
Carbohydrate	g	g
Vitamin A	µg	µg
Vitamin B_6	µg	µg
Vitamin B_{12}	µg	µg
Vitamin C	mg	mg
Vitamin D	µg	µg
Vitamin E	µg	µg
Vitamin K	µg	µg
Biotin	µg	µg
Niacin	mg	mg
Folate	µg	µg
Pantothenic acid	µg	µg
Riboflavin	µg	µg
Thiamin	µg	µg
Calcium	mg	mg
Copper	µg	µg
Iodine	µg	µg
Iron	mg	mg
Magnesium	mg	mg
Manganese	µg	µg
Phosphorus	mg	mg
Selenium	µg	µg
Zinc	mg	mg
Chloride	mg	mg
Potassium	mg	mg
Sodium	mg	mg
(insert any other nutritive substance or inulin-derived substances and galacto-oligosaccharides to be declared)	g, mg, µg	g, mg, µg

***1** – Delete the words 'made up formula' in the case of formulas sold in 'ready to drink' form.
***2** – Delete this column in the case of formulas sold in 'ready to drink' form.

[2.6] *deleting the* Note *at the end of the* Nutrition Information *table in the* Guidelines for Infant Formula Products

[3] ***Standard 2.9.2*** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *omitting paragraph 2(2)(b*) *substituting –*

(b) lactic acid producing cultures; and
(c) either singularly or in combination, no more than 0.8g/ 100 g of inulin-derived substances and galacto-oligosaccharides, as consumed.

(3) For paragraph 2(2)(c) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally occurring and the added substances.

[3.2] *omitting subclause 2(3), the heading to the* Table to paragraph 2(3)(c)*, substituting –*

(4) Food for infants must not contain –

(a) more than 50 mg/100 g of total iron in cereal-based food on a moisture free basis; or
(b) honey, unless it has been treated to inactivate *Clostridium botulinum* spores; or
(c) more than the total quantity of sodium set out in column 2 of the Table to this paragraph for each particular type of food for infants; or
(d) added salt, in the case of ready-to-eat fruit-based foods, fruit drink and vegetable juice.

Table to paragraph 2(4)(c)

[3.3] *omitting subclause 2(4)* and the Editorial note, *substituting –*

(5) Food for infants intended for infants under the age of 6 months must be formulated and manufactured to a consistency that minimises the risk of choking.

Editorial note:

The intent of subclause (5) is to ensure that the food, except in the case of rusks, should have a texture that is soft and free of lumps.

[4] ***Standard 2.9.3*** *of the Australia New Zealand Food Standards Code is varied by –*

[4.1] *inserting in clause 6 –*

(4) Formulated supplementary foods for young children may contain singularly or in combination, no more than 1.6 g of inulin-derived substances and galacto-oligosaccharides per serving.

(5) For subclause 6(4) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally-occurring and the added substances.

Attachment 2

Summary of submissions from the Draft Assessment Report

Executive Summary

In February 2008, FSANZ received 30 submissions in response to the Draft Assessment Report for Proposal P306-Addition of Inulin/FOS and GOS to Food**.**

At Draft Assessment, the following regulatory options were proposed:

Inulin-derived substances and FOS added to the general food supply

Option 1 – the *status quo* – maintain the Code whereby there are no explicit permissions for the addition of inulin-derived substances and FOS in food.

Option 2 – amend the Code to insert a clause in Standard 1.1.1 to the effect that inulin-derived substances and FOS are taken to not be nutritive substances, and therefore do not need explicit permissions for addition to food.

Inulin-derived substances and GOS added to special purpose foods for infants and young children

Option 1 – the *status quo* – maintain the Code whereby there are no explicit permissions for the addition of inulin-derived substances and GOS to infant formula products, infant foods and FSFYC.

Option 2 – amend Standard 2.9.1 to permit the voluntary addition of inulin-derived substances to a maximum of 110 mg/100 kJ (0.3 g/100 mL), or GOS to a maximum of 290 mg/100 kJ (0.8 g/100 g), or a combination of inulin-derived substances and GOS up to a total maximum of 290 mg/100 kJ (0.8 g/100 g) where inulin-derived substances do not exceed 110 mg/100 kJ (0.3 g/100 mL); and amend Standards 2.9.2 and 2.9.3 Division 4 to permit the voluntary addition of inulin-derived substances and GOS, alone or in combination, to infant foods and FSFYC to a total maximum of 0.8 g/100 g and 1.6 g/serve (0.8 g/100 mL), respectively.

The public consultation period for the Draft Assessment Report was approximately eight weeks long, from 21 December 2007 until 22 February 2008. Twenty-two submissions were received from the food industry, six from Government agencies, one from a health professional organisation and one from a consumer group.

Submitters tended to provide separate comments in relation to the general food supply and SPFYC.

The general food supply and proposed amendments to Standard 1.1.1

For the approach taken to the general food supply, in general, submitters including a majority of industry submitters favoured amending Standard 1.1.1 to permit the addition of inulin-derived substances and FOS. However, nearly half of these recommended FSANZ reconsider aspects of the amendment as proposed.

Government submitters presented mixed views regarding their preferred approach including one with no stated preference.

The remaining submitters presented a divergent view, and of the total submitters overall, several did not indicate a preferred regulatory Option.

SPFYC and proposed amendments to Standards 2.9.1, 2.9.2 and 2.9.3

Twenty-three of the total submissions received provided comment on the proposed amendments to the standards relating to SPFYC.

Submitters views were mixed in relation to the regulatory options proposed at Draft Assessment. Just over half of those commenting on SPFYC supported amending the Code to permit inulin-derived substances and GOS to SPFYC. However of these, half recommended modifications to the amendments as proposed at Draft Assessment e.g. alternative definitions, reconsideration of levels and modifications to the proposed variation to the Code.

Several submitters preferred to maintain the *status quo*. Two submitters did not support either Option as presented at Draft Assessment, and several raised issues with regard to SPFYC but did not state a preferred Option.

KEY ISSUES IDENTIFIED FROM SUBMISSIONS

Key issues raised in submissions have been addressed in the Final Assessment Report where possible, or in Attachment 3 and include:

- the need for clarification and consistency of definitions;
- the differing regulatory approaches proposed for general foods (Standard 1.1.1) and SPFYC (Standards 2.9.1, 2.9.2 and 2.9.3);
- the potential for FOS to be added to SPFYC;
- insufficient evidence to demonstrate benefit / efficacy in SPFYC;
- lack of alignment with the Codex Alimentarius Standard for Infant Feeding i.e. in relation to mimicking the effect of breast milk, sufficient amounts to achieve the intended effect and substantiation of benefit;
- insufficient safety evidence in relation to the singular addition of these substances or the addition in a range of ratios;
- the extrapolation of data from infant formula to infant foods and formulated supplementary foods for children;
- a recommendation to include GOS in the amendment to Standard 1.1.1;
- the need for clarity in Standard 2.9.1 in relation to labelling and the potential for claims on infant formula products;
- the lack of suitable methods for the measurement of inulin-derived substances in general foods for compliance and enforcement purposes;
- the need for an education / communication strategy;
- the lack of Ministerial policy guidance on the addition of substances to SPFYC; and
- the pending reviews of Standard 2.9.1 and the definition of a nutritive substance.

Submitter	Submission comments
Government	
South Australian Department of Health Joanne Cammans	**General purpose foods**: does not support the proposed amendment to Standard 1.1.1. **Special purpose foods for young children** (SPFYC): Supports Option 1. *Regulatory approach* **General purpose foods** Supports clarification of the status of inulin-derived substances in general foods and recommends it be permitted for continued use. Suggests inulin-derived substances and FOS should be considered nutritive substance in general foods (in line with the approach to lutein as a nutritive substance). Considers the approach that these substances are taken not to be nutritive substances is inaccurate and contradicts the drafting approach taken for infant formula products. Queries could they be considered additives or biologically active ingredients for general foods. Considers there are potential enforcement issues when accepting these substances not to be nutritive substances in general foods without the same approach in Standard 2.9.1. Considers the drafting approach could allow manufacturers to add FOS without limits in SPFYC. **SPFYC** Does not support further consideration of regulatory amendments suggested in this proposal until the efficacy of adding these substances has been assessed. *Benefit / efficacy* Considers assessment of benefit is crucial where a substance is added for the specific purpose of giving a nutritional benefit especially for a vulnerable population. Proceeding solely on the grounds that there are no safety concerns is not sufficient. *Comparison to breast milk* Considers the proposal does not align with Codex as it does not substantiate benefit or mimic levels of substances found in breast milk. Notes lack of persuasive evidence to support the role of GOS or inulin-derived substances in infant formula to selectively stimulate the growth of the same intestinal microflora contained in breast milk (fed infants). *Level of addition:* Concerned there is little justification for providing oligosaccharides at the levels proposed to infant formula to be potentially consumed for 6 months when breast milk levels may drop substantially after the first few days post partum. *Consultation* Considers one round of consultation mat not clarify all issues. Recommends a second round of targeted consultation before the final assessment. *P609* Does not support the progression of this application on the grounds provided in the P306 DAR.
Department of	**General purpose foods:** supports Option 2

Submitter	Submission comments
Health and Human Services Tasmania Jennifer Savenake	**SPFYC**: supports Option 1 *Regulatory approach* **General purpose foods** Supports the proposed permissions for general foods. Agrees that the continued use of inulin-derived substances in general foods should be permitted. **SPFYC** Considers nutritional benefit should be able to be substantiated for SPFYC with sufficient amounts to achieve the intended effect. Refers to Codex. Would like to see further assessment of health and nutrition benefits to support an amendment of Standard 2.9.1 and 2.9.2. Concerned that 'taken not to be nutritive substances' in Standard 1.1.1 for general foods and the drafting approach in Part 2.9 on the Code *'should not be taken to mean that inulin-derived substances and GOS in infant formula products under Standard 2.9.1 are not 'nutritive substances''* may not resolve the uncertainty.
Queensland Health Tenille Fort	**General purpose foods:** Supports Option 2 **SPFYC:** Supports Option 1 Supports the amendment to Standard 1.1.1. Does not support an amendment to Standards 2.9.1, 2.9.2 or 2.9.3. *Regulatory approach* Concerned about the way different proposals and applications are being considered, and also when 'nutritive substances' and Standard 2.9.1 are yet to be reviewed. **SPFYC** *Definitions* Seeks clarification as to why FSANZ is recommending the addition of inulin-derived substances and GOS rather than long-chain inulin and GOS to infant formula. *Benefit / Comparison to breast milk:* Considers both safety and suitability should be scientifically demonstrated, with sufficient amounts of these substances present to achieve the intended effect - refers to CODEX. Should be able to substantiate the benefit of any substance added for nutritional or health benefits. Considers the efficacy to achieve nutritional or health benefits has not been adequately demonstrated. Considers there is not convincing evidence that long-chain inulin and GOS in infant formula mimic the effects of oligosaccharides in breast milk (in relation to improving gut microflora). *Evidence* Not clear why FSANZ and ICSAG are comfortable with the addition of inulin-derived substances and GOS alone as well as in combination. Considers the effects of inulin-derived substances alone or in combination with GOS are uncertain. Studies have mainly used GOS and long-chain inulin in a ratio of 9:1. Data on the effects of GOS or long-chain inulin alone on stool consistency and frequency, stool pH and SCFA profile is limited and conflicting. *Labelling and claims*

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	Agrees with the proposed labelling requirements for inulin-derived substances and FOS. Considers FSANZ has not given consideration to the labelling of infant foods and FSFYC in relation to content claims. If inulin and GOS are to be nutritive substances then set a minimum claimable level. If they are to be biologically active substances then (under proposed Standard 1.2.7) infant food and FSFYC will need to contain at least 10% of the amount of the substance that is required to be consumed per day to achieve the specific health effect.
NSW Food Authority David Cusack	**General purpose foods**: does not support the proposed amendments to Standard 1.1.1. **SPFYC:** supports Option 1 *Purpose of addition* **General purpose foods** Contends that inulin-derived substances and FOS should be regulated as food additives when added to food to exclusively serve a technological purpose (thickener, emulsifier or stabiliser), or as nutritive substances when added as dietary fibre. When added to general purpose foods to serve as a 'biologically active substance', the Authority contends that claims relating to inulin-derived substances and FOS should be regulated in the same manner as all other permitted biologically active substances in the Code. *Definitions* The Authority has concerns with the proposed definitions in the draft variations to Standard 1.1.1. Considers that FSANZ has deviated from definitions of inulin, FOS and GOS available in the scientific literature (Cummings & Stephen, 2007, *European Journal of Clinical Nutrition* Suppl 1, S5-S18). Requests clarity from FSANZ. *Measurement* Concerned as to how inulin-derived substances and FOS in general foods will be measured. In respect to comments made under 'Compliance with any limits' at page 52 of P306, the Authority does not agree with FSANZ's view that suitable methods exist. **SPFYC** Does not support the proposed amendments to Standards 2.9.1, 2.9.2 or 2.9.3. *Draft variation* In characterising FOS as 'taken *not to be a nutritive substance*' in standard 1.1.1, it appears that a generic permission for the addition of FOS to the infant food applications may have been created. No subsequent drafting in standards 2.9.1 and 2.9.2 overrides the regulatory status granted to FOS in Standard 1.1.1. Considers Clause 6 (1) of standard 2.9.1 may no longer be considered to have any application to FOS and it appears that the proposed drafting may allow for FOS (as defined in standard 1.1.1) to be permitted in foods covered under standard 2.9.1, 2.9.2 and 2.9.3 without limit. Requests FSANZ include specific prohibitive drafting in standards 2.9.1. 2.9.2 and 2.9.3 for the addition of FOS. *Definitions* Queries whether definitions are strictly limited to fructan molecules possessing only 2-1 glycosidic linkages? Queries what about combination of 2-1 and 2-6 glycosidic linkages. Also, will the definition of 'prebiotics' in the DAR will be incorporated into the Code. *Benefit/efficacy* Does not support further consideration of amendments proposed until the efficacy has been assessed. Refers to NFA, CODEX and EU Directive (2006/141/EC). *Evidence*

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	Considers that the addition of inulin-derived substances and GOS to the infant food applications cannot be justified on the basis that human breast milk (HBM) contains larger quantities of oligosaccharides than the draft variations to Standards 2.9.1, 2.9.2 and 2.9.3. Clinical data on safe consumption must be provided. The only ratio where data has been provided is at a ratio of 9:1 to a maximum concentration of 8 g/L. Considers that this may not be extrapolated to the addition of inulin-derived substances and GOS alone or in any combination to a maximum concentration of 8 g/L in infant foods and FSFYC. Suggests FSANZ obtain clinical data to support safe use in all infant food applications being considered in this Proposal. Notes the European Commission (EC) investigation into the addition of inulin-derived substances and GOS in infant foods raised safety concerns with the addition of short chain fructans (not defined) in infant formula. Suggests FSANZ seek clarity on the actual chain length of molecules considered to be short chain fructans for the purposes of the EC investigation and clarify how these relate to the terms proposed in P306. *Labelling* Queries whether, at FAR, inulin-derived substances and GOS will be considered 'nutritive substances' for the operation of clause 20 (f) in standard 2.9.1 of the Code. Seeks clarification of the definition of 'nutrition information statement' in standard 2.9.1 of the Code. Seeks assurance from FSANZ that a nutrition content claim on the label of an infant food product could not be presented as a 'nutrition information statement'. Would not support general level health claims being made with regard to inulin-derived substances and GOS on the label of infant food applications, as does not consider that sufficient evidence has been provided in the DAR for proposal P306, or other sources, to substantiate such claims. *Testing Method* Concerned about how GOS will be measured in powdered, milk based infant food systems. Suggests FSANZ provide guidance at FAR for accurate techniques for measuring GOS in milk based foods.
Victorian Dept. Human Services Victor Di Paola	**General purpose foods and SPFYC**: preferred Options not provided. Has chosen not to indicate which option is supported, as support will depend on how issues are addressed. *Regulatory approach / enforcement* Highlights the need for development of specific policy guidelines for SPFYC. Considers FSANZ is not treating these substances uniformly between general foods and SPFYC. Understands FSANZ does not want to commit to a stance on the status of these substances until the reviews of the concept of 'nutritive substances' and a review of Standard 2.9.1-Infant Formula Products have been completed. Considers this later review is unhelpful in terms of resolving the current regulatory issues in P306. Considers this makes the proposal neither practical nor enforceable. Considers that it remains arguable that inulin-derived substances, FOS and GOS are nutritive substances. Recommend that this standard be reviewed after the concept of nutritive substances is clarified and the review of Standard 2.9.1 is completed. It appears that the proposal does not meet the third requirement of Section 36 regarding

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	minor variations in the FSANZ Act since the imposition of maximum allowable levels can potentially 'alter the legal effect'. *Draft variation* Notes there is no provision for FOS in the proposed drafting for Standards 2.9.1, 2.9.2, and 2.9.3. Refers to Standard 2.9.1, Clause 6(1). Considers it appears that FOS can be added without limit and without any safety assessment, and that a manufacturer can potentially make a content claim. Notes this is consistent with the intent of the proposed change to Standard 1.1.1. *Evidence / safety* Considers it is unacceptable to extrapolate the findings of the specific studies involving inulin to GOS in the ratio of 9:1 to other variations of inulin-derived substances, including the sole addition of either of these substances. Neither the safety nor physiological effects have been established *for these variations* through accepted scientific studies. Considers that there is insufficient evidence in P306 to support the addition of either of these substances alone or in any *other* combination. Notes the EU has permitted the addition of these substances to infant and follow on formula-on in a ratio of 9:1. Suggests it would have been useful to have had available the basis for the European decisions regarding these substances and the available supporting data. Considers FSANZ has extrapolated the data from studies using a specific formulation (inulin- derived substances: GOS in a 9:1 ratio) in infant formula and extrapolated this to foods for infants/young children. Comments there is no information provided in P306 regarding the current permitted amounts of these substances and their ratios in other countries in infant foods. Requests overseas data on permitted levels, ratios, consumption for young children plus safety and outcome studies. *Labelling / claims* The proposed definitions for these substances conflict with generally accepted definitions of inulin in international scientific literature. Need accepted definitions for inulin-derived substances, FOS and GOS and all of the related substances in the Code to enable consistency in approach by manufacturers and consequently allow uniformity in product labelling. Concerned that because the regulatory stance for inulin-derived substances and GOS have not been clarified it will be possible for a manufacturer to be able to make a content claim on the product label. Considers a content claim implies that the product may potentially be viewed as superior to breast milk. Recommends a separate proposal to ensure consistent approach to representation on all infant formula products. Queries whether a manufacturer could make a general level health claim on a special purpose food that contains these substances? Considers it is unclear from a regulatory perspective what the definition of a 'Nutrition information statement' entails. *Education / Communications* Recommends a targeted education and communication strategy Intersection with A609 – requests that both Victoria submissions be considered together.

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New Zealand Food Safety Authority Carole Inkster	**General purpose foods:** supports Option 1. **SPFYC:** Standard 2.9.1 – does not support either Option as proposed. Standards 2.9.2 and 2.9.3 - supports Option 2. Does not support the proposed interim approach for the general food supply (Standard 1.1.1) or infant formula products (Standard 2.9.1). Supports the proposed amendments to Standard 2.9.2 and 2.9.3. *Regulatory approach* **General food supply** Does not agree with amending Standard 1.1.1 as proposed. Considers the status of inulin-derived substances and FOS in general food supply cannot be determined until the definition of nutritive substance is determined, so recommends no change at the present time. **SPFYC** Agrees that infants fed solely on infant formula, older infants and toddlers fed follow-on formula, and infant foods and formulated supplementary foods for young children containing inulin-derived substances and/ or GOS (as defined by FSANZ) in any ratio, are unlikely to be at risk from these foods, provided certain maximum levels are not exceeded. Supports the recommendation that inulin-derived substances and GOS be permitted for addition to infant formula. However does not support the interim approach by FSANZ that 'does not adopt a position either way on the status of inulin-derives substances and GOS when added to special purpose foods for infants and young children'. Supports the purpose of P306 i.e. to provide clarity and regulatory certainty, however does not agree that the interim approach will 'provide clarity for enforcement agencies in Australia and NZ'. The underlying issues remain unresolved and will remain until the proposed review of nutritive substances and Standard 2.9.1. To provide regulatory clarity, NZFSA recommends that inulin-derived substances and GOS (as defined by FSANZ) are permitted as nutritive substances in Standard 2.9.1 and are added to the Table in Clause 7 until any changes are implemented under the review of nutritive substances and Standard 2.9.1. Considers that until these reviews are undertaken no change should be made to the existing 'nutritive substance' definition in Standard 1.1.1. Agrees with the proposed amendment to Standard 2.9.1 – but *subject to* classification of inulin-derived substances and GOS as nutritive substances. Considers there are the following inconsistencies in the DAR: - FSANZ proposes that where inulin-derived substances and GOS are added to IFP a mandatory declaration of these substances will be required which suggests they are NS. However omitting these from the NS list in Table 7 to 2.9.1 indicates they are not NS. - the proposed insertion of a new subclause to clause 20 such that, for the purposes of subparagraph 20(1)(f), inulin-derived substances and GOS are taken to be nutrients, would permit a reference to the presence of inulin-derived substances and GOS only in the statement of ingredients or nutrition information statement. Considers that including inulin-derived substances in the NIP suggests they are nutrients or nutritive substances. - by undertaking a safety assessment and providing express permission for the addition of inulin-derived substances and GOS to infant formula FSANZ is

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	acknowledging these substances are 'nutritive substances'. Believes these inconsistencies could be addressed by listing inulin-derived substances and GOS as nutritive substances in Standard 2.9.1. Agrees with the proposed amendment to Standard 2.9.2 and 2.9.3. *Definitions* Believes terminology is inconsistent with scientific literature and adds to regulatory confusion. Notes in the scientific literature the term FOS and oligofructose have exactly the same meaning and can be used interchangeably. Believes the terms FOS and oligofructose should not be used to describe two substances that have different DP. Recommends this be reflected in the DAR Attachment 1. Also notes the proposal considers using long-chain inulin to describe inulin that has a DP>23 which infers that inulin is not being considered. Recommends FSANZ state the DP range that is being referred to.
Food Industry	
Bayer Australia Ltd Rebekah Folland	**General purpose foods and SPFYC:** preferred Options not stated. Considers that, due to the presence of patents, incorporation of long-chain inulin and GOS into the Code will have an anti-competitive effect in the current Australian marketplace. *Definitions* Bayer agrees with the proposed descriptions of the inulin-derived substances and FOS. *Levels* Bayer supports the proposed limits on addition. *Labelling / Warning statement* Agrees with the suggested approach for declaring the presence of inulin-derived substances and/or GOS in the nutrition information statement on infant formula products Does not believe that a warning statement will be required on a package of infant formula. However, limited safety data is available on the use of these ingredients in non-trial situations as food companies do not follow adverse event reporting procedures. *Impact on industry* Considers the implications are greater than reflected in the Draft Assessment and that the patents would significantly restrict innovation for other manufacturers. Notes they cover not only a preferred 9:1 ratio of GOS to long-chain inulin, but they also cover a broad range of 5-95% of each nutrient in a diverse range of foods not restricted to infant formula products.
BENEO-Orafti Wim Caers	**General purpose foods**: supports Option 2. **SPFYC:** supports Option 2 for Standards 2.9.2 and 2.9.3. Does not support the proposed maximum permitted levels for Standard 2.9.1. Supports the amendment to Standard 1.1.1 as proposed. Supports the proposal to permit the addition of inulin-derived substances and GOS to infant formula but does not support the maximum permitted levels proposed for inulin-derived substances in Standard 2.9.1. Supports the amendment to Standards 2.9.2 and 2.9.3 as proposed. *Regulatory approach*

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	Notes the DAR states these substances are considered to require a pre-market safety assessment and an explicit permission in the Code before they can be added to infant formula. Considers this is not clear in the Code and does not provide for a different interpretation to be applied to the same unstandardised food when added to general foods or SPFYC. Consider this represents an opinion rather than interpretation. *Definitions* Suggests the definitions for oligofructose/FOS derived from inulin or sugar be revised. Provides alternative definitions. Also recommends an editorial note re Degree of polymerisation. However supports inulin and long-chain inulin labelled as inulin for labelling purposes. Considers the interchangeable use of both oligofructose and FOS for labelling purposes could be seen to be misleading and deceptive in the context of fair trading laws. **SPFYC** *Safety* Supports proposal to permit inulin-derived substances and GOS to infant formula. Supports the risk assessment that 0.8 g/100 mL of inulin-derived substances could be safely added to infant formula. However does not support the expert peer review regarding limiting inulin-derived substances to 3 g/L. *Labelling/claims* Supports the proposed approach to declaration and does not support the need for a warning statement. Notes proposal P293 plans to retain the prohibition on nutrient content claims and health claims on infant formula products. Asks for reconsideration in P293 to allow health claims – (provided they can be scientifically supported) for the inclusion in the nutrition information statement.
Nutricia Australia New Zealand Gregg Ward	**General purpose foods and SPFYC**: supports the Proposal but does not support the amendments as proposed. Provides alternatives to the proposed drafting. *Definitions* Considers definitions in the Code need to be consistent with current practice and understanding. Suggests 'short chain oligosaccharides' better describes those compounds with an average DP of <4. Recommends alternatives for the draft variation considered to be more consistent with international academic research and commercial marketing. Also provides specifications. Considers the term FOS can be interchangeable with 'oligofructose'. Considers the present practice and scientific research community is not to limit the definition of FOS as proposed in the DAR. Notes it is compliant with international convention and usage to also recognise the descriptor 'long-chain FOS' for a defined structure with average DP-> 23. Suggests long-chain FOS be referenced in the Code along with the term 'long-chain inulin' to ensure full clarity for stakeholders. Suggests including the source of fructan polymers in the definitions / permissions in the Code. *Labelling* *Warning statement* - considers there is no evidence to support or justify any additional

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	mandatory warning statements. Unclear what is meant by the 'nutrition information statement' as it is not defined in the Code and is open to interpretation. Provides alternative drafting for 2.9.1 Clause 20 replacing nutrition information *statement* with nutrition information *panel.* *Levels of addition* Considers safety data that exists for long-chain inulin /long-chain FOS in a 1:9 ratio with GOS is not currently cited in relation to other ratios and types of inulin-derived substances. Does not consider the evidence presently available would meet the level of satisfaction required before including oligo fructose / FOS with average DP less than 10 (specifically an average of 4.2) in its own infant formula. Refers to 2004 EFSA review of a study by Euler (2005) that supports this view. Considers there are shortcomings in the study noted in the DAR by Kapiti et al 2007. Notes the EU permission only applies to long-chain FOS/long-chain inulin combined in a 1:9 ratio with GOS at a dosage of 0.8 g/100 mL. Considers it prudent to only permit those specific inulin-derived substances that have a body of safety evidence, cited and reviewed by FSANZ. Provides modifications to the proposed standard. Notes also that the changes proposed in this submission will not have significant adverse effect on the interests of anyone (in relation to a s36).
Dairy Goat Co-operative Dianne Lowry Caroline Keast	**General purpose foods**: supports Option 2 *with recommendations* **SPFYC**: supports Option 2 *with recommendations* *Regulatory approach* **General purpose foods** Supports the proposed insertion of clause 9A to Standard 1.1.1 that inulin-derived substances and fructo-oligosaccharides are not nutritive substances, but considers this conflicts with the distinction, even on a temporary basis, between the general food supply and SPFYC. Suggests further explanation needs to be included in the Code. **SPFYC** Standard 2.9.1 – supports the approach to permit the individual or combined use of inulin- derived substances and GOS. Considers the specification for GOS is far too restrictive. Notes GOS is available in powder form as well as liquid/syrup form. Suggests it might be impractical to develop a specific standard for GOS. *Definitions* Supports the BENEO ORAFTI comments and suggested changes for Standard 1.1.1. Has concerns re the definitions proposed by FSANZ for 'oligofructose' and fructo-oligosaccharides (FOS)'. Supports the distinction FSANZ is trying to achieve between oligofructose derived from inulin and the forms derived from sucrose. However considers the proposed terminology is confusing to food industry, consumers, and overseas authorities. Suggest using oligofructose and fructo-oligosaccharides (FOS) interchangeably. Notes FSANZ takes this approach for labelling of general foods – questions whether this applies to SPFYC. Notes this is counter to the terminology distinctions proposed by FSANZ. Supports the revised definition proposed by BENEO-ORAFTI. Suggests using 'inulin-derived' or 'sucrose derived' after 'oligofructose' or 'fructo-oligosaccharides (FOS)'. *Levels* Supports the maximum levels proposed. Notes it may be difficult in some cases to apply

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	a maximum limit to the natural and added levels of inulin-derived substances and/or GOS, due to analytical limitations or the complexity of food matrices tested. Some assumptions may be required to estimate or calculate total levels. Notes no official method will be specifically listed for GOS in the Code, in Standard 1.2.8. This makes it difficult to determine or check levels (natural or added). An AOAC method may exist (AOAC Official Method 2001.02 *trans*-Galactooligosaccharides (TGOS) in Selected Food Products), but are unsure of its suitability for compliance checks. Also complications may be encountered where no, or only a limited number of laboratories have some understanding or experience in testing these compounds (e.g. in New Zealand). *Labelling* Supports the approach to the declaration of presence of inulin-derived substances and/or GOS in the nutrition information panel. Does not support the need for a warning statement. Considers the wording of amendment to clause 16(1) to include paragraph (d) leaves it to the interpretation that even if not added, the average natural levels of inulin-derived substances or GOS (whether present in traces or not) must be declared, and believes this is not FSANZ's intention. Proposed alternative wording for Clause 16(1)(d) to include '***where added*** the average amount of…'. Notes there is no similar annotation in Standards 2.9.2 and 2.9.3 that the maximum levels are to apply to the 'sum of naturally occurring and added substances'. This should be consistent with Standard 2.9.1.
HEINZ Australia and Heinz Wattie's New Zealand Julie Dick	**General purpose foods:** supports Option 2 **SPFYC:** supports Option 2 *Regulatory approach* Supports the preferred regulatory approach for general foods and SPFYC. Notes the approach is consistent with the Heinz Application A598. Considers the issues are best resolved under P306 than through A609. Believes the preferred regulatory approach will protect the health and safety of consumers, including infants, encourage innovation on a level playing field, provide clarity for enforcement agencies, encourage global harmonisation and promote minimal effective regulation. *Definitions* Understands there is some confusion in terminology and that other submitters will seek clarification. Supports the proposed approach for declaration of inulin-derived substances and/or GOS in the nutrition information statement. Does not support a requirement for a warning statement. *Levels* Supports the proposed maximum level of inulin-derived substances in infant formula products at 0.3 g/100 mL. *Safety* Has concerns about the addition of inulin-derived substances to infant formula for very young babies (from birth) due to the potential for this ingredient to cause discomfort in some sensitive infants. Fully support *voluntary* addition of inulin-derived substances when GOS is added to infant formula. This allows industry to exercise more caution as they understand more on the science and real effects of inulin-derived substances in young infants.
Australian Food	**General purpose foods:** supports Option 1

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and Grocery Council Geoffrey Annison	**SPFYC:** supports Option 2 *with recommendations* *Regulatory approach* Supports Option 1 and opposes the preferred regulatory approach. Recommends the FAR should conclude that for general foods inulin and inulin-derived substances and FOS are food ingredients so do not require pre-market approval. Recommends FSANZ does not amend the Code, but clarifies the regulatory status in the FAR. **General foods** Considers there was, and is no ambiguity in the Code in relation to inulin and inulin-derived substances and similar substances. Considers these substances are food ingredients and have been accepted as these for a long period of time. Therefore there is no basis for requiring pre-market regulatory approval. Evidence to support his includes the definition of dietary fibre, Standard 1.2.8. and Application A277 which notes inulin and FOS qualify as dietary fibre. Considers enforcement agencies have been aware of their use for many years and considered such use to be within the Code permissions as dietary fibre. Considers the inherent nature, nutritional and physiological properties and safety of inulin and derived materials at levels used have been extensively reported on in scientific literature. Considers industry is not, and has not been confused regarding their regulatory status. Considers FSANZ should not amend Code in response to a small number of queries. **SPFYC** Notes the inconsistent view of enforcement agencies in Australia and NZ leading to uncertainty for industry and consumers. Supports an amendment to the Code to permit the voluntary addition of inulin-derived substances to SPFYC. Supports Option 2 for SPFYC, but recommends FSANZ reconsider the proposed levels**.** *Levels* Supports a restriction on levels of addition to SPFYC. However notes FSANZ has chosen a relatively low level based on anecdotal evidence of transient intestinal distress when infants are fed higher levels which FSANZ deems safe. *Definitions* Considers the inulin and inulin-derived substances descriptions are correct but notes these are polydispersed materials with variable compositions. Considers exact definitions / chemical descriptors are inappropriate and that permissions will be general and apply to materials from different sources. Suggests there is a need to consider practicalities of the interchangeability between some terms. *Labelling / claims* Supports the amendment to allow health claims (and high level health claims) but does not support use of nutrient profiling scoring criteria.

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	Considers a warning statement is not required. Does not consider mandatory listing of inulin and inulin-derived substances or GOS in the information panel is required.
Allberry House Cecilia Munster	**General purpose foods:** supports Option 2 **SPFYC:** supports Option 2 Endorses overall content of P306 and changes to the Code. *Definitions* Notes the definitions may not fully distinguish the various products available. Considers it is confusing to have different definitions for FOS and oligofructose but that the terms can be used interchangeably. Provides possible definitions as supplied by supplier (believes these have been advised to FSANZ).
Fonterra Co-operative Group Ltd Carol Bate Victoria Landells	**General purpose foods:** supports Option 2 **SPFYC:** supports Option 2 *Definitions* Acknowledges the aim to differentiate between FOS synthesised from sugar, and oligofructose/FOS from inulin. Concerned the product commonly referred to by industry as FOS (the Beneo Orafti product) is different from the proposed FSANZ definition of FOS. Provides alternative definitions (as used by Beneo Orafti). Notes sc-FOS is widely used in Japan but much of the evidence for sc-FOS will be referred to as FOS. **General foods** Endorses the amendment to Std 1.1.1 that inulin-derived substances and FOS are taken as not to be nutritive substances. Queries why GOS is not permitted in the general food supply, as it has been shown to be effective and if considered safe in infants. Therefore questions why it could not be considered safe in adults. **SPFYC** Endorses the preferred approach. Requests clarification of 2.9.2 and 2.9.3 – does the maximum permitted amount include that GOS produced in-situ via hydrolysis of lactose? Also seeks clarification that the 0.8g/100g is the 'consumed' amount (i.e. made up formula) and not the powder.
Robert Forbes and Associates David Panasiak	**General purpose foods:** does not support the amendment as proposed. **SPFYC:** preferred Option not provided. *Regulatory approach* Notes the DAR states *FSANZ considers the regulation of GOS does not need to be included in the Code* as FSANZ is not aware of wide use of GOS (other than in SPFYC) and intakes from the general food supply are likely to be negligible. Considers this is a very narrow view of the potential for GOS in foods. Considers FSANZ has failed to clarify the status of GOS by not including it in the draft

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	Clause 9A of Standard 1.1.1. Its omission leaves industry unclear as to whether it is a nutritive substance. Suggests the clause be redrafted to include GOS. Considers the definition of a nutritive substance is very broad and could encompass a number of substances added to foods without specific permission. Agrees GOS is a newer substance than inulin/FOS in Australia and New Zealand. Notes its major use is as a prebiotic, and it has a non-nutritional purpose in a similar manner to inulin/FOS. Considers GOS should also be able to be added to the general food supply as a dietary fibre. Considers it is equally important to clarify that GOS is not a nutritive substance. Refers to the GRAS status confirmed for GOS mixture Bi2muno® GOS on 29th July 2007. Notes that β-linked galacto-oligosaccharides like Bi2muno® GOS have been used as food ingredients in Japan and Europe for at least 25 years i.e. a longer history of safe use than has been quoted for inulin/FOS in Australia. The US expert panel report notes that foods that contain such galacto-oligosaccharides include baby food and formula, beverages and fermented dairy products. Advises the UK FSA does not consider GOS a novel food. Provides a paper on efficacy of GOS as a prebiotic.
Food Technology Association of Australia David Gill	**General purpose foods:** supports Option 1. **SPFYC:** supports Option 2. *Definitions* Considers the descriptions are adequate. **General food supply** Supports Option 1 to retain status quo – with no explicit permissions for the addition of inulin-derived substances and FOS. Interprets the Code to currently provide permission for these substances to be used through Standard 1.2.8 Division 4. Table to subclause 18(1). Also notes the status of many other food ingredients/substances used for many years are not specifically mentioned in the Code. Considers the concept of listing 'negative' nutritive substances when there is no list of 'positive' nutritive substances is against the principle of a less regulated set of standards. **SPFYC** Supports Option 2 – to amend standard 2.9.1, 2.9.2 and 2.9.3 Notes there is confusion with A609 as it offers a significantly different option. Queries which will take precedence – P306 or A609. Considers the proposal should have only addressed the general food supply.
George Weston Bronwyn Eisenhauer	**General purpose foods:** supports Option 2. Supports amending Standard 1.1.1 by the inclusion of Clause 9A. Considers inulin and oligofructose have been recognised as dietary fibre in the Dietary Fibre standard of the Code. *Definitions:* Recommends combining the definitions of fructo-oligosaccharides and oligofructose as these terms are used interchangeably and this supports section 8.3.1 of the DAR which notes these terms could be used interchangeably. Provides a combined definition. Supports the Orafti definition for Inulin.
Goodman	**General purpose foods:** supports Option 2.

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Fielder Hamish Conway	Fully supportive that inulin/inulin-derived substances and FOS are taken not to be nutritive substances. *Definitions* Considers the proposed separate definitions for FOS and oligofructose, but allowing them to be used interchangeably, is confusing and needs further clarification. Provides alternative definitions.
G C Hahn & Co (Australia) Pty Ltd. Kathryn Milburn	**General purpose foods:** supports Option 2. Provides comment on general foods only and agrees with the proposed amendment to Standard 1.1.1 so that inulin-derived substances and FOS are taken not to be nutritive substances. *Definitions* Proposes an alternative definition for inulin but agrees with the definitions of oligofructose and fructo-oligosaccharides and notes they can be used interchangeably.
Hubbard Foods Ltd. Rachel Bergquist	**General purpose foods:** supports Option 2. Endorses proposed change to the Code regarding inulin/inulin-derived substances and FOS being taken not to be nutritive substance. Not sure the definitions of inulin products fully distinguish the various products available. Also finds it confusing that P306 proposes separate definitions for FOS and oligofructose but states the two terms can be used interchangeably for labelling purposes. Provided alternative definitions
National Foods Katrina Strazdins	**General purpose foods:** supports Option 1. *Regulatory approach* Supports the classification of inulin and inulin-derived substances as food ingredients in the DAR for P306. However does not see a need to amend the Code for general purpose foods. Notes inulin and derived substances have been used safely in general purpose foods for technological purposes and as dietary fibre over 10 years. Notes FSANZ have previously acknowledged these are not food additives but rather are food ingredients/dietary fibre. Also notes they meet the definition of dietary fibre in Standard 1.2.8 of the Code. *Definitions* Does not agree with the terminology in the DAR for inulin – and considers oligofructose and fructo-oligosaccharides are virtually identical with the terms being used interchangeably (provides references). Does not support mandatory declaration of inulin-derived substances and/or GOS in the nutrition information panel. Considers these should only be required to be declared in the nutrition information panel when a claim is made about them.
Naturalac Nutrition Ltd Jacintha Baber	**General purpose foods:** supports Option 2. Endorses overall content of P306 particularly that inulin / inulin-derived substances and FOS are taken not to be nutritive substances. *Definitions* Are not sure the definitions of inulin products fully distinguish the various products available. Considers it confusing that P306 has proposed separate definitions for FOS and oligofructose but also states the two terms can be used interchangeably for labelling

Submitter	Submission comments
	purposes. Have provided alternative definitions.
Nestlé Australia Stephanie Rajczyk	**General purpose foods:** supports Option 2 **SPFYC:** no preferred Option provided. Supports the preferred regulatory approach proposed in the DAR. *Definitions* Supports the proposed description of inulin-derived substances and FOS based on the average and range of degree of polymerisation as stated in the DAR. *Labelling* Supports the proposal to allow manufacturers to use interchangeable descriptions of fructo-oligosaccharides and oligosaccharides on the label. Considers a warning statement is not necessary. Supports the proposal to declare inulin-derived substances and / or GOS separately in the NIP. *Levels* Supports the increase in the maximum permitted level if sound scientific evidence demonstrating safety and efficacy is available.

Submitter	Submission comments
NZ Food and Grocery Council Brenda Cutress	**General purpose foods:** preferred Option not stated. **SPFYC:** supports the Option 2 *with recommendations re maximum permitted levels*. *Regulatory approach* **General foods** Notes inulin-derived substances and FOS have been safely used in the food supply in New Zealand and around the world for many years. Considers there was no ambiguity as to their use as a food ingredient until the legality of their use in infant formula was questioned. Defining them as 'nutritive substances' rather than 'unstandardised foods' caused uncertainty to some manufacturers who had always considered the Food Standards Code was clear that they are unstandardised foods. Pleased to note that FSANZ has now recognised that inulin-derived substances and FOS are not nutritive substances. However, suggests FSANZ further consider whether this recognition is best achieved by amending Standard 1.1.1 as proposed or whether the FAR can confirm that for general foods inulin-derived substances and FOS are food ingredients, not nutrient substances or food additives and therefore do not require premarket approval. **SPFYC** Supports the proposed amendments to SPFYC but recommends reconsideration of permitted levels. *Levels* Considers the maximum permitted levels in SPFYC need to be reconsidered, as the relatively low maximum level proposed differs from the levels that ingredient suppliers of inulin, inulin-derived substances and GOS and infant formula manufacturers have shown to be safe. *Definitions* Recommends FSANZ consider the alternative definitions provided by Beneo-Orafti as they would address any uncertainty. *Labelling and claims* Supports that 'for foods in the general food supply, general level health claims would be permitted for inulin-derived substances and FOS'. Does not support the requirement that such foods would need to meet the Nutrient Profiling Scoring Criteria in order to be eligible to convey a general level health claim (refers to submission to P293). Does not support a need for a warning statement. Supports the mandatory declaration of inulin-derived substances and /or GOS in the label of an infant formula product, if added.
Parmalat Australia Ltd. Tony Coope	**General purpose foods:** supports Option 2 Provides comments only in relation to general food supply. Has marketed dairy products containing inulin added for *technological reasons* in low fat yoghurts and low fat dairy desserts since 1997. Notes the safety of incorporating inulin was never in question. Following the clarification of inulin as a *dietary fibre* in Standard 1.2.8 of the Code, Parmalat introduced liquid milk products onto the Australian market with fibre claims based on the presence of inulin. Understands that within such applications, inulin is captured under the definition of a dietary fibre as contained in Standard 1.2.8 and governed by the same permissions as for other sources of dietary fibre added to general

Submitter	Submission comments
	foods. Notes inulin and FOS are not widely promoted in Australian products for their properties as prebiotics. Claims of a prebiotic nature are commonly used in products in overseas countries where perhaps the health effects associated with stimulation of beneficial gut bacteria are more clearly understood within the general population. *Regulatory approach* Supports Option 2 to amend Standard 1.1.1 of the Code as considers this will provide a 'quick fix' and avoid possible enforcement action. However considers the amendment to Standard 1.11. does not address: • the Health Claims Standard (P293). Notes FSANZ states within the DAR that general levels claims will be possible for inulin-derived substances and FOS even though Standard 1.1.1 defines them as 'non nutritive substances'. Queries how does FSANZ intends to address this anomaly following gazettal of P293? Considers there is an obvious need to provide some clarity within the Code that allows for nutrition and heath claims to be made on these non-nutritive substances. • the omission of GOS from Standard 1.1.1. GOS is finding an application as an alternative to FOS in a number of functional foods on the international market e.g. Finland, Japan, Netherlands. Considers failure to recognise this will create barriers to trade. Considers the core problem is the definition of a nutritive substance, and that, by not undertaking a full review of the definition of a 'nutritive substance', uncertainty will still be present within both industry and enforcement agencies.
Pyx Ltd Lynley Drummond	**General purpose foods:** supports Option 1. **SPFYC:** supports Option 2**.** **General food supply** Supports maintaining the *status quo* whereby there are no explicit permissions for the addition of inulin–derived substances and FOS in foods (other than foods regulated by Part 2.9 of the code). **SPFYC** Supports Option 2 to amend Standards 2.9.1,2.9.2 and 2.9.3 on the basis that: • there is sufficient evidence to suggest that excessive addition of prebiotic substances to foods may cause unacceptable levels of gastrointestinal discomfort (Coussement, 1999); • research demonstrates the ability of prebiotic substances to have a profound physiological effect and therefore regulation of upper levels is required; and • alignment with international legislation – in particular the EU.
Sanitarium Health Food Company Sharon Smith	**General purpose foods:** supports Option 2 Provides comment only in relation to general foods only. Supports amendment to Standard 1.1.1 as proposed. *Definition*s Is not certain the definitions proposed clearly distinguish the various products available. Finds this confusing and supports the need for further clarification.
Coscura Groupe Warcoing and Sensus Cathy Signoret	**General purpose foods:** supports Option 2 **SPFYC:** supports Option 2 Producers of chicory inulin and oligofructose.

Submitter	Submission comments
(Cosucra)	*Definitions* Raise concerns regarding the definitions of proposed ingredients and provide alternatives. *Levels* Supports the limit of 3 g/L of inulin-derived substances in infant formula products. *Labelling and claims* Do not consider a warning statement if required. Agrees with the proposed approach to declaring the presence of inulin-derived substances and GOS on the nutrition information statement.
Health Professionals	
Dietitians Association of Australia Annette Byron	**General purpose foods:** supports Option 2. **SPFYC:** supports Option 2. *Regulatory approach* Has no objections to the proposed approach to amend Standard 1.1.1 and Standards 2.9.2, 2.9.2 and 2.9.3 as proposed. *Benefit / efficacy* Notes that the benefits of the addition of these substances to SPFYC are difficult to assess given the limitations of the studies referred to in the DAR. *Labelling and claims* Believes a warning statement is not warranted. Agrees with the proposed approach for declaring the presence of inulin-derived substances and/or GOS on the nutrition information statement.
Consumer and Community Organisations	
Women's Health Action Louise James	**SPFYC:** supports Option 1. *Regulatory approach* Supports Option 1 for SPFYC but considers toddler milk should be grouped with infant formula products. Considers defining the three levels of formula in the Code to be problematic (infant formula, follow-on formula and toddler milk) and considers these should all fall under the same classification. Considers there has been a lack of wider community consultation outside of industry networks. *Definitions* Satisfied the terminology used is adequate for describing the substances being assessed. Considers describing toddler milk as a food is misleading and puts it outside the Code of Marketing of Breast milk Substitutes and the limitations the Code puts on claims on infant formula. *Objectives* Considers an impact assessment on public health has not been included in the Draft Assessment. Notes new ingredients in formula have been shown to negatively impact on perceptions of the superiority of breast milk despite their actual effect.

Submitter	Submission comments
	Consumer choice Considers FSANZ reasoning that the preferred approach provides customers with choice is irresponsible when one of the choices is breastfeeding. *Review of nutritive substances and policy guidelines* Believes it pre- emptive to support the preferred option that inulin-derived substances and FOS are not to be taken as nutritive substance. Also considers it prudent to wait for the MinCo policy guidelines. *Physiological effects/ safety / benefit* Notes evidence base for benefits for inulin-derived substances and FOS in infant formula products relies solely on stool analysis. However considers there is no evidence that this is beneficial to formula fed infant. Considers there is insufficient evidence for lack of harm and less for demonstrated benefit. Notes European Commission in 2001 permitted addition of these substances but recommended follow-up studies be done. Considers there is no sound scientific evidence to validate the inclusion of new ingredients. Dietary intakes *The consumption of breast milk is not included in the assessment.* *Impact analysis* *Considers anything that has potential to compete with breast milk should be analysed to make sure it has no detrimental impact on breastfeeding beliefs and rates.* Notes there has been no health impact on breastfeeding or the health and wellbeing of Maori.

Attachment 3

Response to Issues Raised by Submitters at Draft Assessment

This section addresses issues raised by submitters at Draft Assessment. A full summary of submitter's comments can be found in Attachment 2.

Submitter comments / issues	FSANZ response
Regulatory Approach	
A submitter noted that it is not clear in the Code that inulin-derived substances and GOS need explicit permission before addition to infant formula. Some submitters considered the different approach proposed for general foods (Standards 1.1.1) and SPFYC (Standards 2.9.1, 2.9.2 and 2.9.3) may not resolve the current uncertainty. It was noted the status of inulin-derived substances and GOS in SPFYC has not been confirmed and the interim approach will not provide clarity for enforcement.	FSANZ prepared Proposal P306 to provide regulatory clarity on this issue. Further explanation for P306 is provided in the Background Section of the Final Assessment Report (FAR). The rationale for FSANZ's assessment and drafting approach is described in the Executive Summary and Sections 5 and 15 of the FAR.
Some submitters presented differing views as to whether inulin-derived substances and FOS should be regulated as nutritive substances (e.g. when added as fibre) or food additives (if added for a technological purpose), or alternatively, they are food ingredients for the general food supply without a need for premarket approval, so there is no need to amend Code. Also, one submitter considered listing a non-nutritive substance in Standard 1.1.1 when there is no list of nutritive substances is against the principle of a less regulated set of standards, noting many other substances used are not listed in the Code.	FSANZ has been aware of the polarity of views among food industry, industry groups and food regulatory agencies as to whether these substances are 'nutritive substances' in the Code. Inulin-derived substances have been added to the general food supply since the mid 1990s, and FSANZ's risk assessment indicates that they have a history of safe use in the general food supply. Also, the approach taken at Final Assessment recognises the status of inulin-derived substances as fulfilling both a technological and nutritional purpose in general foods. In addition, it is planned that the definition of a nutritive substance will be reviewed in the future. For these reasons and for the purpose of providing regulatory clarity in the Code at this time FSANZ has proposed as an interim measure that inulin-derived substances are taken not to be nutritive substances in general foods. The Executive Summary and Section 15 of the FAR provide further explanation.

Submitter comments / issues	FSANZ response
	Also, FSANZ understands that FOS (i.e. fructose polymers derived from sucrose) are not used in the food supply in Australia or New Zealand. Therefore FSANZ has not proposed the regulation of FOS in food at this time, in line with minimal effective regulation. At this time and to align with the approach used internationally, FSANZ does not consider it appropriate or practical to regard inulin-derived substances as food additives even though they perform technological functions in food.
One submitter considered that these substances are already permitted through Std 1.2.8 Division 4 table to subclause 18(1) and requested clarification in the Final Assessment Report.	Standard 1.2.8 relates to methods of analysis for the purposes of nutrition labelling, and does not provide a permission to add these substances.
One submitter commented the Draft Assessment presents an inconsistent approach i.e. the requirement for a mandatory declaration on infant formula products, the new subclause in Standard 2.9.1 clause 20 and providing express permissions for these substances suggests they are nutritive substances, but they are not listed in the Table to clause 7.	An interim approach has been taken as regulatory clarity is required at this time and because FSANZ plans to undertake a review of the definition of 'nutritive substances' and a review of Standard 2.9.1 – Infant Formula Products. FSANZ considered it appropriate to list the proposed permissions for addition to infant formula products outside the Table to Clause 7 so as not to pre-empt the outcome of the planned reviews. It is outside the scope of this section 36 Proposal to review the definition of 'nutritive substance' in the Code to accommodate these and other substances not currently listed in the definition. For further information refer to the Rationale for Drafting Approach in the Executive Summary and Section 15 of the Final Assessment Report.

Submitter comments / issues	FSANZ response
Some submitters considered that this Proposal should be deferred until Ministerial policy is in place and until Standard 2.9.1 and the definition of a nutritive substance are reviewed. The reviews need to be expedited.	The timeframe for the policy development and completion of the reviews is yet to be confirmed. FSANZ considered regulatory clarity is needed at this time and raised P306 as an interim approach to address the current uncertainty.
One submitter suggested that the proposal should only address the general food supply. Another submitter queried whether an amendment to the Code is needed for general foods, and whether the regulatory status can be clarified through the FAR?	As noted in the Background Section of the FAR, some enforcement agencies took enforcement action against the manufacturer of infant formula products with added long-chain inulin44 and GOS as no express permissions exist in the Code. The addition of long-chain inulin and GOS to infant formula products is considered to require a pre-market safety assessment and an explicit permission in the Code. FSANZ is aware that there are differing interpretations of the Code amongst enforcement agencies and food manufacturers, so considered that regulatory clarity with regard to SPFYC was required at this time. An unintended consequence of the enforcement action taken was uncertainty amongst the broader food industry as to the regulatory status of inulin-derived substances/FOS when added to general foods. Food manufacturers were concerned about potential implications for their food products. In response to this concern, FSANZ initiated P306 to provide regulatory clarity in the Code for the general food supply as well as specifically considering SPFYC. The proposed amendments are considered an interim measure to provide regulatory clarity in the Code in response to uncertainty at this time. Amendments to the Code are effected via applications or proposals. In this instance, FSANZ undertook P306 to achieve a change to the Code which will provide regulatory clarity. This is the most effective mechanism to achieve this aim. It is not possible to clarify or permit the necessary amendment for general food unless there is a food regulatory measure amendment. Mere discussion in the FAR is insufficient.

[44] Long-chain inulin has been referred to by some manufacturers as long-chain FOS or high molecular weight FOS.

Submitter comments / issues	FSANZ response
One submitter considered P306 does not meet the 3rd requirement of s36.	The submitter is confusing the provisions of the FSANZ Act which were in force at the time the proposal was prepared and the provisions that are now in force under the same section number. The FSANZ Act was amended in 2007 and the sections were renumbered to accommodate the new provisions. The FSANZ Act, as in force since 1 October 2007 and not applicable to P306, provides at s.36 for the application of subdivision E – Modification of general procedure for minor variations. This is not the relevant section for consideration of this proposal. S.36 of the FSANZ Act (as was in force prior to 1 Oct 2007) provides that the Authority (the Board) may simplify the proposal procedure by deciding not to do something that it is required to do if satisfied that: (a) omitting to do the thing will not have a significant adverse effect on the interests of anyone; or (b) the application or proposal raises issues of minor significance or complexity only.
Some submitters considered assessing A609 at the same time as P306 is confusing as it offers a significantly different option. It was queried which will take precedence?	FSANZ prepared P306 in response to enforcement measures, regularity confusion within industry, manufacturers and the general public. P306 intends to clarify the situation for general foods and SPFYC. Application A609 is a paid application lodged after work on the proposal had commenced, therefore both progress simultaneously. Under instruction of the FSANZ Board, the proposal was prepared and considered under s36 of the FSANZ Act which allows for FSANZ to omit one round of public comment. FSANZ retains its statutory obligation to progress A609 within the legislated timelines. In accordance with the FSANZ Act and the direction of the FSANZ Board, the Proposal will take precedence.

Submitter comments / issues	FSANZ response
Definitions / terminology	
Several submissions considered the proposed definitions differ from international scientific literature and should to be consistent with international convention and current usage (for gazettal). • It was noted to be confusing to have separate definitions (for fructo-oligosaccharides and oligofructose) yet with the ability to use these interchangeably. • Clarification was requested as to whether the interchangeable use of fructo-oligosaccharides and oligofructose in general foods also applies to SPFYC (especially if FOS is not permitted in SPFYC). • It was also queried whether the definitions are strictly limited to fructan molecules possessing only 2-1 glycosidic linkages; are molecules possessing a combination of β 2-1 and β 2-6 glycosidic linkages included; why are inulin-derived substances and GOS being permitted, and not long-chain inulin and GOS; and will a definition for prebiotics be included in the Code? It was also considered that exact definitions or chemical descriptors are inappropriate as permissions will apply to different sources. It was suggested the source of fructan polymers needs to be included in definitions and permissions in the Code. An editorial note on the degree of DP was also recommended.	FSANZ acknowledges the comments in submissions and proposes that the range of relevant fructose polymers be consolidated into the single generic term of 'inulin-derived substances' in the draft variation. 'Inulin-derived substances' would include inulin and would be mixtures of those fructose polymers with predominantly β (2→1) fructosyl-fructose linkages with or without a terminal glucose molecule but would not include those polymers produced from sucrose by enzymatic action. This approach would: • avoid the need for a range of terms to be defined, which is not practical or necessary given the varying nature of fructose polymers; • avoid any confusion with the existing common names used to describe fructose polymers, including inulin-derived substances; and • be likely to be more practical from a compliance perspective. Long-chain inulin is included under inulin-derived substances. Refer to Section 1.4.1 Terminology. A scientific definition for prebiotics is included in the FAR, as the term is commonly used by industry. A definition will not be included in the drafting as these foods have been used in the general food supply for a number of other purposes (Refer to Section 1.4). FSANZ acknowledges that these substances are difficult to characterize chemically and has redrafted the definitions to reflect this. The source of inulin-derived substances may vary and it is therefore not appropriate to prescribe the source. FSANZ has redrafted the definitions to remove the need for an editorial note on degree of polymerisation.
Evidence of benefit / efficacy	
It was suggested FOS from sucrose should be considered and a review of the data suggested.	FSANZ has been informed that FOS i.e. fructose polymers derived from sucrose, is not used in the food supply in Australia or New Zealand and that there is therefore no need to consider it at this time as part of this Proposal. This does not prevent a future consideration of these substances if required.
Several submitters considered assessment should demonstrate nutritional benefit/efficacy in SPFYC, not safety alone, especially for this vulnerable population	There are currently no Ministerial Policy Guidelines on the addition of substances to special purpose foods for infants and young children. As a result, FSANZ, in

Submitter comments / issues	FSANZ response
group. It was noted benefits of these substances in SPFYC are difficult to assess given the limitation of the studies in the Draft Assessment.	accordance with its statutory objectives, has confined the risk assessment to considering safety as well as nutritional equivalence with breast milk as assessed by comparable physiological and microbiological effects. Refer to the Executive Summary and Section 7 for further information.
Some submitters considered the Proposal does not align with the Codex approach that infant formula should mimic breast milk, specifically that the suitability for particular nutritional uses for infants be scientifically demonstrated, that infant formula should mimic the levels in and effects of breast milk, provide sufficient amounts to achieve the intended effect, or provide other benefits similar to the outcome of breastfed infants. One submitter also referred to the EU Directive 2006/141/EC noting Article 5 refers to a systematic review of expected benefits in the assessment process.	FSANZ seeks to harmonise with international regulations whenever possible. As noted above. in the absence of Ministerial Policy Guidelines on the addition of substances to SPFYC, FSANZ has confined the risk assessment to considering safety as well as nutritional equivalence with breast milk as assessed by comparable physiological and microbiological effects. FSANZ's assessment found that at levels up to 10 g/L there is evidence of similar physiological (softer stools and increased stool frequency) and microbiological effects (increased growth of colonic bifidobacteria) in some studies comparing breastfed and formula fed infants. Also, FSANZ's assessment of nutritional equivalence to breast milk estimated that exclusively breastfed three month old infants would consume 12 g/day of 'human milk oligosaccharides' and infants consuming formula containing up to 8 g/L of inulin-derived substances and GOS would consume an estimated 6 g/day. Health benefits attributed to a substance when added to infant formula has not been considered in the risk assessment of this Proposal. For further information refer to sections 7.2, 7.2.2 and 7.3.2.
One submitter noted the evidence provided relies on stool analysis, with no evidence this is of benefit to formula fed infants.	In the absence of policy guidance, the potential benefits of these substances on the health of infants and young children have not been assessed. FSANZ's assessment found that at levels up to 10 g/L there is evidence of similar physiological (softer stools and increased stool frequency) and microbiological effects (increased growth of colonic bifidobacteria) in some studies comparing breastfed and formula fed infants. For further information refer to sections 7.2, 7.2.2 and 7.3.2.
One submitter noted the dietary analysis does not include breast milk.	As inulin-derived substances/FOS are not present in breast milk and the concentration of GOS in breast milk is negligible, a 'breast milk' assessment was calculated using the intakes of oligo- and polysaccharides for infants at three months

Submitter comments / issues	FSANZ response
	of age. Section 7.4.1 further describes the breast milk assessment undertaken for the Final Assessment Report.
One submitter considered the analysis should include the impact on breastfeeding	FSANZ supports the New Zealand Food and Nutrition Guidelines for Healthy Infants and Toddlers (Aged 0-2 years)45 and the Dietary Guidelines for Children and Adolescents in Australia46 that recognise that breast milk is the ideal food for infants. However, in the absence of policy guidelines it is not within the scope of P306 for FSANZ to assess the impact of this Proposal on breast-feeding beliefs and rates.
Safety	
A number of submitters expressed concern over the use of ratios of GOS to inulin other than the 9:1 ratio, on which most safety studies were based. This included concern about the single addition of either GOS or inulin. Some considered it was not appropriate to extrapolate from specific studies (inulin/GOS at a 9:1 ratio) to other variations, or singular use of these substances.	A range of studies have been conducted with GOS and inulin in infant formula products. Although the majority of these used the 9:1 ratio at a maximum level of 8 g/L, other studies have been done with GOS alone, and with inulin alone. At least one study has been done with the 9:1 ratio at a level of 10 g/L. Based on these studies, and what is known about how inulin and GOS are fermented in the colon, FSANZ has concluded that these products are unlikely to pose any risk when used either alone or in combination at the levels recommended in this proposal. This is further discussed in the Safety Assessment Report at Attachment 8.
One submitter suggested that the higher levels of human milk oligosaccharides in breast milk should not be used to justify the safety of inulin and GOS in the absence of clinical data to support the levels proposed.	In putting forward the recommendations for maximum levels of inulin and GOS in infant formula products, FSANZ has used the levels that have been shown to be safe in clinical studies. The safety of these levels is further supported by the much higher levels found naturally in human milk, however FSANZ does not base the safety assessment solely on levels of human milk oligosaccharides.
One submitter suggested the safety of inulin with an average DP of less than 10 relies on two studies of only 2-3 weeks duration (Kapiki *et al*., 2007; Kim *et al*., 2007).	The safety assessment does not rely on any single study in order to make the stated recommendations. In addition to the two studies cited above, each of which may have had shortcomings, three other studies have been published on the use of longer chain inulin alone in infant formula products (Euler et al., 2005; Bettler and Euler, 2006; Veereman-Wauters et. al., 2008). One of these studies (Bettler and Euler, 2006) had almost 300 infants and was conducted over 12 weeks. The recommendations aim to restrict the addition of very short fructans (i.e. FOS), however inulin is generally made up of a distribution of fructans of different lengths, and it is impossible to draw a line at which point the fructans become too short, nor

[45] New Zealand Ministry of Health, Food and Nutrition Guidelines for Healthy Infants and Toddlers (Aged 0-2): A Background Paper. (1999)
[46] National Health and Medical Research Council, Dietary Guidelines for Children and Adolescents in Australia. (2003)

Submitter comments / issues	FSANZ response
	would it be possible to enforce such a recommendation. Even long-chain inulin preparations will have some proportion of short chain fructans. FSANZ is of the opinion, supported by the external reviewers, that the recommendations put forward are unlikely to pose any risk to young infants. References are provided in Section 7.3.1 of the FAR.
One submitter expressed concern regarding the potential effect on very young babies (from birth) due to the potential to cause discomfort in some sensitive infants.	The only potential hazard identified in relation to the use of inulin-derived substances or GOS in infant formula products is the chance of increased osmotic pressure in the colon leading to diarrhoea and dehydration. This is of greater concern in very young infants (from birth), who lack fully developed renal systems and may not have full colonisation of the colon with bacteria capable of breaking down added oligosaccharides. This potential hazard has been addressed in a range of studies in very young infants, and is discussed in Attachment 8, Safety Assessment Report, which concluded that the addition of inulin-derived substances and GOS at the proposed levels is unlikely to pose any risk to very young infants.
The lack of data on the use of GOS and inulin in infant foods and FSFYC was of concern to one submitter. It was considered data on safety of a specific formulation in infant formula (9:1 ratio and max level of 8 g/L) cannot be extrapolated to infant food or formulated supplementary foods for young children (FSFYC).	Although fewer direct studies have been done for older infants (aged 4-6 months and above) and young children (aged 1-3 years) who might be consuming infant foods and FSFYC, these infants are much less sensitive to potential dehydration as their kidneys are more developed and they have the ability to concentrate urine. Therefore, as inulin-derived substances and GOS are considered safe for very young infants, there will be an equally low risk to older infants and young children.
One submitter noted that the European Commission had some concern with the addition of 'short chain fructans' and suggests it would be useful to have the basis of the European decisions.	The European regulatory assessment of inulin and GOS is described in Section 3 of the Safety Assessment Report (Attachment 8). Some concern was expressed by the Scientific Panel on Dietetic Products, Nutrition and Allergies about the use of oligofructose in infant formula. FSANZ is unaware of any use of short chain fructans derived from sucrose (i.e. FOS) in the food supply in Australia or New Zealand so their exclusion from the term 'inulin-derived substances' is not seen as problematic. Short chain fructans have not been sufficiently studied in infants and young children, therefore these are being excluded from the recommendations of this Report.
Levels of addition	

Submitter comments / issues	FSANZ response
One submitter noted there was little justification for the levels proposed for infants when breast milk levels drop post partum. Several submitters suggested FSANZ reconsider levels. Some industry submitters comment that the relatively low levels permitted in SPFYC differ from the levels shown to be safe by suppliers of these products, and infant formula manufacturers, and that a relatively low level is proposed based on anecdotal evidence of transient gastro intestinal effects. One submitter did not agree with one of the expert views regarding limiting the addition of inulin-derived substances to 3 g/L.	In putting forward the recommendations for maximum levels of inulin and GOS in infant formula products, FSANZ has used the levels that have been shown to be safe in clinical studies. The only potential hazard identified in relation to the use of inulin-derived substances or GOS in infant formula products is the chance of increased osmotic pressure in the colon leading to diarrhoea and dehydration. The levels recommended are based on safety in very young infants. At Draft Assessment the safety assessment concluded that up to 8 g/L inulin-derived substance is unlikely to pose a public health and safety risk to infants. However, it was noted that inulin may cause increased flatulence and bloating in adults at supplementary intakes of 10 g inulin/day. It was not clear if this would occur in infants due to differences in colonic microflora and overall diet. Although both expert peer reviewers considered that these substances when added to infant formula would be safe for infants of all ages, one suggested that in the absence of appropriate studies with inulin-derived substances at higher levels in infants it would be justified to limit the addition of these to the levels that have been directly studied in infants (3 g/L) (see Section 7.5.1). The other expert reviewer had no similar concern. Therefore, at Draft Assessment, FSANZ considered it prudent to limit the addition of inulin-derived substances to levels which have been shown to be well tolerated in infants i.e. 3 g/L. However, since Draft Assessment more recent data has been made available to FSANZ that indicates that inulin-derived substances at levels up to and including 8 g/L were well tolerated by infants, with no serious adverse effects (see section 7.3.1). Therefore, FSANZ has reconsidered the maximum permitted levels based on the totality of evidence available, and has used the levels that have been shown to be safe in clinical studies to recommend maximum levels of inulin and GOS in infant formula products. At Final Assessment the following levels[47] are proposed: for infant formula products a permitted maximum level of 290 mg/100 kJ (0.8 g/100 mL) for the total combined inulin-derived substances and GOS, or for the singular addition of either inulin-derived substances or GOS. This is further discussed in the Safety Assessment Report at Attachment 8 and throughout Section 7 of the Report.

[47] The maximum permitted amounts only apply when the substance is added and then apply to the total of the naturally occurring and added substances.

Submitter comments / issues	FSANZ response
One submitter asked whether the permission for 0.8g/100g refers to made up formula (or powder).	This permission for 0.8g/100g refers to infant *foods* regulated by Standard 2.9.2 and does not apply to infant formula products i.e. FSANZ has proposed for *infant foods* a permitted maximum level of 0.8 g/100 g for total combined inulin-derived substances and GOS, or for the singular addition of either inulin-derived substances or GOS in infant *foods* as consumed. The permissions for infant formula products relate to the made up formula and are expressed per 100 kJ (or per 100 mL).
Methods of measurement	
Some submitters considered suitable measurement methods do not exist (for Compliance), and that no official method is listed in Standard 1.2.8 of the Code. It was suggested FSANZ provide guidance for accurate techniques for measuring GOS in powdered milk-based foods. One submitter also noted it is difficult to measure natural and added levels due to analytical limitations and complex food matrices.	FSANZ understands that methods have been published for determining these substances in foods. Ordinarily this would mean that compliance agencies and their appointed analysts could consider developing and validating their own methods that are suitable for monitoring compliance. FSANZ is not able to develop and validate methods for compliance agencies or their appointed analysts. In addition, methods have not been prescribed for the analysis of fructose polymers or galacto-oligosaccharides in infant foods and so compliance agencies could consider developing their own methods that are suitable for these matrices. Given the uncertainty in relation to galacto-oligosaccharides in some milk-based foods, FSANZ considers that it is not appropriate to prescribe the AOAC method for determining galacto-oligosaccharides. This approach will enable industry, compliance agencies and appointed analysts to continue to develop the methods to address any concerns with determining these substances in milk-based foods. FSANZ has not sought expert analytical advice on the methods of analysis for a number of reasons: methods are not prescribed for determining fructose polymers or galacto-oligosaccharides in food as part of this Proposal; and the appropriateness of any method used for compliance purposes is not subject to any expert analytical advice obtained by FSANZ. In terms of methods of analysis, FSANZ acknowledges that compliance agencies may need time to develop compliance strategies, including validated methods with their appointed analysts.
Labelling and claims	
Several submitters raised issues with regard to labelling and the potential for making claims on infant formula products including: Will inulin-derived substances and GOS be considered a nutritive substance for	FSANZ has addressed these concerns as follows: FSANZ has proposed a specific amendment to clause 16 requiring that where inulin-derived substances and GOS are added to infant formula products, they must be declared and certain information provided, together with the information required for

Submitter comments / issues	FSANZ response
Clause 20(f) in Standard 2.9.1? The meaning of nutrition information statement is not clear or defined in the Code. Could a nutrition content claim be presented as a 'nutrition information statement'.	energy, protein, fat, carbohydrate, and permitted vitamins and minerals and other nutritive substances FSANZ also proposes a new subclause to clause 20 that will only permit a reference to the presence of inulin-derived substances and GOS in the statement of ingredients and the nutrition information statement. Clause 20 will also be amended so that the reference to 'nutrition information statement' links back to Clause 16, where the provisions require the statement to contain certain nutrition information. These amendments aim to clarify the intent that a nutrition information statement is a single statement that is to contain all the information specified in Standard 2.9.1 Clauses 16(1) and (2) and that further reference to inulin-derived substance or GOS on the label of an infant formula product is not permitted.
Could a general level claim be made on SPFYC?	Under the Code, Standard 1.1A.2 – Transitional Standard Health Claims prohibits all food from carrying any health claim, unless the food is listed in the Table to subclause (3)(e). This Table lists specific foods which are permitted to carry the health claim in relation to maternal folate consumption and a reduced risk of neural tube defects. No SPFYC are listed in the Table and therefore none are permitted to carry this claim. Under Proposal P293 – Nutrition, Health and Related Claims (draft Standard 1.2.7), FSANZ is proposing to retain the prohibition of nutrition content claims and health claims on infant formula products. Health claims will be permitted on foods for infants (as regulated by Standard 2.9.2) and Formulated supplementary foods for young children (as regulated by Standard 2.9.3), including claims relating to inulin-derived substances and GOS. Claims made on these foods will not be subject to the nutrient profile scoring criteria due to prescriptive compositional requirements that already apply to these foods. All other requirements of draft Standard 1.2.7 will apply.

Submitter comments / issues	FSANZ response
The use of *either* oligofructose *or* FOS for labelling could be misleading / deceptive for fair trading.	This issue is addressed as part of Section 9.3.1.1. In summary, the current Editorial note to clause 4 of Standard 1.2.4 provides clarification by stating that the names of ingredients should be sufficiently detailed and accurate to ensure that that they are not false, misleading or deceptive, or likely to mislead or deceive. The use of names such as oligofructose and FOS are not misleading provided they are a true representation of the ingredient. The FSANZ Ingredient Labelling User Guide also provides clarification on the use of terms for labelling purposes.
Considers general level claims will be possible for inulin-derived substances and FOS even though they are defined as non-nutritive substances in Standard 1.1.1. Queries how will this anomaly be addressed after gazettal of P293?	Under draft Standard 1.2.7 (recommended as part of Proposal P293), general level health claims are not restricted to nutritive substances. General level health claims will be permitted for inulin-derived substances in general purpose foods, subject to meeting substantiation requirements, the nutrient profiling scoring criteria and other requirements as detailed in draft Standard 1.2.7.
One submitter recommended a separate proposal to ensure consistency of representation on all infant formula products.	FSANZ plans to conduct a review of Standard 2.9.1 Infant Formula Products. This will include a review of Subdivision 4 – General labelling and packaging requirements.
Several submitters considered that if inulin-derived substances are added as biologically active substances a minimum claimable level is required.	Under the Code, biologically active substance nutrition claims may be made on general purpose foods and no minimum or maximum threshold is set. Suppliers are required to declare the average quantity that is present, in accordance with the provisions contained in paragraph 5 (1)(g) of Standard 1.2.8. With regard to SPFYC, FSANZ recommends that where inulin-derived substances are added, only the maximum permitted amount should be regulated for health and safety purposes. Should suppliers wish to make biologically active substance nutrition claims for inulin-derived substances, they will be required to meet labelling conditions stated in paragraph 5 (1) (g) of Standard 1.2.8. Draft Standard 1.2.7 – Nutrition, Health and Related Claims is intended to supersede claim conditions currently set out in Standard 1.2.8. In the draft Standard, FSANZ is proposing that where a biologically active substance general level health claim is made, a serve of the food must contain at least 10% of the amount of the substance that is required to be consumed per day to achieve the specific health effect. The

Submitter comments / issues	FSANZ response
	supplier of the food will be required to substantiate the claim. Other claim conditions for nutrition content claims and general level health claims will also apply. FSANZ considers that current and proposed labelling requirements for biologically active substance claims provide sufficient regulation for claims and therefore a minimum permitted level for inulin-derived substances is not required in the Code.
Drafting	
One submitter commented that the specification for GOS is too restrictive in Standard 1.3.4.	The information available to FSANZ indicates that the specification proposed at Draft Assessment is unnecessarily restrictive. Given the range of formulations that may contain galacto-oligosaccharides, it is considered that the prescription of a specification is no longer considered appropriate and the draft variation will be amended to delete it. This approach would also be consistent with the approach taken for inulin-derived substances where a prescriptive specification is also not proposed. However, these substances would still need to comply with the general requirements in Standard 1.3.4 – Identity and Purity
The wording of Standard 2.9.1 clause 16(1) paragraph (d) is considered open to interpretation and needs clarification.	The proposed amendments to Standard 2.9.1 clause 16(1) paragraph (d) and clause 16(2)(e) have been amended to clarify the requirements. Refer to Attachment 1, Draft Variation to the Code.
Some submitters considered the current drafting potentially allows for the addition of FOS to SPFYC, without limits and with the ability to make a claim. One submitter recommended a specific prohibition for FOS in SPFYC.	At Final Assessment, the definitions proposed at Draft Assessment have been consolidated (refer to section 1.4). FOS (i.e. those fructose polymers derived from sucrose) is excluded from the definition of inulin-derived substances. Therefore at Final Assessment the proposed amendments to the Code that would permit the addition of inulin-derived substances to SPFYC would exclude FOS from this permission.
The drafting for Standards 2.9.2 and 2.9.3 is considered to be inconsistent with Standard 2.9.1 with regard to the maximum permitted levels applying to the 'sum of naturally occurring and added substances'.	FSANZ has revised the proposed draft variation to ensure that the requirement that the maximum permitted levels apply to the 'sum of naturally occurring and added substances' is consistent across Standards 2.9.1, 2.9.2 and 2.9.3. Refer to Attachment 1.

Submitter comments / issues	FSANZ response
GOS	
A submitter considered GOS should be included in the amendment to Standard 1.1.1 as there is potential for greater use in the general food supply, it is considered safe by FSANZ for SPFYC, and is not taken to be a nutritive substance. It was also noted that failure to recognise GOS in general foods will create trade barriers. Further explanation was requested for why GOS is not permitted in general foods when it is safe for infants. A submitter queried whether the maximum permitted amount proposed for GOS includes GOS produced in-situ via hydrolysis of lactose.	There is no history of safe use in there general food supply in Australia and NZ and FSANZ is not aware of the wide use of GOS added to food (other than to infant formula products, infant foods and FSFYC). It is also considered that intakes from the general food supply from naturally-occurring GOS are likely to be negligible. Therefore, FSANZ considers the regulation of GOS in food does not need to be included in the Code at this time, other than for its use in infant formula products, infant foods and FSFYC. The limit would apply to the GOS in the food naturally occurring, added, or formed during production and processing of the food. The drafting has been amended to ensure consistency across Standards 2.9.1, 2.9.2 and 2.9.3.
Education / communications	
A targeted education / communication strategy is needed.	FSANZ will undertake targeted communication and education on the proposed draft variations to the Code with key stakeholders including health professionals, the food industry and enforcement agencies. Also, information will be provided on the FSANZ website and for the FSANZ Code enquiry line, particularly regarding the proposed permissions for addition of inulin-derived substances and GOS to special purpose foods for infants and young children. This will ensure consumers and health professionals have access to appropriate information.
Consultation	
Recommends a 2nd round of consultation may be needed to address issues.	FSANZ has undertaken targeted consultation during development of the Final Assessment, following submissions to the Draft Assessment.

Attachment 4

Chemical and Technological Uses Assessment

This document has been amended from that which was circulated for comment following Draft Assessment.

Summary

Inulin-derived substances and to a lesser degree galacto-oligosaccharides, are used in food for various reasons including technological and nutritional reasons. The purpose of this Report is to describe these substances and characterise them for the purposes of further assessment of their nutritional and general ingredient properties.

Galacto-oligosaccharides

The term 'galacto-oligosaccharide' is used consistently to describe those substances comprised of between two and eight saccharide units with one of these units being a terminal glucose and the remaining saccharide units being galactose, and disaccharides comprised of two galactose units. While the disaccharide lactose is present in 'galacto-oligosaccharide' mixtures, it is not regarded as a galacto-oligosaccharide. Galacto-oligosaccharides are produced from lactose by enzymatic action and are also referred to as 'trans-galacto-oligosaccharides'.

Galacto-oligosaccharides are added to infant formula products, infant foods and formulated supplementary foods for young children for nutritional reasons. FSANZ is unaware of any technological reason for the addition of galacto-oligosaccharides to other foods. For this reason, FSANZ has not considered the technological aspects of the addition of galacto-oligosaccharides to these other foods.

Fructose polymers (inulin/oligofructose/fructo-oligosaccharides)

The following terms are used in this Report:

- The term 'inulin-derived substances' is used to collectively describe inulin, long-chain inulin and oligofructose. This term does not include those fructose polymers derived from sucrose;

- the term 'inulin' is used to describe those fructose polymers with β (2→1) fructosyl-fructose linkages, where the average Degree of Polymerisation (DP)[48] is equal to or greater than ten;

- the term 'long-chain inulin' is used to describe those fructose polymers with β (2→1) fructosyl-fructose linkages, where the average DP is equal to or greater than 23;

- the term 'oligofructose' is used to describe those fructose polymers with β (2→1) fructosyl-fructose linkages, derived from inulin, where the average DP is less than ten; and

[48] Degree of polymerisation is the number of fructose or saccharide units in a substance.

- the term ‘fructo-oligosaccharide’ (FOS) 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 enzymatic condensation of sucrose.

FOS could be regarded as a subset of oligofructose because it contains some similar compounds as oligofructose. However, it is not typically produced from inulin and is therefore not considered to be derived from inulin.

The substance that has been used overseas in infant formula products, infant foods and formulated supplementary foods for young children has been represented as ‘high molecular weight fructosyl-saccharose’, ‘long-chain fructo-oligosaccharides’, ‘long-chain inulin’ or ‘high molecular weight inulin’. Based on the terms described above, this substance is considered to be a fraction of processed ‘inulin’. This is supported by the specifications for these substances that have been provided to FSANZ. Throughout this Report the term ‘long-chain inulin’ will be used to describe the processed inulin fraction that has been added or has been proposed to be added to infant formula, infant foods and formulated supplementary foods for young children.

Taking into account the comments in submissions and following further assessment, FSANZ considers that it is appropriate to retain the terminology for specific fructose polymer groups stated above. However, in relation to definitions in the draft variation, FSANZ acknowledges the comments in submissions and proposes that the range of relevant fructose polymers could be consolidated into the single generic term of ‘inulin-derived substances’.

‘Inulin-derived substances’ would include inulin and would be mixtures of those fructose polymers with predominantly β (2→1) fructosyl-fructose linkages with or without a terminal glucose molecule but would not include those polymers produced from sucrose by enzymatic action. This broad term would include all fructose polymers derived from inulin. This approach would also reflect the natural variation in these polymers which may have some β (2→6) fructosyl-fructose linkages.

Inulin type fructose polymers may be added to foods for technological reasons or nutritional reasons (e.g. dietary fibre). The technological reasons for the addition of inulin, oligofructose or fructo-oligosaccharides to foods include as an emulsifier, thickener, stabiliser and sweetener. These functions vary with the nature of the inulin-derived mixture (e.g. chain length), its concentration in a food and the food itself. These technological purposes relate to the gelling properties of inulin, in particular its ability to form stable gels with water to replace fat or to impart textural qualities in foods. Some inulin-derived products (e.g. oligofructose) and fructo-oligosaccharides are used as sweeteners. Based on the information available, FSANZ understands that FOS (i.e. the fructose polymers derived from sucrose) is not used in the food supply in Australia or New Zealand.

Specifications

Substances added to foods must comply with the requirements in Standard 1.3.4 – Identity and Purity of the Australia New Zealand Food Standards Code (the Code), where applicable. These requirements include specifications for specific substances where appropriate.

Based on the 'galacto-oligosaccharide' proposed to be added to infant formula, infant foods and formulated supplementary foods for young children, a specification for this substance was originally proposed. Additional information has been provided to FSANZ indicating that a range of galacto-oligosaccharide containing formulations are available. This information indicates that the specification originally proposed is unnecessarily restrictive and is no longer considered appropriate.
For this reason, the inclusion of a specification for galacto-oligosaccharide in Standard 1.3.4 is no longer proposed. However, the general provisions in Standard 1.3.4 would still be applicable to these substances.

The specifications for inulin, oligofructose, and ingredients derived from inulin will vary in accordance with the variety of different compositions that are available. It is therefore impractical to develop specific specifications for these substances. However, the general provisions in Standard 1.3.4 would still be applicable to these substances.

Stability data

Inulin type fructose polymers are generally stable in most food matrices but under acid conditions (e.g. certain beverages when not refrigerated) hydrolysis may occur. Based on information provided to FSANZ galacto-oligosaccharides are represented as having good stability to heat and acid conditions. FSANZ considers that these substances are likely to have acceptable stability in most dry foods but that inulin type fructose polymers may not be suitable in low pH liquid foods, as inulin potentially might be hydrolysed to fructose.

Compliance with any limits

FSANZ has noted that methods for determining fructose polymers or galacto-oligosaccharides in food have been published by the Association of Official Analytical Chemists. FSANZ has not sought expert analytical advice on the methods of analysis because methods are not prescribed for determining fructose polymers or galacto-oligosaccharides in food as part of this Proposal, and because the appropriateness of any method used for compliance purposes is not subject to any expert analytical advice obtained by FSANZ. FSANZ acknowledges that published methods may need to be modified by compliance agencies and their appointed analysts to be suitable for compliance purposes.

1. Structure of Inulin, Oligofructose, Fructo-oligosaccharides (FOS) and Galacto-oligosaccharides (GOS)

In general terms an 'oligosaccharide' is a carbohydrate that consists of a relatively small number of linked monosaccharide units, typically between three and ten units. The term 'oligosaccharide' has been further characterised by adjectives used to describe specific substances or fractions of substances e.g. Long-chain oligosaccharides.

1.1 Inulin/Oligofructose/Fructo-oligosaccharides

To clarify the use of the terms 'inulin', 'oligofructose' and 'fructo-oligosaccharides', the following information is provided about the terms used throughout this Report. The information and terms below are based upon terms used by Carabin and Flamm[49].

[49] Carabin, I and Flamm, G. Evaluation of Safety of Inulin and Oligofructose as Dietary Fiber. Regulatory Toxicology and Pharmacology 30, 268-282 1999.

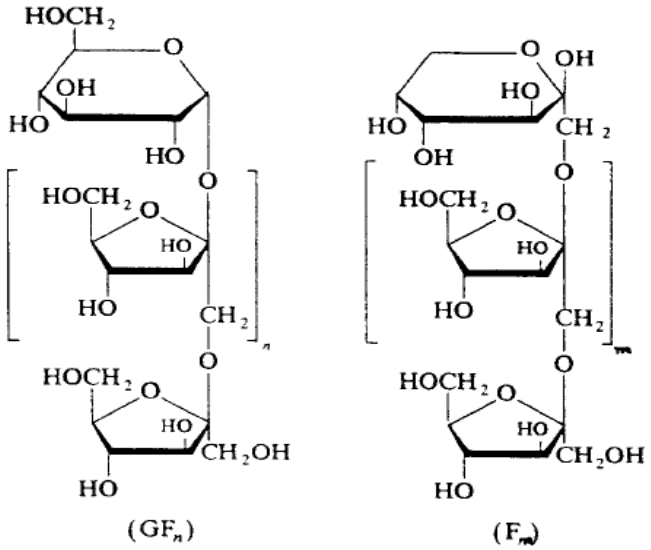
Polymers of fructose are referred to as 'fructans' with the fructose units primarily joined by two types of molecular linkages, inulin type β (2→1) and levan type β (2→6). These linkages refer to the numbering of the carbon atoms on the six carbon fructose molecule.

Inulin is a mixture of inulin type fructose polymers (polysaccharides) that are extracted from plant material. It occurs naturally in many plants and depending on the degree of refinement, the substance will vary in terms of its physical and chemical characteristics.

In general terms, inulin is a substance composed of molecules of fructose units of differing lengths or degrees of polymerisation (DP), typically with a terminal glucose molecule. The differences between the terms used to describe fructose polymers are characterised by the range of the DP, including the average DP. The DP is a measure of the number of fructose molecules or saccharide units in the chain and the degree of polymerisation is therefore a key compositional component in characterising fructose polymers. The proportions of monosaccharides and disaccharides present in a mixture of substances are also considered to be characterising aspects of these ingredient mixtures.

Standard inulin contains a small amount of mono (glucose & fructose), di (sucrose) and other longer chain saccharides. Inulin can also contain branched or linear chains of fructose units, which may or may not be terminated with a glucose molecule. Inulin extracted from most plant sources typically has only a small degree of branching and is predominantly composed of linear chains of fructose, the blue agave being an exception. The major commercial source of inulin is chicory and the DP is between two and seventy fructose units with an average DP above ten. Refining of standard inulin can result in partial removal of the shorter chain molecules and increase the average DP to approximately 25.

The term 'oligofructose' has been used to describe those mixtures of substances that are produced from the partial enzymatic hydrolysis of inulin, typically with a degree of polymerisation in the range of two to eight, although a range of three to nine has also been quoted. The term 'fructo-oligosaccharide' has been used to mainly describe those mixtures of substances with a degree of polymerisation in the range of three to five, although this term has also been used to describe oligofructose like substances and inulin.



Structure of inulin[50] where G =glucose, F=fructose and where *n* and *m* represent the number of fructose units

[50] A Franck, De Leenheer, ORAFTI,

The number of saccharide units in inulin and other polysaccharide mixtures is not defined specifically, although the DP for the substances in inulin is described as between 2 and seventy. Terms such as 'oligofructose' and 'fructo-oligosaccharides' are generally used to describe substances where the average DP is less than ten. The term 'fructo-oligosaccharides' also appears to be used more commonly (but not exclusively) to describe those short chain fructose polymers (usually with a glucose terminating molecule) that are prepared from enzymatic condensation of sucrose and fructose. The term 'fructo-oligosaccharides' has also been used to describe all inulin type fructans, both long and short chain.

To ensure that there is clarity about the substances, this Report will use the term 'inulin-derived substances' to collectively describe inulin, long-chain inulin and oligofructose. This term does not include those fructose polymers derived from sucrose. The term 'inulin' will be used to describe those fructans, with β (2→1) fructosyl-fructose linkages, where the average DP is equal to or greater than ten. The term 'oligofructose' will be used to describe those fructans, with β (2→1) fructosyl-fructose linkages, where the average DP is less than ten. Consistent with the view of Carabin and Flamm, the term 'fructo-oligosaccharide' will only be used to describe those fructans, with β (2→1) fructosyl-fructose linkages, where the average DP is less than four. In accordance with this terminology and on the basis of the information available to FSANZ, 'fructo-oligosaccharides' do not appear to be the substances that are proposed to be added or that are being added to infant formula or infant foods as 'FOS'.

The substances used overseas in infant formula, infant foods and formulated supplementary foods for young children have been represented as 'high molecular weight fructosyl-saccharose', 'long-chain fructo-oligosaccharides' or 'high molecular weight inulin'. Based on the terms described above, this substance is considered to be a fraction of processed 'inulin'. This is supported by the specifications for these substances that have been provided to FSANZ. Throughout this Report the term 'long-chain inulin' will be used to describe the processed inulin fraction that has been added or is proposed to be added to infant formula, infant foods and formulated supplementary foods for young children.

Substance	Degree of Polymerisation	Average Degree of Polymerisation
Inulin	**2 - 70**	**≥10**
Oligofructose	**2 – 10**	**< 10**
Long-chain Inulin	**10 - 70**	**≥ 23**
Fructo-oligosaccharide	**3 - 5**	**< 4**

1.1.1 Comments on the Draft Assessment

FSANZ developed the terms above for a range of fructose polymers to ensure there was clarity about these terms in assessing or considering the assessments for this Proposal and a number of related Applications. These terms were included in the Draft Assessment Report for this Proposal as well as the definitions in the draft variation. Comment was sought on them. The comments on the definitions in the draft variation ranged from full support to requests to modify them. The reasons for the modifications were given as:

1. there was a need for the definitions to reflect that fructose polymers are derived from natural sources and subject to natural variations;

2. fructose polymers are described with terms or common names that have a long history of use and the definitions did not reflect this use; and

3. distinctions based around 'average degree of polymerisation' may not be readily enforceable or consistent with current conventions, and the source of the fructose polymers may be a more practical distinction between these polymers.

FSANZ acknowledges that there are 'generally accepted' terms used to describe fructose polymers but is not convinced that these are used universally or consistently. Despite the varying use of these terms, FSANZ has not been informed of any misuse of these terms. In addition, the natural variation in these substances means that it is not possible to develop prescriptive characterisations for these substances. For this reason, FSANZ has proposed a less prescriptive approach for the definitions in the draft variation which reflects the status quo in relation to representations about these substances.

Taking into account the comments in submissions and following further assessment, FSANZ proposes to retain the terminology for specific fructose polymers used in the Draft Assessment Report. However, in relation to definitions in the draft variation, FSANZ acknowledges the comments in submissions and proposes that the range of relevant fructose polymers could be consolidated into the single generic term of 'inulin-derived substances'. This approach would:

- avoid the need for a range of terms to be defined, which is not practical or necessary given the varying nature of fructose polymers;

- avoid any confusion with the existing common names used to describe fructose polymers, including inulin-derived substances; and

- be likely to be more practical from a compliance perspective.

'Inulin-derived substances' would include inulin and would be mixtures of those fructose polymers with predominantly β (2→1) fructosyl-fructose linkages with or without a terminal glucose molecule but would not include those polymers produced from sucrose by enzymatic action. This broad term would include all fructose polymers derived from inulin but would exclude those derived from sucrose. This term would also reflect the natural variation in these polymers which may have some β (2→6) fructosyl-fructose linkages. The use of this term in the draft variation would also be equivalent to the term 'inulin-derived substances' used throughout this Report and in the draft variation.

Use of this term would mean that it is not necessary to differentiate between the different types of fructose polymers from inulin in the draft variation and the status quo is maintained in relation to existing representations (e.g. common names) about these substances in the general food supply. The approach of consolidating the definitions in the draft variation to a more generic expression and excluding those polymers derived from sucrose, is considered a pragmatic approach taking into account that:

- on the basis of current knowledge, sucrose derived fructose polymers are always of shorter chain length than polymers derived from inulin and it is this shorter chain length group of polymers which the original definition of 'fructo-oligosaccharide' was intended to capture; and

- FSANZ is unaware of any use of short chain fructose polymers from sucrose in the food supply in Australia or New Zealand and so their specific exclusion from the term 'inulin-derived substances' is not seen as problematic.

It should be noted that the exclusion of sucrose derived fructose polymers is not based on a concern about the safety of these substances. It is based on insufficient data demonstrating their safety in infant foods and the need to develop a sufficiently practical means of capturing those substances that are currently used in the food supply in Australia and New Zealand. This approach does not prevent the fructose polymers from sucrose being reconsidered at some time in the future including in the context of whether they are nutritive substances or food additives.

1.2 Galacto-oligosaccharides

The term 'galacto-oligosaccharide' is used more consistently to describe those substances comprised of between two and eight saccharide units with one of these units being a terminal glucose and the remaining saccharide units being galactose, and disaccharides comprised of two galactose units. Galacto-oligosaccharides produced from lactose by enzymatic action and are also referred to as 'trans-galacto-oligosaccharides'. This mixture of substances is available as a syrup or powder and the lactose content (disaccharide) is typically regarded as part of the 'galacto-oligosaccharide' mixture.

1.2.1 Comments on the Draft Assessment

FSANZ developed the term above for galacto-oligosaccharides to ensure it was sufficient for the range of substances available. The term was included in the Draft Assessment Report for this Proposal as well as the definitions in the draft variation. Comment was sought on it.

The comments received were in relation to the disaccharide portion of galacto-oligosaccharides. The term 'galacto-oligosaccharides' does not include lactose (a disaccharide) but includes those substances produced from lactose by enzymatic action. This includes disaccharides which are made from two units of galactose. To clarify this, the definition for 'galacto-oligosaccharides' will be amended to reflect this.

1.3 Specifications

Substances added to foods must comply with the requirements in Standard 1.3.4 – Identity and Purity, where applicable. These requirements include specifications for specific substances where appropriate.

The specifications for inulin, oligofructose and inulin-derived ingredients will vary in accordance with the wide variety of proprietary mixtures that are available. This variation makes it impractical to ascribe a particular specification for these mixtures. However, these substances would still need to comply with the general requirements in Standard 1.3.4.

In relation to infant formula, infant foods and formulated supplementary foods for young children, and based on information provided to FSANZ, the syrup form of galacto-oligosaccharides is proposed to be added to infant formula, infant foods and formulated supplementary foods for young children. A specification for the syrup form was proposed at Draft Assessment and this was included in the Draft Assessment Report.

1.3.1 Comments on the Draft Assessment

One submission indicated that a powder form of galacto-oligosaccharides was also available and questioned whether it was practical to develop a specification for galacto-oligosaccharides. Additional information was also provided to FSANZ indicating that a range of galacto-oligosaccharide containing formulations are available. This information indicates that the specification proposed at Draft Assessment was unnecessarily restrictive.

Given the range of formulations that may contain galacto-oligosaccharides, it is considered that the prescription of a specification is no longer considered appropriate and the draft variation will be amended to delete it. This approach would also be consistent with the approach taken for inulin-derived substances where a prescriptive specification is also not proposed. However, these substances would still need to comply with the general requirements in Standard 1.3.4 – Identity and Purity.

1.4 Stability

1.4.1 Fructose polymers (inulin/oligofructose/fructo-oligosaccharides)

Inulin type fructose polymers are generally stable in most food matrices but under acid conditions (certain beverages if not refrigerated) hydrolysis can occur. FSANZ considers that these substances are likely to have acceptable stability in most dry foods but that inulin type fructose polymers may not be suitable in low pH unrefrigerated liquid foods. The significance of this unsuitability would depend on the purpose for the addition and whether any breakdown substantially reduced the capability of the inulin type fructose polymers to fulfil the technological or nutritional purpose. In such cases, inulin type fructose polymers may be partially hydrolysed to oligofructose.

1.4.2 Galacto-oligosaccharides

Based on information provided to FSANZ galacto-oligosaccharides are represented as having good stability to heat and acid conditions. FSANZ considers that these substances are likely to have acceptable stability in most foods.

1.5 Analysis

The Association of Official Analytical Chemists (AOAC) has published methods for determining the amount of inulin and certain 'oligosaccharides' in food. These methods are primarily based on the saccharide analysis of products following selective enzyme action. In the Draft Assessment Report, FSANZ considered that suitable methods exist for compliance purposes and these methods have been published, including by the Association of Official Analytical Chemists.

FSANZ did not propose to prescribe any methods of analysis as part of this Proposal but did propose to update the terminology for a method currently prescribed in the Code for determining inulin in foods. This was proposed to align the terminology in the Code with the terminology in the AOAC published method.

1.5.1 Comments on the Draft Assessment

The comments from one submitter included concerns about monitoring compliance and specifically the methods of analysis for determining fructose polymers and galacto-oligosaccharides in food. This submitter also stated that they were unaware of any analytical capability for measuring fructose polymers in foods in Australia. On the basis that methods have been published for determining these substances in foods, FSANZ understood that this would mean that compliance agencies and their appointed analysts would be able to develop and validate their own methods that are suitable for monitoring compliance.
In addition, FSANZ has not proposed that any methods should be prescribed. On this basis, compliance agencies and their appointed analysts can use any appropriate method for monitoring compliance for these substances in food.

One point of potential confusion was the inclusion in the draft variation of an editorial change to the currently prescribed methods for determining fructose polymers in foods. This change was proposed to ensure that the terminology used in clause 18 of Standard 1.2.8 in the Code was the same as the terminology used in the AOAC method. It was not intended to indicate that this method would be prescribed for generally measuring fructose polymers in food and no change is now proposed to the terminology for the methods stated in Clause 18 of Standard 1.2.8. In summary, compliance agencies and their appointed analysts can use any appropriate method for monitoring compliance with any requirements for fructose polymers in foods, except where it relates to nutrition labelling. In this case the methods prescribed in clause 18 of Standard 1.2.8 are to be used.

One submitter questioned whether the method for determining galacto-oligosaccharides was appropriate for milk based products. FSANZ has been informed that the AOAC method may not be suitable where there are high levels of lactose in the food as this can interfere with the detection phase of the analysis. FSANZ understands that the method published by the AOAC was used to determine galacto-oligosaccharides in a range of foods including milk based foods. On this basis, FSANZ is of the view that the method should be appropriate for determining galacto-oligosaccharides in a number of foods. Given the uncertainty in relation to galacto-oligosaccharides in some milk-based foods, FSANZ considers that it is not appropriate to prescribe the AOAC method for determining galacto-oligosaccharides in all foods. This approach will enable industry, compliance agencies and appointed analysts to continue to develop the methods to address any concerns with determining these substances in milk-based foods.

FSANZ has not sought expert analytical advice on the methods of analysis because methods are not prescribed for determining fructose polymers or galacto-oligosaccharides in food as part of this Proposal, and because the appropriateness of any method used for compliance purposes is not subject to any expert analytical advice obtained by FSANZ. In terms of methods of analysis, FSANZ acknowledges that compliance agencies may need time to develop validated methods with their appointed analysts.

1.6 Mode of Action

1.6.1 Fructose polymers (inulin/oligofructose/fructo-oligosaccharides)

Inulin, inulin-derived substances and fructo-oligosaccharides may be added to foods for technological reasons or nutritional reasons. In the case of infant formula, infant foods and formulated supplementary foods for young children, from the data available to FSANZ, the use of inulin or inulin-derived substances is for nutritional reasons and not for technological reasons associated with the food. For this reason, this Report will focus on technological uses for inulin, inulin-derived substances and fructo-oligosaccharides in foods other than infant formula, infant foods and formulated supplementary foods for young children.

The technological purposes for the addition of these substances to foods include as an emulsifier, thickener and stabiliser as well as fat and sugar replacement ingredients. These purposes vary with the nature of the inulin-derived mixture (e.g. chain length), its concentration in a food and the food itself. These technological purposes relate to the dispersing properties of inulin, in particular its ability to mimic fat droplets dispersed in water. These dispersions can then be used in foods to replace fat or to impart textural qualities in foods.

The amount of these inulin-derived ingredients used to fulfil these purposes will vary in the food application as it will be necessary to specifically consider the technological aspects in each situation, given the varying composition of the foods to which it will be added and the precise technological purpose to be fulfilled. Therefore different levels of inulin-derived ingredients will be added to foods to achieve these functions.

It has been reported that specific applications for inulin and inulin-derived products include:

- beverages (including for nutritional purposes);
- bread or cereal products for fat or sugar replacement or processing benefits (also for nutritional purposes); and
- dairy products for fat or sugar replacement or texture improvement.

Some inulin-derived products (e.g. oligofructose) and fructo-oligosaccharides are also used as sweeteners with the relative sweetness being dependent on the degree of polymerisation and the proportion of the monosaccharide and disaccharide content in these products. While inulin and inulin-derived products may be refined to fulfil specific technological characteristics, the substances in these products occur naturally in many foods. While some foods would not be expected to contain inulin or inulin-derived products or substances, foods containing these substances would be part of the diet of most if not all people. This is not the case for FOS (i.e. fructose polymers derived from sucrose) which based on the information available to FSANZ, is not used in the food supply in Australia or New Zealand.

1.6.2 Galacto-oligosaccharides

From the information available to FSANZ the addition of galacto-oligosaccharides to infant formula, infant foods and formulated supplementary foods for young children is for nutritional reasons and not for any technological purpose in the foods. In addition, FSANZ is unaware of any technological reason for the addition of galacto-oligosaccharides to other foods. For this reason, FSANZ has not considered the technological aspects of the addition of galacto-oligosaccharides to general purpose foods.

1.6.3 Comments on the Draft Assessment

The comments in some submissions stated that fructose polymers, including inulin-derived substances, should be regarded as food additives given their technological function in food. All food ingredients can perform technological functions in a food and this of itself does not classify a food ingredient as a food additive. Recognising the wide range and permutations of ingredients that could be added to food, it would be impractical to declare all food ingredients as food additives.

A practical approach is to consider each case on its merits and where its recognition as a food additive is appropriate then the substance can be included in the food additive standard (Standard 1.3.1) and the commensurate restrictions and obligations would then apply to these food additives. At this time and to align with the approach used internationally, FSANZ does not consider it appropriate or practical to regard inulin-derived substances as food additives even though they perform technological functions in food.

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Attachment 5

Human Milk Carbohydrates

Summary

Human breast milk contains a carbohydrate component that is composed of mixed saccharide monomers connected by bonds that are resistant to hydrolysis in the small intestine. The structures range from simple tri-saccharides to complex multiply-branched polysaccharides. These oligosaccharides with a degree of polymerization (DP) of 3-10 and polysaccharides with a DP > 10 are comprised of neutral and acidic compounds, of which the neutral fraction is the major component. The number of structurally different oligo- and polysaccharides may exceed 1,000. Some of the structures in breast milk are determined by maternal genetics and regional differences in breast milk composition have been found.

The total oligo- and polysaccharide content of human milk may be up to 25 g/L during the first few weeks following birth. From one to four months the concentration is likely to be around two-thirds of the concentration in early lactation and the concentration may continue to decline with time. Neutral oligo- and polysaccharides have been found in concentrations of up to 15 g/L in Italian women over the first 3 months of lactation. There is a large variation in the breast milk concentration of oligosaccharides among individual women, as much as a four-fold difference. The effect of maternal diet on the carbohydrate content of breast milk has not been extensively studied. Between and within country comparisons indicate similar lactose concentrations in breast milk independent of the mother's state of nourishment or economic status.

1. Structure

The carbohydrates in greatest abundance in human milk comprise lactose (~7% of the milk) and oligosaccharides (1-2%). Polysaccharides are described as being in low abundance (Stahl *et al*., 1994). The monomers found in oligo- and polysaccharides include galactose, fucose, N-acetyl-glucosamine, N-acetyl-galactosamine, and N-acetyl-neuraminic acid (NeuAc; sialic acid). These sugar bases are all hexoses and fucose should not be confused with the fruit sugar fructose, a pentose that is not present in human milk (Huisman *et al*., 1996). The oligo- and polysaccharide fraction contains a complex mixture of compounds. Citing a number of articles, Ninonuevo and colleagues estimate that more than 200 oligo- and polysaccharides have been identified (Ninonuevo *et al*., 2006). However, due the occurrence of isomeric structures that are not easily identified from each other, the number of different oligo- and polysaccharides may exceed 1000 (Boehm, 2005).

Oligo- and polysaccharides are synthesized in the mammary gland by monomer-specific enzymes (transferases). The disaccharide lactose is used as a starting substance to which sugar monomers are added to form larger linear or branched structures. A simple tri-saccharide in high abundance is 2'-fucosyllactose. Other major components of human milk are 'core' oligosaccharides. These structures are formed from the elongation of lactose with N-acetyl-glucosamine and galactose. Two of these core structures, lacto-N-tetraose and lacto-N-neo-tetraose are in high abundance in human milk; the structure of lacto-N-tetraose is shown in **Figure 1**. In addition to their presence in human milk, core oligosaccharides also represent the starting structures of more complex oligosaccharides.

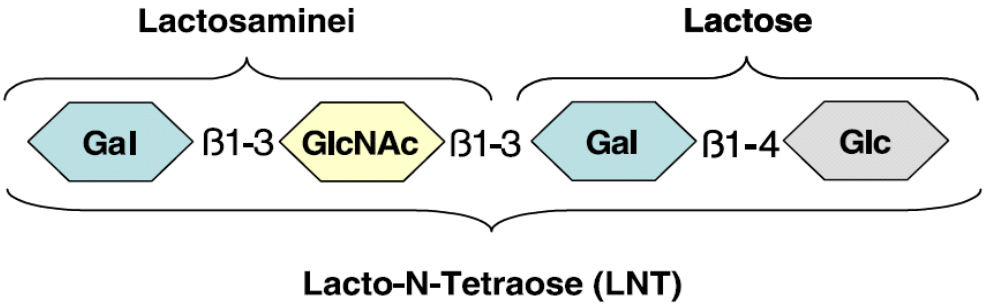

Figure 1: Lacto-N-tetraose (source: Kunz & Randolf, 2006)

Branching and elongation of the core oligosaccharides with additional monosaccharides creates longer oligosaccharides and polysaccharides with a degree of polymerization of 50 or more. If one or more fucose molecules are added to lactose or to a core oligosaccharide the resulting compound is classified as a fucosyl-oligosaccharide. Similarly, if sialic acid is added to lactose or to a core oligosaccharide it is classified as a sialyl-oligosaccharide. Compounds containing both fucose and sialic acid have been identified (Smith *et al*., 1987). Human milk oligosaccharides are sometimes classified on the basis of charge according to the presence of sialic acid into neutral and acidic (sialylated) compounds. The majority fraction is comprised of neutral compounds with the sialylated acidic compounds comprising 16% of the total oligo- and polysaccharides found in the breast milk of five milk-bank donors (Ninonuevo *et al*., 2006). The proportion of acidic compounds is not fixed and varied from 3% to 36% among the five samples of breast milk. The galacto-oligosaccharide 6'-galactosyl-lactose has been found in human milk at a low concentration of around 0.003 g/L (Yamashita & Kobata, 1974), and 3'- galactosyl-lactose has been identified (Donald, 1988). Some of the oligosaccharides found in human milk in relatively high concentrations are shown in **Table 1**.

Table 1: Some of the major oligosaccharides in human milk sampled 30 days postpartum (Coppa *et al*., 1999)

Classification	Sub-classification	Oligosaccharide	Concentration (g/L)
	Fucosyl-oligosaccharide	2'-fucosyl-lactose	2.78 (0.94)
		3-fucosyl-lactose	0.28 (0.07)
		Trifucosyl-lacto-N-hexaose	3.10 (1.40)
		Difucosyl-lacto-N-hexaose	2.62 (0.82)
Neutral		Lacto-N-fucopentaose I	0.99 (0.25)
	Core oligosaccharide	Lacto-N-tetraose	0.71 (0.21)
		Lacto-N-neo-tetraose	1.40 (0.55)
		6'-sialyl-lactose	0.44 (0.14)
Acidic	Sialyl-oligosaccharide	Sialyl-lacto-N-tetraose c	0.21 (0.08)
		Disialyl-lacto-N-tetraose	0.67 (0.57)

The expression of enzymes that facilitate the addition of fucose, the fucosyltransferases, are influenced by the Secretor and Lewis blood group genotype of the lactating woman. Hence the structures of some of the fucosylated compounds in human milk are genetically determined. The majority of Caucasian women (~70 - 80%) are secretors of A and B antigenic material and their milk contains lacto-N-fucopentaose I. In non-secretors, the milk oligosaccharide is Lewis gene dependent and lacto-N-fucopentaose II is the major form (**Figure 2**). Other forms may be present dependent upon maternal genetics.

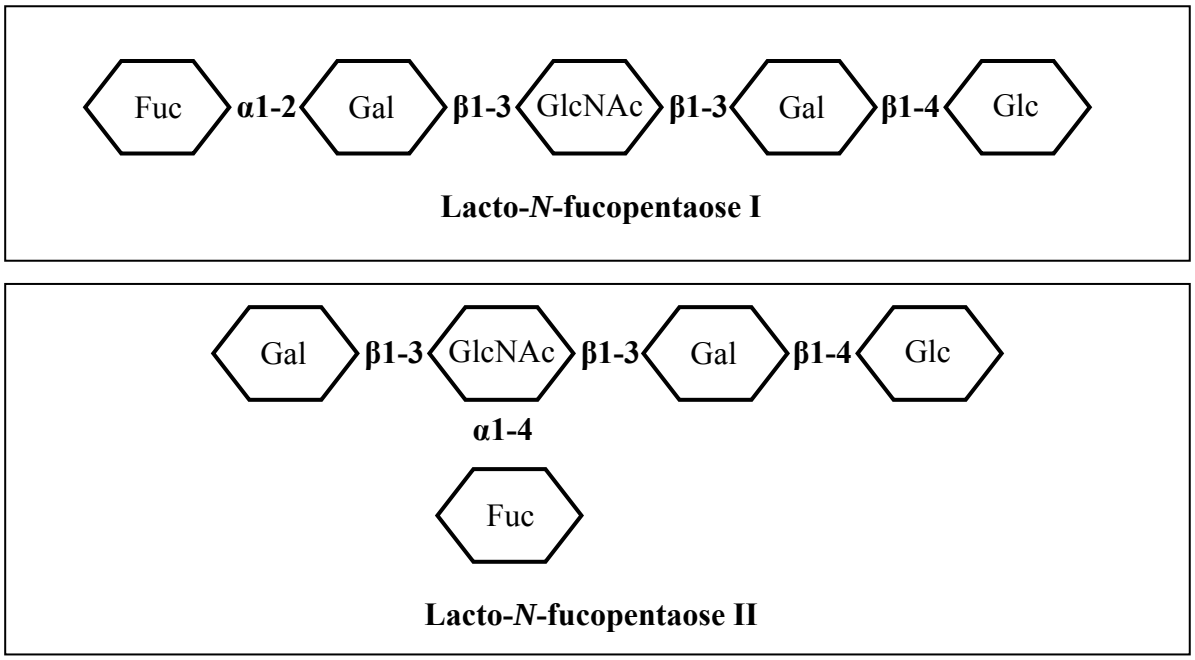

Figure 2: Genetically-determined structures of two lacto-N-fucopentaoses

Regional variation in breast milk oligosaccharide composition has been found (Erney *et al*., 2000). The presence and concentration of nine neutral oligosaccharides were determined in the breast milk of women living in 10 countries. Results of two of the major oligosaccharides, 2'-fucosyl-lactose and 3-fucosyl-lactose, are shown in **Table 2**. The breast milk of almost all of the women in all countries contained 3-fucosyl-lactose. The proportion of women whose breast milk contained 2'-fucosyl-lactose varied over a range of 46 to 100%.

Table 2: **Percentage of women whose breast milk contains 2'-fucosyl- and 3-fucosyl-lactose**

Country	n	2'-fucosyl-lactose (% of women)	3-fucosyl-lactose (% of women)
Chile	44	84	100
China	32	78	100
France	22	91	89
Germany	18	83	100
Italy	29	86	100
Mexico	156	100	100
Philippines	22	46	96

Country	n	2'-fucosyl-lactose (% of women)	3-fucosyl-lactose (% of women)
Singapore	26	72	92
Sweden	7	100	Not determined
United States	79	68	98

These data demonstrate the diversity in the composition of human milk oligosaccharides that differ with respect to size, sequence, charge and abundance (Ninonuevo *et al*., 2006). The number of structurally different oligo- and polysaccharides may exceed 1000. The structures range from simple tri-saccharides to complex multiply-branched polysaccharides. Some of the structures are genetically determined.

2. Concentration

The oligosaccharide concentration of breast milk obtained from 46 Italian women was measured over a period of four months postpartum and the results are shown in **Table 3** (Coppa *et al*., 1993).

Table 3: Mean (SD) oligosaccharide concentration in the breast milk of 46 women

Day after delivery	Oligosaccharide concentration (g/L)
4	20.9 (4.81)
10	20.1 (3.95)
30	15.5 (3.44)
60	12.9 (2.60)
90	12.4 (2.80)
120	12.9 (3.30)

In a later study by the same group involving 18 women delivering term infants, oligosaccharide fractions (fucosyl-, sialyl- and core oligosaccharides) were reported separately as shown in **Table 4** (Coppa *et al*., 1999).

Table 4: Mean oligosaccharide concentration in the breast milk of 18 women.

Day after delivery	Oligosaccharide concentration (g/L)		
	Fucosyl-	Core	Sialyl-
4	13.88	3.13	3.30
10	12.60	2.71	2.70
30	11.59	2.26	2.14
60	12.13	2.73	1.79
90	11.45	3.1	1.58

The total oligosaccharide concentration at 4 days was in excess of 20 g/L followed by a decline of around 20% at 30 days and relatively constant thereafter. The long-term neutral oligosaccharide concentration (excluding sialyl-oligosaccharides) was around 14-15 g/L. Among the fractions, the concentration of fucosyl-oligosaccharides tended to decrease slightly from early to late lactation, core oligosaccharides remained relatively constant, and the sialyl-oligosaccharide fraction fell by approximately half from day 4 to day 90. Within each fraction, the concentrations of individual oligosaccharides were not necessarily constant over time; for example, the concentration of 2'-fucosyl-lactose decreased over the first month of lactation after which the concentration rose again.

The mean concentration of oligosaccharides in the milk of 15 French women whose milk was sampled from day 2 to day 8 postpartum ranged from 13-17 g/L (Viverge *et al*., 1990). These values may be compared with neutral oligosaccharide concentrations found in the breast milk of 12 North American women (Chaturvedi *et al*., 2001). The mean total neutral oligosaccharide concentration during the first 14 weeks of lactation was 9 g/L, somewhat lower than concentrations found in other studies. Chaturvedi *et al*. suggested that this may be due to different populations or as a consequence of their analytical method that did not measure oligo- and polysaccharides with a degree of polymerization of 9 or more. Samples of breast milk were taken over a period of one year and the concentration declined from the concentration found at 14 weeks to less than half at one year. Variability among women was large, the neutral oligosaccharide concentration averaged throughout the year for individual women differed four-fold.

Coppa et al. have found that the oligo- and polysaccharide concentration in the colostrum of mothers delivering pre-term infants is higher than that of mothers of term infants (Coppa *et al*. 1997). From 26 mothers delivering pre-term infants, the mean (SD) oligo- and polysaccharide concentration of their milk at four days postpartum was 25.61 (5.19) g/L, higher than the concentration of 20.9 (4.81) g/L found in a study of term infants ($P < 0.001$) (Coppa *et al*., 1993). Differences did not persist beyond the 4-day sample.

These data indicate that the total oligo- and polysaccharide content of human milk may be up to 25 g/L during the first few weeks following birth. From one to four months the concentration is likely to be around two-thirds of the concentration in early lactation and the concentration may continue to decline with time. The total oligo- and polysaccharide content of human milk is comprised of neutral and acidic compounds, of which the neutral fraction is the major component. The neutral oligo- and polysaccharide content of human milk has been found in concentrations of up to 15 g/L over the first 3 months of lactation.

3. Maternal dietary influence

The oligosaccharides found in human milk are produced in the mammary gland from lactose, which itself is synthesized principally from plasma glucose with some *de novo* generation of glucose and galactose in the breast (Sunehag *et al*., 2002). Whether maternal diet affects the oligosaccharide content or composition of breast milk has not been extensively studied. A comparison of milk sampled from women living in a number of countries variously described as being 'well' or 'poorly' nourished found little difference in the lactose content of milk among countries (Jelliffe & Jelliffe, 1978). Similarly, within a country there was little difference in lactose concentration between healthy and malnourished Egyptian women (6.65 *cf*. 6.48 g/100 mL) or between Brazilian women of low or high economic status (6.5 *cf*. 6.8 g/100 mL).

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Attachment 6

Microbiological assessment

Summary

The microbiological assessment evaluates the effect of inulin-derived substances and galacto-oligosaccharides (GOS) in combination or alone as a component in infant formula and infant formula products on gut microflora.

The dominance of *Bifidobacterium* and *Lactobacillus* species in the intestinal tract of breast-fed infants and their associated beneficial effects to the host appear to be the result of a combination of factors present in human breast milk. Oligosaccharides in human breast milk promote *Bifidobacterium* and *Lactobacillus* dominated intestinal microflora, however the effect results from a number of interactive factors including the presence of oligosaccharides, lactoferrin, lactose, nucleotides and low concentration of proteins and phosphates in the human breast milk.

There is some evidence to suggest that supplementation of infant formula with GOS and inulin-derived substances in a ratio of 9:1 (at a level not exceeding 10 g/L) or inulin-derived substances comprising of oligofructose: long-chain inulin at the 1:1 ratio (at a level not exceeding 8 g/L) may selectively stimulate the growth of intestinal *Bifidobacterium* populations in infants. There is a lack of persuasive evidence to support the suggestion that supplementation by GOS in isolation, in infant or toddler formula selectively stimulates the growth of intestinal *Bifidobacterium* and *Lactobacillus* in infants.

It should be noted that many of the published studies summarised in this Report have small sample sizes and variable supplementation methodology and hence it is difficult to draw firm conclusions from the data currently available. Further research is needed to strengthen this evidence.

There has been no research conducted or evidence found associated with the addition of fructo-oligosaccharide (FOS) to infant formula products and hence these substances have not been considered in this Report.

1. Biology of gut microflora in infants and young children

1.1 Distribution of microflora in human intestinal tract

The number of microorganisms inhabiting the human gastrointestinal tract is estimated in the order of 10^{14} cells per person, about 10 times the total cell number making up the entire human body (Bengmark, 1998). Microorganisms in the gastrointestinal tract are distributed as an increasing gradient from the stomach to the colon. This is largely the result of the low pH of the luminal content in the upper digestive tract, the digestive fluids produced by the gallbladder and the pancreas, and the phasic propulsive motor activity of the small intestinal tract, rendering an environment inhospitable to bacteria (Guarner and Malagelade, 2003). With reduced availability of oxygen in the intestinal tract from the stomach to the colon, this gradient of intestinal microflora becomes increasingly dominated by obligate anaerobes towards the colon.

Helicobacter pylori is the only recognised bacterium capable of survival in the gastro-stomach environment due to its unique survival attributes, this organism can invade the epithelial cells of the stomach and may cause stomach and duodenum ulcers (Suerbaum and Michetti, 2002). The gastrointestinal tract from the duodenum to the caecum contains a few species of microorganisms including Gram-positive, acid tolerant lactic acid bacteria like *Streptococcus* and *Lactobacillus*. Their concentration is usually in the order of 10^3 organisms/ml of lumen. According to Marteau *et al.*, (2001) and Ramakrishna (2007), lactic acid bacteria like *Lactobacillus*, *Streptococcus* and *Enterococcus*, and facultative anaerobes like *Escherichia coli* can reach very high densities in the caecum, up to 10^8 bacteria/g of the content. Beyond the caecum, and into the ascending colon, strict anaerobic bacteria become dominant. The ratio of anaerobes to aerobes in the colon is estimated in the order of 100:1 to 1000:1 (Simon and Gorbach, 1984, and Salminen *et al.*, 1998). The predominant anaerobes found in the colon include *Bacteroides*, *Bifidobacterium*, *Eubacterium*, *Clostridium*, *Peptococcus*, *Peptostreptococcus* and *Ruminococcus*. Table 1 lists the major bacteria present in the human colon. Bacterial cell density reaches approximately 10^{12}/g of faeces in the colon (Ramakrishna, 2007). Such microbial biomass contributes to around 60% of the faecal solids (Stephen and Cummings, 1980).

Table 1: Major bacteria present in human colon (Ramakrishna, 2007)

Oxygen requirement	Gram stain and shape	Genus	Estimated concentration (log/gram faeces)
Strict anaerobes	**Gram-negative bacilli**	***Bacteroids***	**11**
	Gram-negative bacilli	***Fusobacterium***	**9**
	Gram-positive bacilli	***Eubacterium***	**10**
		Bifidobacterium	**10**
		Clostridium	**10**
	Gram-negative cocci	***Ruminococcus***	**10**
		Peptostreptococcus	**NA**
Facultative anaerobes	**Gram-negative rods**	***E. coli, Citrobacter, Enterobacter, Proteus, Klebsiella* etc**	**NA**
Aerotolerant	**Gram-positive bacilli**	***Lactobacillus***	**4-8**
	Gram-positive cocci	***Streptococcus***	**NA**

NA: Estimation not available

1.2 Process of microbial colonisation of human intestinal tract

Microbial colonisation of the human gastrointestinal tract starts immediately after birth. The initial microorganisms are acquired from the mother through contamination during the birth, as a result of breast feeding, caring, and from the environment. Birth delivery methods of newborns strongly influence the composition of the intestinal microflora in the very early days of the infant (Bezirtzoglou, 1997; Coppa *et al.*, 2004a). It is generally accepted that the critical stage of bacterial colonisation of the colon occurs after birth and during weaning. During the early days and weeks of infant life, bacterial colonisation of the colon is a symbiotic process where the stimulation caused by the presence of the bacteria and their activities contribute to the formation of the immune system of the host (Edwards and Parrett, 2002; Gibson and Roberfroid, 1995). The interactive process between the bacteria and the human intestine results in gradually formed recognition, tolerance and coexistence of the specific intestinal bacteria population.

Because of the differences in exposure to the initial bacterial species and population from one individual to another, the exact pattern/distribution of the intestinal microflora is unique to the individual (Guarner and Malagelade, 2003; Ramakrishna, 2007).

1.3 Bifidogenic effect

Approximately 90% of the intestinal microflora of breast-fed infants is made up of *Bifidobacterium* and *Lactobacillus* species, collectively referred to in the literature as **bifidogenic flora** (Coppa *et al.*, 2004a, and Edwards and Parrett, 2002). In comparison, the proportion of *Bifidobacterium* present in the gastrointestinal tract of formula-fed infants is relatively small, approximately 40-60% of the overall intestinal microflora, and the rest is shared by *Streptococcus*, *Bacteroids*, *Clostridium*, *Staphylococcus* and a few genera belonging to the family of Enterobacteriaceae (Coppa *et al.*, 2004a, and Edwards and Parrett, 2002). The intestinal microflora of mixed-fed (breast and formula fed) infants is different from, and between those found in the breast-fed and formula-fed infants (Edwards and Parrett, 2002). Figure 1 below illustrates the difference in intestinal microflora in infants according to their food intake, and the evolution of intestinal microflora as food intake changes over time. The dominance of *Bifidobacterium* in the intestinal tract of breast-fed infants is described as the **bifidogenic effect** (Coppa *et al.*, 2004a).

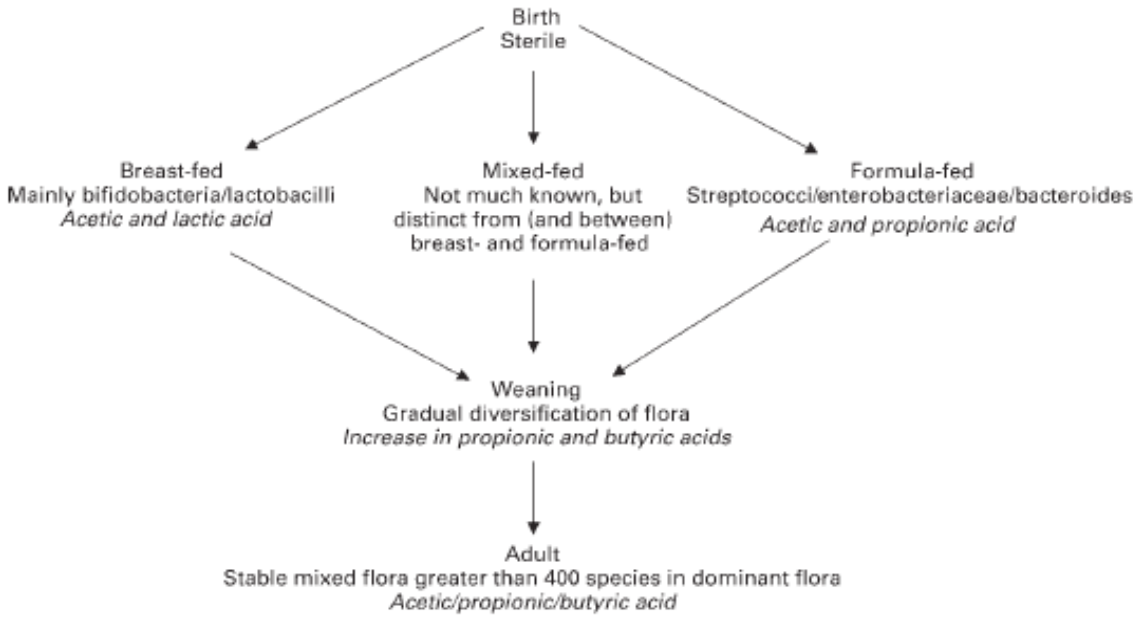

Figure 1: Development of intestinal microflora in infants (Edwards and Parrett, 2002)

During the weaning stage, the intestinal microflora becomes gradually more diverse. By the second year of life, the intestinal microflora of a child becomes increasingly similar to the stable mixed intestinal microflora found in adults where greater than 400 different species are present and 30-40 of them are in a dominant state (Edwards and Parrett, 2002; Guarner and Malagelade, 2003, and Ramakrishna, 2007).

1.4 Effect of gut microflora on the host

Gastrointestinal bacteria and their activities play important roles in host physiology including in nutrition, health and wellbeing.

It is increasingly recognised that intestinal bacteria and their host intestinal environment share a mutual and symbiotic relationship that affects the nutritional and physiological status of the host (Backhed *et al.*, 2005, Hooper and Gordon, 2001, and Sears, 2005). The fermentative activities of the intestinal bacteria in the colon result in the breakdown of complex carbohydrates and proteins leading to recovery of nutrients and energy that otherwise would not be available to the human body because the human digestive system alone cannot breakdown these complex molecules.

Animal experimental data indicate that without the activities of the intestinal bacteria, an additional 30% more calories is required to enable sterile animals (animal free of intestinal microorganisms) to maintain the same body mass as that of a normal animal where intestinal bacteria are active (Wostmann *et al.*, 1983).

Gastro-intestinal bacteria and their activities contribute also to the formation and function of the host immune system, the protection of the host against infection by pathogenic microorganisms, the synthesis of vitamins and the absorption of some minerals (O'Hara and Shanahan, 2006), and also certain physiological disorders of the host, for example colon cancer and inflammatory bowel diseases (Guarner and Malagelada, 2003).

Among the intestinal microflora, the *Bifidobacterium* and *Lactobacillus* are recognised as the fraction whose presence/population and activities largely benefit the host (Edwards and Parrett, 2002, Guarner and Malagelade, 2003, and Ramakrishna, 2007). This is not to say that other factions of the intestinal microflora exert only a negative effect on host health and wellbeing. Metabolic activities of key *Bacteroides* species, such as *B. thetaiotaomicron*, have been found to be beneficial to the host (Sears, 2005). It is apparent that there is a significant knowledge gap about the complex interactions between the human host and major anaerobes of the gastrointestinal tract, such as *Bacteroides*, *Clostridium* and *Eubacterium*.

Bifidobacterium and *Lactobacillus* are recognised for their ability to ferment oligosaccharides present in human breast milk that are non-digestible by the host. Short chain fatty acids (SCFA) produced by these bacteria in the metabolism of oligosaccharides modulates the formation of the immune structure of the host, through their stimulation of the host intestinal epithelial cells (Binder *et al.*, 1994). These stimulations facilitate the development and differentiation of the host epithelial cells. SCFA also promotes the absorption of sodium and chloride by the host and promotes host lipid metabolism (Binder *et al.*, 1994, Ramakrishna, 2007). Another beneficial role played by *Bifidobacterium* and *Lactobacillus* results from their preferential metabolism of human milk oligosaccharides, which includes the increased dominance of this population in the colon that contributes to a bulking effect that may benefit the laxation of the host. Increased dominance of *Bifidobacterium* and *Lactobacillus* leads to a reduced pH of the colon content, and this has been claimed to restrict the proliferation of other intestinal microorganisms in the colon. The competition for nutrients available in the colon by *Bifidobacterium* and *Lactobacillus* is also claimed to lead to an exclusion effect on other intestinal microorganisms (Moro and Arslanoglu, 2005). These suppressive effects on other intestinal microorganisms, particularly those that are pathogenic to the host, are attributed as probiotic effects that are generally regarded as beneficial to the host, although direct and convincing evidence to support these claims is lacking.

2. Human breast milk oligosaccharides and their effect on gut microflora

2.1 Prebiotic and probiotic approach to food for young children

Because of the perceived health promoting effects of *Bifidobacterium* and *Lactobacillus* dominated intestinal microflora, attempts have been made to increase the proportion and population levels of these gut bacteria in infants and toddlers fed with infant and toddler formula. Three approaches have been developed to increase the number and activity of these bacteria in the intestinal tract for young children who are fed by infant/toddler formula according to Coppa *et al.*, (2004a).

The first approach is a direct ingestion of live probiotic bacteria[51]. Organisms considered to be probiotic include selected *Lactobacillus* and *Bifidobacterium* species. The second approach is to incorporate prebiotics[52] into the foods for young children. The third approach incorporates both probiotics and prebiotics into foods for young children.

2.2 Oligosaccharides from human breast milk

Oligosaccharides with a degree of polymerization (DP) of 3-10 are found in human milk (FAO/WHO, 1998). These human milk oligosaccharides (HMOs) account for the third largest component of human milk, with the peak concentration of around 25 g/L in the colostrum during the first few weeks following birth and decline there after in normal human milk (Coppa *et al.*, 1994, and Coppa *et al.*, 1999).

Human milk oligosaccharides are synthesized by the glycosyltransferase in the mammary gland by adding sequentially monosaccharide units (galactose, fucose, N-acetyl-glucosamine, sialic acid) to lactose. Human milk oligosaccharides are resistant to enzymes present in the infant digestive system, and most human milk oligosaccharides pass to the colon of the infants undigested. These oligosaccharides facilitate selective proliferation of *Bifidobacterium* and *Lactobacillus* through fermentative metabolism by these bacteria and production of SCFA leading to the beneficial effect to the host as outlined above (Coppa et al, 2004a).

The amount of oligosaccharides in normal infant formula is considerably less than those found in human breast milk, and cow's milk contains <1 g oligosaccharides/L (Coppa *et al.*, 2004a). Deliberate fortification of infant formula with oligosaccharides is part of the approach to simulate the composition of human breast milk.

2.3 Prebiotic effect of human breast milk oligosaccharides

Human breast milk oligosaccharides are recognised prebiotics, because of their resistance to digestion by host enzymes and their ability to selectively promote the growth of *Bifidobacterium* and *Lactobacillus* in the colon (Coppa *et al.*, 2004a).

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[51] Probiotic bacteria are *Live microorganisms which when administered in adequate amounts confer a health benefit on the host* (FAO/WHO, 2001).

[52] Prebiotic are defined as *non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health* (Gibson and Roberfroid, 1995).

The overall prebiotic effect of the human oligosaccharides in young children is a combination of the roles played by *Bifidobacterium* and *Lactobacillus* in the intestinal tract and the roles played by oligosaccharides as dietary fibres.

Despite the recognition that HMOs promote *Bifidobacterium* and *Lactobacillus* dominated intestinal microflora, this is most likely the result of a number of complex and interactive factors present in the human milk including the lactoferrin, lactose, nucleotides and low concentration of proteins and phosphates present in the human breast milk (Coppa *et al.*, 2006). The exact role of these other factors found in human breast milk on the formation of *Bifidobacterium* and *Lactobacillus* dominated intestinal microflora is not clear at this stage.

2.4 Effect of inulin-derived substances and GOS on gut microflora

2.4.1 Carbohydrates simulating human breast milk oligosaccharides

Researchers have used commercially available carbohydrates in an attempt to mimic the prebiotic qualities of human milk oligosaccharides (HMOs). The most frequently studied include inulin-derived substances including inulin, long-chain inulin and oligofructose (as defined in attachment 2) as well as galacto-oligosaccharides (GOS). Other oligosaccharides tested for their potential prebiotic effect include lactulose, soybean oligosaccharides, lactosucrose, isomalto-oligosaccharides, gluco-oligosaccharides and xylo-oligosaccharides. In clinic trial studies, inulin preparations, with degree of polymerisation greater than 10 (defined as Inulin) are used to simulate the high molecular fraction of the human breast milk oligosaccharides.

2.4.2 Effect of Inulin-derived substances and GOS in combination on gut microflora

A clinical trial using a combination of a GOS preparation and a high molecular weight fraction of inulin preparation at the ratio of 9:1 supplemented into an infant formula demonstrated a significant stimulation to the growth of bifidobacteria and lactobacilli (Moro *et al.*, 2002). Table 2 shows a summary of the changes in the population of *Bifidobacterium* and *Lactobacillus* bacteria over the course of the trial. The trial involved 90 full term infants, and the infant formula was fortified at 4 g/L and 8 g/L respectively. The results indicated that *Lactobacillus* and *Bifidobacterium* cell numbers in infant colons were positively correlated to the presence of GOS and the inulin preparation. While changes to the *Bifidobacterium* population appeared to correlate to the inulin-derived substance (defined as high molecular weight inulin) and GOS concentration present in the infant formula, this wasn't the case for *Lactobacillus* population. The authors did not attempt to interpret such differences encountered in the experiment. Due to the lack of information about microbiological analysis and how the original data was treated, it is difficult to ascertain the variations of the parameters presented in the publication.

The same trial conducted with 42 preterm infants (Boehm *et al.*, 2002) found approximately a 3 log increase of *Bifidobacterium* in infants fed with 10 g/L of GOS and high molecular mass inulin (defined as high molecular mass FOS in the reference) supplemented infant formula against a control where less than 1 log increase of *Bifidobacterium* was observed. The authors in this study found supplementation of the GOS and inulin preparation showed no effect on the population of faecal *Lactobacillus* and no effect on the population of faecal *Bacteroids*, *Clostridium*, *E. coli*, *Enterococcus*, *Citrobacter*, *Proteus*, *Klebsiella* and *Candida*.

Table 2: Summary of data presented of the effect of supplemented GOS and inulin-derived (defined as FOS in the table) preparations on the population of bifidogenic bacteria in full term infants (Moro *et al*., 2002)

	Bifidobacterium **$\log_{10}$ CFU/g wet faeces (mean)**			***Lactobacillus*** **$\log_{10}$ CFU/g wet faeces (mean)**		
	Control*	**GOS:FOS** 4 g/L**	**GOS:FOS** 8 g/L**	**Control**	**GOS:FOS** 4 g/L**	**GOS:FOS** 8 g/L**
Day 1	**8.8**	**8.5**	**7.7**	**3.4**	**3.3**	**3.4**
Day 28	**7.2**	**9.3**	**9.7**	**3.4**	**5.9**	**5.6**
Difference	**- 1.4**	**+ 0.8**	**+ 2.0**	**0**	**+ 2.6**	**+ 2.2**

* Control refers to infants been fed with control infant formula.

** Please note that in this table 'FOS' refers to 'inulin-derivedsubstances' for the purpose of this Report.

Bakker-Zierikzee *et al.* (2005) assessed the effect of a GOS and inulin (Raftiline HP, supplied by Orafti; now redefined at Beneo HP) supplementation (ratio at 9:1) during the first 4 months of life of infants and compared the analysis with controls and breast-fed infants. The study involved 91 infants and another 101 breastfed infants as the reference group, and the GOS and inulin combination was supplemented at a level of 6 g/L. Their study found that the combination of GOS and inulin supplemented infant formula stimulated the growth of lactobacilli and 6.1% in the total colon bacteria at the end of feeding trial was lactobacilli. This was comparable to the lactobacilli counts in infants fed with human breast milk. Supplementation of GOS alone to the infant formula or infant formula without supplementation of either inulin or GOS did not stimulate colon lactobacilli growth.

A summary of the all the above studies together with several other human trials using GOS and inulin-derived substances used in combination are presented in Table A. The available information suggests that the supplementation of infant formula with a combination of GOS and inulin-derived substances at a dosage not exceeding 10 g/L, may selectively stimulate the growth of colon bifidobacteria in infants.

Studies looking at the effects of GOS and Inulin-derived substances at ratios that differ from the commonly assessed ratio of 9:1 are currently limited. Future studies employing consistent methodology, (e.g. the proportion and actual counts of faecal bifidobacteria, increased faecal sampling and microbiological analysis as well as additional studies into variations of ratios and dosages), may assist in generating objective information and strengthen the evidence surrounding selective growth stimulation of intestinal bifidobacteria by GOS and inulin-derived substances used in combination.

2.4.3 Effect of inulin-derived substances alone on gut microflora

A recent study by Veereman-Wauters *et al.,* (2008) assessed the effects of three different formulas:

- Oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1') 4 g/L and
- Oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1') 8 g/L and
- GOS: Inulin-derived substances at a 9:1 ratio 8 g/L

against a control group consuming non-supplemented infant formula.

This study involved 81 neonates enrolled within the first 5 days of life and lasted for a period of 28 days. Microbiological analysis of faecal samples showed that whilst the total number of faecal bacteria remained unchanged in the control group, there was an increase in total faecal bacteria levels over time for all supplemented groups tested, with these increases in levels being similar across all groups. There was no significant difference found between the supplemented groups over time and between groups by days for specific faecal numbers of Lactobacilli, Bacteroides and Clostridia. However with both the 8 g/L formulas of GOS: Inulin-derived substances at the 9:1 ratio and Oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1'), faecal bifidobacteria numbers increased significantly and remained high from day 14 onwards, compared with day 3 levels. The results of this study indicate that the supplementation of infant formula with a combination of Oligofructose and long-chain inulin at the specific ratio of 1:1 as well as GOS: Inulin-derived substances at the 9:1 ratio may similarly selectively stimulate the growth of intestinal bifidobacteria in infants when used at a level of 8 g/L. At the level of 4 g/L the Oligofructose: long-chain inulin ('Orafti Synergy1') supplemented formula did not produce a significant increase in faecal bifidobacteria numbers.

In a study involving 20 young children attending a day care centre aged between 7 and 19 months, consumption of inulin-derived oligofructose (Beneo® P95 supplied by Orafti) at 2 g/day was found to only slightly stimulate the growth of bifidobacteria, with the population increasing by 0.4 log (from 9.1-9.4 log CFU/g) over a period of 20 days (Waligora-Dupriet *et al.* 2007). In a separate report of the same study, Waligora-Dupriet *et al.* (2005) presented data that indicates that while there was a small increase in the levels of faecal bifidobacteria over the trial period the differences of bifidobacteria counts between the infants fed with oligofructose supplemented formula and the control were not significant.

Kapiki *et al.* (2007) reported that bifidobacteria in 36 infants fed with inulin (4 g/L) supplemented formula increased above those in the control group (20 infants).

Euler *et al.* (2005) assessed the effect of inulin (Raftilose®95 supplied by Orafti; now redefined at Beneo P95) on full term healthy infants. Inulin was supplemented in infant formula at 1.5 g/L or 3.0 g/L using human breast milk fed infants as control, and the study involved a total of 72 subjects. The study found that inulin supplemented at 1.5 or 3.0 g/L had minimal effect on the intestinal microflora including bifidobacteria, lactobacilli, bacteroids, clostridia and enterococci.

In a study involving 14 infants aged at an average of 12.4 weeks, where inulin was tested for prebiotic effect, the authors claimed that inulin (Frutafit® IQ supplied by Sensus, defined in the study as native inulin) fed at 1.5 g/day stimulated both bifidobacteria and lactobacilli growth (Kim *et al.*, 2007). The author claimed that a significant stimulation to these intestinal microorganisms by exposure to inulin is associated with a lower initial bifidobacteria population in the colon. Data presented in the report provides insufficient detail to enable appropriate peer review of how the conclusion was derived.

A summary of these studies is presented in Table A. There is evidence to suggest that the supplementation of infant formula with inulin-derived substances (Oligofructose: long-chain inulin at the 1:1 ratio – 'Orafti Synergy1'), at the level of 8 g/L, selectively stimulates the growth of intestinal *Bifidobacterium* populations in infants, similar to the effects seen when GOS: Inulin-derived substances are used in combination at a ratio of 9:1 in infant formula.

In general, consistent information on the effect of inulin-derived substances alone on the growth and activities of intestinal lactobacilli and bifidobacteria in infants is still limited and further evidence would be advantageous to strengthen the available information.

2.4.4 Effect of GOS alone on gut microflora

As reported earlier, Bakker-Zierikzee *et al.* (2005) found supplementation of GOS alone (at 6 g/L for a period of 12 weeks) to the infant formula did not stimulate *Lactobacillus* growth in newborn infants. The authors did not examine the effect of GOS supplementation on the growth and activity of bifidobacteria.

Ben *et al.* (2004) reported that GOS supplemented at 2.4 g/L stimulated selectively the growth of bifidobacteria and lactobacilli and the concentrations of faecal bifidobacteria and lactobacilli at 3 months and 6 months were similar to those found in subjects fed with human breast milk.

Further research employing consistent methodology in the future may assist to elucidate the role of GOS alone on the growth and activity of intestinal microflora.

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Table A: Studies on the Effect of Inulin-derived and Galacto-oligosaccharide (GOS) on Intestinal Microflora

Dose	Subject Details	Study Duration	Effect on gut microflora	References
GOS and Inulin-derived substances in combination				
6 g/L GOS : Inulin at 9:1 (Raftiline HP) Or GOS alone	91 + 101 - breastfed reference (infants of average age 5 days)	12 weeks	GOS and Inulin combination supplemented infant formula stimulated the faecal lactobacilli, with its proportion matching that found in breast-fed infants. No stimulation of lactobacilli was observed with standard infant formula, or after the addition of 6/L GOS to the standard infant formula.	Bakker-Zierikzee et al., (2005)
10 g/L GOS : Inulin at 9:1 (high molecular mass inulin)	30 + 12 - breastfed reference (preterm infants, average age 8 days)	28 days	Supplementation of GOS and Inulin in combination stimulated the growth of bifidobacteria, but had no effect on the growth of Lactobacillus, Bacteroids, Clostridium, E. coli, Enterococcus, Citrobacter, Proteus, Klebsiella and Candida.	Boehm et al., (2002)
4 g/L GOS : Inulin at 9:1 (high molecular weight fraction of inulin)	140 (infants of average age 5 days old)	6 weeks	Proportion of faecal bifidobacteria increased significantly (5.36% at week 0 to 39.69% at week 6) in GOS and Inulin supplemented infants whereas the increase was small in the control infants (8.04% at week 0 to 14.87% at week 6).	Costalos C. et al., (2007)
6 g/L GOS :Inulin at 9:1 (high molecular mass inulin) 2 g/L of acidic oligosaccharides	46 (infants with average of 3 days old)	6 weeks	Counts of faecal bifidobacteria of infants fed with GOS and Inulin supplemented formula (in the presence of acidic oligosaccharides (AOS) derived from enzyme hydrolysed citrus pectin at week 6 was approximately 1.5 log higher than those found in the infants fed with control formula or control formula with AOS.	Fanaro et al., (2005)
8 g/L GOS : Inulin-derived substance at 9:1 (Assumed Inulin described as FOS in the study, no further definition given)	53 (infants age at 7 to 8 weeks)	6 weeks	Proportion of faecal bifidobacteria increased from 45.2% (week 0) to 59.5% (week 6) in infants fed with GOS and Inulin supplemented formula, and those in the control changed from 47.3% to 49.5%. Proportion of bifidobacteria at week 6 (59.5%) in infants fed with GOS and Inulin supplemented infant formula is comparable to that (67.7%) in breast-fed infants.	Knol et al. (2005)

Dose	Subject Details	Study Duration	Effect on gut microflora	References
8 g/L GOS : Inulin-derived substance at 9:1 (long-chain FOS)	206 (infants approximately 6 weeks old)	6 months	Significant increases in the number of faecal bifidobacteria were found with infants fed with infant formula supplemented with GOS and Inulin. Supplementation of infant formula with GOS and Inulin resulted in no significant influence on the faecal lactobacilli counts as comparing with the control subjects.	Moro et al., (2006)
4 – 8 g/L GOS : Inulin at 9:1 (high molecular weight inulin)	90 (infants average age at 7 days)	28 days	Supplementation of GOS and Inulin in combination stimulated the growth of bifidobacteria and lactobacilli. The growth stimulation was Inulin and GOS dose dependent for bifidobacteria, but no for lactobacilli.	Moro et al., (2002)
8 g/L GOS : Inulin-derived substance at 9:1 (FOS with a reduced proportion of DP<10)	102 (infants < 2 weeks)	10 weeks	The number of faecal bifidobacteria in infants fed with GOS and Inulin-derived substance supplemented formula increased from 3.87 x 109 to 10.3 x 109/g from day 0 to week 6 whereas those in the control increased from 3.50 x 109 to 5.60 x 109/g.	Schmelzle et al., (2003)
4.5 g/day GOS : Inulin at 9:1 (Raftiline HP)	35 (infants 4 to 6 months)	6 weeks	Inclusion of GOS and Inulin in solid infant food induced an increase in the faecal proportion of bifidobacteria of fully formula fed infants.	Scholtens et al., (2006)
4 g/L and 8 g/L Oligofructose: long-chain inulin at the 1:1 ratio (Orafti Synergy1) 8 g/L GOS: Inulin at 9:1	81 (neonates within the first 5 days of life)	28 days	The total numbers of faecal bacteria increased over time for all supplemented groups when compared to the control infant formula group. There was no significant difference found between the supplemented groups over time and between days for faecal numbers of Lactobacilli, Bacteroides and Clostridia. Faecal bifidobacteria numbers however increased significantly from day 14 onwards, when compared to day 3, with both the 8 g/L formula of GOS: Inulin 9:1 and the 8 g/L formula of Oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1'). Faecal bifidobacteria numbers did not significantly increase with the 4 g/L Oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1') formula group.	Veereman-Wauters et al., (2008)

Dose	Subject Details	Study Duration	Effect on gut microflora	References
Inulin-derived substances in combination				
4.5 g/L (minimum 500 ml/day) **Oligofructose (RaftiloseP95®) and Inulin (Raftiline)**	**140** **(12-24 month infants)**	**28 days**	**Faecal population of Bifidobacterium increased in oligofructose and inulin supplemented infants by 0.37 log and reduced in control infants by 0.27 log at day 7. Faecal population of Lactobacillus and Enterococcus increased in oligofructose and inulin treated infant by 0.67 log and reduced in control by 0.10 log at day 7. No observable changes with Bacteroides, E. coli, Clostridium lituseburense and C. histolyticum.**	**Brunser et al. (2006)**
4 g/L and 8 g/L Oligofructose: long-chain inulin at the 1:1 ratio (Orafti Synergy1) **8 g/L GOS: Inulin at 9:1**	**81** **(neonates within the first 5 days of life)**	**28 days**	**The total numbers of faecal bacteria increased over time for all supplemented groups when compared to the control infant formula group. There was no significant difference found between the supplemented groups over time and between days for faecal numbers of Lactobacilli, Bacteroides and Clostridia. Faecal bifidobacteria numbers however increased significantly from day 14 onwards, when compared to day 3, with both the 8 g/L formula of GOS: Inulin 9:1 and the 8 g/L formula of oligofructose: long-chain inulin at the 1:1 ratio ('Orafti Synergy1'). Faecal bifidobacteria numbers did not significantly increase with the 4 g/L oligofructose: long-chain Inulin at the 1:1 ratio ('Orafti Synergy1') formula group.**	**Veereman-Wauters et al., 2008**
Inulin-derived substances Only				
1.5 – 3.0 g/L **Oligofructose (RaftiloseP95®)**	**72** **(2 – 6 weeks old infants)**	**5 weeks**	**Supplementation of oligofructose in infant formula had minimal effect on faecal counts of Bifidobacterium, Lactobacillus, Enterococcus, Bacteroids and Clostridium. Faecal counts of these faecal bacteria did not change significantly in infants fed with human milk.**	**Euler et al., (2005)**
4 g/L **Inulin**	**56** **(0-14 days preterm infants)**	**14 days**	**Faecal counts of bifidobacteria of infants fed with Inulin supplemented formula increased from day 1 to day 7 by 0.5 log and were 0.5 log higher than those from control infants at day 7. Faecal E. coli and enterococci counts apparently reduced by 1.8 to 0.8 log from day 1 to day 7 in infants fed with Inulin supplemented formula.**	**Kapiki et al., (2007)**
2 g/day **Oligofructose (RaftiloseP95®)**	**20** **(7-19 months)**	**42 days**	**Bifidobacteria increased slightly in infants fed with oligofructose supplemented formula. While there was a small increase in the levels of faecal bifidobacteria over the trial period, the differences between the infants fed with oligofructose supplemented formula and the control infants were insignificant. Lactobacilli species were seldom identified from both the treatment and control groups.**	**Waligora-Dupriet et al., (2007)** **Waligora-Dupriet et al., (2005)**

Dose	Subject Details	Study Duration	Effect on gut microflora	References
GOS Only				
6 g/L **GOS : Inulin at 9:1 (Raftiline HP)** **Or GOS alone**	**91** **+ 101 - breastfed reference** **(infants of average age 5 days)**	**12 weeks**	**GOS and Inulin combination supplemented infant formula stimulated the faecal lactobacilli, with its proportion matching that found in breast-fed infants. No stimulation of lactobacilli was observed with standard infant formula, or after the addition of 6/L GOS to the standard infant formula.**	**Bakker-Zierikzee et al., (2005)**
2.4 g/L **GOS**	**271**	**6 months**	**Faecal bifidobacteria and lactobacilli counts of infants fed with GOS supplemented formula were similar to those found in infants fed with breast milk at 3 months and 6 months. These counts were approximately 2-log higher than those found in infants fed with control formula.**	**Ben, (2004)**

Attachment 7

Nutrition Assessment

Summary

Breastfed infants generally have softer and more frequent stools than those given infant formula. They also have a lower stool pH and a different faecal short chain fatty acid (SCFA) profile; one in which acetate and lactate predominate. This is at least partly due to the oligo- and polysaccharides that are unique to breast milk. The range of oligo- and polysaccharides in human milk is large. It is not possible for infant formula product manufacturers to copy this diversity, but attempts have been made to achieve the same result through the addition of commercially available oligo- and polysaccharides. The most frequently studied have been long-chain inulin, inulin, oligofructose and galacto-oligosaccharides (GOS).

Combined Addition of Galacto-oligosaccharides and Long-chain Inulin

The bulk of research has been done comparing standard infant formula to formula supplemented with GOS and long-chain inulin at a ratio of 9:1 and concentrations of 4-10 g/L of formula. The majority of these studies reported softer stools, with a lower pH, when infant formulas were supplemented. The one study that examined faecal SCFA also reported that supplemented formula resulted in a SCFA profile similar to that reported for breastfed infants. The ability of GOS and long-chain inulin to increase stool frequency is less well established, possibly because this effect gets smaller with age. The addition of GOS and long-chain inulin to infant foods did not influence stool frequency or softness, nor did it significantly lower stool pH.

Single Addition of Inulin-derived Substances or Galacto-oligosaccharides

Sole addition of derived substances to infant formula products or infant foods has sometimes been shown to increase stool frequency or stool weight in infants less than 12 months of age. The limited data available suggests they have little effect on stool pH. There appears to be little impact on stool frequency or consistency in infants over 12 months of age.

The one study that examined the addition of GOS to infant formula in isolation, i.e. without also adding other poly- or oligosaccharides, reported higher stool frequency in GOS-fed infants. The frequency was similar to that of a breastfed reference group. More data are needed to draw a firm conclusion. Data on the effect of formula supplemented with GOS alone on stool pH and faecal SCFA is limited and contradictory, thus no conclusion can be made.

Single Addition of Fructo-oligosaccharides

It should be noted that fructo-oligosaccharides, as defined in the Draft Assessment Report, have not been sufficiently studied to draw any conclusions about their effect on stool characteristics in infants or young children.

Study Limitations

When considering these results it is important to keep in mind that many of the studies done in this area had one or more of the following limitations: loss of a large proportion of participants, small sample size, and industry sponsorship. Stool consistency was measured simply by rating the stool on a scale that often varied across studies; it therefore has an element of subjectivity.

Mineral Interaction

In adults there does not appear to be any interference of mineral absorption from the small intestine when fructo-oligosaccharides (FOS), inulin-derived substances are added to diets in amounts typically in the range of 8-20 g/d. There is evidence to suggest that mineral absorption from the large intestine may be increased due to the presence of added fermentable fructan polymers, the evidence being particularly strong for an enhanced effect on calcium absorption.

1. Inulin, Long-chain Inulin, FOS and GOS in Infant Formula Products, Infant Food, and Formulated Supplementary Foods for Young Children – Effect on Stool Frequency and Consistency

1.1 Stool Frequency and Consistency

A recognised difference between formula-fed and breastfed infants is that the latter have softer and more frequent stools (Quinlan *et al*, 1995). One of the potential functions of inulin-derived substances and/or GOS added to infant formula and infant food is to promote stool frequency and consistency similar to that observed in breastfed infants. The other, and perhaps related, proposed function of these compounds is to modify the microflora of the colon, but this aspect is discussed further in section 2 below, and in detail in Attachment 4. The laxative properties of inulin-derived substances, FOS and GOS in adults are discussed in Attachment 7.

1.1.1 Search Strategy

An electronic literature search was conducted via pubmed (www.ncbi.nlm.nih.gov/sites/entrez/) using the following search terms:

- (galacto-oligosaccharide OR galactooligosaccharide OR fructo-oligosaccharide OR fructooligosaccharide OR inulin OR fructan) AND (infant OR formula OR stool)
- Limited to: Human, English, German, All Infant (0-23 months), Clinical Trial, Meta-Analysis, Review, Randomized Controlled Trial

Particularly relevant journals were also searched individually including the American Journal of Clinical Nutrition and the Journal of Pediatric Gastroenterology and Nutrition. Terms used were *galactooligosaccharide* and *fructooligosaccharide* and the results examined manually without further electronic filtering.

References were also provided by Nutricia Ltd and H.J. Heinz Co Ltd, including abstracts from conference proceedings published in peer reviewed journals.

Where an apparently relevant abstract was identified an author search was conducted on pubmed to identify if the research had since been published as a full paper. The reference list of key papers was also consulted to identify other potentially relevant research.

1.1.2 Summary of Identified Studies

Seventeen randomised controlled trials comparing oligo- and/or polysaccharide supplemented foods for infants with an unsupplemented control, and in some cases breast milk, were identified in the peer reviewed literature. A further two studies published in conference proceedings as abstracts were also identified and included. Breastfed reference groups were not randomised.

The studies are summarised in the tables and text below. Where authors provided the trade name or other details about the oligosaccharide(s) tested and/or the commercial formula used this is included. If no such information was provided the generic term for the oligosaccharide(s) is given. Formula that was made up for the study from generic recipes are listed as *experimental*. Table 1 provides a basic guide to the products tested. The sample sizes that are reported here are based on the number in each treatment group at the end of the study.

Table 1: Guide to Branded Oligosaccharides Used in Identified Studies

Manufacturer	Brand Name	Description	Generic Term
Orafti	Raftiline® HP	Inulin with no mono- or disaccharides	Long-chain inulin
	Raftilose® P95/ Beneo® P95	Hydrolysed inulin from chicory; 5% di- and monosaccharides	Oligofructose
	Synergy 1®	Inulin and hydrolysed ~8% di and mono-saccharides	Long-chain inulin
Sensus	Frutafit IQ	Instantised inulin from chicory	Inulin
Friesland Foods Domo	Vivinal	Galacto-oligosaccharide	Galacto-oligosaccharide

1.1.3 Study Limitations

Studying infants is arguably a difficult undertaking and many of the studies had one or more of the following limitations:

- small sample size,
- loss of a large proportion of subjects to follow-up,
- incomplete descriptions of the poly- and/or oligosaccharides used, i.e. no data on brand name, manufacturer or descriptors such as the degrees of polymerisation;
- no indication that an intention to treat analysis was conducted/failure to conduct an intention to treat analysis;

A further problem is that none of the studies that used maltodextrin as a control specified its characteristics. As maltodextrin refers to a range of products including some resistant to digestion, this may not have been a neutral control. It is reasonable to assume that digestible maltodextrins were used.
However, *in vitro* evidence indicates that if maltodextrins were to reach the colon they would be fermented by colonic bacteria (Probert *et al*, 2002).

Further, it has been demonstrated, at least *in vitro*, that maltodextrin administration can lead to increased numbers of specific bacterial groups including *bifidobacteria* and *lactobacilli* (Olano-Martin *et* al, 2000; Rycroft *et al*, 2001). Thus it is possible that some studies underestimate the effect of the test formula.

Many studies were funded by industries with financial interest in the outcome and conducted by industry employees.

1.1.4 Measuring Stool Frequency and Consistency

Stool frequency has been measured in terms of number of defecations per day usually reported by parents or other care givers. Stool consistency has been assessed by observation and graded using a numeric scale of 1-4 or 1-5. In some studies the lower numbers indicate softer stools; in others the higher numbers indicate softer stools. Most studies compare average scores but some compare the number or proportion of soft stools in each study group. The lack of a single consistent grading method makes numeric comparisons between studies impractical, results are therefore reported as either (statistically significantly) different or similar.

1.2 Inulin-derived Substances or Fructo-oligosaccharide Alone in Infant Formula Products, Weaning Foods, and Formulated Supplementary Foods for Young Children

The main details of the studies in this section, including age at entry, study design, sample size and outcome in terms of stool characteristics, are presented in Table 2.

Euler et al (2005) compared stool frequency and consistency before and after infants received infant formula supplemented with 1.5 or 3.0 g/L oligofructose in a crossover design. Stool frequency increased and consistency softened when infants received 3.0 g/L. Conversely, frequency decreased and consistency stayed the same relative to pre-supplementation when infants were only given 1.5 g/L. Kapiki et al (2006) reported more frequent stools but similar consistency with inulin supplemented pre-term formula compared to unsupplemented control formula. Veereman-Wauters et al (2008) reported no effect of inulin supplemented formula at 4 or 8 g/L on stool frequency after four weeks. However, formula supplemented at 8 g/L did lead to softer stools than did control formula, this was not observed with just 4 g/L.

Kim et al (2007) reported no difference in stool frequency or consistency between supplemented and control formula-fed infants. The group did report greater stool weight in infants given inulin supplemented infant formula; this measure was not reported by the other studies. Stool weight was measured by weighing nappies and therefore without indication that the urinary content of the nappy was accounted for.

Waligora-Dupriet et al (2007) examined the effect of mixing oligofructose at 2 g/d with food and drink in 7-19 month olds and observed no difference in stool frequency or consistency between supplemented and unsupplemented groups. Brunser et al (2006) compared a formulated supplementary food for young children with and without inulin at 4.5 g/L in 12-24 month olds after treatment with amoxicillin for acute bronchitis, and observed no difference in stool frequency or consistency.

However, 16-46 week olds given infant cereal supplemented with FOS, at an average FOS intake of 0.74 g/d, had a higher stool frequency and more stools described as soft than those fed formula containing the same amount of maltodextrin (Moore et al, 2003).

Studies to date are equivocal with respect to the effect of inulin-derived substances on stool frequency and consistency. The reason for the discrepancies in outcome cannot readily be related back to dose as higher doses did not always result in a greater effect. The duration of the studies, generally less than a month, are also not clearly related to outcome. As several different preparations of inulin-derived substances were tested across, but not within, studies this may explain some of the conflicting outcomes, but there are too few studies to draw in conclusions about the effect of individual preparations.

1.3 Combination of Galacto-oligosaccharides and Long-chain Inulin at a Ratio of 9:1 added to Infant Formula Products and Infant Foods

Twelve studies have reported stool frequency and/or consistency in infants receiving formula supplemented with long-chain inulin in combination with GOS. All but two of these studies clearly identified the ratio as 1:9; Moro *et al* (2006) and Mihatsch *et al* (2006) are unclear though the use of this ratio is implied by referencing earlier work that used a 1:9 ratio. Key study details including age at entry, study design, sample size and outcome in terms of stool characteristics are provided in Table 3.

Five studies published as six papers have looked at the addition of long-chain inulin and GOS to infant formula without also adding other components that may influence stool characteristics (Boehm *et al*, 2002; Boehm *et al*, 2003; Moro *et al*, 2002; Moro *et al*, 2006; Litov *et al*, 2006; Costalos *et al*, 2007). The two largest studies reported greater stool frequency with supplemented formula at 4 and 8 g/L (Moro *et al*, 2006; Costalos *et al*, 2007). Only the small short duration study by Litov *et al* (2006) reported lower stool frequency at 4 g/L. The relative increase in stool frequency has been shown to be maintained at least until the age of six months, but the magnitude of the difference reduces over time (Moro *et al*, 2006). All four studies that reported stool consistency observed softer stools in supplemented groups (Boehm *et al*, 2002; Boehm *et al*, 2003; Moro *et al*, 2002; Moro *et al*, 2006; Costalos *et al*, 2007). Only 8 g/L of oligosaccharide mix resulted in similar stool consistency in supplemented and breastfed groups (Moro *et al*, 2002).

Three studies tested long-chain inulin and GOS in combination with high concentration β-palmitic acid in infant formula (Schmelzle *et al,* 2003; Bongers *et al*, 2007; Fuentes *et al*, 2005). All three studies report a greater proportion of soft stools in those receiving supplemented formula. Only Fuentes *et al* (2005) observed a greater of frequency of defecation with supplemented formula. They were the only group to include breastfed infants a further comparison; stool characteristics were similar between supplemented formula-fed and breastfed infants. When evaluating the outcome of these studies, it must be considered that β-palmitic acid added to infant formula alone has previously been shown to result in softer stools (Kennedy *et al*, 1999). As it was not also tested in isolation in these three studies, it is unclear what contribution the GOS and long-chain inulin made to the reported findings.

Formula supplemented with long-chain inulin and GOS in combination with *Bifidobacterium longum* BL999 resulted in softer and more frequent stools (Puccio et al, 2007).

However, as there was no comparison group that received Bifidobacterium longum BL999 alone, it is not clear what if any impact the oligosaccharides had.

Fanaro et al (2005) sought to mimic the oligosaccharide composition of breast milk more closely by adding an acidic carbohydrate, i.e. hydrolysed pectin, as well as the neutral long-chain inulin and GOS.

Hydrolysed pectin alone and in combination long-chain inulin and GOS resulted in softer stools. Hydrolysed pectin alone did not alter stool frequency relative to control formula. Supplementation of weaning foods with long-chain inulin and GOS at up to 4.5 g/d made no difference to stool frequency or softness (Scholtens et al, 2006).

Despite some variation in findings and confounding in several studies, it appears likely that inclusion of long-chain inulin and GOS at a ratio 9:1 in infant formula products leads to a softening of stools similar to those of breastfed infants. The impact on stool frequency is less clear with many studies reporting no statistically significant difference between fortified and unfortified formula-fed infants. The available evidence suggests that any increase in frequency declines with age. Supplementation at 8-10 g/L was more likely to result in softer and/or more frequent stools than 4 g/L.

With only one small study examining long-chain inulin and GOS in weaning foods at up to 4.5 g/d, no conclusion on its impact can be made.

1.4 Galacto-oligosaccharides Alone Added to Infant Formula

Using a six month parallel study design, Ben *et al* (2004) compared infants receiving standard formula supplemented with GOS at 2.4 g/L (n=69) with those given unsupplemented control formula (n=52) or breast milk (n=26). Stool frequency was the same in breastfed infants and those receiving supplemented formula, but higher in both these groups than in infants receiving control. This result somewhat inconsistent with the findings of studies using a combination of GOS and long-chain inulin, which suggest only a small, and sometimes non-significant impact on stool consistency with 4 g/L of GOS and long-chain inulin at a ratio of 9:1, i.e. 3.6 g/L of GOS. Further studies examining the sole addition of GOS to formula are needed before firm conclusions can be made.

1.5 Galacto-oligosaccharides in Combination with Non-inulin Oligo- and Polysaccharides added to Infant Formula

Ziegler et al (2007) studied an alternative combination of oligosaccharides also using a parallel design, but with a study duration of four months. Infants received standard formula (n=58), the same formula supplemented with polydextrose and GOS in a one-to-one ratio at 4 g/L (n=58), or polydextrose, GOS and lactulose in a ratio of 50:33:17 at 8 g/L (n=48). Both treatment groups had softer stools than control infants at 30, 60 and 90 days of age. Only those receiving the polydextrose, GOS and lactulose supplemented formula had more frequent stools than controls and only at 30 days of age. This work serves to highlight the possibility that a range of oligo- and/or polysaccharides may help to soften stools in infants.

1.6 Conclusion

The available evidence indicates that the addition of GOS and long-chain inulin at a ratio of 9:1 and concentration 4-10 g/L to infant formula is likely to result in softer stools. The ability of this mixture to increase stool frequency is less well established, possibly because this effect gets smaller with age.

Sole addition of inulin-derived substances to infant formula products or infant foods has sometimes been shown to increase stool frequency or stool weight in infants less than 12 months of age. The limited data available suggests they have little effect on stool pH. There appears to be little impact on stool frequency or consistency in infants over 12 months of age.

The one study that examined the addition of GOS to infant formula in isolation, i.e. without also adding other poly- or oligosaccharides, reported higher stool frequency in GOS-fed infants. The frequency was similar to that of a breastfed reference group. More data are needed to draw a firm conclusion. Data on the effect of formula supplemented with GOS alone on stool pH and faecal SCFA is limited and contradictory, thus no conclusion can be made.

2. Long-chain Inulin and GOS in Infant Formula: Impact on Stool pH and Short Chain Fatty Acid Profile

2.1 Colonic/Faecal pH and Short Chain Fatty Acids

The microflora of breastfed infants tends to be more heavily dominated by lactic acid bacteria, particularly *Bifidobacteria* and *Lactobacilli*, than that of formula-fed infants, which is more diverse (Edwards and Parrett, 2002). As a result of the metabolic activity of the lactic acid bacteria dominated microflora, breastfed infants have a lower colonic pH and a different, acetate and lactate dominated, short chain fatty acid (SCFA) profile than those fed formula (Coppa *et al*, 2004; Edwards and Parrett, 2002).

Such a lactic acid dominated microflora is considered to be beneficial to the infant and has been at least partially attributed to the influence of oligo- and polysaccharides inherent to human milk (Edwards and Parrett, 2002). Supplementation of infant formula with inulin-derived substances and/or GOS is seen as a potential way to simulate human milk's influence on colonic pH and the SCFA profile (Boehm *et al*, 2005). As it is not practical to measure colonic conditions directly, stool pH and faecal SCFA are used as a surrogate.

For a more detailed description of the microflora of both breastfed and formula-fed infants see Attachment 4.

2.1.1 Search Strategy, Study Limitations

The search strategy and study limitations were the same as those previously described in sections 1.1.1 and 1.1.3 respectively.

2.2 Effect of GOS and Long-chain Inulin and at a Ratio of 9:1 in Infant Formula or Infant Foods on Stool pH and Faecal Short Chain Fatty Acids

Five studies comparing stool pH in infants fed unsupplemented formula or formula supplemented with GOS and long-chain inulin at a 9:1 ratio were identified (Bakker-Zierikzee *et al*, 2005; Costalos *et al*, 2007; Fuentes *et al*, 2005; Moro *et al*, 2002; Scholtens *et al*, 2006). The main details of these studies, including age at entry, study design, sample size and outcome in terms of stool characteristics, are presented in Table 3.

Bakker-Zierikzee *et al* (2005) and Fuentes *et al* (2005) were the only researchers to include a breastfed control group. Both reported a lower stool pH in breastfed infants and those receiving formula supplemented with either 6 or 8 g/L oligosaccharide than in infants receiving unsupplemented formula. However, Bakker-Zierikzee *et al* (2005) reported that stool pH is lowest in breastfed infants, and that the faecal SCFA profile was similar in breastfed and supplemented formula-fed infants; i.e. both groups had higher proportions of lactate and lower proportions of butyrate and propionate than unsupplemented formula-fed infants. The study by Fuentes *et al* (2005) was only available as an abstract; it is not clear if this group found a difference in stool pH between breastfed and supplemented formula-fed infants, or if they measured faecal SCFA.

Infants given formula supplemented with 4 g/L of GOS and long-chain inulin mixture were reported to have a similar stool pH to those on standard formula (Costalos *et al*, 2007). An earlier study also reported no difference in stool pH between infants fed unsupplemented formula or formula supplemented with 4 g/L of GOS and long-chain inulin mixture, but did report a lower stool pH at a concentration of 8 g/L (Moro *et al*, 2002).

Scholtens *et al* (2006) were the only group to compare the effect of GOS and long-chain inulin when added to weaning food. Stool pH in infants fed up to 4.5 g of mixture was similar to those not given GOS and long-chain inulin supplemented foods.

Collectively these findings suggest that the addition of a 9:1 mixture of GOS and long-chain inulin to infant formula, at a concentration above of 6-8 g/L, would be expected to lower stool pH. The very limited available data suggest that such a formula may also promote a faecal SCFA profile more akin to that commonly observed in breastfed infants.

2.3 Effect of GOS Alone in Infant Formula or Infant Foods on Stool pH

Ben *et al* (2004) compared infants receiving standard formula supplemented with GOS at 2.4 g/L (n=69) with those given unsupplemented control formula (n=52) or breast milk (n=26) using a six month parallel study design. Infants receiving GOS supplemented formula or breast milk were reported to have had lower stool pH and higher faecal acetate concentrations than those on unsupplemented formula. Conversely, Bakker-Zierikzee *et al* (2005) report similar stool pH and faecal SCFA profile in infants receiving either unsupplemented formula (n=17) or formula supplemented with GOS at 6 g/L over a sixteen week period. The group also reported that stool pH was lower and faecal SCFA profile different in breastfed controls (n=unreported). It should be noted that this study was only available as an abstract from a conference proceeding.

With two studies conflicting so completely, no conclusion can be reached at this time.

2.4 Effect of Inulin Alone in Infant Formula or Infant Foods on Stool pH

Kim *et al* (2007) reported similar stool pH in infants fed either unsupplemented formula or formula supplemented so that each infant received 0.25 g/kg of inulin per day. Further details of the study can be found in Table 2.

2.5 Conclusion

The available evidence indicates that the addition of GOS and long-chain inulin at a ratio of 9:1 and concentration 6-8 g/L, but not 4 g/L makes infant formula more similar to human milk than unsupplemented formula with respect to stool pH and faecal SCFA profile. This was not observed when weaning foods were supplemented.

The influence of sole addition of GOS or inulin-derived substances to infant formula is unclear.

Table 2: Inulin or Oligofructose Alone in Infant Formula Products, Weaning Foods, and Formulated Supplementary Foods for Young Children

Reference	Study Participants	Comparisons	Oligosaccharide(s)	Concentration	Duration & Design	Outcome(s)
Brunser *et al* 2006	12-24 month old term infants after treatment with amoxicillin for acute bronchitis	test formula - Prebio 1 (Nestle de Chile) n=57 control formula - as per test without oligosaccharide n=56	Raftilose 95® & Raftiline at 7:3	4.5 g/L (2.25 g/d)	21 day parallel	No difference in stool frequency or consistency between groups
Euler *et al* 2005	2-6 week old term infants	test formula - S26® Gold (Wyeth Nutrition, Collegeville, PA) + oligosaccharide vs. no oligosaccharide n=58 breast milk n=14	Raftilose 95®	1.5 or 3.0 g/L	5 week total, but 1 week per treatment + 1 week washout	Greater stool frequency with either concentration, softer stools with higher concentration of oligosaccharide relative to no oligosaccharide. Softer and more frequent stools in the breastfed infants.
Kapiki *et al* 2006	preterm infants with maximum gestation age of 36 weeks	test - standard preterm formula + oligosaccharide n=36 control - standard preterm formula + maltodextrin n=20	inulin	4 g/L	14- days, measurements at 7 days	Greater stool frequency with oligosaccharide
Kim *et al* 2007	5-24 week old orphan term infants	test: standard formula + inulin n=14 control: standard formula n=14	Frutafit IQ®	0.25 g/kg/d	3 week cross-over	Greater faecal weight with oligosaccharide
Moore *et al* 2003	16-46 week old term infants	test: Nestle Carnation Premium Baby Cereal ® (Nestle, USA) + oligosaccharide n=27 control: Nestle Carnation Premium Baby Cereal ® + maltodextrin n= 29	*Fructo-oligosaccharide* no further details provided	0.75 g per 25 g serving of cereal	28 days	Greater stool frequency with oligosaccharide Stools were more likely to be soft with oligosaccharide cereal
Veereman-Wauters *et al* 2008	term infants 5 days old and under	test: standard formula + inulin n=20 x 2 test: standard formula + 1:9 mixture n= 20 control: standard formula n=20 control: breast milk n+28	Synergy1® or 90% galacto-oligosaccharide & 10% long-chain inulin	4 g/L inulin, or 8 g/L inulin, or 8 g/L 9:1 mixture	28 days	Stool frequency was the same in across formula-fed infants at week 4. Stool consistency was softer with 9:1 mixture and inulin at 8 g/L than with control.
Waligora-Dupriet *et al* 2007	7-19 month old term infants in day care	test: food & drink + with oligosaccharide n=9 control: food & drink + maltodextrin n=10	Beneo P95®	2 g/d	21 days parallel	Frequency & consistency of the stools were similar between groups

Table 3: Combination of GOS and Long-chain Inulin at a Ratio of 9:1 Added to Infant Formula Products and Infant Foods

Reference	Study Participants	Comparisons	Oligosaccharide(s)	Concentration	Duration & Design	Outcome(s)
Bakker-Zierikzee *et al* 2005	~ 1 week old term infants	test 1: Nutrilon I (Nutricia, Zoetermeer, The Netherlands) + oligosaccharides n=19 test 2: Nutrilon I + Bifidobacterium animalis Bb-12 n=19 control: Nutrilon I; Nutricia, Zoetermeer, The Netherlands) n=19 breastfed n=63	90% Vivinal® & 10% Raftiline HP®	6 g/L	16 week parallel	Lowest stool pH in breastfed infants. Oligosaccharide supplemented formula-fed infants had lower stool pH than standard formula-fed infants. No difference in total SCFA. Proportions of SCFA were similar in breast- and supplemented formula-fed infants with higher proportions of lactate and lower proportions of butyrate & propionate than in standard formula-fed infants.
Boehm *et al* 2002/3	preterm infants	test: experimental formula + oligosaccharides n=12 control: experimental formula + maltodextrin n=15 breastfed n=15	90% galacto-oligosaccharide & 10% long-chain inulin	10 g/L	28 days parallel	Breastfed and supplemented formula-fed infants had similar stool consistency, both had softer stools than control formula-fed infants
Bongers *et al* 2007*	constipated infants aged 3-20 weeks	test: Nutrilon Omneo (Nutricia, Zoetermeer, The Netherlands) n=12 control: 75% Nutrilon 1 & 25% Aptamil HA l (Nutricia, Zoetermeer, The Netherlands) n=12	90% galacto-oligosaccharide & 10% long-chain inulin	8 g/L	3 weeks cross-over	No difference in stool frequency, but oligosaccharide fed infants had more soft stools.
Costalos *et al* 2007	0-14 day old term infants	test: standard formula + oligosaccharides (Numico Research, the Netherlands) n=70control: standard formula n=70	90% galacto-oligosaccharide & 10% long-chain inulin	4 g/L	12 week parallel	Softer and more frequent stools with oligosaccharides. Similar stool pH between groups.
Moro *et al* 2002	~7 day old term infants	test: experimental formula + oligosaccharides n=30 for lower concentration & n=27 for higher concentration control: experimental formula + maltodextrin n=33	90% galacto-oligosaccharide & 10% long-chain inulin	4 & 8 g/L	28 day parallel	Same stool frequency across groups, softer stools with 8 g/L relative to control and similar to breast milk. Lower stool pH in those on supplemented formula with a dose response.

Reference	Study Participants	Comparisons	Oligosaccharide(s)	Concentration	Duration & Design	Outcome(s)
Moro *et al* 2006†	0-14 day old term infants	test: experimental formula + oligosaccharides n=102 control: experimental formula + maltodextrin n=104	90% galacto-oligosaccharide & 10% long-chain inulin	8 g/L	~26 week parallel	Softer and more frequent stools with oligosaccharides
Schmelzle *et al* 2003†	0-14 day old term infants	test: experimental formula + oligosaccharides n=76 control: Pre-Aptamil with Milupan (Milupa, Friedrichsdorf, Germany) n=78	90% galacto-oligosaccharide & 10% long-chain inulin	8 g /L	12 week parallel	More soft stools with oligosaccharide
Scholtens *et al* 2006	4-6 month old formula fed term infants being weaned	test: food with added oligosaccharides n=9 control: unsupplemented food n=7	90% Vivinal® & 10% Raftiline HP®	4.5 g/day	6 week parallel	Similar stool consistency and frequency between groups. Similar stool pH and faecal SCFA across groups.
Puccio *et al* 2007	0-14 day old term infants	test: Nan (Nestlé, Vevey, Switzerland) + oligosaccharides + *Bifidobacterium longum* BL999 n=49 control: Nan n=55	90% galacto-oligosaccharide & 10% long-chain inulin	4 g/L	112 day parallel	Higher stool frequency with fortified formula, more yellow/fewer green stools with symbiotic, lower risk of constipation
Litov *et al* 2006†‡	~ 2 month old infants	test: experimental + oligosaccharides control: experimental	90% galacto-oligosaccharide & 10 & long-chain inulin	4 g/L	14 +/- 3 day crossover	Less frequent stools with oligosaccharide
Fuentes *et al* 2005*‡	term infants	test: Nutrilon Omneo n=25 control: Nutrilon Premium n=23 breastfed n=20	90% galacto-oligosaccharide & 10 & long-chain inulin	8 g/L	6 months	More frequent and softer stools with oligosaccharides, similar faecal appearance as in breastfed infants. Lower stool pH in breast- and oligosaccharide supplemented formula-fed infants than in standard formula fed infants.
Mihatsch et al 2006†	Healthy stable preterm infants	test: standard preterm (whey/casein) formula + experimental supplement n=10 control: standard preterm (whey/casen) formula +	Not clearly stated. Assumed 90 % galacto-oligosaccharide & 10 % fructo-oligosaccharides	10 g/L	14 days	Reduced viscosity with GosFos supplements. Accelerated GI transport time with GosFos supplements

Reference	Study Participants	Comparisons	Oligosaccharide(s)	Concentration	Duration & Design	Outcome(s)
		maltodextrin n=10				

* Test formula also contains a high concentration of β-palmitic acid
† Test formula contains hydrolysed whey protein
‡ Study only available as an abstract

3. Nutrient interactions

Fibre intakes in the form of wheaten wholemeal or thickening agents made from soluble fibre have been found to interfere with mineral absorption (Reinhold et al., 1976; Bosscher et al., 2001). Although inulin is often added to food in the form of a purified extract it shares some of the characteristics of intact dietary fibre suggestive of the potential for nutrient interaction.

3.1 Magnesium, iron, zinc, copper and selenium

A positive effect of oligofructose consumption on magnesium absorption has been reported (Tahiri et al., 2001). Using a two-way crossover design, 14 healthy postmenopausal women were randomized to receive 10 g/d (5 g at lunch and 5 g at dinner) oligofructose (Actilight®; Eridania Beghin-Say, Vilvoord, Belgium) or sucrose for 35-days on each treatment. A stable isotope was given on day 28 after which faeces were collected for 5 to 7 days. Apparent absorption was defined as the difference in isotope intake and excretion expressed as a percentage of intake. Mean (SD) percentage intestinal absorption of isotopic magnesium increased from 30.2 (5.0)% to 33.9 (7.2)% after the placebo and oligofructose periods, respectively. Using the same protocol and isotopes of copper, zinc and selenium, the apparent absorption of copper was increased during the oligofructose intervention period compared with the control period ($P = 0.042$) whereas there was no difference in the absorption of zinc and selenium between treatments (Ducros et al., 2005). Iron absorption, as assessed by stable iron isotope enrichment in erythrocytes, was not different among treatments when 12 men took part in a randomized multi-crossover study involving a control diet or diets supplemented with 15 g/d inulin, FOS or GOS, each diet consumed for 21 days (van den Heuval et al., 1998).

An indirect way to assess mineral absorption along the small intestine is to measure the mineral content in the effluent of people with ileostomies, a surgical procedure in which an opening is created at the end of the small intestine that bypasses the colon. In a three-way crossover study, 10 people with ileostomies were randomized to receive a standard diet supplemented either with 17 g inulin (Raftiline ST; Orafti, Tienen, Belgium) 17 g oligofructose (Raftilose P95; Orafti, Tienen, Belgium), or 7 g sucrose as a control. The inulin or oligofructose were added to meals throughout the day and each diet was given for a period of three days (Ellegard et al., 1997). The excretion of magnesium, zinc, iron and calcium were not different among treatments indicative that 17 g inulin or 17 g oligofructose did not affect the absorption of these minerals along the small intestine compared with the sucrose control. A similar study design was used in healthy adults in which faeces were collected for the determination of mineral content (Coudray et al., 1997). In a three-way crossover study, nine young men were randomized to a control diet or to the same diet supplemented with 40 g/d inulin extracted from chicory roots (Agro Industries, Compiegne, France). Each experimental period lasted 28 days during which there was a progressive increase in inulin intake followed by 12 days at full dose. Sixty percent of the daily inulin intake was added to bread and 40% to beverages. The apparent absorptions assessed as mineral intake minus the mineral content of the faeces were not different between the inulin and control diet for magnesium, iron or zinc, but were increased for calcium ($P < 0.01$). These data suggest that the addition of inulin or oligofructose to food does not interfere with the absorption of magnesium, iron or zinc along the small intestine.

3.2 Calcium

In adults, positive differences in calcium absorption whilst consuming inulin supplemented diets with respect to controls has been shown using 15 g/d partially hydrolyzed inulin (Raftilose P95; Orafti, Tienen, Belgium) and 10 g/d of a 1:1 mix of short:long-chain inulin (Synergy 1; Orafti, Tienen, Belgium) (van den Heuvel et al., 1999; Holloway et al.,2007).

Calcium absorption measured using a double stable isotope technique was assessed in 60 female adolescents randomized in a crossover design to receive 8 g/d oligofructose (Raftilose; Orafti, Tienen, Belgium) or 8 g/d of a mix of inulin and oligofructose (Synergy 1; Orafti, Tienen, Belgium) or a control diet, each for a period of 3-weeks (Griffin et al., 2002). Calcium absorption was not different following the control and the oligofructose supplemented dietary periods but there were both fractional and absolute increases in calcium absorption following the inulin and oligofructose (Synergy 1) period. A clinical consequence of increased calcium absorption may be to increase bone mineralization. Results of a randomized controlled trial in which 100 adolescents were assigned to receive 8 g/d inulin and oligofructose (Synergy 1; Orafti, Tienen, Belgium) or maltodextrin for 1-year showed greater changes from baseline in bone mineral content and bone mineral density in the inulin-treated group (Abrams et al., 2005).

An enhancement in calcium absorption has not been found in all studies. In a doubly-labelled stable isotope study in 12 young men, there was no difference in calcium absorption assessed using 24-hour urinary calcium excretion between a control diet and diets containing 15 g/d inulin or fructo-oligosaccharides (van den Heuvel et al., 1998). The authors suggested that a 24-hour period may have been too short to observe an effect for an enhancement in calcium absorption occurring in the large intestine. Fourteen postmenopausal women were randomized to diets for 5-weeks containing 10 g/d FOS or a control (Tahiri et al., 2003). Calcium absorption was assessed by difference, intake less excretion, and by the amount of calcium isotope in plasma and urine. There was no difference in any of the parameters when comparing the control diet with the diet containing added FOS. The authors suggested that the prolonged ingestion of FOS might have down-regulated active calcium absorption in the small intestine, thus offsetting a possible increase in calcium absorption in the large intestine, although this could not be confirmed using this study design.

Calcium absorption in 15 young adults was estimated using a doubly-labelled technique in a short-term study in which FOS (Ebro-Puleva, Spain) were added to semi-skimmed milk at a concentration of 5 g/L (Lopez-Huertas et al., 2006). Following consumption of a test drink containing approximately 1 g FOS, calcium absorption was not different when compared with a control. The lack of effect may have been because the amount FOS was small or that the short-term nature of the study did not allow enough time for intestinal changes conducive to calcium enhancement to occur. An acute study in which inulin was added to cheese or to a calcium supplement did not show differences in serum ionized calcium postprandially over eight hours or calcium in urine collected for up to 24 hours (Teuri et al., 1999). Preterm infants were randomized to receive a 9:1 mix of GOS and long-chain inulin added to formula in an amount that equated to a concentration of 10 g/L in the made-up formula, or a control formula containing maltodextrine (Lidestri et al., 2003). After four weeks, mean serum and spot urinary calcium concentrations were not different between the groups. No difference in fasting urinary calcium excretion was found in 10 wheelchair-bound adults randomised to receive 15 g/d inulin added to thickened drinks for 3-weeks (Dahl et al., 2005).

Variability in results among studies might be expected given diversities in the population groups, the amount and type of oligosaccharide, duration of studies, and methods of determining calcium absorption, some of the details of which are shown in Table 4. Nevertheless, although an enhancement in calcium absorption has not been found in all studies, in no case has a negative effect of added inulin-derived substances or FOS on calcium absorption been reported.

Table 4: Calcium absorption in randomized controlled trials with a crossover design, unless otherwise indicated

Reference	Treatment[1,2]	Amount (g/d)	n and duration	Main outcome
Ellegard et al., 1997	Inulin (Raftiline ST) Oligofructose (Raftilose P95)	17 17	10 people with ileostomies, 3 days	Ca excretion 29.8 mmol (inulin); 31.2 mmol (oligofructose); *cf*. 29.3 mmol (control) (P > 0.05)
Coudray et al., 1997	Inulin (Agro Industries)	40	9 young men, 28 days	Apparent Ca absorption on treatment 33.7% *cf*. 21.3% on control (P < 0.01)
van den Heuvel et al., 1998	Inulin Oligofructose (Raftilose P95)	15 15	12 young men, 21 days	Fractional Ca absorption 25.8% (inulin); 26.3% (oligofructose); *cf*. 28.1% (control) (P > 0.05)
van den Heuvel et al., 1999	Oligofructose (Raftilose)	15	12 male adolescents, 9 days	Fractional Ca absorption on treatment 60.1% *cf.* 47.8% on control (P < 0.05)
Teuri et al., 1999	Inulin (Raftiline)	15	15 young women, acute study (1 day)	Inulin in cheese: Urinary Ca on treatment 1.60 *cf*. 1.45 mmol on control (NS). Serum ionized Ca 8-h area under the curve on treatment 0.010 *cf*. 0.002 mmol/L on control (NS). Inulin in a Ca supplement: Urinary Ca on treatment 1.47 *cf*. 1.46 mmol on control (NS). Serum ionized Ca 8-h area under the curve on treatment 0.011 *cf*. 0.009 mmol/L on control (NS).
Griffin et al., 2002	Oligofructose (Raftilose P95) Inulin oligo- and polysaccharides (Synergy 1)	8 8	60 female adolescents, 21 days	Fractional Ca absorption on oligofructose 31.8% *cf.* 31.8% on control (P = 0.75) Ca absorption on inulin and oligofructose 38.2% *cf.* 32.3% on control (P= 0.007)

Reference	Treatment[1,2]	Amount (g/d)	n and duration	Main outcome
Tahiri et al., 2003	Short-chain FOS	10	14 young women, 5 weeks	True Ca absorption on treatment 36.6% *cf*. 35.6% on control (P > 0.05)
Lidestri et al., 2003	9:1 mix galacto- and fructo-oligosaccharides	2.7 + 0.3	30 healthy pre-term infants, 4 weeks	Urinary Ca on treatment 1.63 *cf*. 0.93 mmol/L on control (P = 0.055)
Abrams et al., 2005[3]	Inulin oligo- and polysaccharides (Synergy 1)	8	100 adolescents, 1 year	Fractional Ca absorption 37.7% on treatment *cf*. 31.7% on control (P = 0.04)
Dahl et al., 2005	Inulin (Frutafit IQ)	15	15 wheelchair-bound adults, 3 wk	Urinary Ca on inulin 0.53 *cf*. 0.55 nM/mM Cr on control (P > 0.05)
Lopez-Huertas et al., 2006	Short-chain FOS (Ebro-Puleva)	1	15 young adults, acute	Fractional Ca absorption on treatment 25.6% *cf*. 24.5% on control (P > 0.05)
Holloway et al.,2007	Inulin oligo- and polysaccharides (Synergy 1)	10	15 post-menopausal women, 6-wk	Change in true absorption +5.1% on treatment *cf*. -3.3% on control (P < 0.05)

[1] The following branded products were used:
Orafti Raftiline ST – Inulin as extracted from the Chicory plant
Raftiline HP – Long-chain inulin - inulin with the oligosaccharide fraction removed
Raftilose P95 – Partially hydrolyzed inulin (5% monosaccharides, 95% oligosaccharides)
Synergy1 – A 1:1 mix of long-chain inulin and partially hydrolyzed inulin
Sensus Frutafit IQ - Instantised powdered inulin
Ebro-Puleva FOS – Fructo-oligosaccharide enzymatically synthesized from sucrose

[2] Other products:
Coudray et al - Agro Industries Research and Development – Inulin extracted from Chicory roots
Tahiri et al – No manufacturers details. Possibly Actilight FOS synthesized from sugar as this product was used by this group in another study.
Lidestri et al – The fructan part of the mix was described as inulin with a reduced amount of low molecular mass fraction; and as fructo-oligosaccharides with a degree of polymerization greater than 10. This description matches that of Raftiline HP.

[3] Parallel study design

The variety of products used, differences in the amounts used, and the small number of studies would make comparisons of effect among the products difficult to assess.

However, the data strongly suggest that inulin-derived substances and FOS added to diets do not inhibit the absorption of magnesium, iron, zinc, copper, selenium or calcium along the small intestine. In addition, some of the data is indicative of an enhancement of calcium, copper and magnesium absorption in the large intestine when inulin-derived substances are included in the diet.

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Attachment 8

Safety Assessment

Summary

Inulin (average Degree of Polymerisation ≥10), oligofructose (average DP <10) and fructo-oligosaccharides (FOS, average DP<4) have been used in the general food supply for over ten years without any reported adverse effects. This Proposal (P306) has been prepared to consider whether oligofructose, inulin and galacto-oligosaccharides (GOS) with an average DP 2-8 ought to be permitted to be voluntarily added to infant formula products and infant foods with the purpose of providing a prebiotic effect for formula-fed infants. This assessment aims to determine the safety of these indigestible oligosaccharides when added to infant formula products (including infant formula and follow-on formula), toddler formula and infant foods. For the purpose of this Report the term 'inulin-derived substances' refers to oligofructose and inulin.

Inulin-derived substances, composed primarily of fructose, are not present in human milk. Trace amounts of GOS (composed primarily of galactose) may be present. Human milk contains a mixture of complex oligo- and polysaccharides (referred to in this Report as human milk oligosaccharides) at levels up to 25 g/L in colostrum and somewhat less in mature milk. These human milk oligosaccharides (HMOs) are not digested in the upper gastrointestinal tract but enter the colon where they are partially fermented by the colonic microflora to short chain volatile fatty acids (SCFAs). These SCFAs may be absorbed, fermented further to form carbon dioxide, or excreted in the faeces.

FSANZ has assessed the evidence on the potential for inulin-derived substances and GOS to cause adverse effects in infants and young children. These soluble oligosaccharides, like naturally occurring HMOs, are not digested to any great extent in the small intestine, and reach the large intestine intact where they are also fermented by colonic bacteria to SCFAs and carbon dioxide. There is virtually no systemic exposure to these intact oligosaccharides, therefore the only possible adverse effect identified was an increased osmotic potential within the colon, potentially leading to increased water loss and dehydration. This possibility had also previously been considered by the European Scientific Committee on Food.

FSANZ has considered this potential risk. It was concluded that inulin-derived substances and GOS either alone or in combination at concentrations up to 8 g/L will beneficially contribute to increased osmotic potential in the colon of infant formula-fed infants; the increase is considered to be no greater than in breast-fed infants where undigested HMOs also enter the colon. To reach this conclusion FSANZ has considered the following evidence:

- HMOs in breast milk at levels up to 25 g/L are safe for breast-fed infants;
- GOS and long-chain inulin (9:1) preparations at 8 g/L are safe for formula-fed infants;
- Oligofructose preparations at 3 g/L are safe for formula-fed infants;
- Preparations of oligofructose and long-chain inulin (1:1) are safe for formula-fed infants at up to 8 g/L; and
- *In vitro* evidence that inulin-derived substances and GOS are fermented by colonic microflora to a similar or greater extent than HMOs.

It is concluded that up to 8 g/L inulin-derived substances are unlikely to pose a public health and safety risk to infants. Evidence from adult studies which suggested that some individuals may experience increased flatulence and bloating upon consumption of high levels of inulin-derived substances, were not significant observations in a recent infant study and may be due to differences in colonic microflora and overall diet. While clinical quantitation of gastrointestinal discomfort in young infants is difficult, similar clinical signs may be experienced by young infants when changing from breast milk or conventional formula to oligosaccharide-supplemented formula. In addition, the phenomenon of changed gastrointestinal effects is not uncommon for infants when changing from one formula to another formula. It is anticipated that this effect will be less evident in older infants (e.g. 6 months and over).

Unlike infant formula products, toddler formula and infant foods do not represent the sole source of nutrition for young children. It follows that if inulin-derived substances GOS, are safe for newborns and infants, they will be equally safe for older infants and young children.

Limited information is available on the safety of FOS in infant formula and foods for young children, therefore FSANZ did not consider FOS for infants as part of this Proposal.

1. Safety assessment of inulin-derived substances and GOS

FSANZ has not previously assessed the safety of inulin-derived substances or GOS in infant formula products, formulated supplementary foods for young children (FSFYC), e.g. toddler formula, and infant foods. Therefore, the aim of the current assessment was to review the published data on the chemical characteristics, use and effects of inulin-derived substances and GOS to determine their safety in these products. This covers the age group zero to three years. The use of inulin-derived substances as ingredients in the general food supply has also been considered.

1.1 Human milk oligosaccharides – Chemistry and metabolism

In human milk, a mixture of complex oligosaccharides is present. Complex oligosaccharides are branched oligosaccharides with a range of monosaccharides. To date over 200 complex oligosaccharides have been identified in breast milk, however, it is thought that the total number may be in the thousands (Boehm *et al*., 2005; Ninonuevo *et al*., 2006). The total oligo- and polysaccharide content of human milk is reported to be up to 25 g/L during the first few weeks following birth (Coppa *et al*., 1993; Coppa *et al*., 1997). Of this, up to 15 g/L are neutral oligo- and polysaccharides. It appears that levels are usually highest in colostrum, with lower levels reported in mature milk. These oligosaccharides generally have a lactose unit at their reducing end, linked to other monosaccharides by β1-3 or β1-6 linkages, although other β-glycosidic and α-glycosidic bonds may also be present. The saccharides present include glucose, galactose, fucose and N-acetylglucosamine. The degree of polymerisation of these oligosaccharides has been reported to be predominantly up to 8, but polysaccharides are present with DPs of greater than 20 (Boehm *et al*., 2003). Other sources reports the DP to range between three and thirteen (Stahl *et al.*, 2005) and over 50 (Attachment 3 – Breast milk composition).

Fructose and inulin-derived substances are not found in human milk; however the galacto-oligosaccharides 6'-galactosyl-lactose and 3'- galactosyl-lactose have been found at trace levels. Further information on the types and concentrations of oligo- and polysaccharides in human milk is in Attachment 3 – Breast milk composition.

It appears that human milk oligosaccharides (HMOs) are resistant to hydrolysis in the upper gastrointestinal tract. HMOs have been shown to be resistant to *in vitro* degradation by enzymes present in human and porcine brush border membranes, and human duodenal aspirates (Engfer *et al.,* 2000). Gnoth et al. also demonstrated that HMOs are resistant to acidic hydrolysis *in vitro* and are not digested by human salivary amylase or porcine pancreatic amylase (Gnoth *et al*., 2000).

Trace amounts of HMOs have been detected in preterm breast-fed infants' urine (Rudloff *et al*., 1996), supporting the evidence that they are resistant to digestion by amylases and glycosidases in the small intestine. Intact oligosaccharides are generally not absorbed by adults; the presence of HMOs in infant urine may be due to the higher intrinsic permeability of the infants' gut, however the mechanism by which absorption occurs is not known (Engfer *et al.,* 2000).

In the large intestine, HMOs are fermented by colonic microflora (Engfer *et al*., 2000) where they are converted to short chain volatile fatty acids (predominantly acetate, propionate and butyrate) which are mostly absorbed, preventing osmotic diarrhoea (Parrett and Edwards, 1997). The exact fermentation end products will vary depending on the genera of micro-organisms principally involved in their breakdown. In one-month old breast-fed infants, fermentation of HMOs is only partial, with around 40-50% of those ingested being excreted in the faeces (Coppa *et al*., 1999; Coppa *et al*., 2001). After one month of lactation the HMO concentration in breast milk is reported to be around 16 g/L (See Table 3, Attachment 3).

1.2 Inulin-derived substances, FOS and GOS – Chemistry and metabolism

Inulin is a polydisperse β2-1 fructan, with an average chain length of greater than 10 fructose units. The fructose units are linear, typically with a glucose unit at one end linked by an α1-2 bond, although glucose is not always present (Niness, 1999; Flickinger *et al*., 2003; Gibson *et al*., 2005). Inulin has high solubility in water and alcohol, and is not detected by traditional dietary fibre analyses (Flickinger *et al.,* 2003). Oligofructose is defined as having a chain length of less than 10 fructose units, while FOS has a chain length of less than 4 fructose units.

GOS is comprised of a glucose residue joined to galactose by a β1-4 glycosidic bond, to form lactose. Additional galactose units are joined to the first galactose by predominantly β1-4 or β1-6 glycosidic bonds (Schmelzle *et al*., 2003). β1-3 glycosidic bonds may also be present. The chain length of GOS is generally between 2-8 monosaccharide residues.

The β -glycosidic linkages present in inulin-derived substances and GOS (as well as HMOs) are broken down by different enzymes to those that break down α -glycosidic bonds. In general, β-glycosidic bonds are not digested by human gastrointestinal enzymes, whereas α -glycosidic bonds (such as those in starch) are quickly hydrolysed.
For this reason, inulin-derived substances and GOS will not be hydrolysed to any great extent in the upper gastrointestinal tract; rather they will be transported mostly intact to the colon where bacterial fermentation occurs.

This was confirmed in a study on the *in vitro* digestibility of GOS by human intestinal enzymes. It was shown that small intestinal β-galactosidase activity on GOS was less than 10% of its activity on lactose (Boehm *et al.,* 2005). Similarly, for inulin, studies with ileostomists have shown on average 86-89% of ingested inulin is not digested in the small intestine and can be recovered from the terminal ileum (Cummings *et al*., 2001b).

Inulin and GOS have been detected in the faeces of infants fed formula containing 8 g/L of the 9:1 (GOS:inulin) formulation (Moro *et al*., 2005). However, the amount detected was not quantified so it is unclear what proportion this represents. Another study similarly detected inulin and GOS in the faeces of 4-week old, pre-term infants fed formula containing the 9:1 preparation. The authors concluded that inulin-derived substances and GOS are at least partially unfermented, however, again the amount of oligosaccharides in the faeces was not quantified (Moro *et al*., 2004). In an *in vitro* study colonic bacteria in the faeces of breast-fed and formula-fed infants were capable of fermenting GOS and inulin (9:1) into the short chain volatile fatty acids acetate, propionate and butyrate (Boehm *et al*., 2004).

In human adults, inulin is completely fermented in the large intestine (Cherbut, 2002). No fructans were detected in the faeces of 6 healthy adults given 20 g FOS/day for 11 days (Molis *et al*., 1996), 24 volunteers given 5 and 15 g FOS/day for seven days (Alles *et al*., 1996) or three volunteers given 50 g inulin/day for 16 days (Castiglia-Delavaud *et al*., 1998). These findings are consistent with what would be expected given the chemical structure of inulin and its similarities with other fermentable carbohydrates. That is, it is soluble in water, typically non-viscous and does not appear to bind bile acids (Schneeman, 1999).

Tolerance studies

Laboratory animals

A conventional 90-day oral (gavage) toxicity study conducted in young adult rats dosed with 2500 or 5000 mg/kg bw/day Vivinal ® GOS syrup (45% GOS) reported the No Observed Adverse Effect Level (NOAEL) to be 5000 mg/kg/bw/day (the highest dose tested) (Anthony JC. *et al*., 2006). This is equivalent to 2250 mg/kg bw/day of GOS.

Humans

A number of clinical studies have been conducted in human infants fed infant formula containing GOS and inulin-derived substances, in varying ratios and concentrations and for a range of durations (up to 6 months). The most commonly used GOS:inulin preparation is a 9:1 GOS:inulin preparation, added to infant formula at a level of 8 g/L. Concentrations of 4, 6 and 10 g/L have also been studied, as has GOS alone. The infants' ages vary between studies from preterm infants up to over 12 month-olds. Most of these studies have focused on the effect of GOS:inulin fortified formula on stool characteristics (frequency, consistency, bacterial content) and other gastrointestinal symptoms, compared to infants fed unfortified formula or breast milk. More detail on the effects of GOS and inulin-derived substances on stool frequency and consistency is given in Attachment 5 – Nutrition Assessment. The highest level studied is 10 g/L (9:1 GOS:inulin) in a 28-day study in preterm infants.
In general, no adverse effects have been reported (see for example (Boehm *et al*., 2003; Moro *et al*., 2003; Schmelzle *et al*., 2003; Bakker-Zierikzee *et al*., 2005; Knol *et al*., 2005; Fanaro *et al*., 2005a; Ziegler *et al*., 2007; Alliet *et al*., 2007; Costalos *et al*., 2007; Bongers *et al*., 2007).

Other studies examined effects of GOS and oligofructose supplemented formula on the occurrence of atopic dermatitis, cholesterol, and HDL and LDL levels. No adverse effects were reported in these studies (Moro *et al*., 2006; Alliet *et al.,* 2007).

Some studies reported on gastrointestinal effects in infants given non-digestible oligosaccharides in infant formula products. Twenty-three infants less than 14-days received formula containing 4 g/L of the 9:1 ratio for 7 months. (Puccio *et al*., 2007). The formula also contained *Bifidobacterium longum* BL999. Occurrence of flatulence, spitting up/vomiting, comfort of the infant based on frequency of crying, restlessness and irritability and occurrence of parent diagnosed colic were recorded. More serious events (rhinitis, wheezing, cough, respiratory tract infection, diarrhoea, constipation, colic, fever, and rash) were also recorded based on inquires to the parents. Results indicated that compared with the control group, infants in the supplemented group were less likely to have flatulence. Data on frequency of crying, restlessness, colic, spitting, and vomiting showed no statistically significant differences between the two study groups. Occurrence of these events, serious or otherwise, was similar between groups.

In a 6-week study, 46 term infants were divided into three groups and fed formula supplemented with 2 g/L acidic oligosaccharides and 6 g/L maltodextrin, 2 g/L acidic oligosaccharides and 6 g/L of the 9:1 GOS:inulin preparation, or control formula containing 8 g/L maltodextrin. Possible side effects (crying, vomiting and regurgitation) were recorded and no differences were observed among the test groups (Fanaro *et al*., 2005b)

In other studies, similar results have been seen. Three and six month supplementation of formula-fed term infants with 2.4 g/L GOS alone had no influence on incidence of side effects (including crying, regurgitation, and vomiting) (Ben *et al*., 2004). In term infants given 0, 4 or 8 g/L of the 9:1 ratio for 28 days, supplementation had no influence on the incidence of side effects (crying, regurgitation, vomiting) or growth (Moro *et al*., 2002). Ninety-six infants younger than 4 months with colic given formula supplemented with 8 g/L of the 9:1 preparation for 14 days, had significantly decreased episodes of crying related to colic than those given a formula containing only 4 g/L GOS and inulin (Savino *et al*., 2006). Term infants with atopic dermatitis were given formula supplemented with 8 g/L 9:1 (GOS:inulin) for up to 6 months. Formula was well tolerated and there were significantly lower reports of regurgitation and crying in the group fed the GOS:inulin-supplemented formula relative to a group fed formula containing maltodextrin. There was no difference in the reported incidence of vomiting (Moro *et al*., 2006).

In a double-blind, randomised, controlled study of 120 days duration, 14-day old term infants were given either control formula (containing no oligosaccharides), or formula containing either 4 g/L GOS and polydextrose (50:50) or 8 g/L of polydextrose, GOS and lactulose (50:33:17) (Ziegler *et al*., 2007). Levels of GOS were therefore 0, 2 or 2.6 g/L. Parents rated infants' fussiness, fussiness relative to normal, gas, and gas relative to normal. Dropout rates were not statistically significantly different between groups; of 226 infants commencing the study, 164 completed it (24%, 22% and 36% dropout in each group).
The most common reason for dropout (including the control group) was intolerance to the formula, including gas, fussiness and diarrhoea. Infants receiving the test formulas had more gastrointestinal effects (e.g. gas and diarrhoea) however given the presence of other prebiotics (polydextrose and lactulose) it is difficult to attribute this to the presence of GOS. The two test formulas had similar GOS levels (2 and 2.6 g/L), which are lower than those used in other studies where no adverse effects were observed.

There are a small number of published studies on the effects of formula supplemented with oligofructose alone in young infants. The longest study was in 297 healthy, term infants (<14 days old) given formula supplemented with 0, 1.5 or 3 g oligofructose (raflilose95)/L for 12 weeks (Bettler and Euler, 2006). Growth, clinical chemistry at baseline and 12 weeks (albumin, blood urea nitrogen, calcium, magnesium, phosphorus, creatinine, triglycerides, low-density lipoprotein, and cholesterol), and adverse events (*e.g.* abdominal pain, allergic reaction, constipation, diarrhoea, flatulence, irritability, loose stools, rash, spitting up and vomiting) were measured. Two-hundred and twelve infants completed the study (67%, 73% and 73% from the control, low- and high-dose groups respectively). Growth, tolerance of the formula and reported adverse events were similar between the groups. Mean values for growth and clinical chemistry results at 12 weeks were within the normal range, and it was concluded that both test formulas were safe for young infants. Fifty-five percent of infants had at least one event that was considered to be formula-related. The 3 g/L group had less formula-related events compared with the other groups. The 1.5 g/L group had slightly more events than the control group. None were considered serious.

In other studies on oligofructose alone, no adverse effects were reported in 36 preterm infants (mean gestational age 33.9 weeks, 0-14 days old) receiving supplemented formula (4 g/L) for 14 days relative to a control group of 20 similar infants receiving un-supplemented formula (Kapiki *et al*., 2007). More frequent stools were also observed in this study. Softer stools and increased stool frequency were also observed in a study in 14 infants with an average age of 12 weeks, given an average of 0.25g inulin /kg bw/day (average 1.5 g/day) for 3 weeks (Kim *et al*., 2007).

In a prospective, randomised, cross-over study in 58 infants (term, 2-6 weeks old) given formula containing either 1.5 g/L or 3 g/L oligofructose for one week out of five, an increased incidence of flatulence and regurgitation were reported during the week of oligofructose supplementation (Euler *et al*., 2005). Looser stools were also observed during the week of supplementation. These effects were less frequent in the 1.5 g/L dose group relative to the 3 g/L group: seven infants (21%) versus 10 (31%) with flatulence, four infants (12%) versus nine (28%) with regurgitation and five infants (15%) versus 10 (31%) with looser stools. No comparison of occurrence of flatulence or regurgitation was made with the control group of 14 human milk-fed infants, however stool frequency was increased and stool consistency was looser in the human milk-fed infants compared with either formula-fed groups.

More recently, four groups of 20 term infants (received standard formula, formula containing 4 g/L or 8 g/L of inulin-derived substances (1:1 oligofructose and long-chain inulin, SYN1), or formula containing 8 g/L of 9:1 GOS to long-chain inulin (FOS) from as early as day 4 post-birth for 28 days (Veereman-Wauters et al, 2008). Samples were collected on days 1, 2 and 3; 12, 13 and 14; and 26, 27 and 28 and then averaged to represent week 0+, week 2 and week 4 of supplementation, respectively. Regurgitation of formula, stool frequency and stool consistency were recorded in study diaries.

Microbiology analysis of stool used the following probes/parameters: DAPI nucleotide stain as a broad indication of overall bacterial load, but would also stain positive with increased viral and yeast presence; Bac303 (BAC) for the detection of most *Bacteroides* and *Prevotella* species, all *Parabacteroides* species, *Barnesiella viscericola* and *Odoribacter splanchnicus*; Bif164 (BIF) for the detection of most *Bifidobacterium* species and *Parascardovia denticolens*; Chis150 for the detection of most members of *Clostridium* Cluster I and all of Cluster II strains; and Lab158 (LAB) for the detection of most *Lactobacillus* species,

all *Vagococcus, Melissococcus*, *Tetragenococcus*, *Enterococcus*, *Catelicoccus*, *Pediococcus*, *Paralactobacillus* and *Oenococcus* species, *Lactococcus lactis* and most *Weissella* and *Leuconostoc* species. Non-compliance/non-completion rates were similar across all treatment groups and would not have affected the interpretation of the study findings.

Infant weight, height and food intake were similar between groups at all sample intervals and the infants fed and grew normally. Observations of vomiting and assessment of crying were considered to be low and similar in all groups and no serious adverse events were observed.

The stool frequency for infants that received control formula, 8 g/L SYN1 or 8 g/L GOS:FOS decreased significantly from a mean score of about 2.8/day to about 2.1 after 4 weeks. The frequency in infants who received 4 g/L SYN1 decreased slightly but was not significant. The frequency in breast-fed infants increased from 2.8 to about 4 over the same period. Stool consistency of control formula-fed infants was significantly harder *cf.* breast-fed infants. Infants who were fed formula supplemented with 4 g/L SYN1, 8 g/L SYN1 or 8 g/L GOS:FOS had significantly decreased stool consistency at week 2 and week 4 was approximately mid way between values from breast-fed infants and infants who received the control formula. Faecal microbe analysis indicated that there were no unexpected changes in total bacteria, *Bacteroides*, *Clostridia*, or *Lactobacilli*. Mean values of *Bifidobacteria* increased significantly in samples from infants who received 8 g/L SYN1 or 8 g/L GOS:FOS. Non-significant increases were noted in infants who received 4 g/L SYN1 or those who were breast-fed. There was no significant change in infants who received the control formula.

Overall, the study authors concluded that formula supplementation with the SYN1 and GOS:FOS were well tolerated and led to an increase in faecal *Bifidobacteria*. There were no apparent adverse effects at up to 8 g/L SYN1 or 8 g/L as 9:1 GOS:FOS mixture.

Fewer studies have been performed in older infants that investigated the safety of FOS. Oligofructose has been studied in older infants (4-24 months) in toddler formula or cereal, at levels from 0.67 g/day for 6 months (Duggan *et al*., 2003), 2 - 2.25 g /day for 3 weeks (Brunser *et al*., 2006; Waligora-Dupriet AJ *et al*., 2007), an average of 1.05 g/day with a maximum of 3 g/ day (Moore *et al*., 2003) and an average of 1.1 g/day or up to 0.8 g/kg body weight per day (duration not stated) (Saavedra and Tschernia, 2002) without adverse effects. Brunser *et al* observed gastrointestinal signs (flatulence, restlessness, cramping, pain, crying and vomiting), and the results indicated these were similar in the treated and control groups (Brunser *et al*., 2006). Scholtens et al reported feeding GOS/inulin (9:1 ratio) supplemented weaning products to 11 infants with a mean age of 4 months for 6 weeks (mean intake 4.05 g/day) but no comment was made on the tolerance of the weaning foods (Scholtens *et al*., 2006).

Inulin-derived substances and GOS in the general food supply

Inulin is considered to be a dietary fibre in the general food supply. Dietary fructans including inulin occur naturally in plant foods such as wheat, bananas, Jerusalem artichokes, artichokes, onions and leeks. Average daily consumption of fructans has been estimated as 1-4 g in the United States and 3-11 g in Europe (Roberfroid and Delzenne, 1998). Other estimates of dietary exposure to inulin suggest adults may consume up to 10 g inulin per day from a range of foods containing naturally occurring or added inulin and inulin-derived substances.

Up to 20-30 g/day of inulin-derived substances and FOS can be tolerated by many adults (Briet *et al*., 1995), although increased flatulence was observed in adults taking 10 g/day 'fructo oligosaccharides' (DP not reported) for four weeks (Cummings *et al*., 2001a). However, out of 117 people starting the study in the fructo-oligosaccharide group, only three dropped out due to flatulence. A statistically significant increase in perceived well-being was also noted in the fructo-oligosaccharide group relative to a control group. A high level of consumption (e.g. over 30 g/day) may result in increased flatulence, and may cause more severe side effects such as stomach cramps and diarrhoea, however, these are common effects of over consumption of any dietary fibre. Gastrointestinal tolerance varies between individuals and is also influenced by diet (Coussement, 1999). In addition excessive consumption is likely to be self-limiting due to the unpleasant side effects (TGA, 1998).

There are two published reports of individual patients with an allergy to inulin (Gay-Crosier *et al*., 2000; Franck *et al*., 2005). Both individuals exhibited allergies to artichoke, and some processed foods containing inulin. However, the rarity of these cases indicates that from a public health and safety perspective inulin is an insignificant allergen. It is not recognised as a major allergen in Australia and New Zealand or elsewhere.

GOS is generally not present in foods, although it may be present at low levels in some processed dairy products, such as lactose reduced milk and yoghurt. Short term studies in adults have been done with GOS including 10 g GOS/day for 21 days, 15 g/day for 6 days and single intakes of 30 g, without reported adverse effects (cited in (Boehm *et al.,* 2005). However, intakes of GOS from the general food supply are likely to be negligible. The addition of GOS to the general food supply is not being considered as part of this proposal.

2. Discussion

Infants consuming breast milk tend to have a lower renal solute load[53] than those on conventional infant formula products. Similarly breast-fed infants tend to have softer stools than formula-fed infants. These effects are thought to be due to the presence of undigested or partially digested HMOs in the colon exerting an osmotic potential[54]. This osmotic effect is expected to be greatest in very young breast-fed infants without established colonic microflora as HMOs in milk will not fermented at all.

Following microbial colonisation, around 60% of the HMOs are fermented, with only the remaining 40% having the potential to exert osmotic pressure and being excreted in the faeces.

Similar to HMOs in breast milk, inulin-derived substances and GOS are not digested to any great extent in the small intestine and reach the colon largely intact. In considering the safety of inulin-derived substances and GOS in infant formula products, it was important to consider whether the presence of undigested oligosaccharides in the colon could lead to excess water excretion in the faeces, causing diarrhoea and dehydration. A newborn infant's renal system is not fully developed and so has a limited capacity to concentrate urine.

[53] The potential renal solute load of infant food is the sum of dietary nitrogen (expressed as mmol of urea divided by 28), sodium, potassium, chloride and phosphorus.

[54] Osmotic potential occurs when two solutions with differing solute concentrations are separated by a membrane that is only permeable to water. To achieve equilibrium, water is drawn from the side of the membrane that has a lower solute concentration to the side with the higher concentration in an effort to equalise the concentration on either side of the membrane.

If excess water loss through faeces occurs then the renal concentrating ability may be exceeded leading to a negative water balance (dehydration). This issue was considered in two parts: for newborns without the ability to ferment oligosaccharides (no significant colonic microflora); and for young infants (< 12 months) with the ability to ferment oligosaccharides (colonic microflora).

In newborn formula-fed infants, prior to the establishment of colonic microflora, inulin-derived substances and GOS would not be fermented in the large intestine, and are excreted unchanged in the faeces. This is likely to contribute to a slightly increased osmotic potential relative to infants fed formula not containing 8 g/L GOS:inulin. However, in comparison to breast-fed infants, where the HMO concentration is up to 25 g/L, the levels of undigested oligosaccharides in the colon of infants fed GOS and inulin-supplemented infant formula products will be less than half those of breast-fed infants. Therefore, it is unlikely that there is any risk to these very young infants from the presence of inulin-derived substances and GOS in infant formula at the levels suggested.

In regard to young infants where the colonic microflora has become established, some of the undigested oligosaccharides will be fermented. In 1-month old, breast-fed infants only around 60% of ingested HMOs (16 g) are fermented; if a similar proportion of GOS and inulin-derived substances (at 8 g/L) are fermented in formula-fed infants, the remaining undigested oligosaccharides would be unlikely to pose a risk to infants. There is evidence which indicates that this is likely to be the case. Based on the presence of short chain fatty acids in formula-fed infants' stools, and *in vitro* studies indicating that colonic bacteria from formula-fed infants produce short chain fatty acids in the presence of GOS and inulin, it appears that a significant portion of GOS and inulin are fermented. It has also been shown that inulin is totally fermented in the large intestine of human adults; although there may be differences between young infants and adults in regard to fermentation capacity, where a substance is entirely fermented in adults, it is likely that some fermentation also occurs in infants. In addition, an *in vitro* study on the differences in fermentation capabilities between breast-fed and formula-fed infants suggests both groups have similar capability to ferment complex oligosaccharides into short chain fatty acids (Parrett and Edwards, 1997). Thus there is a high likelihood that GOS and inulin-derived substances would be fermented effectively in infants. Only around a quarter of the intake of added undigested oligosaccharides would need to be fermented to give a similar level in the colon as HMOs (given around 15 g/L HMOs of which 50-60% are fermented). The very high probability that such a level of fermentation occurs reduces the level of concern that water balance could be adversely affected by an increase in osmotic potential due to undigested inulin-derived substances and GOS in the colon. Furthermore, the level of proposed addition of non-digestible oligosaccharides to infant formula (8 g/L) is lower than the level of oligosaccharides in human milk (up to 25 g/L); even if no fermentation of inulin-derived substances occurred, the amount of oligosaccharides in the colon would be in the same range as breast-fed infants.

The contention that GOS and inulin are at least partially fermented in the colon, similarly to HMOs, and are therefore unlikely to affect water balance when used at levels no greater than those in breast milk, is supported by indirect evidence from a range of studies conducted in preterm, term and older infants. These studies indicate that the use of a 9:1 ratio of GOS to inulin in formula at a level of 8 g/L does not cause problems with water balance or other adverse effects.

In regard to the use of other ratios of oligosaccharides, or inulin-derived substances alone in infant formula, FSANZ has considered a concern expressed by EFSA relating to water balance. The available evidence that oligofructose and inulin are fermented by colonic microflora in formula fed infants as described above (presence of SCFA in stool, *in vitro* stool studies, and evidence from adult toleration studies), reduces the concern that water balance could be adversely affected by an increase in osmotic potential due to undigested inulin-derived substances in the colon. In addition, a 12-week study in term infants which indicated oligofructose at 3 g/L had no significant effect on growth, blood chemistry, or reported adverse events, supports the safety of inulin-derived substances in infant formula products. It has been shown that 8 g/L of GOS:long-chain inulin is safe, levels as high as 25 g HMOs/L in breast milk is safe, and inulin-derived substances are likely to be fermented to a similar degree to GOS and HMOs, therefore, FSANZ concludes up to 8 g/L added inulin-derived substances will be safe for young infants. This is supported by a recent 28-day study on up to 8 g/L of a 1:1 oligofructose and long-chain inulin combination. This conclusion applies equally to the use of GOS alone or any ratio of GOS:inulin-derived substances so long as the total level of oligosaccharides is no greater than 8 g/L.

The use of ratios of GOS to inulin other than 9:1 has not been reported in the published literature to any extent, therefore the safety of other ratios relies on a theoretical argument that the any effects will be similar to the 9:1 ratio. This seems reasonable provided the total concentration of oligosaccharides does not exceed 8 g/L.

Prebiotics such as GOS and inulin-derived substances are intended to selectively stimulate the growth and/or activity of beneficial bacteria (e.g. bifidobacteria and lactobacilli) in the colon. These bacteria do not generate gas as part of their metabolism; however other bacteria may also be stimulated, and therefore increased flatulence compared to standard formula-fed infants may occur.

In addition, evidence from studies in adults suggests that inulin-derived substances at a daily dose of 10 g cause gastrointestinal symptoms including flatulence and bloating in some individuals. The data from two studies where infants were fed formula containing oligofructose at 3 g/L do not provide clear evidence whether this would also occur in infants, although the recent study suggests that up to 8 g/L is safe. There may be differences in colonic microflora between adults and formula-fed infants, and adults have a much more varied diet compared to infants; both these factors would impact on gas production. However, intestinal discomfort in very young infants is undesirable and appropriate studies (e.g. *in vitro* comparison of the volume of gas produced through fermentation of inulin-derived substances with the complex oligosaccharides found in human breast milk, or direct studies of gastrointestinal symptoms in infants with higher levels of intake) to demonstrate this would not occur are lacking.

Some gastrointestinal discomfort may initially be experienced by young infants changing from breast milk or conventional formula to oligosaccharide-supplemented formula. The phenomenon of changed gastrointestinal effects is not uncommon for infants when their formula is changed. It is anticipated that this effect will be less evident in older infants (e.g. 6 months and over).

The effects of FOS have not been studied to any extent in infant formula and so it has not been assessed in this Report.

Formulated Supplementary Foods for Young Children (FSFYC) and infant foods

Young children (1-3 years) have a more developed renal system that is able to more effectively concentrate urine relative to young infants. Therefore dehydration is much less of a concern in the older age group. For this group, FSFYC (toddler formula) and infant foods will not be the sole source of nutrition, so even if inulin-derived substances and GOS concentrations in these foods are higher than those in infant formula, exposure on a body weight basis is likely to be lower than for young infants exclusively consuming oligosaccharide supplemented formula. FSANZ considers the addition of GOS and inulin-derived substances to toddler formula and infant foods at levels similar to those added to infant formula is unlikely to pose a risk to children consuming these foods. Further information on exposure to inulin-derived substances and GOS by different age groups is detailed in Attachment 7 – Dietary Exposure Assessment.

Inulin in the general food supply

FSANZ considered the safety of inulin as part of Application A277 – Inulin and fructo-oligosaccharides as dietary fibre (FSANZ., 2001). Inulin, oligofructose and FOS are currently permitted as food ingredients and have been since prior to 1995, when Application A277 was first made. Since 2001, added inulin has been required to be labelled as dietary fibre, and has been added as an ingredient to a wide range of foods with the aim of increasing the fibre content. It is also used in some foods (e.g. margarine) as a bulking agent.

Although there are two reports of allergy to inulin, it is not considered to be a major allergen. Otherwise, no adverse effects have been reported due to the consumption of foods containing inulin, and FSANZ considers inulin-derived substances and FOS to have a history of safe use as food ingredients in the general food supply.

3. European regulatory assessments of GOS and inulin

The safety of GOS and inulin-derived substances in infant formula and in follow-on formula was considered by the Scientific Committee on Food (SCF) in 2001, initially in September (SCF, 2001b) and then again in December (SCF, 2001a). The data considered included six clinical studies in preterm and term infants given infant formula containing 4 or 8 g/L GOS and ‘high molecular weight oligofructose’ (at a 9:1 ratio) or ‘low molecular weight oligofructose’ alone (concentration not stated).

Stool frequency and consistency were found to differ significantly with the two concentrations of GOS and oligofructose. Increased stool frequency and greater watery or fluid stools were observed in the treated groups compared to infants fed non-supplemented infant formula.

Although it was noted that breast-fed infants generally have looser and more frequent stools than formula fed infants, human milk has a lower renal solute load than infant formula, and concern was expressed that increased faecal water losses might occur in infants fed formula containing oligosaccharides. This was of greater concern for infants already suffering from stress factors that may affect water balance.

It was also concluded that as by four to six months of age, infants have a more mature renal function and lower water turnover per unit body weight, that the adverse potential of added oligofructose and GOS would be very low in this group (SCF, 2001b).

Following this statement, further studies were submitted to the committee, which included two preliminary studies on growth and water balance. Growth data in both preterm and term infants fed different concentrations of GOS and oligofructose were considered. Other data submitted included individual observations of urine creatinine in preterm infants, observations of individual stool frequency, stool consistency, and indicators of protein metabolism in term infants, data on levels of minerals and potential renal solute load of different infant formula, and preliminary information of urine osmolarity in term infants.

The SCF concluded that there was no evidence of adverse effects from the use of a formula with up to 8 g/L of a combination of 90% 'oligogalactosyl-lactose' (GOS) and 10% 'high molecular weight oligofructosyl-saccharose' (high molecular weight inulin). This conclusion was confirmed in 2003 in the SCF's Report on the Revision of Essential requirements of Infant Formula and Follow-on Formula (SCF, 2003).

The European Food Safety Authority (EFSA) Scientific Panel on Dietetic Products, Nutrition and Allergies considered the safety of oligofructose supplemented infant formula in 2004 (EFSA, 2004). Oligofructose at 0, 1.5 and 3.0 g/L in infant formula was given to healthy, term infants for 12 weeks. Growth, serum markers of protein and mineral status and kidney function were all within the normal range. The committee stated that variable effects on the consistency and frequency of the infants' stools were observed, including increased adverse events (e.g. loose stools), in infants fed formula with added oligofructose. No measures were made to demonstrate satisfactory water balance, and the committee therefore could not exclude the possibility of increased risk of dehydration. A study on the effect of FOS on faecal microflora was also assessed at this time, and it was observed that oligofructose-supplemented formula (1.5 and 3 g/L) led to increased flatulence, regurgitation, irritability and looser stools (Euler *et al*., 2005). The committee concluded that there was no evidence of benefits to infants from the addition of oligofructose at the studied levels, and believed that there are reasons for safety concerns.

4. Conclusions

FSANZ has assessed the evidence for the potential of inulin-derived substances and GOS to cause adverse effects in infants and young children. In particular, the possibility of oligosaccharides increasing the osmotic potential in the colon, which could lead to increased water loss and dehydration was considered.

The results presented indicate that inulin-derived substances and GOS, like naturally occurring HMOs, are not digested to any great extent in the small intestine. The oligosaccharides/ inulin-derived substances, were found in the large intestine mostly intact and contributed to a small increase in osmotic potential in the colon. However, this slight increase in osmotic potential for GOS and inulin-derived substances was not considered to be undesirable because breast-fed infants also have levels of undigested HMOs present in the colon.

A number of studies on the 9:1 GOS to long-chain inulin preparation in infant formula products supported the conclusion that 8 g/L of oligosaccharides would not pose a risk to young infants. This conclusion applies to GOS, inulin and oligofructose at any ratio to a total level of 8 g/L, based on data indicating that these oligosaccharides are fermented to a similar or greater extent than HMOs. The safety of this level (8 g/L) is further supported by the presence of higher levels of indigestible oligosaccharides (up to 25 g/L) in human milk, 3-fold higher than tested in the formula-supplementation study.

The evidence in adults that intakes of inulin-derived substance may lead to gastrointestinal signs (e.g. flatulence and bloating), when compared to the lack of adverse findings in 4 day-old infants for 4 weeks, was insufficient to propose a mid range limit (e.g., 4 g/L) for the amount of these substances to be permitted in infant formula.

The consumption of GOS and oligofructose or inulin by young children (*via* toddler formula and infant foods) or by very young infants at maximum levels 8 g/L, or less than one third that present in breast milk, is very unlikely to pose a risk to young children.

FSANZ considers inulin and FOS to have a history of safe use as food ingredients in the general food supply.

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Attachment 9

Dietary Intake Assessment

Summary

A dietary intake assessment was deemed necessary for Proposal P306 in order to estimate the potential dietary intakes of inulin-derived substances and GOS in special purpose foods for infants and young children <3 years of age (i.e. infant and follow-on formula, infant foods and formulated supplementary foods for young children (FSFYC), for example, toddler formula).

FSANZ has received two Applications (from Heinz Wattie's Limited and Nutricia Australia), requesting amendments to the Code to allow addition of inulin-derived substances and GOS to infant formula products and in the case of Nutricia, to infant foods. The Applications and literature reviewed by FSANZ were used as the basis for assigning concentrations for the addition of inulin-derived substances and GOS in infant formula products, infant foods and FSFYC.

Dietary intakes of inulin-derived substances and GOS have been estimated in two ways:

- ***'Combined' Assessment*** – represents estimated intakes of inulin-derived substances and GOS collectively for each population group assessed in this proposal, i.e. based on the concentration of inulin-derived substances and GOS in special purpose foods for infants and young children as a combined total of 0.8 g/100 mL; and

- ***'Separate' Assessment*** – represents estimated intakes of inulin-derived substances and GOS separately for each of the population groups assessed in this proposal, based on the concentration at a maximum proposed level (inulin-derived substances or GOS at 0.8 g/100 mL in special purpose foods for young children).

Baseline dietary intakes of inulin-derived substances and GOS were estimated based on natural sources and added sources according to the current market uptake of these substances in processed food products. An additional intake estimate was then calculated to account for potential intakes from infant formula products, infant foods and FSFYC supplemented with inulin-derived substances and GOS.

As food consumption data were not available for children aged <2 years in Australia and <5 years in New Zealand, model diets were constructed for infants aged 3, 9 and 12 months for Australia and aged 3 months and 1-3 years for New Zealand for use in the intake assessments. FSANZ developed the model diets for Australian children based on the Australian National Nutrition Survey and New Zealand model diets were derived from the New Zealand total diet study. The model diets include the estimated intakes of infant formula (800 mL/day for a 3 month old), follow-on formula (545 mL/day for a 9 month old), toddler formula (between 285 and 425 mL/day for 1-3 year olds) and infant foods along with consumption of other foods where appropriate.

The estimates indicate that following the addition of inulin-derived substances and GOS to infant formula, 3 month old infants are likely to have the highest increase in mean intakes but the lowest total intake of these substances among the young children <3 years of age.

Infants aged 3 months were assumed to be exclusively fed infant formula, thus their intake of inulin-derived substances and GOS at baseline is zero and the only contributor to intakes of inulin-derived substances and GOS for this age group is infant formula. As young children grow, they consume smaller amounts of formula, more of other foods, and greater amounts of food in total; hence their dietary intake of inulin-derived substances and GOS from added and the natural sources also increases. The estimated dietary intakes of inulin-derived substances and GOS increased for each age group assessed from 3 months to the 3 years age group.

The main source of inulin-derived substances and GOS in the diets of young children in Australia and New Zealand for the *baseline* for the combined assessment and GOS only assessment was from yoghurt. If the addition of inulin-derived substances and GOS to special purpose foods for infants and young children <3 years of age were to be approved, formula products[55] would be the main source of these substances for infants (≤1 year of age). The main source of inulin-derived substances and GOS intakes for New Zealand children (aged 1-3 years) were from yoghurts. Toddler formula was also a major contributor but was lower than yoghurts.

Intakes from naturally-occurring food sources and added sources in processed foods did not make a large contribution to the estimated intakes of inulin-derived substances and GOS for infants 9 months and 1 years of age.

1. Background

A dietary intake assessment was deemed necessary for Proposal P306 in order to estimate the potential dietary intakes of inulin-derived substances and GOS in special purpose foods for infants and young children <3 years of age (i.e. infant and follow-on formula, infant foods and FSFYC).

FSANZ had received two Applications (from Heinz Wattie's Limited and Nutricia Australia), requesting amendments to the Code to allow addition of inulin-derived substances and GOS to infant formula products and in the case of Nutricia, to infant foods also. These Applications were used as the basis for setting the concentration of added inulin-derived substances and GOS in infant formula products (Tables 1 and 2).

Table 1: Proposed concentration of inulin-derived substances and GOS in infant formula products, as a *Ratio (FOS:GOS as a 1:9 ratio, maximum of 0.8 g/100 mL)*

Substance	Infant Formula Products and Infant Foods
	Ratio
Inulin	0.08
GOS	0.720

[55] Formula products include infant formula for 3 month old, follow-on formula for <1 year old.

Table 2: Proposed concentration of inulin-derived substances and GOS in infant formula products, as *Minimum and Maximum (mg/100 kJ)*

Substance	Infant and follow-on formula (mg/100 kJ)	
	Minimum	**Maximum**
Inulin	30	110
GOS	145	290

2. Dietary modelling conducted to estimate inulin-derived substances and GOS intakes

2.1 What is dietary modelling?

Dietary modelling is a tool used to estimate dietary exposure/intakes to food chemicals, including nutrient intakes, as part of the FSANZ risk assessment process. To estimate dietary exposure to food chemicals, records of what foods people have eaten are needed along with reports of how much of the food chemical of interest is in each food. The accuracy of these dietary exposure estimates depends on the quality of the data used in the dietary models. Sometimes, all of the data needed are not available or their accuracy is uncertain so assumptions have to be made, either about the foods eaten or about chemical levels, based on previous knowledge and experience. The models are generally set up according to international conventions for food chemical dietary exposure estimates. However, each modelling process requires decisions to be made about how to set the model parameters and what assumptions to make. Different decisions may result in different answers. Therefore, FSANZ documents clearly all such decisions, model assumptions and data limitations to enable the results to be understood in the context of the data available and so that FSANZ risk managers can make informed decisions.

2.2 Population groups assessed

The primary target group was identified as young children (<3 years of age). Within this population group, dietary inulin-derived substances and GOS intakes were investigated for different age groups (Table 3).

Table 3: Population groups assessed for this Proposal

Australia: • Model diet for 3 month old infant; • Model diet for 9 month old infant; • Model diet for 1 yr old infant;
New Zealand: • Model diet for 3 month old infant; • Model diet for 1-3 years children.

2.3 Dietary survey data

DIAMOND contains dietary survey data for both Australia and New Zealand; the 1995 NNS from Australia that surveyed 13,858 people aged 2 years and above, and the 1997 New Zealand NNS that surveyed 4,636 people aged 15 years and above. Both of these surveys used a 24-hour food recall methodology.

As there were no data available from the 1995 Australian NNS for children aged < 2 years, theoretical diets were constructed to estimate dietary inulin-derived substances and GOS intakes for the target groups of children aged 3 months, 9 months and 12 months. Similarly, as there were no data available from the 1997 New Zealand NNS or 2002 New Zealand Children's NNS for children aged < 5 years, theoretical diets were used to estimate dietary inulin-derived substances and GOS intakes for the New Zealand children aged 3 months and 1-3 years. See Appendix 1 for further details on how the theoretical diets were constructed.

2.4 Dietary intake assessment approach

The dietary intakes of inulin-derived substances and GOS were estimated by combining usual patterns of food consumption, as derived from the theoretical diets, with current concentrations of inulin-derived substances and GOS in foods and the proposed levels of use of inulin-derived substances and GOS in infant formula, follow-on formula and toddler formula. Concentrations were also assigned to infant foods where data was available. The dietary modelling approach used for the intake assessment of inulin-derived substances and GOS for Australian and New Zealand population groups is as shown in Figure 1.

Dietary Intake = concentration x food consumption amount

Dietary intake assessments were estimated for both inulin-derived substances and GOS combined and also separately.

2.5 Inulin-derived substances and GOS concentration data

The proposed levels of inulin-derived substances and GOS added to special purpose foods for infants and young children (<3 years of age) that were used in the dietary intake assessment were derived from the aforementioned Applications. International analysis/literature (Appendix 2), industry use data and FSANZ analysis (Food Standards Australia New Zealand, 2002) provided current levels of inulin-derived substances and GOS in a range of other different foods consumed by the young children (<3 years of age).

Concentrations of inulin-derived substances and GOS, as described in Tables 1 and 2, were assigned to each of the food groups in the theoretical diets.

Concentration data from the literature were assigned to food groups as inulin-derived substances together (i.e. summed). For the purpose of dietary intake assessment, if levels of both inulin and FOS were available, the highest concentration available was used and if only levels of FOS were available for a food that FOS value was used. Where the concentration data were available as a range, an average of the lowest and highest values in the range was used. Some literature did not clearly distinguish between long-chain and short chain oligosaccharides and in this case, also, the value cited was assigned to inulin-derived substances.

Where the concentration data available did not distinguish between naturally-occurring or added to foods, the value was included in the dietary intake assessments (for example, yoghurt).

FSANZ's assessment is based on the proposed maximum concentrations of inulin-derived substances and GOS in two ways:

- GOS and inulin-derived substance, with a maximum combined concentration of 0.8 g/100 mL; and
- proposed maximum concentrations of inulin-derived substances and GOS added separately.

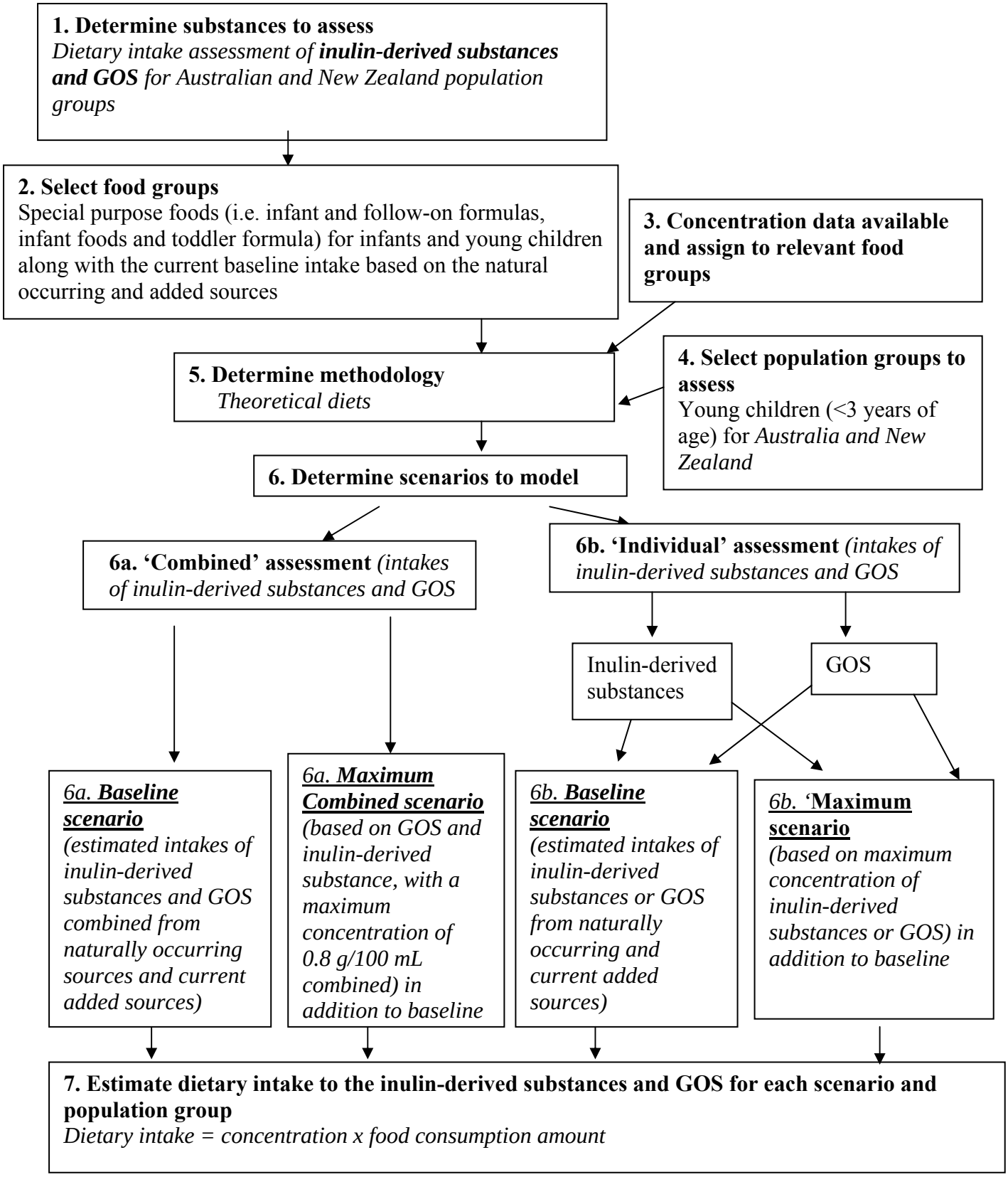

Figure 1: Dietary modelling approach used for the intake assessment of inulin-derived substances and GOS for the Australian and New Zealand population groups

The proposed maximum concentrations for infant formula products and foods for infants were also assigned to toddler formulas. The inulin-derived substances and GOS concentrations that were used in the dietary intake assessments are outlined in Table 4a for infant and follow-on formulas and Table 4b for infant foods and toddler formula.

Table 4: Inulin-derived substance and GOS concentrations used in the dietary intake assessments

a: Infant and follow-on formula concentrations

Substance	Infant and follow-on formula concentration (g / 100 mL)
	Maximum
Inulin-derived substance	0.80
GOS	0.80
Inulin-derived substance and GOS as combined	0.80

b: Infant foods and toddler formula concentrations

Substance	Infant foods and toddler formula concentration (g / 100 mL)
	Maximum
Inulin-derived substances	0.80
GOS	0.80
Inulin-derived substance and GOS as combined	0.80

2.6 Scenarios for dietary intake assessments

The scenarios that were investigated in the dietary intake assessments are outlined in Sections 2.6.1 and 2.6.2.

2.6.1 *Combined assessment* (intakes of inulin-derived substances and GOS, collectively)

The *combined assessment* estimates intakes of inulin-derived substances and GOS combined for each population group assessed in this proposal. The two scenarios modelled for the *combined assessment* were the *baseline* scenario and the *maximum combined* scenario.

2.6.1.1 Baseline Scenario

Baseline scenario represents estimated intakes from naturally-occurring inulin-derived substances and GOS in foods along with added sources based on the current market uptake for inulin-derived substances and GOS in processed foods. The concentration data used in dietary intake assessments are shown in Appendix 2.

2.6.1.2 Maximum combined scenario

The Applications are seeking a maximum concentration of 0.8 g/100 mL of total oligosaccharides. The *maximum combined* scenario takes into account estimated intakes of inulin-derived substances and GOS of 0.8 g/100 mL in infant and follow-on formulas, toddler formulas and foods for infants in addition to baseline intakes of inulin-derived substances and GOS from naturally-occurring sources in foods and added sources in other processed foods.

2.6.2 *Separate assessment* (intakes of inulin-derived substances and GOS individually)

The *separate assessment* represents estimated intakes of inulin-derived substances and GOS separately for each population group assessed in this proposal. The two scenarios modelled for each *separate assessment* were the *baseline* scenario and the *maximum* scenario.

2.6.2.1 *Baseline* Scenario

As per the *baseline* scenario in *combined assessment* (Section 2.6.1.1), but assessing inulin-derived substances and GOS separately.

2.6.2.2 Maximum Scenario

The Applications also provided proposed maximum concentrations of inulin-derived substances and GOS in infant formula for inulin-derived substances and GOS separately. The *maximum* scenario takes into account the proposed maximum levels of use for inulin-derived substances and GOS in addition to baseline intakes of inulin-derived substances and GOS from naturally-occurring sources and added sources. In processed foods the proposed maximum levels of use for inulin-derived substances and GOS are as 0.8 g/100 mL.

2.6.3 'Breast milk' assessment (intakes of oligo- and polysaccharides for infants at 3 months of age)

In order to assess the dietary intake of oligo- and polysaccharides for infants at 3 months of age that are fully breastfed, the quantity of breast milk consumed and the concentration of oligo- and polysaccharides in breast milk needed to be determined. Reilly *et al.* (2005) found that infants at 3 months of age from presumably well-nourished populations, including Australia, consumed a mean amount of 796 grams of breast milk per day (weighted for sample size). The oligo- and polysaccharide concentration of breast milk is up to 15g/L (Coppa et al, 1999). Inulin-derived substances/FOS are not present in breast milk and the concentration of GOS in breast milk is negligible, therefore the concentration of oligo- and polysaccharides was used for this calculation.

For breastfed infants, the following assumptions were made:

- milk was the only food consumed for infants at 3 months; and
- one gram of breast milk is equal to one millilitre of breast milk.

2.7 How were the estimated dietary inulin-derived substances and GOS intakes calculated?

A detailed explanation of how the estimated dietary intakes were calculated can be found in Appendix 1.

3. Assumptions used in the dietary modelling

The aim of the dietary intake assessment was to make as realistic an estimate of dietary inulin-derived substances and GOS intakes as possible. However, where significant uncertainties in the data existed, conservative assumptions were generally used to ensure that the dietary intake assessment did not underestimate intake.

The assumptions made in the dietary intake assessment are listed below, broken down into several categories.

3.1 Consumer behaviour

- Consumption of foods as outlined in the theoretical diets represent current food consumption amounts for Australian and New Zealand young children (<3 years of age);
- consumers select products that, on average, contain inulin-derived substances and GOS at the concentrations specified;
- consumers do not alter their food consumption habits upon inulin-derived substances and GOS fortified products becoming more available on the market;
- infants aged 3 months are exclusively infant formula fed;
- infants aged 9 months consume follow-on formula and infant foods in addition to solid foods;
- all children aged 1-3 years consume Toddler formula and infant foods in addition to other solid and liquid foods;
- all milks consumed by children aged 1-3 years in the theoretical New Zealand diet is assumed to be toddler formula; and
- the substitution of Toddler formula for milk is on a 'volume for volume' basis rather than on an energy basis.

3.2 Concentration Data

- It was assumed that the inulin-derived substances and GOS concentrations in foods were representative of Australian and New Zealand foods;
- where a food was not included in the intake assessment, it was assumed to contain a zero concentration of inulin-derived substances and GOS;
- the inulin-derived substances and GOS concentration of infant formula, follow-on formula, Toddler formula and infant foods is currently zero (i.e. at *'Baseline'*);
- the proposed inulin-derived substances and GOS concentration of follow-on formula was same as the concentration of infant formula;
- there was no contribution to inulin-derived substances and GOS intakes through the use of complementary medicines (Australia) or dietary supplements (New Zealand); and
- concentration data available were imputed to similar food groups for the dietary intake assessments (for example the concentration data from root vegetables (average value of burdock, murnong, yacon, salsify) were imputed to other root vegetables like carrot and potato).

3.3 General

- For the purpose of this assessment, it was assumed that 1 millilitre is equal to 1 gram for all liquid and semi-liquid foods (e.g. infant formula).

4. Limitations of the dietary modelling

Dietary modelling based on 1995 or 1997 NNS food consumption data provides the best estimate of actual consumption of a food and the resulting estimated dietary intake of a nutrient for the population. However, it should be noted that the NNS data do have limitations. These limitations relate to the age of the data and the changes in eating patterns that may have occurred since the data were collected. Generally, consumption of staple foods such as fruit, vegetables, meat, dairy products and cereal products, which make up the majority of most people's diet, is unlikely to have changed markedly since 1995/1997 (Cook, Rutishauser, and Seelig, 2001; Cook, Rutishauser, and Allsopp, 2001).

Over time, there may be changes to the ways in which manufacturers and retailers make and present foods for sale. Since the data were collected for the Australian and New Zealand NNSs, there have been significant changes to the Code to allow more innovation in the food industry.

As a consequence, a limitation of the dietary modelling is that some of the foods that are currently available in the food supply were either not available or were not as commonly available in 1995/1997 (e.g. toddler formula). Additionally, since the data were collected for the NNSs, there has been an increase in the range of products that are fortified with nutrients. FSANZ does update the food composition database through analytical programs and scans of the market place. However, with the market place continually changing it is difficult to account for all fortified products at a given point in time.

A limitation of estimating dietary intake over a period time using information from a recall method is that people may over- or under-report food consumption, particularly for certain types of foods. Over- and under-reporting of food consumption has not been accounted for in this dietary intake assessment.

Since the 1995 Australian NNS does not report on respondents aged below 2 years, the 1997 New Zealand NNS does not report on respondent aged below 15 years and the 2002 New Zealand National Children's Nutrition Survey (CNS) does not report on respondents aged below 5 years, theoretical diets were used to estimate dietary inulin-derived substances and GOS intakes for children in the target group of up to 3 years. FSANZ developed the model diets for Australian children based on an extrapolation from 2 years diet from Australian National Nutrition Survey and New Zealand model diets were derived from the New Zealand total diet study. Theoretical diets for Australian children aged 3 months, 9 months and 1 year and New Zealand children aged 1-3 years were used in this assessment. Mean food consumption amounts in the theoretical diets are used to represent food consumption patterns for an age group as a whole and may not be as accurate as the data derived for other population groups from the NNSs that use food consumption data of individuals.

Although some data on the use of complementary medicines (Australia) or dietary supplements (New Zealand) were collected in the NNSs, data were either not in a robust enough format to include in DIAMOND or have simply not been included in the DIAMOND program to date. Consequently, intakes of substances consumed via complementary medicines or dietary supplements could not be included directly in the theoretical diets.

While the results of national nutrition surveys can be used to describe the usual intake of groups of people, they cannot be used to describe the usual intake of an individual (Rutishauser, 2002). In addition, they cannot be used to predict how consumers will change their eating patterns as a result of an external influence such as the availability of a new type of food.

Concentration data available on natural sources and added sources based on the current market uptake of inulin-derived substances and GOS were limited, therefore extrapolation of values from some foods to many other food groups was conducted. Concentration data and comments on data extrapolation used for the dietary intake assessments are as in Table A2.2. Also, the form or chain length of inulin-derived substances or GOS was often not indicated. How these limitations were dealt with was explained earlier.

5. Dietary intake assessment results

5.1 Estimated dietary intake of inulin-derived substances and GOS

Mean and 95th percentile dietary intakes of inulin-derived substances and GOS were estimated for the *combined* and *separate assessments* based on maximum levels for inulin-derived substances and GOS. The results are shown in Figures 2 and 3 (full results in Tables 5 and 6). As young children grow, they consume smaller amounts of formula, more of other foods and greater amounts of food in total; hence their dietary intake of inulin-derived substances and GOS from supplemented and natural sources also increases. The estimated dietary intakes of inulin-derived substances and GOS increased for each age group assessed from 3 months to the 3 years age group.

This assessment has assumed infants aged 3 months were exclusively fed infant formula. Thus, the estimated dietary intakes of inulin-derived substances and GOS for this age group were exclusively from infant formula and, *baseline* inulin-derived substances and GOS intakes for infants aged 3 months were zero for both *combined* and *separate assessments f*or Australia and New Zealand.

5.1.1 Combined assessment

Combined assessments represent estimated intakes of inulin-derived substances and GOS combined for each of the population groups assessed in this proposal, based on the concentrations at a maximum proposed level (0.8 gm/ 100 mL).

Infants 3 months for Australia and New Zealand:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances and GOS for the *maximum combined* scenario were 6 g and 16 g per day respectively.

Infants 9 months for Australia:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances and GOS were 5 g and 12 g per day respectively for the *baseline* scenario and 9 g and 23 g/day for the *maximum combined* scenario.

Infants 1 years of age for Australia:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances and GOS were 7 g and 17 g per day respectively for the *baseline* scenario and 10 g and 26 g/day for the *maximum combined* scenario.

Children 1-3 years of age for New Zealand:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances and GOS were 17 g and 42 g per day respectively for the *baseline* scenario and 19 g and 49 g/day for the *maximum combined* scenario.

5.1.2 *Separate assessments*

Separate assessments represents estimated intakes of inulin-derived substances and GOS separately for each of the population groups assessed in this proposal, based on the concentrations at different maximum proposed levels.

The intakes for the combined maximum scenarios will not be a sum of the two separate maximum scenarios and this is because of the special foods for young children. Adding the intakes from the two separate assessments would result in some 'double-counting' of inulin-derived substances and GOS from these foods.

5.1.2.1 Inulin-derived substances only Scenarios

Inulin-derived substances only scenarios represent estimated intakes of inulin-derived substances when added at 0.8 g/100 mL.

Infants 3 months for Australia and New Zealand:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances for the *maximum* scenario were 2 g and 6 g per day, respectively.

Infants 9 months for Australia:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances were 4 g and 9 g per day, respectively, for the *baseline* scenario and 5 g and 14 g/day for the *maximum* scenario.

Infants 1 years of age for Australia:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances were 5 g and 14 g per day, respectively, for the *baseline* scenario and 7 g and 18 g/day for the *maximum* scenario.

Children 1-3 years of age for New Zealand:
The estimated mean and 95th percentile dietary intakes of inulin-derived substances were 12 g and 31 g per day, respectively, for the *baseline* scenario and 14 g and 34 g/day for the *maximum* scenario.

5.1.2.2 GOS only Scenarios

GOS only scenarios represent estimated intakes of GOS when added at 0.8 g/100 mL to special purpose foods for young children.

Infants 3 months for Australia and New Zealand:
The estimated mean and 95th percentile dietary intakes of GOS for the *maximum* scenario were 6 g and 16 g per day, respectively.

Infants 9 months for Australia:
The estimated mean and 95th percentile dietary intakes of GOS were 1 g and 3 g per day, respectively, for the *baseline* scenario and 5 g and 14 g/day for the *maximum* scenario.

Infants 1 years of age for Australia:
The estimated mean and 95th percentile dietary intakes of GOS were 1 g and 4 g per day, respectively, for the *baseline* scenario and 5 g and 12 g/day for the *maximum* scenario.

Children 1-3 years of age for New Zealand:
The estimated mean and 95th percentile dietary intakes of GOS were 5 g and 12 g per day, respectively, for the *baseline* scenario and 7 g and 18 g/day for the *maximum* scenario.

5.1.3 Breast milk assessment

In this assessment 3 month old infants were assumed to have a diet consisting entirely of breast milk. The estimated intake of oligo- and polysaccharides from breast milk for 3 month old infants is 12.0 g/day (i.e. 796 g/d x 15 g/L). This is higher than the mean dietary intake of total oligosaccharides for 3 month old infants from infant formula only of 6 g/day based on the maximum proposed concentration of 8 g/L total oligosaccharides (see Table 5).

5.2 Major contributing foods to dietary intakes of inulin-derived substances and GOS for infants consuming infant formula, follow on formula or toddler milks

5.2.1 Combined assessment

The major contributors (≥ 5%) to intakes of inulin-derived substances and GOS for the 'combined' assessment for Australian and New Zealand young children (<3 years of age) are shown in Table 7.

With the exception of special purpose foods, the major contributors (≥ 5%) for all population groups assessed were similar between the *baseline* and *maximum combined* scenarios. For the *maximum combined* scenario, the highest contribution was from infant formula products for the 9-month old and the 1 year old (47% and 33%, respectively) for Australia. The major contributors for *baseline* and *maximum combined* scenarios for New Zealand 1-3 year olds were from yoghurt (45% and 39%) and potatoes[56] (15% and 13%), respectively. Major contributors for *maximum combined* scenarios for New Zealand 1-3 year olds also includes toddler formula (11%).

5.2.2 *Separate assessments*

The major contributors (≥ 5%) to intakes of inulin-derived substances and GOS for the *separate assessments* for Australian and New Zealand young children (<3 years of age) are shown in Table 8.

[56] The concentration data for potato has been imputed from other root vegetables.

The highest contributors for inulin-derived substances for the *maximum scenarios* among 9 month olds and 1 year olds in Australia were from infant formula products (30% and 23%), potatoes (19% and 20%) and yoghurt (11% and 12%), respectively. The highest contributors for *baseline* and the *maximum* scenarios among New Zealand 1-3 year olds were from yoghurt (29% and 27%) and potatoes (21% and 19%), respectively. Contributions from toddler formula were 9% for the *maximum* scenario for New Zealand 1-3 year olds.

The highest contributors for GOS for the *'maximum scenarios'* among the 9 month olds and 1 year olds in Australia were from infant formula products (80% and 69%) and yoghurt (12% and 19%), respectively. The highest contributors for GOS among New Zealand 1-3 year olds for the *baseline* scenario were yoghurt (84%) and cheese (7%) and for the *maximum* scenario were yoghurt (54%) and toddler formula (29%).

Figure 2: Estimated mean dietary intake of inulin-derived substances and GOS for combined *and* separate assessments *for Australia and New Zealand population groups*

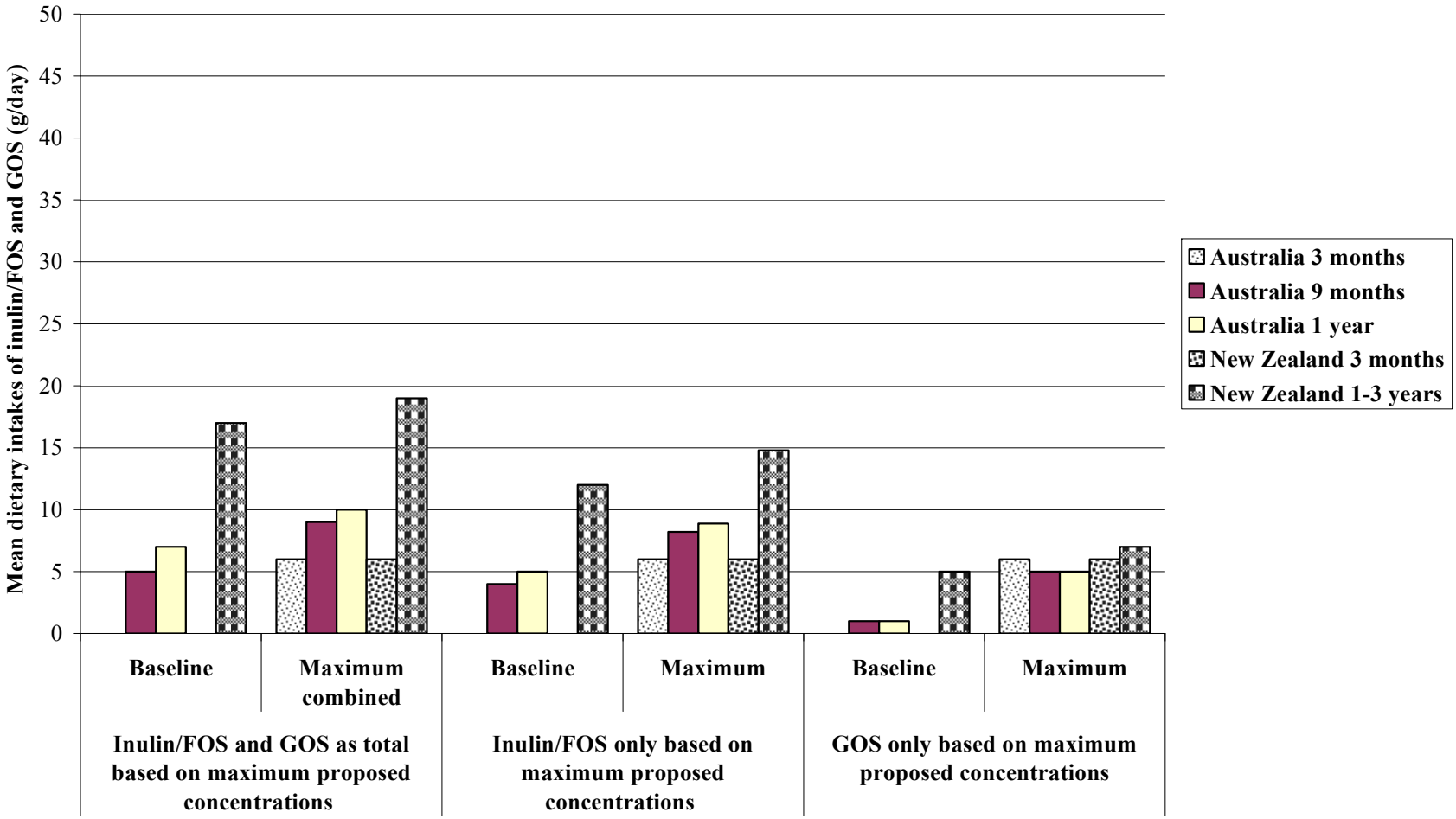

Figure 3: Estimated 95th percentile dietary intake of inulin-derived substances and GOS for combined *and* separate assessments *for Australia and New Zealand population groups*

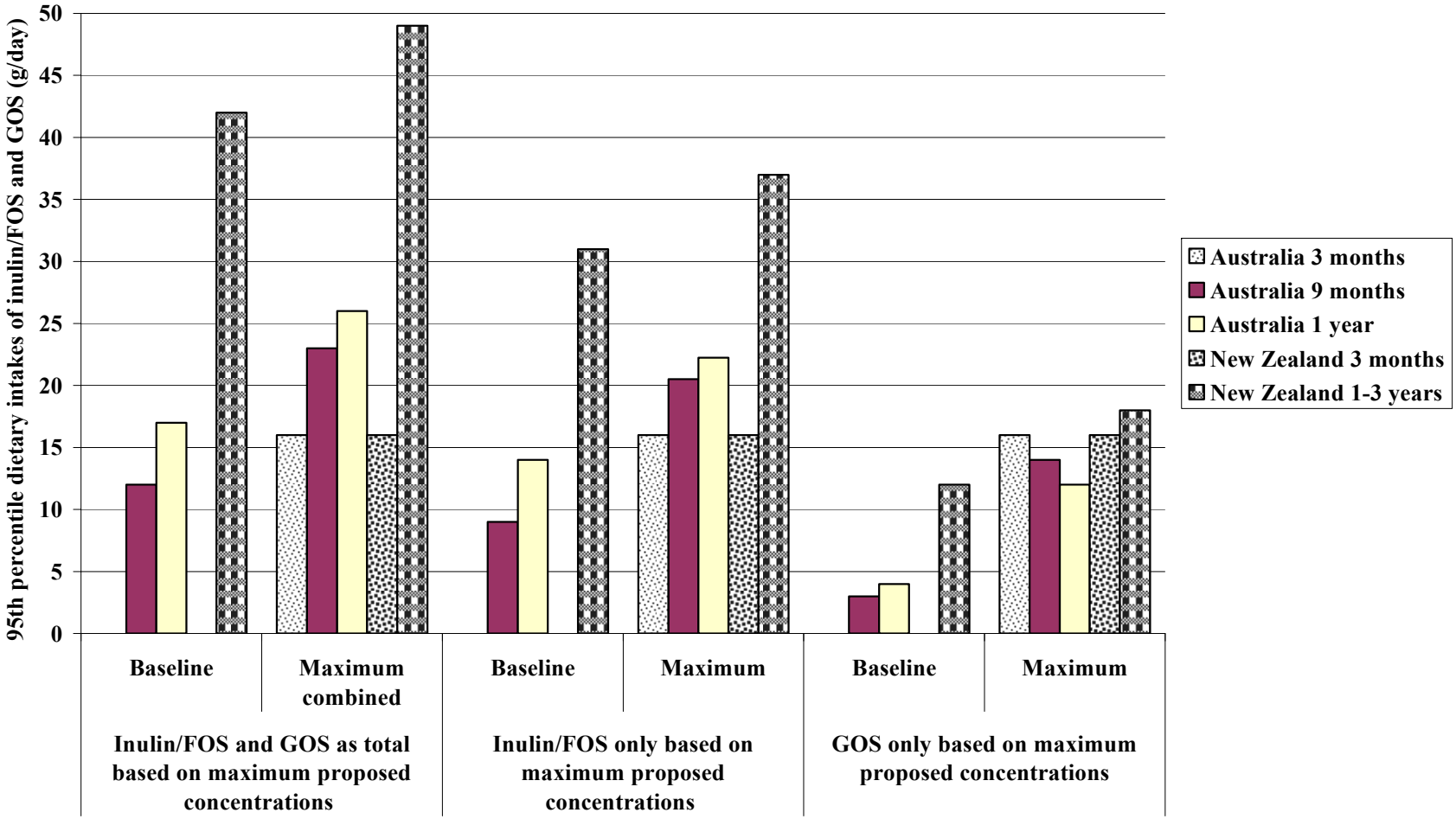

Table 5: Estimated mean dietary intake of inulin-derived substances and GOS for *combined* and *separate assessments* for Australia and New Zealand population groups

Population groups	Age	50th percentile body weight (kg)	Estimated energy requirement (kJ/kg bw/day)	Estimated intake of formula# (mL/day)	Combined assessment		Separate assessment			
					Inulin-derived substances and GOS as total based on maximum proposed concentrations		Inulin-derived substances only based on maximum proposed concentrations		GOS only based on maximum proposed concentrations	
					Mean (g/day)					
					Baseline	***Maximum combined***	***Baseline***	***Maximum***	***Baseline***	***Maximum***
Australia	3 months	6.4	343	800	0	6	0	6	0	6
	9 months	8.9	335	545	5	9	4	8	1	5
	1 year	9.6	345	425	7	10	5	9	1	5
New Zealand	3 months	6.4	343	800	0	6	0	6	0	6
	1-3 years	9.6	NA	280	17	19	12	15	5	7

Energy content of cow's milk based infant formula = 274 kJ/100 g
NA Not applicable

Table 6: Estimated 95th percentile dietary intake of inulin-derived substances and GOS for *combined* and *separate* assessments for Australia and New Zealand population groups

Population groups	Age	50th percentile body weight (kg)	Estimated energy requirement (kJ/kg bw/day)	Estimated intake of formula# (mL/day)	Combined assessment		Separate assessment			
					Inulin-derived substances and GOS as total based on maximum proposed concentrations		Inulin-derived substances only based on maximum proposed concentrations		GOS only based on maximum proposed concentrations	
					95th percentile (g/day)					
					Baseline	***Maximum combined***	***Baseline***	***Maximum***	***Baseline***	***Maximum***
Australia	3 months	6.4	343	800	0	16	0	16	0	16
	9 months	8.9	335	545	12	23	9	21	3	14
	1 year	9.6	345	425	17	26	14	22	4	12
New Zealand	3 months	6.4	343	800	0	16	0	16	0	16
	1-3 years	9.6	NA	280	42	49	31	37	12	18

Energy content of cow's milk based infant formula = 274 kJ/100 g
NA Not applicable

Table 7: Major contributors for Australia and New Zealand for the *combined assessments*

1: Australia

Foods	% contribution					
	3 month old		9 month old		1 year old	
	Baseline	Maximum combined	Baseline	Maximum combined	Baseline	Maximum combined
Formula products*	NA	100	NA	47	NA	33
Yoghurt, fruit, full fat	NA	NA	26	13	25	17
Potatoes	NA	NA	21	11	21	14
Rice, white	NA	NA	9	<5	9	6
Bread, white	NA	NA	7	<5	7	<5
Ice cream, full fat, vanilla	NA	NA	6	<5	6	<5
Carrots	NA	NA	5	<5	5	<5

2: New Zealand

Foods	% contribution			
	3 month old		1-3 year old	
	Baseline	Maximum combined	Baseline	Maximum combined
Formula products*	NA	100	NA	11
Yoghurt	NA	NA	45	39
Potatoes	NA	NA	15	13

*Formula products include infant formula for 3 month old, follow-on formula for <1 year old and toddler formula for children 1-3 years old.
NA - Not applicable

Table 8: Major contributors for Australia and New Zealand for the *separate assessments*

a: Inulin-derived substances

1: Australia

Foods	% contribution					
	3 month old		9 month old		1 year old	
	Baseline	*Maximum*	*Baseline*	*Maximum*	*Baseline*	*Maximum*
Formula products*	NA	100	NA	53	NA	38
Potatoes	NA	NA	27	12	27	16
Yoghurt, fruit, full fat	NA	NA	16	7	16	10
Bread, white	NA	NA	10	<5	9	6
Ice cream, full fat, vanilla	NA	NA	8	<5	8	5
Carrots	NA	NA	7	<5	7	<5
Lettuce, raw	NA	NA	6	<5	6	<5
Rice, white	NA	NA	6	<5	6	<5

2: New Zealand

Foods	% contribution			
	3 month old		1-3 year old	
	Baseline	*Maximum*	*Baseline*	*Maximum*
Formula products*	NA	100	NA	14
Yoghurt	NA	NA	29	25
Potatoes	NA	NA	21	18
Bread, white	NA	NA	6	<5
Carrots	NA	NA	6	<5

*Formula products include infant formula for 3 month old, follow-on formula for <1 year old and toddler formula for children 1-3 years old.
NA - Not applicable

b: GOS

1: Australia

Foods	% contribution					
	3 month old		9 month old		I year old	
	Baseline	*Maximum*	*Baseline*	*Maximum*	*Baseline*	*Maximum*
Formula products*	NA	100	NA	80	NA	69
Yoghurt, fruit, full fat	NA	NA	63	12	63	19
Rice, white	NA	NA	21	<5	21	6

2: New Zealand

Foods	% contribution			
	3 month old		1-3 year old	
	Baseline	Maximum	Baseline	Maximum
Formula products*	NA	100	NA	29
Yoghurt	NA	NA	84	54
Cheese	NA	NA	7	<5

*Formula products include infant formula for 3 month old, follow-on formula for <1 year old and toddler formula for children 1-3 years old.
NA -Not applicable

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Appendix 1

Theoretical diets used in the risk assessment

A1.1 How were the estimated dietary inulin-derived substances and GOS intakes calculated?

As there were no data available from the 1995 Australian NNS for children aged <2 years, FSANZ developed theoretical diets for Australian children to estimate dietary inulin-derived substances and GOS intakes for the target groups of children aged 3 months, 9 months and 12 months.

Similarly, as there were no data available from the 1997 New Zealand NNS or 2002 New Zealand Children's NNS for children aged < 5 years, New Zealand theoretical diets from New Zealand total diet study were used to estimate dietary inulin-derived substances and GOS intake for the New Zealand children aged 3 months and 1-3 years.

Research conducted by UMR Research and the New Zealand Food Safety Authority reported that, for children aged 1-3 years who consume at least 200 ml of toddler formula per day, the average consumption was 460 ml per day (New Zealand Food Safety Authority, 2006). The theoretical diet for Australian children aged 1 year contained 423 g/day of Toddler formula; the theoretical diet for New Zealand children aged 1-3 years contained 267 g/day Toddler formula and approximately 15 g/day of infant formula/ follow-on formula. Therefore, the theoretical diets used in this assessment considered the complete replacement of milk with Toddler formula.

Since the theoretical diets were based on mean food consumption amounts only, individual records were not available to derive a distribution of food consumption amounts and hence a distribution of inulin-derived substances and GOS intakes. The 95th percentile dietary inulin-derived substances and GOS intakes were estimated using the internationally accepted formula (WHO, 1985) of:

$$95^{th} \text{ percentile intake} = \text{mean intake} \times 2.5$$

A1.1.1 Australian and New Zealand infants aged 3 months

The diet for the 3 month old was based solely on infant formula based on the assumption that milk could be the only food source for this age group. The recommended energy intake for a three-month-old boy (FAO, 2004) at the 50th percentile weight (WHO, 2007) was used as the basis for the theoretical diet. Boys' weights were used because boys tend to be heavier than girls at the same age and therefore have higher energy and food requirements. Dietary intakes of inulin-derived substances and GOS were calculated as follows:

1. Calculate the energy requirements for 3 month old infant:

= Estimated energy requirement (kJ/kg bw/day) x body weight (kg)
= 343 kJ/kg bw/day x 6.4 kg
= 2195 kJ/day

2. Calculate the amount of infant formula required to meet energy requirements:

= Estimated energy requirement (kJ/day) ÷ energy content of infant formula (kJ/100g)

$$= \frac{2195 \text{ kJ/day}}{274 \text{ kJ/100 g formula}}$$

= 800 g infant formula per day

3. Calculate the estimated mean dietary intake of inulin-derived substances and GOS:

= Daily amount of infant formula x concentration of (inulin-derived substances and GOS) in formula

= 0.8 kg infant formula/day x concentrations (inulin-derived substances and GOS) per kg infant formula

A1.1.2 Australian infants aged 9 months

The theoretical diet for Australian children aged 9 months was based on information on recommended energy intakes, mean body weight and the proportion of milk and solid foods in the diet for a 9 month old child, and data from the 1995 NNS on foods consumed by a 2 year old child.

The recommended energy intake for a nine-month-old boy (FAO 2004) at the 50th percentile weight (WHO 2007) was used as the basis for the theoretical diet. The body weight of a 50th percentile 9 month old boy was 8.9 kg.

It was assumed that 50 per cent of energy intake was derived from follow-on formula and 50 per cent from solids (Hitchcock *et al*., 1986). The patterns of consumption of a two-year-old child from the 1995 NNS were scaled down and used to determine the solid portion of the 9 month old's diet. Certain foods such as nuts, tea, coffee and alcohol were removed from the diet since nuts can be a choking risk (National Health and Medical Research Council, 2001) and coffee and alcohol are unsuitable foods for infants (ACT Community Care, 2000). Consumption of breakfast cereals was assumed to be in the form of either infant cereal or single grain breakfast cereals, excluding bran-based cereals. All milk consumption was assumed to be in the form of follow-on formula.

A detailed description of the theoretical diet used for Australian children aged 9-month old can be found in Table A1.1

A1.1.3 Australian children aged 1 year

The theoretical diet for Australian children aged 1 year was based on information on recommended energy intakes, mean body weight and the proportion of milk and solid foods in the diet for a 1 year old child, and data from the 1995 NNS on foods consumed by a 2 year old child.

The recommended energy intake for a one year old boy (FAO 2004) at the 50th percentile weight (WHO 2007) was used as the basis for the theoretical diet. The body weight of a 50th percentile 1 year old boy was 9.6 kg.

It was assumed that 35 per cent of energy intake was derived from milk and 65% from solids (Hitchcock *et al*., 1986). The patterns of consumption of a two-year-old child from the 1995 NNS were scaled down and used to determine the solid portion of the 1-year old's diet. Certain foods such as nuts (excluding peanut butter), coffee and alcohol were removed from the diet since nuts can be a choking risk (National Health and Medical Research Council, 2001) and coffee and alcohol are unsuitable foods for infants (ACT Community Care, 2000).

A detailed description of the theoretical diet used for Australian children aged 1 year can be found in Table A1.1

A1.1.4 New Zealand children aged 1-3 years

As there were no data available from the 1997 or 2002 New Zealand NNSs for children aged < 5 years, a theoretical diet was used to estimate dietary inulin-derived substances and GOS intakes for New Zealand children aged 1-3 years. The Simulated Diet for 1-3 year old toddlers that was used in the analysis of the 2003/04 New Zealand Total Diet Survey (NZ TDS) was used to estimate the mean dietary inulin-derived substances and GOS intake in this assessment (Vannoort and Thomson, 2005b). The Simulated Diet was a 14-day diet constructed to represent average consumers and was derived from regional studies, rather than national studies of food and nutrient consumption (Vannoort and Thomson, 2005a). Intakes of inulin-derived substances and GOS were divided by 14 to obtain daily intakes. In order to assume a 'worst-case' scenario, the body weight of a 1 year old child was used in the calculations of inulin-derived substances and GOS intakes in mg/kg bw/day.

A detailed description of the theoretical diet used for New Zealand children aged 1-3 years can be found in Table A1.2.

Table A1.1: Theoretical diet for Australian children aged 9 months and 1 year

Food/Food Group	**Food Consumption Amount (grams per day)**	
	9 months	1 year
Almonds	0.0	0.0
Apple, unpeeled	18.5	26.6
Avocado	0.2	0.4
Bacon	0.2	0.2
Baked beans, in tomato sauce, canned	3.1	4.4
Bananas	9.6	13.9
Beans, green	0.5	0.7
Beef steak, rib/ribeye/sirloin, grilled	1.1	1.6
Beer, 3.5% alcohol	0.0	0.0
Beetroot, canned	0.4	0.6
Biscuits, savoury	1.2	1.7
Biscuits, sweet, plain	2.7	3.9
Bread, multigrain	1.0	1.5
Bread, white	15.0	21.6
Bread, wholemeal	3.4	5.0

Food/Food Group	Food Consumption Amount (grams per day)	
	9 months	1 year
Breakfast cereal, mixed grain	0.0	4.3
Breakfast cereal, single grain	3.3	4.7
Broccoli, cooked	2.1	3.0
Butter, regular	0.4	0.5
Cabbage, cooked	0.3	0.5
Cake, chocolate, iced	2.7	3.9
Carrots, cooked	2.8	4.0
Celery, raw	0.5	0.7
Cheese, cheddar, full fat	2.2	3.1
Cheese, cottage	0.2	0.2
Cheese, processed, cheddar type	1.5	2.1
Chicken, breast, fillet	3.3	4.8
Chocolate, milk	2.1	3.0
Coconut, desiccated	0.5	0.7
Cream, pure (not thickened)	0.9	1.3
Cucumber, raw	1.0	1.5
Dairy blend (not reduced fat)	0.1	0.1
Eggs, boiled	2.3	3.3
Fish fillets	0.3	0.5
Fish, battered, takeaway	0.4	0.6
Fish, crumbed, oven bake	0.1	0.2
Grapes	2.6	3.7
Ham	1.8	2.5
Hamburger	0.0	0.0
Ice cream, full fat, vanilla	5.6	8.0
Infant cereal, mixed	3.0	0.0
Infant dessert, dairy based	1.8	1.3
Infant dessert, fruit based	2.0	1.1
Infant dinner, containing meat, chicken or fish	2.6	1.3
Infant formula	0.0	0.0
Juice, orange	113.7	163.8
Lamb chops, loin, grilled	0.6	0.9
Lettuce, raw	0.8	1.1
Liver, sheep	0.0	0.0
Mango	0.6	0.9
Margarine or margarine spread, polyunsaturated	1.4	2.1
Milk, full fat	0.0	0.0
Milk, modified, low fat	0.0	0.0
Mushrooms	0.4	0.6

Food/Food Group	Food Consumption Amount (grams per day)	
	9 months	1 year
Nori sheets	0.0	0.0
Oats, rolled	1.0	1.5
Oil, canola	0.3	0.5
Olives	0.0	0.0
Onions	1.7	2.5
Orange	8.5	12.2
Parsley, fresh	0.0	0.0
Pasta, white	7.0	10.1
Peach, canned in natural juice	3.4	4.9
Peach, fresh	2.8	4.0
Peanut butter	0.0	0.9
Peas, frozen, cooked	1.2	1.8
Pie, meat, individual size	3.2	4.6
Pineapple, fresh	1.1	1.6
Pizza, meat & vegetable containing	0.5	0.6
Pork chops, grilled	0.4	0.6
Potato crisps	2.3	3.3
Potatoes, cooked	12.3	17.8
Prawns, cooked	0.1	0.1
Pumpkin, cooked	1.7	2.5
Rice, white	8.8	12.6
Salmon, canned in brine	0.0	0.0
Salt, iodised	0.0	0.0
Salt, non-iodised	0.0	0.0
Sauce, tomato	0.9	1.3
Sausages, beef	2.4	3.5
Soft Drink	16.1	23.2
Soy Beverage, plain	0.0	0.0
Spinach, fresh, cooked	0.1	0.1
Strawberries	0.8	1.2
Sugar, white	5.9	8.4
Sultanas	1.6	2.3
Sweet corn, kernels, frozen	1.7	2.5
Tea	0.0	0.0
Tomatoes, raw	4.3	6.2
Tuna, canned in brine	0.3	0.5
Water, bottled still	0.0	0.0
Water, tap	0.0	0.0
Watermelon	2.2	3.2

Food/Food Group	Food Consumption Amount (grams per day)	
	9 months	1 year
Wine, white	0.0	0.0
Yoghurt, fruit, full fat	10.1	14.5

Table A1.2: Theoretical diet for New Zealand children aged 1-3 years

Food	Food Consumption Amount	
	(grams per 14 days)	(grams per day)
Apple-based juice	380	27
Apples	350	25
Apricots, canned	60	4
Avocado	20	1
Bacon	30	2
Banana	490	35
Beans	15	1
Beans, baked	100	7
Beef, mince	120	9
Beef, rump	50	4
Beer	0	0
Beetroot	0	0
Biscuit, chocolate	115	8
Biscuit, cracker	60	4
Biscuit, plain sweet	165	12
Bran flake cereal, mixed	30	2
Bread, mixed grain	30	2
Bread, wheatmeal	115	8
Bread, white	425	30
Broccoli/Cauliflower	70	5
Butter	55	4
Cabbage	15	1
Caffeinated beverage	0	0
Cake	60	4
Capsicum	10	1
Carbonated drink	300	21
Carrot	115	8

Food	Food Consumption Amount	
	(grams per 14 days)	(grams per day)
Celery	15	1
Cheese	145	10
Chicken	60	4
Chicken nuggets	50	4
Chinese takeaway dish	0	0
Chocolate beverage	300	21
Chocolate, plain milk	20	1
Coffee beans, ground	0	0
Coffee instant	0	0
Confectionery	35	3
Corn, canned	30	2
Corned beef	35	3
Cornflakes	60	4
Courgette	10	1
Cream	20	1
Cucumber	15	1
Dairy dessert (child)	460	33
Egg	110	8
Fish fingers (child)	40	3
Fish in batter	45	3
Fish, canned	20	1
Fish, fresh	30	2
Flavoured snacks (child)	60	4
Fruit drink, powdered	830	59
Toddler formula	3,740	267
Grapes	20	1
Ham	70	5
Hamburger, plain	80	6
Honey	20	1
Ice-cream	150	11
Infant & follow-on formula	200	14
Infant weaning food, cereal based	0	0
Infant weaning food, custard/fruit dish	0	0
Infant weaning food, savoury dish	120	9

Food	Food Consumption Amount	
	(grams per 14 days)	(grams per day)
Jam	20	1
Kiwifruit	50	4
Kumara	30	2
Lamb/Mutton	40	3
Lambs liver	0	0
Lettuce	15	1
Margarine/Table Spread	35	3
Meat pie	90	6
Melon	30	2
Milk, flavoured	0	0
Milk, trim (0.5%)	0	0
Milk, whole	0	0
Muesli	15	1
Muffin/scone	70	5
Mushrooms	15	1
Mussels	0	0
Nectarines	30	2
Noodles, instant	160	11
Oats, rolled	120	9
Oil	35	3
Onion	15	1
Orange juice	280	20
Oranges	260	19
Oysters	0	0
Pasta, dried	150	11
Peaches, canned	50	4
Peanut butter	20	1
Peanuts	0	0
Pears	70	5
Peas	60	4
Pineapple	20	1
Pizza	70	5
Pork chop	20	1
Potato crisps	35	3

Food	Food Consumption Amount	
	(grams per 14 days)	(grams per day)
Potato, hot chips	210	15
Potatoes, peeled	240	17
Potatoes, with skin	60	4
Prunes	20	1
Pumpkin	80	6
Raisins/Sultanas	99	7
Rice, white	55	4
Salad dressing	0	0
Sausages, beef	150	11
Silverbeet	20	1
Snack bars	30	2
Soup	50	4
Soy, milk	100	7
Spaghetti in sauce (canned)	150	11
Strawberries	20	1
Sugar	25	2
Taro	0	0
Tea	0	0
Tomato	65	5
Tomato sauce	50	4
Tomatoes in juice	45	3
Water	3,500	250
Weet-bix	210	15
Wine, still red	0	0
Wine, still white	0	0
Yeast extract	25	2
Yoghurt	870	62

Appendix 2

Concentration data

Table A2.1: Concentration data obtained from the literature

Concentration Data	Concentration (g/100g)			Data Derivation
Food	**Inulin**	**FOS**	**GOS**	
Bar, Cereal And Milk Solids, Snack Or Breakfast Style	1			(Food Standards Australia New Zealand, 2007)
Artichoke, Jerusalem, Boiled	3.2			
Artichoke, Jerusalem, Raw, Peeled	3.0			
Capsicum	0.1			(Food Standards Australia New Zealand, 2002)
Raw Green Peas	0.5			
Onion, White	0.3			
Carrot, raw	0.3			
Banana				(Van Loo *et al*., 1995)
Raw	0.5	0.5		
Raw- Dried	1.4	1.4		
Asparagus				
Canned	0.2	0.2		
Raw	2.5	2.5		
Boiled	1.7	1.7		
Fried	3.4	3.4		
Chicory Root	41.6	22.9		
Dandelion Greens				
Raw	13.5	10.8		
Cooked	9.1	7.3		
Garlic				
Raw	12.5	5g		
Dried	28.2	11.3		
Globe Artichoke	4.4	0.4		
Jerusalem Artichoke	18	13.5		
Leeks				
Raw	6.5; 3	5.2		
Onions				
Raw	4.3	4.3		
Raw - Dried	18.3	18.3		
Cooked	3	3		
Baked	5	5		
Fried	5.8	5.8		
Wheat				
Bran - Raw	2.5	2.5		
Flour - Baked	2.4	2.4		
Flour - Boiled	0.4	0.4		
Barley				
Raw	0.8	0.8		
Cooked	0.2	0.2		
Rye				
Rye Flour - raw	0.75	0.75		
Rye Flour -baked	0.7	0.7		
Burdock - root	3.5-4			
Camas - bulb	12-20			

Concentration Data	Concentration (g/100g)			Data Derivation
Food	**Inulin**	**FOS**	**GOS**	
Murnong - root	8-13			
Yacon - root	3-19			
Salsify - root	4-11			
Tomato		0.15		(Spiegel *et al*., 1994)
Brown sugar		0.30		
Honey		0.75		
Soy Beans				(Espinosa-Martos and Ruperez, 2006)
Ripe Yellow Soybean Seeds			1.84-1.95	
Unripe Green Soybean Seeds			1.43-1.61	
Sweet Cookies	0.34			(Zuleta and Sambucetti, 2001)
Salted Cookies	0.55			
Skim Milk	1			
Ice-cream				
Lemon	5.09			
Vanilla	5.2			
Chocolate	4.91			
Cereal Bar	16.57			
Diet Cheese	1.61			
Breast Milk			7-12 g/L oligosaccharides	(Boehm and Stahl, 2007)
Bar	*			Confidential commercial information
Spreads Lite	*			
Spreads Olive Lite	*			
Yoghurt			*	Confidential commercial information
infant yoghurt			*	
infant dessert			*	
cheese			*	
smoothie			*	
spread			*	
Infant Formula	*		*	Based on proposed uptake
Infant food	*		*	

Table A2.2: Concentration data used for the dietary intake assessments and comments on data extrapolation

Concentration Data	Concentration (g/100g)			Comments
Food	**Inulin**	**FOS**	**GOS**	
Almonds				No values reported
Apple, Unpeeled				No values reported
Avocado	0.5	0.5		Value for banana = 0.5. Avocado in same category as banana (tropical fruit - inedible peel).
Bacon				No values reported
Baked beans, in tomato sauce, canned			1.52	Average of range (1.43-1.61) for unripe green soybean seed. Beans in same category as soy bean.
Bananas	0.5	0.5		Natural levels reported in raw banana.
Beans, Green			1.52	Average of range (1.43-1.61) for unripe green soybean seed. Common bean in same category as soy bean.
Beef Steak, Rib/Ribeye/Sirloin, Grilled				No values reported
Beer, 3.5% Alcohol				No values reported
Beetroot, Canned	8.19			Average of 4 values for burdock root, murnong root, yacon root and salsify root. Jerusalem artichoke and chicory also in same category but not used in averaged result due to very high levels in these foods in particular.
Biscuits, Savoury	0.55			Value derived from 'salted cookie'.
Biscuits, Sweet, Plain	0.34			Value derived from 'sweet cookie'
Bread, Multigrain	2.4	2.4		Value derived from 'wheat flour - baked'
Bread, White	2.4	2.4		Value derived from 'wheat flour - baked'
Bread, Wholemeal	2.4	2.4		Value derived from 'wheat flour - baked'
Breakfast Cereal, Mixed Grain	1			Value derived from 'Bar, Cereal And Milk Solids, Snack Or Breakfast Style'.
Breakfast Cereal, Single Grain	1			Value derived from 'Bar, Cereal And Milk Solids, Snack Or Breakfast Style'.
Broccoli, Cooked				No values reported
Butter, Regular	*			Confidential commercial information
Cabbage, Cooked				No values reported
Cake, Chocolate, Iced	2.4	2.4		Value derived from 'wheat flour - baked'

Concentration Data	Concentration (g/100g)			Comments
Food	**Inulin**	**FOS**	**GOS**	
Carrots, Cooked	8.19			Average of 4 values for burdock root, murnong root, yacon root and salsify root. Jerusalem artichoke and chicory also in same category but not used in averaged result due to very high levels in these foods in particular.
Celery, Raw	3.45			Average of raw asparagus and globe artichoke values (2.5g and 4.4g respectively). These foods are categorised in the same group as celery
Cheese, Cheddar, Full Fat	*			Confidential commercial information
Cheese, Cottage	*			Confidential commercial information
Cheese, Processed, Cheddar Type	*			Confidential commercial information
Chicken Breast, Fillet				No values reported
Chocolate, Milk				No values reported
Coconut, Desiccated				No values reported
Cream, Pure (Not Thickened)	*			Confidential commercial information
Cucumber Raw				No values reported
Dairy Blend (Not Fat Reduced)	*			Confidential commercial information
Eggs, Boiled				No values reported
Fish Fillets				No values reported
Fish, Battered, Takeaway				No values reported.
Fish, Crumbed, Oven Bake				No values reported.
Grapes				No values reported
Ham				No values reported
Hamburger				No values reported
Ice Cream, Full Fat, Vanilla	5.2			Value derived from 'Ice-cream'
Infant Cereal, Mixed		*		Confidential commercial information
Infant Dessert, Fruit Based	0.5	0.5		Assumes banana based
Infant Dinner, Containing Meat, Chicken Or Fish				No values reported
Infant Formula	*		*	Values imputed based on the information from the applications and maximum proposed levels for each scenarios
Juice, Orange				No values reported
Lamb Chops, Loin, Grilled				No values reported
Lettuce, Raw	27.55	16.85		Average taken from chicory root (41.6) and dandelion greens, raw (13.5) = 27.55 for Inulin. FOS = 16.85 (Average of 22.9 for chicory root and 10.8 for dandelion

Concentration Data	Concentration (g/100g)			Comments
Food	**Inulin**	**FOS**	**GOS**	
				greens).
Liver, Sheep				No values reported
Mango	0.5	0.5		Value for banana = 0.5. Mango in same category as banana (tropical fruit - inedible peel).
Margarine Or Margarine Spread, Polyunsaturated	*			Confidential commercial information
Milk, full fat	0.0	0.0		No values reported
Milk, modified, low fat	1			Value derived from skim milk
Mushrooms				No values reported
Nori Sheets				No values reported
Oats, Rolled	1.65	1.65		Value averaged from wheat (2.5) and barley (0.8) values for inulin and FOS.
Oil, Canola	*			Confidential commercial information
Olives				No values reported
Onions	4.3	4.3		
Orange				No values reported
Parsley, Fresh				No values reported
Pasta, White	0.4	0.4		Value derived from wheat, flour - boiled
Peach, Canned In Natural Juice				No values reported
Peach, Fresh				No values reported
Peanut Butter				No values reported
Peas, Frozen, Cooked			1.52	Value averaged from range of 1.43-1.61 for 'Unripe Green Soybean Seeds' = 1.52
Pie, Meat, Individual Size				No values reported
Pineapple, Fresh	0.5	0.5		Value for banana = 0.5. Pineapple in same category as banana (tropical fruit - inedible peel).
Pizza, Meat & Vegetable Containing				No values reported
Pork Chops, Grilled				No values reported
Potato Crisps	8.19			Average of 4 values for burdock root, murnong root, yacon root and salsify root. Jerusalem artichoke and chicory also in same category but not used in averaged result due to very high levels in these foods in particular.
Potatoes, Cooked	8.19			Average of 4 values for burdock root, murnong root, yacon root and salsify root. Jerusalem artichoke and chicory also

Concentration Data	Concentration (g/100g)			Comments
Food	**Inulin**	**FOS**	**GOS**	
				in same category but not used in averaged result due to very high levels in these foods in particular.
Prawns, Cooked				No values reported
Pumpkin, Cooked				No values reported
Rice, White		2.5	2.5	Value derived from wheat bran - raw as in same category
Salmon, Canned in Brine				No values reported
Salt, Iodised				No values reported
Salt, Non-Iodised				No values reported
Sauce, Tomato				No values reported
Sausages, Beef				No values reported
Soft Drink				No values reported
Soy Beverage, Plain			1.895	Value averaged from range of 1.84-1.95 for 'Ripe Yellow Soybean Seeds' = 1.895
Spinach, Fresh, Cooked	25.35	15.1		Average taken from chicory root (41.6) and dandelion greens, cooked (9.1) = 25.35 for Inulin. FOS = 15.1 (Average of 22.9 for chicory root and 7.3 for dandelion greens).
Strawberries				No values reported
Sugar, White				No values reported
Sultanas				No values reported
Sweet corn, Kernels, Frozen				No values reported
Tea				No values reported
Tomatoes, Raw				No values reported
Tuna, Canned In Brine				No values reported
Water, Bottled Still				No values reported
Water, Tap				No values reported
Watermelon				No values reported
Wine, White				No values reported
Yoghurt, Fruit, Full Fat	*		*	Confidential commercial information

FIRST REVIEW REPORT

PROPOSAL P306

ADDITION OF INULIN/FOS & GOS TO FOOD

For information on matters relating to this Assessment Report or the assessment process generally, please refer to http://www.foodstandards.gov.au/standardsdevelopment/

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Decision

FSANZ re-affirms its approval of the draft variations to the *Australia New Zealand Food Standards Code* as notified to the Ministerial Council, with amendments (see Attachment 1).

This decision clarifies that for general foods inulin-derived substances are taken not to be nutritive substances thus providing regulatory certainty for general food manufacturers who currently add inulin-derived substances to a range of general foods.

This decision also permits the voluntary addition of inulin-derived substances and galacto-oligosaccharides (GOS) to infant formula products, infant foods and formulated supplementary foods for young children (FSFYC) because:

- these substances are considered not to pose a risk to the health and safety of infants and young children at the proposed maximum levels;

- the permissions will provide infant formula manufacturers with regulatory certainty regarding the addition of these substances to infant formula products; and

- the permissions are broader than, but consistent with, overseas recommendations such as the addition of long chain inulin and GOS to infant and follow-on formula in Europe.

This decision does not permit the addition of fructo-oligosaccharides (FOS), as defined in the P306 Final Assessment Report, to these foods as there is insufficient evidence to support their addition.

FSANZ has made the following amendments to the draft variations:

- the maximum amount of inulin-derived substances that can be added to infant formula products has been reduced from 290 mg per 100 kJ (8 g/L) to 110 mg per 100 kJ (3 g/L);

FSANZ is proposing this amendment because infant formula manufacturers are not seeking to add inulin-derived substances to infant formula at levels up to 8 g/L at this time; a maximum of 3 g/L will meet their needs.

Summary Table

Matters Addressed in the First Review

MINISTERIAL COUNCIL ISSUE	FSANZ'S RESPONSES
Consistency with the objectives of the FSANZ Act	The approach taken in this Proposal is consistent with the objectives of the FSANZ Act However, FSANZ acknowledges that the outcomes of P306 are an interim regulatory response that provides short term regulatory certainty for general food manufacturers, as well as providing express permissions in the Code to voluntarily add inulin-derived substances and GOS to infant formula products, infant foods and toddler formula. FSANZ agrees that this interim regulatory response does not provide the regulatory certainty for substances that do not meet the definition of substances requiring pre-market approval (such as nutritive substances). This situation will be addressed during the review of Standard 2.9.1 which will commence once the Policy Guideline on Infant Formula Products has been completed. It is outside the scope of this section 36 Proposal to give consideration to broader issues such as the definition of nutritive substances but FSANZ will undertake a review of the definition of 'nutritive substance' in Standard 1.1.1 and its application in the Code at a later date when considering the response to the Policy Guideline on the Addition to Food of Substances Other Than Vitamins and Minerals. The definition of nutritive substances is fundamental to considering any changes to the Code arising from the policy guidance. A section 36 Proposal is not an 'urgent' Proposal but simply omits one round of public comment. The basis for a decision to raise a Proposal under this section of the FSANZ Act (as was in force prior to 1 July 2007) includes that it will not have a significant adverse effect on any party. FSANZ remains satisfied that omitting one round of public consultation prior to making the Draft Assessment does not have significant adverse effects on the interests of anyone. By adopting this course of action all relevant issues have been addressed. While it has been argued that FSANZ should not have raised this Proposal ahead of receiving the policy guidance on infant formula, three Applications have been submitted which relate to these issues and which can only have been delayed pending policy guidance with the agreement of the applicants.
Protection of public health and safety	FSANZ's safety assessment was informed by studies involving the addition of GOS and inulin-derived substances alone or in combination, to infant formula products, infant food, and toddler formula. Although the majority of studies used the 9:1 ratio of these substances at a maximum level of 8 g/L, other studies have been undertaken with GOS or inulin-derived substances alone. At least one study was conducted with the 9:1 ratio at a level of 10 g/L. On this basis, FSANZ concludes that there are no safety concerns with regard to the addition of inulin-derived substances and/or GOS to infant and follow-on formula, infant foods and toddler formula, singularly or combined, in any ratio, up to 8 g/L. FSANZ's assessment of the maximum permitted level of inulin-derived substances permitted to be added to infant formula products (8 g/L) is based on the totality of evidence available shown to be safe in clinical studies. The safety of this level is further supported by the presence of higher levels of HMOs (up to 25 g/L) in breast milk. FSANZ acknowledges that at Final Assessment, one member of the Infant and Child Health Scientific Advisory Group did not support the proposed increase from 3 g/L to 8 g/L in the maximum amount of inulin-derived substances permitted to be added to infant formula products.

MINISTERIAL COUNCIL ISSUE	FSANZ'S RESPONSES
	However, there was support from the two international experts consulted for the higher level and thus, FSANZ considered that the views of the majority of external experts consulted did not differ from FSANZ's recommendation. While satisfied that there are no safety concerns with up to 8 g/L of inulin-derived substances added to infant formula products, FSANZ is recommending a reduced maximum of 3 g/L as this level will satisfy the needs of infant formula manufacturers at this time.
Consistency between domestic and international food standards	Independent risk assessments are an integral part of FSANZ's approach to developing food standards for Australia and New Zealand. In this context, FSANZ considers, but is not bound by, relevant international regulations. The European Commission (EC) Directive permits the addition of GOS and long chain inulin to infant and follow-on formula but also indicates that other substances can be added subject to a systematic review of the available data. At Final Assessment, FSANZ undertook an independent systematic review of both the published and unpublished literature and assessed the safety of all inulin-derived substances, not just long chain inulin, and GOS when added to infant formula products. Thus, there is no inconsistency in the forms of the permitted substances between the proposed domestic and international standards. FSANZ acknowledges that there is no agreed and consistent terminology used to describe these substances internationally. As a result there is confusion and misunderstanding when various terms are used. FSANZ has attempted to resolve this confusion by using the generic term 'inulin-derived substances' which includes oligofructose, inulin and long chain inulin, but not FOS. As such, the proposed draft variations to Standards 2.9.1, 2.9.2 and 2.9.3 use the terms inulin-derived substances and GOS to clarify the compositional permissions (which are inclusive of, but broader than, the EC Directive) but do not prescribe the terms to be used in labelling. This approach allows manufacturers to use the terms of their choice on labels thus promoting consistency with the varying international terms used for inulin-derived substances. There are insufficient data to support the addition of FOS (described at Final Assessment as being fructose polymers produced from the enzymatic condensation of sucrose) to infant formula products, infant foods and toddler formula; nor is there any evidence that FOS is added to these special purpose foods elsewhere in the world.
Enforcement and compliance.	In the absence of ISC consideration or Ministerial Council policy guidance, FSANZ considers that it is the role of laboratories or enforcement agencies to develop analytical capability for monitoring inulin-derived substances and GOS in foods. Thus, methods of analysis for these substances have not been prescribed. This approach allows enforcement agencies and their appointed analysts to develop and agree on their own means of monitoring compliance thereby reducing the costs of developing suitable capability.

1. Introduction

In September 2008, the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) requested a First Review of Proposal P306 – Addition of Inulin/FOS & GOS to Food. This section 36 Proposal seeks to amend the *Australia New Zealand Food Standards Code* (the Code) to confirm the regulatory position for the food industry regarding the addition of inulin-derived substances, including inulin, to general foods (and some special purpose foods) and to consider permissions for the addition of inulin-derived substances, FOS and GOS to special purpose foods for infants and young children including infant and follow-on formula, infant foods and formulated supplementary foods for young children (FSFYC), such as toddler formula.

The grounds for the First Review broadly relate to:

whether the draft variations provide regulatory certainty for infant formula manufacturers regarding the addition of these substances to infant formula products;

whether the proposed maximum amounts of GOS and inulin-derived substances are safe when added to infant formula products in amounts and ratios other than the EC recommendation of a maximum of 8 g/L in a ratio of 9:1;

the use of different terminology in the proposed standard compared with international terminology for these substances; and

methods and costs of analysing these substances in food.

FSANZ has addressed these issues by reviewing its assessment of the safety of these substances when added to infant formula products and reviewing its commentary in the Final Assessment[57] Report and responding to each of the identified issues in turn (see Section 6).

2. Terminology

FSANZ acknowledged at Final Assessment that there are no widely agreed definitions for the substances inulin, FOS and GOS. Therefore, in keeping with the terminology used at Final Assessment the following terms are used in this First Review Report: inulin, long chain inulin, oligofructose, FOS and GOS. The term 'inulin-derived substances' is used throughout this report to collectively refer to inulin, long chain inulin and oligofructose – it does not include FOS. The identity of these substances was described in Section 1.4 of the Final Assessment Report, but to ensure clarity in this Report this section has been repeated at Attachment 2.

3. Objective of the review

The objective of this First Review Report is to address the Ministerial Council's concerns expressed in the Review Request and to reconsider the draft variations (at Attachment 1) notified to the Ministerial Council by FSANZ in July 2008.

[57] The Final Assessment Report and the its attachments can be found at http://www.foodstandards.gov.au/standardsdevelopment/proposals/proposalp306addition3639.cfm

4. Grounds for the review

The Ministerial Council requested a First Review on the grounds that approval of the draft variations:

- is not consistent with the objectives of the legislation which establishes FSANZ (or the Authority);
- does not protect public health and safety;
- does not promote consistency between domestic and international food standards where these are at variance; and
- will be difficult to enforce or comply with in both practical and resource terms.

Additional comments provided by Ministers included the following:

- The draft variations do not provide regulatory clarity and certainty in relation to the status of the substances which are arguably of a nutritive character in infant formula products. The Final Assessment Report for Proposal P306 does not clarify that these substances are either nutritive or non-nutritive; thus setting a precedent for other non-nutritive substances to be added to infant formula products in the future without requiring pre-market approval.
- The absence of Ministerial policy guidance on the addition of substances to special purpose foods – Part 2.9 of the Code – is resulting in piecemeal interim regulatory responses that do not provide long-term regulatory certainty for food manufacturers. In light of this uncertainty, policy guidance should not be pre-empted.
- Urgent standards, particularly for vulnerable populations such as infants, should not be used to do anything other than address the presenting problem and provide a regulatory response which is consistent with international permissions and which has been demonstrated to protect public health and safety.
- The majority of the studies used in FSANZ's risk assessment are based on a maximum of 8 g/L in a ratio of 9:1 of GOS to long chain inulin which is now included in the EC Directive. Thus, there is stronger case for the safety of this level and ratio compared with other ratios, particularly when either substance is added alone to infant formula products.
- Why is FSANZ recommending the addition of GOS and inulin-derived substances when the EC Directive recommends GOS and 'long chain inulin' and this appears to be the substances commonly added to infant formula products?
- Why is FSANZ recommending the use of oligofructose as an inulin-derived substance but not FOS when oligofructose has an average chain length of less than 10 and can vary from a DP of 2-10?

- There was no consensus among experts on FSANZ's Infant and Child Health Scientific Advisory Group (ICSAG) regarding the increase in the maximum amount of inulin-derived substances permitted to be added to infant formula products from 3 g/L at Draft Assessment to 8 g/L at Final Assessment. FSANZ based this increase on just one study undertaken by a manufacturer of inulin, however, the methodology and sample size of this study are not sufficiently robust to justify the increase. There was not wide consultation on this change and concerns were raised by the jurisdictions when the proposed increase in the maximum permitted amount was conveyed to them.

- The terminology, in particular the term inulin-derived substances, is not consistent with international terminology used for these carbohydrates and may confuse industry, particularly importers, as to whether products approved in other jurisdictions may lawfully be imported into Australia. The Australian and New Zealand food regulatory system should strive for consistency between our food standards and international food standards, especially where international standards clearly protect public health and safety.

- There appears to be no reliable and agreed methodology at present for the analysis of inulin/FOS and GOS in infant formula, and no acceptable laboratory in Australia which is capable of achieving reproducible and reliable results. Furthermore, there is considerable cost to be incurred by regulators with the development and verification of such methods. This and other costs to regulators are not itemised in the benefit cost analysis and no quantitative values are assigned to these costs.

5. Background

FSANZ initiated Proposal P306 in July 2007 in response to enforcement action taken in early 2007 against an infant formula manufacturer who had launched a brand of infant formula products containing added inulin-derived substances (specifically long chain inulin) and GOS in Australia and New Zealand. The addition of these substances to infant formula products is considered to require a pre-market safety assessment and an explicit permission in the Code.

An unintended consequence of this enforcement action was confusion among the broader food industry as to the regulatory status of inulin-derived substances when added to general foods. Food manufacturers have added inulin-derived substances to the general food supply in Australia and New Zealand since the mid 1990s.

In June 2008, the FSANZ Board approved draft variations to the Code and notified the Ministerial Council. This decision stated that inulin-derived substances were taken not to be nutritive substances and permitted the voluntary addition of GOS and inulin-derived substances in any ratio up to a maximum amount of 8 g/L in infant formula products, infant foods and FSFYC[58].

[58] The maximum amount proposed in the draft variation which is equivalent to 8 g/L is 290 mg/100 kJ in infant formula products; 0.8 g/100 g in infant foods and 1.6 g per serve in FSFYC.

6. Ministerial Council Review Grounds

The First Review of the draft variations to the Code has been undertaken addressing the matters stated in the Ministerial Council's request (as listed above). FSANZ's response to each of the issues raised is discussed in detail below.

6.1 Consistency with the objectives of the legislation that establishes FSANZ

6.1.1 Provision of regulatory certainty when adding these substances to infant formula products

6.1.1.1 The Review Request states that regulatory certainty is not provided if the nutritive status of inulin-derived substances and GOS, when added to infant formula products, is not acknowledged

FSANZ acknowledges that the proposed amendments to the Code reflect an **interim regulatory response** but provide the required regulatory certainty at this time.

The proposed draft variations to Standard 2.9.1, 2.9.2 and 2.9.3, provide express permissions for the addition of inulin-derived substances and GOS to special purpose foods for infants and young children, such as infant formula products. This approach confirms the regulatory position (i.e. express permission based on pre-market safety assessment) for the food industry as well as providing certainty for enforcement agencies. The regulatory certainty of this permission is not dependent on deeming inulin-derived substances and GOS to be 'nutritive substances'.

FSANZ also notes that it is outside the scope of this section 36 Proposal to give consideration to broader issues such as the nutritive status of these substances but has indicated that it will undertake a review of the definition of 'nutritive substance' in Standard 1.1.1 and its application in the Code at a later date. Preliminary work has begun on FSANZ's response to the Ministerial Council's Policy Guideline on the Addition to Food of Substances other than Vitamins and Minerals. This work will include a review of the definition of 'nutritive substance'. In addition, Application A613, to be commenced soon, will also consider the issues raised by this definition.

Therefore, FSANZ reaffirms its decision at Final Assessment, to retain clause 9A in Standard 2.9.1 which provides express permissions to add inulin-derived substances and GOS to infant formula products. This clause does not indicate the nutritive status of these substances but, as indicated above, this decision may be reviewed at a later date.

6.1.2 Interim approach sets a precedent for other non-nutritive substances to be added to infant formula products

6.1.2.1 The Review Request states that because the substances have not been declared to be either nutritive or non-nutritive this sets a precedent for other non-nutritive substances to be added to infant formula products in the future without requiring pre-market approval

FSANZ agrees that this **interim regulatory response** for inulin-derived substances and GOS does not provide the regulatory certainty for substances that do not meet the definition of substances requiring pre-market approval (such as nutritive substances).

However, currently all substances not considered to be ingredients require express permission in Standard 2.9.1, irrespective of their nutritive status; other standards cross-referenced in Standard 2.9.1 provide additional guidance in relation to the addition of food additives as well as microbiological limits. This situation will remain following the gazettal of the draft variations to the Code.

FSANZ acknowledges, however, that what is regarded as an ingredient[59] in an infant formula product is open to interpretation as this has not been explicitly defined in Standard 2.9.1. However, this anomaly is expected to be addressed in the proposed future review of the infant formula Standard following development of a Policy Guideline for Infant Formula Products. (see Section 6.1.3 for further information on the development of the Policy Guideline).

6.1.3 Lack of relevant policy guidance at present

6.1.3.1 The Review Request states that the absence of Ministerial policy guidance is resulting in piecemeal interim regulatory responses that do not provide long term regulatory certainty for any stakeholder. In light of this uncertainty, policy guidance should not be pre-empted

FSANZ affirms that **interim regulatory responses** are sometimes necessary to address situations that raise uncertainty for the food industry. Thus, FSANZ undertook this work to provide short term regulatory certainty for general food manufacturers who have for some years been adding inulin and oligofructose to a range of foods for a variety of technical and nutritional reasons in Australia and New Zealand. The interim regulatory response also provides short term certainty to infant formula manufacturers seeking to market products containing inulin-derived substances in Australia and New Zealand.

A Policy Guideline for Infant Formula Products is currently being developed by a Food Regulation Standing Committee (FRSC) Working Group on Infant Formula Products. The development of the Policy Guideline has been precipitated by recent applications and proposals seeking to amend Standard 2.9.1 and the range of issues arising from this work, in particular the vulnerability of infants and that infant formula may be the sole source of nutrition for an infant. The three current Applications[60] received by FSANZ that relate to these issues can only be delayed, pending policy advice, with agreement from the applicants.

An indicative timeframe for completion of the Policy Guideline is late 2009. As a result of this proposed timeframe, FSANZ considers it appropriate to progress Proposal P306 as quickly as possible and will reconsider the implications of the Policy Guideline on the infant formula standard (Standard 2.9.1) when it becomes available.

[59] An ingredient is not defined generically in the Code, but only in Standard 1.2.4 for the purposes of labelling.
[60] Applications A598, A609 and A613.

6.1.4 'Urgent' standards should only address the presenting problem

6.1.4.1 The Review Request states that 'urgent' standards, particularly for vulnerable populations such as infants, should not be used to do anything other than address the presenting problem and provide a regulatory response which is consistent with international permissions and which has been demonstrated to protect public health and safety

This Proposal was not prepared under the urgency provisions contained in what was section 24 (declaration of urgency) of the FSANZ Act (as was in force prior to 1 July 2007), but rather was prepared as a section 36 Proposal (FSANZ may simplify proposal procedure).

In the interest of dealing with this regulatory matter in a timely and responsive manner, FSANZ decided, pursuant to section 36 of the FSANZ Act (as was in force prior to 1 July 2007), to omit to one round of public consultation. Consequently one round of public consultation was not called for prior to making the Draft Assessment. FSANZ remains satisfied that omitting one round of public consultation prior to making the Draft Assessment does not have significant adverse effects on the interests of anyone – one of the criteria for using this provision of the FSANZ Act. By adopting this course of action, all relevant issues have been addressed. Manufacturers, consumers, health care providers and government agencies that have an interest in ensuring the health and safety of a vulnerable population group have had opportunity to provide comment and engage with the relevant agencies.

It should also be noted that had this Proposal been prepared after 1 October 2007, it would have had only one round of public consultation in accordance with the General Category provisions of the amended FSANZ Act.

6.2 Protection of public health and safety

6.2.1 Maximum level of inulin-derived substances proposed to be permitted to be added to infant formula products

6.2.1.1 The Review Request states that the increase in the proposed maximum amount of inulin-derived substances permitted to be added to infant formula products from 3 g/L at Draft Assessment to 8 g/L at Final Assessment was based on one study with a questionable methodology

The conclusions reached by FSANZ on the safety of inulin-derived substances and GOS, including the proposed maximum concentration of 8 g/L to be added to infant formula, do not rely on any one study or piece of evidence. FSANZ has used a weight-of-evidence approach, underpinned by the following considerations:

Similar to naturally-occurring human milk oligosaccharides (HMOs), inulin-derived substances and GOS are undigested in the small intestine. When they reach the large intestine, mostly intact, there is a small beneficial increase in osmotic potential in the colon. This increase in osmotic potential from inulin-derived substances and GOS is similar to that observed from HMOs and therefore no more likely to cause dehydration.

Data from clinical trials that have provided formulas supplemented with up to 10 g/L of inulin-derived substances and GOS to infants for various durations were without evidence of harm.

Evidence that inulin-derived substances and GOS are fermented by colonic microflora to a similar or greater extent than HMOs.

Evidence that addition of inulin-derived substances and GOS and inulin-derived substances alone up to 10 g/L, added to infant formula products result in similar physiological effects i.e. softer stool consistency and lower pH of stools; and microbiological effects i.e. selective growth stimulation of intestinal *Bifidobacterium* to those of breastfed infants.

Approximately 1-2% of human breast milk comprises HMOs, with a large variation in their concentration among individual women. The natural levels of HMOs in colostrum (25 g/L) and mature breast milk (15 g/L) are safe for newborn and older infants.

While there are fewer data in older infants and young children, older children are much less sensitive to potential dehydration because their kidneys are more developed, and have the ability to concentrate urine. Further, infant foods and toddler formula do not represent the sole source of nutrition in this group. It follows that if inulin-derived substances and GOS are safe for newborns and young infants, they will be equally safe for older infants and young children.

Following Draft Assessment, FSANZ received an unpublished supplementary study by Veereman-Wauters *et al.* (2008), also referred to as the Beneo study, which examined the effect of 4 g/L or 8 g/L of inulin-derived substances, or formula containing 8 g/L of 9:1 GOS to long-chain inulin in newborn infants. The Review Request questioned the suitability of this study in terms of its sample size, duration, statistical power and whether it could 'fully assess the effects of the substances on infant health, growth and development'.

The study of Veereman-Wauters *et al.* (2008) was evaluated by FSANZ based on its scientific merits (see Attachments 7 and 8 in the Final Assessment Report). The study examined approximately 20 infants per group for 28 days in a randomised, blinded design. The study analysed a number of independent indicators of infant health, growth and development including length, weight, food intake, stool frequency and consistency, faecal microbe analysis, crying, regurgitation and vomiting. The study found no adverse effects on any of these parameters. The group size and duration of 20 and 28 days, respectively, were not limitations to the interpretation of the study. It is noteworthy that the interpretation of any study is not based solely on statistical analysis, but more importantly, on biological relevance, which is underpinned by sound scientific judgement and comparisons with other studies in the scientific database. The group size and study duration are consistent with a range of clinical studies conducted in variously aged infants up to 6 months of age.

The Review Request raised the issue of infants as a vulnerable population group and the need to take a conservative approach. It is important to recall that soluble oligosaccharides, like naturally occurring HMOs, are not digested to any great extent in the small intestine, and reach the large intestine intact where they are also fermented by colonic bacteria to short-chain volatile fatty acids and carbon dioxide.

There is virtually no systemic exposure to these intact oligosaccharides and therefore the only possible adverse effect identified in infants was an increased osmotic potential within the colon due to the excretion of unchanged oligosaccharides, potentially leading to increased water loss and dehydration. This effect is more likely in very young infants because they lack a fully developed renal system and may not have full colonisation of the colon with bacteria capable of breaking down added oligosaccharides.

However, in comparison to breastfed infants, where the HMO concentration is up to 15 g/L, the levels of undigested oligosaccharides in the colon of infants fed infant formula containing inulin-derived substances and GOS will be about half those of breastfed infants. Therefore, it is unlikely that there is any risk to these very young infants from the presence of inulin-derived substances and GOS in infant formula at the levels suggested. This is supported by evidence that inulin-derived substances and GOS are fermented by colonic microflora to a similar or greater extent than HMOs.

To reiterate, FSANZ views the supplementary study by Veereman-Wauters *et al.* (2008) as supporting rather than pivotal evidence for the safety of the proposed maximum concentration. Therefore, FSANZ's assessment of the maximum permitted levels is based on the totality of evidence available, and has used the levels that have been shown to be safe in clinical studies to recommend maximum levels of inulin and GOS in infant formula products. No new data have been found to alter this conclusion after a comprehensive search of the published scientific literature, covering the period since the completion of the Final Assessment Report.

6.2.2 Established safety of the 9:1 ratio of GOS to long chain inulin compared with other ratios

6.2.2.1 The Review Request raised concerns that the majority of studies used in FSANZ's risk assessment have been conducted on the 9:1 of GOS to long chain inulin, while the proposed permissions are to add inulin-derived substances and GOS alone and in combination in any ratio. Thus, there is a stronger case for the safety of this level and ratio compared with other ratios, particularly when either substance is added alone to infant formula products.

FSANZ's safety assessment was informed by studies involving the addition of GOS and inulin-derived substances alone or in combination, to infant formula products, infant food, and toddler formula, and includes studies using concentrations of 4, 8 and 10 g/L. Although the majority of studies used the 9:1 ratio at a maximum level of 8 g/L, other studies have been undertaken with GOS or inulin-derived substances alone. At least one study was conducted with the 9:1 ratio at a level of 10 g/L. Based on the available evidence, FSANZ concluded that addition of a total level of 8 g/L of inulin-derived substances and GOS, alone or combined, at any ratio in infant formula products is unlikely to pose a risk to young infants.

This conclusion is based on data from clinical trials which have provided formulas supplemented with up to 10 g/L of inulin-derived substances and GOS to infants without evidence of harm. Data also indicated that these oligosaccharides are fermented to a similar or greater extent than HMOs. The safety of this level (8 g/L) is further supported by the presence of higher levels of HMOs (up to 25 g/L) in colostrum and (up to 15 g/L) in mature breast milk.

On the basis of the above considerations, FSANZ concludes that there are no safety concerns with regard to the addition of inulin-derived substances and/or GOS to infant and follow-on formula, infant foods and toddler formula, singularly or combined, in any ratio, up to 8 g/L.

6.2.3 Views of external experts regarding the conclusions of the safety assessment

6.2.3.1 The Review Request states that there was not consensus among experts on FSANZ's Infant and Child Health Scientific Advisory Group (ICSAG) regarding the increase in the maximum amount of inulin-derived substances permitted to be added to infant formula products from 3 g/L to 8 g/L

FSANZ established the ICSAG to provide scientific advice to FSANZ on matters relating to infant and child health. ICSAG comprises six members in addition to the FSANZ Chair[61] ICSAG met for the first time in December 2007. As this is an Advisory Group, minutes were not taken at this meeting, but outcome notes were provided to members following the meeting. The outcome notes indicated ICSAG members' agreement with FSANZ's proposed maximum level of inulin-derived substances added to infant formula products of 3 g/L although concerns were raised about the quality of the studies at the time.

Prior to completion of the Final Assessment, FSANZ sought additional comment from ICSAG members on the proposed increase in the maximum amount of inulin-derived substances from 3 g/L to 8 g/L permitted to be added to infant formula products. In response, three of the six external members provided comment. FSANZ did not expect a response from all members, as not all members have expertise in infant carbohydrate nutrition. Of those that did respond, two members were generally supportive of increasing the maximum amount of inulin-derived substances added to infant formula products from 3 g/L to 8 g/L based only on the additional evidence in the Veereman-Wauters *et al.* (2008) study referred to above in Section 6.2.1. Similar to the issues raised in the Review Request, the third member was not supportive of the increase on the basis that the study was not large enough to identify statistically significant differences (there were 20 infants in each treatment group), the short duration of the study (28 days post birth and up to five days old) and the categories of crying behaviour, vomiting and regurgitation were not sufficiently sensitive to detect differences.

Because of the lack of agreement among ICSAG members, FSANZ also sought advice from Professor Cummings[62] who considered that the additional evidence did provide reassurance of the safety of 8 g/L of inulin-derived substances in infant formula. His conclusion was based on no significant differences in terms of growth, weight gain and food intake between infants fed either 8 g/L of inulin-derived substances or those fed 8 g/L of GOS and inulin-derived substances in a ratio of 9:1. He also noted that stool frequency was well below that of the breastfed infants indicating that infants fed this formula were not at risk of dehydration. FSANZ did not contact Professor Gibson[63] again because he had concurred with FSANZ's risk assessment conclusions at Draft Assessment that 8 g/L in any combination of GOS, oligofructose and inulin, either alone or combined, was safe.

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[61] ICSAG's membership is located at the following FSANZ website http://www.foodstandards.gov.au/aboutfsanz/scientificcapabilities/infantandyoungchilds3960.cfm.

[62] Professor John Cummings is Emeritus Professor of Experimental Gastroenterology, University of Dundee, Scotland and has expertise in dietary fibre and carbohydrates.

[63] Professor Glenn Gibson is Head of Food Microbial Sciences, University of Reading, England and has expertise in prebiotics.

Thus, FSANZ acknowledges that there was not complete agreement among all members of ICSAG. FSANZ has, however, maintained its conclusion that a maximum of 8 g/L of inulin-derived substances added to infant formula products is unlikely to pose a risk to the growth and development of infants fed this formula from birth onwards. This conclusion accords with the majority of reviewers including the international experts consulted.

6.3 Consistency with international food standards

6.3.1 Use of the term 'inulin-derived substances'

6.3.1.1 The Review Request states that the terminology, in particular the term inulin-derived substances, is not consistent with international terminology used for these substances. The Australian and New Zealand food regulatory system should strive for consistency between our food standards and international food standards, especially where international standards clearly protect public health and safety.

FSANZ has outlined its response to the safety concerns of these substances, particularly inulin-derived substances, when added to infant formula products in Section 6.2 above.

FSANZ considers that there are no international standards permitting the addition inulin-derived substances and GOS to infant formula products. FSANZ, has however, acknowledged the one overseas standard, the EC Directive on infant formula and follow-on formula (see Section 6.3.3 below) in its consideration of this Proposal.

In regard to terminology, FSANZ has consistently noted the use of a variety of terms used to describe inulin-derived substances in Australia, New Zealand and internationally. There are also no relevant Codex Alimentarius Commission standards that define inulin-derived substances. As a result there is confusion and misunderstanding when various terms are used. FSANZ has attempted to resolve this confusion by using the generic term 'inulin-derived substances' which includes oligofructose, inulin and long chain inulin, but not FOS.

As such, the proposed draft variations to Standards 2.9.1, 2.9.2 and 2.9.3 use the term inulin-derived substances and GOS to clarify the compositional permissions (which are inclusive of, but broader than, the EC regulations) but do not prescribe the terms to be used in labelling. For example, infant formula manufacturers could use other names, such as 'long chain FOS', in labelling to describe the addition of long chain inulin to their products, provided that these names describe the true nature of these substances. This approach provides flexibility for manufacturers to name inulin-derived substances to reflect the relevant and different target audiences for all the foods that may contain inulin-derived substances. This approach also allows the current differing terminology to continue to be used in the different contexts and therefore promotes consistency with the varying international terms used to describe inulin-derived substances.

6.3.2 Oligofructose as an inulin-derived substance

6.3.2.1 The Review Request queries why FSANZ is recommending the use of oligofructose as an inulin-derived substance but not FOS when oligofructose has an average chain length of less than ten but whose degree of polymerisation (DP) can vary from two to ten

Fructose polymers (fructans) are characterised by the range of the Degree of Polymerisation (DP), including the average DP. The DP is a measure of the number of fructose molecules or saccharide units in the substance. The DP ranges for the different fructans can vary with these ranges overlapping for the different substances. For this reason, the terms used to describe fructans in the Final Assessment Report have been described on the basis of the DP as well as their source (see Attachment 4 – Chemical and Technological Uses Assessment Report – of the Final Assessment Report for more information on the average DP, DP ranges and sources for particular substances).

The Final Assessment Report stated that inulin-derived substances includes 'oligofructose' that is produced from the partial enzymatic hydrolysis of inulin, typically with a DP in the range of 2-8, although a range of 3-9 has also been quoted. For the purpose of the Final Assessment Report, FOS was regarded as mixtures of fructose polymers produced from the enzymatic condensation of sucrose and they have a more narrow degree of polymerisation range (DP 3-5) than inulin-derived substances.

FOS, as described in the Final Assessment Report, has not been sufficiently studied in infants and young children to allow any conclusions about their physiological effects to be made. Therefore, there is insufficient data to support their addition to infant formula and special purpose foods for young children.

Based on this insufficiency of data, the draft variations needed to be worded so that fructose polymers produced from the enzymatic condensation of sucrose (i.e. FOS) were not permitted in infant formula products, infant foods and FSFYC. This was achieved by limiting the definition of 'inulin-derived substances' to inulin as the source. This excluded FOS from the definition of inulin-derived substances, removed the need to define FOS, and simplified the definitions in the draft variations by allowing them to be consolidated into two general terms.

In addition, FSANZ is not aware of the use of FOS in the general food supply in Australia or New Zealand, so their exclusion from the term inulin-derived substances is not seen as problematic.

6.3.3 Recommendation to permit the addition of inulin-derived substances to infant formula products and not restrict this to long chain inulin

6.3.3.1 The Review Request queries why FSANZ is recommending the addition of GOS and inulin-derived substances when the European Commission Directive recommends GOS and 'long chain inulin' and this appears to be the substances commonly added to infant formula products?

Independent risk assessments are an integral part of FSANZ's approach to developing food standards for Australia and New Zealand. In this context, FSANZ considers, but is not bound by, relevant international regulations.

However, FSANZ has acknowledged the EC Directive 2006/141/EC on infant formula and follow-on formula[64] published in December 2006. In relation to infant formula, this Directive states that:

Fructo-oligosaccharides and galacto-oligosaccharides may be added to infant formula. In that case their content shall not exceed: 0.8 g/100 mL in a combination of 90% oligogalactosyl-lactose and 10% high molecular weight oligofructosyl-saccharose.

Other combinations and maximum levels of fructo-oligosaccharides and galacto-oligosaccharides may be used in accordance with Article 5.

As noted in Attachment 2, 'oligogalactosyl-lactose' is the same substance as GOS and 'high molecular weight oligofructosyl-saccharose' is the same substance as long chain inulin.

Article 5 states that:

Infant formula shall be manufactured from protein sources defined in point 2 of Annex I and other food ingredients, as the case may be, whose suitability for particular nutritional use by infants from birth has been established by generally accepted scientific data.

Such suitability shall be demonstrated through a systematic review of the available data relating to the expected benefits and to safety considerations as well as, where necessary, appropriate studies, performed following generally accepted expert guidance on the design and conduct of such studies.

The Directive also states that similar amounts and ratios may be voluntarily added to follow-on formula.

Thus, while the Directive permits the addition of GOS and long chain inulin to infant and follow-on formula, it also indicates that other substances can be added subject to a systematic review of the available data. FSANZ undertook an independent systematic review of both the published and unpublished literature and documented these findings in the Microbiological, Nutrition and Safety Assessments (see Attachments 5, 6 and 7, respectively, in the Final Assessment Report). The clinical studies reported in the literature included the inulin-derived substances: oligofructose (Raftilose® P95 and Beneo® P95) and inulin (Frutafit IQ) in addition to long chain inulin (Raftiline® HP and Synergy 1®).

The Assessments did not consider potential health benefit but the Microbiological and Nutrition Assessments compared the amounts of these and similar substances in breast milk, and whether they result in similar microbiological and physiological effects to breastfed infants. FSANZ indicated at Final Assessment that it will await the outcomes of the Policy Guideline on Infant Formula Products before considering potential health benefit in greater detail than has been considered in this interim regulatory response.

Thus, FSANZ considers that is has adequately met the systematic review process outlined in the EC Directive regarding the amounts and ratios of inulin-derived substances and GOS which can be safely added to infant formula products.

[64] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. *Official Journal of the European Union, L 401/1, 30/12/2006.*

6.4 Enforcement and compliance

6.4.1 Analysis of inulin-derived substances and GOS in foods

6.4.1.1 The Review Request states that there is 'no reliable or agreed methodology' for the analysis of inulin-derived substances or GOS

Under the outcomes based approach to developing the Code, FSANZ does not prescribe analytical methods. While this approach is consistent with the philosophy engendered in the move to the Code, the issue of analytical methods has been raised in the context of a number of standards and by a range of stakeholders. It appears to be an issue that is best considered by the Implementation Sub-Committee (ISC) or FRSC as the appropriate bodies to determine what, if any, action should be taken to resolve this broader issue. If FSANZ received guidance or a request from the Ministerial Council to move to a more prescriptive approach in developing standards, a proposal would be raised to consider this issue and to provide opportunities for interested parties to provide input to this process.

In the absence of ISC consideration or Ministerial Council policy guidance, FSANZ considers that it is the role of laboratories or enforcement agencies to develop analytical capability for monitoring inulin-derived substances and GOS in foods. FSANZ cannot develop this capability on their behalf because method development and validation must be undertaken by appointed analysts to reflect their individual capability, their available analytical facilities and their commercial priorities. In addition, enforcement agencies can collaborate or develop agreements among themselves as to which methods they consider suitable for monitoring compliance. FSANZ considers that this is the most appropriate means for enforcement agencies to agree on methods suitable for monitoring enforcement.

Thus, methods of analysis for inulin-derived substances and GOS have not been prescribed to allow enforcement agencies and their appointed analysts to develop and agree on their own means of monitoring enforcement and thereby reduce the costs of developing suitable capability.

6.4.2 Cost of the methods of analysis

6.4.2.1 The Review Request states that there are 'considerable costs' to develop and verify methods but does not include information on these costs

In the Final Assessment Report, FSANZ acknowledged that published methods may need to be modified to be suitable for enforcement monitoring purposes. Depending on the analytical facility, method modification or validation may result in costs to enforcement agencies that have analytical facilities.

FSANZ has noted that methods for inulin-derived substances are already used for dietary fibre analysis and therefore capability for this analysis should already exist. On this basis, there should be no costs to enforcement agencies associated with the analysis of inulin-derived substances in food as the costs associated with developing this capability should already have been incurred.

As acknowledged at Final Assessment, costs for developing capability for GOS analysis may result in costs for enforcement agencies that have analytical facilities.

The Association of Official Analytical Chemists published method for GOS analysis has not been prescribed in the draft variations to assist enforcement agencies and their appointed analysts in developing alternative appropriate methods and therefore to reduce their costs for developing enforcement capability.

The potential costs to jurisdictions have not been itemised because this information was not provided to FSANZ. However, FSANZ expects any additional costs to be not significant given that most enforcement agencies would have this capability at least for inulin-derived substances. In any case, the costs for developing or validating methods would be unlikely to outweigh the benefits associated with this Proposal.

Moreover in accordance with Best Practice Regulation guidelines, FSANZ undertook a preliminary assessment that indicated negligible compliance costs for this Proposal. This assessment was forwarded to the Office of Best Practice Regulation (OBPR) the government's central body to promote and monitor the effectiveness and efficiency of regulation. The OBPR have cleared the Regulatory Impact Statement, including the impact analysis as adequate.

7. Proposed amendments to the draft variations

7.1 Maximum amount of inulin-derived substances permitted to be added to infant formula products

As indicated above in Sections 6.2.1 and 6.2.2, FSANZ's assessment of the maximum permitted level based on the totality of evidence re-affirms that 8 g/L of inulin-derived substances added to infant formula products is unlikely to pose a risk to the growth and development of infants fed this formula from birth onwards.

However, FSANZ notes that infant formula manufacturers[65] are not seeking permissions to add up to 8 g/L of inulin-derived substances to infant formula products at this time.

FSANZ also acknowledges that work on the Ministerial Council's Policy Guideline on the regulation of infant formula products has commenced. Once this policy guidance is received FSANZ intends to review Standard 2.9.1. Also, as noted above (see Section 6.1.4), FSANZ has undertaken this Proposal in accordance with section 36 of the FSANZ Act so that the immediate problem is addressed and regulatory certainty is provided in a timely and responsive manner.

Therefore at First Review, in noting the interim nature of the regulatory response and the levels being sought for use by the infant formula industry, FSANZ is proposing to amend the maximum level of inulin-derived substances permitted to be added to infant formula products from 8 g/L proposed at Final Assessment to 3 g/L as proposed at Draft Assessment.

[65] FSANZ has received two Applications seeking to add inulin-derived substances to infant formula products. Application A609 from Nutricia Australia Pty Limited is seeking permission to add GOS and long chain inulin up to 8 g/L in a ratio of 9:1. Application A598 from Heinz Wattie's Limited is seeking permission to add GOS alone up to 8 g/L or FOS alone up to 3 g/L. The specification for FOS has yet to be clarified with Heinz.

8. Review options

Three options were considered in this Review:

1. re-affirm approval of the draft variations to the Code as notified to the Ministerial Council;

2. re-affirm approval of the draft variations to the Code subject to any amendments FSANZ considers necessary; or

3. withdraw approval of the draft variations to the Code as notified to the Ministerial Council.

9. Conclusion

The First Review concludes that the preferred option is Option 2 – re-affirm approval of the draft variations to the Code subject to any amendments FSANZ considers necessary (at Attachment 1).

References

Veereman-Wauters, G., Staelens, S., Vandebroek, H., Plaskie, K. *et al.* (2008) Study of the effects of prebiotics on the intestinal flora of the neonate. Unpublished Report.

Attachments

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Terminology

Attachment 1

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

Standards or variations to standards are considered to be legislative instruments for the purposes of the Legislative Instruments Act (2003) and are not subject to disallowance or sunsetting.

To commence: on gazettal

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

[1.1] *inserting in clause 2 –*

galacto-oligosaccharides means a mixture of those substances produced from lactose by enzymatic action, comprised of between two and eight saccharide units, with one of these units being a terminal glucose and the remaining saccharide units being galactose, and disaccharides comprised of two units of galactose.

inulin-derived substances means mixtures of polymers of fructose with predominantly β (2→1) fructosyl-fructose linkages, with or without a terminal glucose molecule and includes inulin, but does not include those polymers of fructose produced from sucrose by enzymatic action.

[1.2] *inserting after clause 9 –*

9A Certain substances not nutritive substances

Inulin-derived substances are taken not to be nutritive substances.

[2] ***Standard 2.9.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting after clause 9 –*

9A Permitted inulin-derived substances and galacto-oligosaccharides

(1) Infant formula product may contain no more than –

(a) 110 mg per 100 kJ of inulin-derived substances; or
(b) 290 mg per 100 kJ of galacto-oligosaccharides; or
(c) 290 mg per 100 kJ of combined inulin-derived substances and galacto-oligosaccharides, where the inulin-derived substances is no more than 110 mg per 100 kJ.

(2) For subclause (1) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally occurring and the added substances.

[2.2] *omitting paragraph 16(1)(c), substituting –*

(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL; and

(d) when added, the average amount of –

(i) a combination of inulin-derived substances and galacto-oligosaccharides; or
(ii) inulin-derived substances; or
(iii) galacto-oligosaccharides

expressed in weight per 100 mL.

[2.3] *omitting paragraph 16(2)(d), substituting* –

(d) a declaration –

(i) of the weight of one scoop in the case of powdered infant formula; and
(ii) of the proportion of powder or concentrate required to reconstitute the formula according to directions; and

(e) when added, the average amount of –

(i) a combination of inulin-derived substances and galacto-oligosaccharides; or
(ii) inulin-derived substances; or
(iii) galacto-oligosaccharides

expressed in weight per 100 mL.

[2.4] *omitting clause 20, substituting* –

(1) The label on a package of infant formula product must not contain –

(a) a picture of an infant; or
(b) a picture that idealises the use of infant formula product; or
(c) the word 'humanised' or 'maternalised' or any word or words having the same or similar effect; or
(d) words claiming that the formula is suitable for all infants; or
(e) information relating to the nutritional content of human milk; or
(f) subject to clause 28, a reference to the presence of any nutrient or nutritive substance, except for a reference to a nutrient or nutritive substance in –

(i) clause 30 – claims relating to lactose free formula or low lactose formula; or
(ii) Standard 1.2.4 – labelling of ingredients; or
(iii) clause 16-declaration of nutrition information; or

(g) subject to Division 3, a representation that the food is suitable for a particular condition, disease or disorder.

(2) Subject to clause 28, the label on a package of infant formula product must not contain a reference to inulin-derived substances or galacto-oligosaccharides except for a reference to either substances in –

(a) a statement of ingredients; or
(b) the nutrition information statement.

[2.5] *omitting the* Nutrition Information *table in the* Guidelines for Infant Formula Products, *substituting* –

NUTRITION INFORMATION

	Average amount per 100 mL made up formula *1	**Average amount per 100 g of powder (or per 100 mL for liquid concentrate) *2**
Energy	kJ	kJ
Protein	g	g
Fat	g	g
Carbohydrate	g	g
Vitamin A	µg	µg
Vitamin B_6	µg	µg
Vitamin B_{12}	µg	µg
Vitamin C	mg	mg
Vitamin D	µg	µg
Vitamin E	µg	µg
Vitamin K	µg	µg
Biotin	µg	µg
Niacin	mg	mg
Folate	µg	µg
Pantothenic acid	µg	µg
Riboflavin	µg	µg
Thiamin	µg	µg
Calcium	mg	mg
Copper	µg	µg
Iodine	µg	µg
Iron	mg	mg
Magnesium	mg	mg
Manganese	µg	µg
Phosphorus	mg	mg
Selenium	µg	µg
Zinc	mg	mg
Chloride	mg	mg
Potassium	mg	mg
Sodium	mg	mg

(insert any other nutritive substance or inulin-derived substances and galacto-oligosaccharides to be declared)	g, mg, µg	g, mg, µg

***1** – Delete the words 'made up formula' in the case of formulas sold in 'ready to drink' form.
***2** – Delete this column in the case of formulas sold in 'ready to drink' form.

[2.6] *deleting the* Note *at the end of the* Nutrition Information *table in the* Guidelines for Infant Formula Products

[3] ***Standard 2.9.2*** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *omitting paragraph 2(2)(b) substituting –*

(b) lactic acid producing cultures; and
(c) either singularly or in combination, no more than 0.8g/ 100 g of inulin-derived substances and galacto-oligosaccharides, as consumed.

(3) For paragraph 2(2)(c) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally occurring and the added substances.

[3.2] *omitting subclause 2(3) and the heading to the* Table to paragraph 2(3)(c)*, substituting –*

(4) Food for infants must not contain –

(a) more than 50 mg/100 g of total iron in cereal-based food on a moisture free basis; or
(b) honey, unless it has been treated to inactivate *Clostridium botulinum* spores; or
(c) more than the total quantity of sodium set out in column 2 of the Table to this paragraph for each particular type of food for infants; or
(d) added salt, in the case of ready-to-eat fruit-based foods, fruit drink and vegetable juice.

Table to paragraph 2(4)(c)

[3.3] *omitting subclause 2(4)* and the Editorial note, *substituting –*

(5) Food for infants intended for infants under the age of 6 months must be formulated and manufactured to a consistency that minimises the risk of choking.

Editorial note:

The intent of subclause (5) is to ensure that the food, except in the case of rusks, should have a texture that is soft and free of lumps.

[4] ***Standard 2.9.3*** *of the Australia New Zealand Food Standards Code is varied by –*

[4.1] *inserting in clause 6 –*

(4) Formulated supplementary foods for young children may contain singularly or in combination, no more than 1.6 g of inulin-derived substances and galacto-oligosaccharides per serving.

(5) For subclause 6(4) the maximum permitted amount only applies when the substances are added. In that case the maximum permitted amount then applies to the sum of the naturally-occurring and the added substances.

Attachment 2

Terminology

1. Inulin-derived substances and fructo-oligosaccharides

Given the differences in the terminology currently in use, FSANZ developed terminology for fructose polymers to ensure there was clarity about these terms in assessing or considering the assessments for Proposal P306. FSANZ acknowledges that there are diverse opinions regarding the description of inulin-derived substances and that a number of different terms and expressions are used to describe these substances. To ensure that there is clarity about the terminology and identity of these substances, the following terms are used:

The term '**inulin-derived substances**' is used to collectively describe inulin, long-chain inulin and oligofructose. This term does not include those fructose polymers derived from sucrose;

the term 'inulin' is used to describe those fructans[66], with β (2→1) fructosyl-fructose linkages, where the average degree of polymerisation[67] (DP) is equal to or greater than ten:

- the term '**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;

the term '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. Chicory inulin, for example, contains about 30% oligofructose; and

the term '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.

FSANZ also acknowledges that sometimes oligofructose and inulin are referred to as 'FOS' and FOS is sometimes referred to as 'oligofructosyl-saccharose'. In addition, the terms oligofructose and FOS are sometimes used interchangeably. Given the differences in the terminology currently in use, the terms described above have been used to ensure clarity in the FSANZ assessment process and related consultations.

Fructans are characterised by the range of the DP, including the average DP. The DP is a measure of the number of fructose molecules or saccharide units in the substance. The DP ranges can vary for the different fructans with these ranges overlapping for the different substances. For this reason, the terms used above have been described on the basis of the average DP.

[66] Polymers of fructose.
[67] Degree of polymerisation is the number of fructose or saccharide units.

The term '**long-chain inulin'** is used to describe the processed inulin fraction that is currently added to infant formula, follow-on formula, infant foods and FSFYC internationally. The terms **inulin**, **oligofructose** and **FOS** is used where appropriate.

2. Galacto-oligosaccharides

The term '**galacto-oligosaccharides'** (sometimes referred to as oligogalactosyl-lactose) is used consistently to describe those substances comprised of between two and eight saccharide units with one of these units being a terminal glucose and the remaining saccharide units being galactose and disaccharides comprised of two molecules of galactose. While disaccharide lactose is present in GOS mixtures, it is not regarded as a galacto-oligosaccharide. GOS is produced from lactose by enzymatic action and is also referred to as 'trans-GOS'.

3. Oligosaccharides and polysaccharides

The terms oligosaccharides and polysaccharides are used throughout this Report.

Oligosaccharides refer to component sugars with a DP range 3-10.

Polysaccharides contain several simple sugars (DP > 10) linked together and are often referred to as complex carbohydrates.

Human milk oligosaccharides (HMOs) is a collective term used to refer to the oligosaccharide and polysaccharide content of human breast milk.