20 December 2019
[106-19]

Approval report – Application A1155

2′-FL and LNnT in infant formula and other products

Food Standards Australia New Zealand (FSANZ) has assessed an application made by Glycom A/S to permit the voluntary addition of 2′-O-fucosyllactose (2′-FL) alone or in combination with Lacto-N-neotetraose (LNnT), produced by microbial fermentation, in infant formula products and formulated supplementary foods for young children.

On 22 July 2019, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received twenty one submissions.

The FSANZ board approved the draft variation on 4th December 2019. The Australia and New Zealand Ministerial Forum on Food Regulation was notified of FSANZ's decision on 19th December 2019.

This Report is provided pursuant to paragraph 33(1)(b) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act).

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Supporting documents

The following documents which informed the assessment of this Application are available on the FSANZ website:

SD1 Health effects assessment (at Approval)
SD2 Policy Guidelines (at Approval)
SD1 Risk Assessment (at 2nd CFS)

Executive summary

Glycom A/S applied to amend the Australia New Zealand Food Standards Code (the Code) to permit the voluntary addition of 2′-O-fucosyllactose (2′-FL), either alone or in combination with Lacto-N-neotetraose (LNnT) to infant formula products (IFP) and formulated supplementary foods for young children (FSFYC). The application sought to include 2′-FL and LNnT as novel foods in the table to S25—2 of Schedule 25 (Permitted novel foods) and also noted amendments to Standard 2.9.1 (Infant formula products), Standard 2.9.3, Division 4 (Formulated supplementary foods for young children) and Schedule 3 (Identity and purity) may be required. The applicant also requested exclusive permission for their brand of 2′-FL and LNnT for a period of 15 months after gazettal.

The two oligosaccharides are found in human milk and have been identically produced by microbial fermentation from genetically modified (GM) *Escherichia coli* K12 production strains SCR6 and MP572, respectively. Several countries in Europe, Asia and the Americas permit the addition of 2′-FL and LNnT to a range of foods including infant formula products and formulated supplementary foods for young children.

FSANZ concluded that there are no public health and safety concerns associated with adding the applicant's 2′-FL and LNnT to infant formula products and FSFYC at the permitted levels.

The purpose for adding 2′-FL and LNnT was to create products that better reflect the oligosaccharide profile of human milk. In addition, the substances are claimed to: exert bifidogenic effects, adhere to pathogens in the gut with anti-infective benefits, provide immune modulation, improved intestinal barrier function and alleviation of allergic responses.

FSANZ undertook a comprehensive safety, technical and health effects assessment. This assessment considered two maximum use levels for 2′-FL: the applicant's request of 1.2 g/L, and a higher level of 2.4 g/L consistent with average levels in human milk. When combined with maximum 0.6 g/L LNnT, these respective use levels are 1.8 g/L and unaltered 2.4 g/L.

The higher maximum use level was also assessed in light of several companies' interest in applying for their proprietary brand of one or both oligosaccharides, based on overseas approvals up to 2.4 g/L. FSANZ's assessment of the safety and health effects up to this maximum level means that, if A1155 were approved, subsequent applications[1] would reduce in scope to an assessment of the safety of the method of production and product specification. This would simplify future assessments consistent with the Ministerial priority to maintain an agile food regulatory system.

The assessment considered a body of evidence including in vitro studies, animal studies including those in neonatal animals, and human studies including clinical trials in infants. It concluded that a protective specific binding mechanism exists between 2'-FL and invasive strains of *Campylobacter jejuni,* and that both oligosaccharides promote an increase in the relative abundance of bifidobacteria in the intestinal microflora. These effects may be enhanced as concentrations of 2′-FL are increased. The assessment also concluded there is insufficient evidence to support a role of 2′-FL and LNnT in immune modulation or improved intestinal barrier function.

The evidence assessed demonstrates 2'-FL & LNnT have a bifidogenic effect. Also that 2'-FL binds to invasive strains of *Campylobacter jejuni*.

[1] A1190: 2'Fl in infant formula products and FSFYC at 2g/L; PA1197: 2'FL in infant formula products, infant food, and FSFYC at 2.4 g/L (withdrawn)

The generic GM labelling Code requirements apply to these substances. As there is no novel protein or DNA present in the 2'FL and LNnT they will not be required to be labelled as GM. In response to issues raised by some submitters there are prohibitions on terms that can be used in the labelling: human milk identical oligosaccharides and similar abbreviations. The generic term oligosaccharide, the chemical name and the chemical name abbreviations can all be used. The prohibition applies to both IF & FSFYC to prevent risk of consumers being misled about the equivalency of these products with breast milk.

On 22 July 2019, FSANZ published an assessment report and sought submissions on a draft variation. The draft variation permitted the use of 2′-FL and LNnT on the basis that: the proposed use is safe, can provide beneficial health effects; allows alternative options to existing oligosaccharide permissions; supports international consistency and provides trade opportunities.

Labelling restrictions on the terminology that can be used aim to minimise the risk of consumers being misled.

Addition of new substances to infant formula can be a contentious topic. FSANZ received 21 submissions to the 2nd CFS. Submissions expressed divergent stakeholder views. Twelve of these supported the overall addition of 2′-FL and LNnT. Issues raised related to FSANZ's consideration of the labelling restrictions, the prohibition of use with existing GOS and ITF and regard to the policy guidelines. FSANZ has taken all the views into consideration in the decision process.

The addition of 2′-FL and LNnT to IFP and FSFYC at the levels proposed is safe and consistent with the average level in human milk; and can provide beneficial health effects to infants and young children. The permission supports international consistency and trade opportunities. It also allows for industry innovation and provides an alternative to currently permitted oligosaccharides (FOS and GOS) in infant formula products and FSFYC.

Having considered the submissions and weighed all aspects of the assessment against the statutory requirements including the ministerial policy guidelines, FSANZ approved the draft variation to the Code with one amendment. The amendment was to correct a typographical error.

2′-FL and LNnT are permitted to be added to these foods in many countries: the EU, Asia and the Americas at a range of levels. The permission provides industry with alternative oligosaccharide options for use in infant formula products and FSFYC, allowing opportunities for innovation.

Glossary of terms

2'-FL	2'-*O*-fucosyllactose
FSFYC	Formulated supplementary foods for young children (or 'toddler milk')
Follow-up Formula'	Defined by Codex as a food intended for use as a liquid part of the weaning diet for the infant from the 6th month on and for young children (12-36 months).
GOS	Galacto-oligosaccharide
HMO	Human milk oligosaccharide
HiMO	Human identical milk oligosaccharide
ITF	inulin-type fructans
LNnT	Lacto-*N*-neotetraose
Mature milk	In this report refers to human milk provided from a mother's breast from 60 days post-partum to distinguish it from colostrum.
scFOS	Short-chain fructo-oligosaccharide

1 Introduction

Infants are a vulnerable population group. Breastfeeding is the recommended way to feed an infant; however a safe and nutritious substitute for breast milk is required for infants who are not breastfed.

1.1 The Applicant

The application was submitted by Glycom A/S (Glycom), a Danish food ingredient manufacturer.

1.2 The Application

The application sought to amend the Australia New Zealand Food Standards Code (the Code) to permit the voluntary addition of 2′-O-Fucosyllactose (2′-FL), either alone or in combination with Lacto-N-neotetraose (LNnT), in infant formula products[2] and formulated supplementary foods for young children (FSFYC)[3]. 2′-FL and LNnT are oligosaccharides that naturally occur in human milk. The application is specifically for 2′-FL and LNnT produced by microbial fermentation from genetically modified (GM) *Escherichia coli* production strains SCR6 and MP572, respectively. The applicant claimed these oligosaccharides produced by microbial fermentation are structurally and chemically identical to 2′-FL and LNnT found in human milk.

Permission was sought for the addition of 1.2 g/L of 2′-FL alone, or with an additional 0.6 g/L of LNnT (i.e. totalling 1.8 g/L), to infant formula products and FSFYC[4]. The application stated these requested levels are within the ranges of 2′-FL and LNnT found naturally in mature human milk. The applicant's stated purpose was to better reflect the compositional profile of oligosaccharides of human milk. 2′-FL and LNnT produced by microbial fermentation are purported to provide the following favourable health effects typically associated with the oligosaccharide component of human milk: anti-infective effect against pathogens; bifidogenic effect; immune modulation, improved intestinal barrier function and alleviation of allergic responses.

The application sought to include 2′-FL and LNnT as novel foods in the table to S25—2 of Schedule 25 (Permitted novel foods) and noted amendments to Standard 2.9.1 (Infant formula products), Standard 2.9.3, Division 4 (Formulated supplementary foods for young children) and Schedule 3 (Identity and purity) may be required. The applicant also requested exclusive permission for their brand of 2′-FL and LNnT for a period of 15 months after gazettal.

The Applicant did not apply for a permitted health claim for FSFYC. FSANZ considers that this assessment could not be used as the basis of a health claim, since asessment of any health claim, including claims of a preventive nature, was not part of FSANZ's consideration of this application.

[2] 'Infant formula products' used throughout this report captures infant formula, follow-on formula and infant formula products for special dietary use.
[3] Toddler milk is the main type of FSFYC currently available.
[4] Specified in Table D.1-1 of the application dossier.

1.3 The current Standards

1.3.1 Australia and New Zealand Food Standards Code (the Code)

Australian and New Zealand food laws require food for sale to comply with the following Code requirements.

1.3.1.1 Permitted use

Paragraphs 1.1.1—10(5)(c) and (6)(g) of Standard 1.1.1 require that, unless expressly permitted, a food for sale must not be a *food produced using gene technology*, or have as an ingredient or component a *food produced using gene technology*. 2′-FL and LNnT are both *food produced using gene technology* (section 1.1.2—2) as they are derived from an organism modified using gene technology (i.e. derived from GM *E. coli* K12 strains). If approved, express permission for 2′-FL and LNnT is required in accordance with Standard 1.5.2 – Food produced using gene technology (i.e. listed in Schedule 26), rather than permission for a novel food in Schedule 25.

In addition, paragraph 1.1.1—10(6)(b) of Standard 1.1.1 requires that, unless expressly permitted, a food for sale must not have as an ingredient or component a substance that was *used as a nutritive substance* (section 1.1.2—12). 2′-FL and LNnT are both *used as a nutritive substance* because their addition to food is intended to achieve specific nutritional purposes. Therefore, if approved, express permission for 2′-FL and LNnT to be *used as a nutritive substance* is required in the Code in addition to the permission as *food produced using gene technology* above.

1.3.1.2 Infant formula products

The composition of infant formula is regulated in Standard 2.9.1 – Infant Formula Products and Schedule 29 – Special Purpose Foods in the Code. The standard (and associated schedule) set out specific compositional and labelling requirements for the following infant formula products:

- infant formula (for infants aged 0-<12 months)
- follow-on formula (for infants aged from 6-<12 months)
- infant formula products for special dietary use (for infants aged 0-<12 months).

Regulation of the composition of infant formula is appropriately prescriptive to ensure that infant formula provides sufficient energy and nutrients to promote normal growth and development of formula-fed infants, without posing a risk to infant health.

1.3.1.3 Formulated Supplementary Food for Young Children

Specific compositional and labelling requirements for FSFYC (for children aged 1-<4 years) are set out in Division 4 of Standard 2.9.3 and in Schedules 17 and 29.

1.3.1.4 Labelling requirements

Paragraph 1.1.1—10(8) requires that food for sale must comply with all relevant labelling requirements in the Code for that food. In addition to specific labelling requirements in Standards 2.9.1 and 2.9.3 (Division 4), the following general labelling requirements also apply.

Standard 1.2.4 generally requires food products to be labelled with a statement of ingredients.

Standard 1.2.7 sets out the requirements and conditions for voluntary nutrition, health and related claims made about food (FSFYC only). The Standard prohibits claims to be made about an infant formula product. Section 1.2.7—8 prohibits claims that are therapeutic in nature for any food.

Standard 1.2.8 generally requires food products to be labelled with nutrition information. This Standard does not apply to infant formula products (specific nutrition labelling requirements are set out in Standard 2.9.1).

Section 1.5.2—4 sets out labelling requirements for foods for sale that consist of or have as an ingredient, food that is a *genetically modified food*. A *genetically modified food* is defined in subsection 1.5.2—4(5) as a *food produced using gene technology* that contains novel DNA or novel protein or is listed in section S26—3.

1.3.1.5 Identity and purity

Paragraph 1.1.1—15(1)(a) requires a substance that is *used as a nutritive substance* to comply with any relevant identity and purity specifications listed in Schedule 3.

1.3.1.6 Current oligosaccharide permissions

The Code currently permits galacto-oligosaccharides (GOS) and inulin-type fructans (ITF) (section 1.1.2—2) to be added to infant formula products and FSFYC (sections 2.9.1—7 and 2.9.3—7). These are also permitted in general foods by their specific exclusion from the definition of *used as a nutritive substance* in section 1.1.2—12 and general provisions in section 1.1.1—10. ITF includes substances such as fructo-oligosaccharides (FOS), short-chain FOS (scFOS), oligofructose and inulin (FSANZ 2013). Unlike 2′-FL and LNnT, ITF are not present in human milk and GOS is found only in trace amounts (FSANZ 2008).

For infant formula products, the Code permits the addition of ITF alone (up to 110 mg/100 kJ), GOS alone (up to 290 mg/100 kJ), or ITF and GOS combined (up to 290 mg/100 kJ, with no more than 110 mg/kJ of ITF). These amounts were converted to the respective mg/100 kJ units for Code purposes from 8 g/L of GOS (alone or combined with ITF) and 3 g/L of ITF. For FSFYC, the total amount of ITF or GOS must not be more than 1.6 g/serving (converted from 8 g/L). The permitted maximum amounts take into account both the added and naturally occurring substances. These permissions were gazetted under Proposal P306 – Addition of inulin/FOS & GOS to food and Application A1055 – Short-chain Fructo-oligosaccharides.

1.3.2 International regulations

2′-FL and LNnT produced by microbial fermentation and by chemical synthesis are permitted for use in infant formula products, FSFYC and many other foods in at least 37 countries at a range of levels. A summary outlining some of the permissions for infant formula, follow-on formula and toddler milk products is shown in table 1.

Labelling permissions and restrictions differ across countries, some specify the terminology that must be used for the ingredients on labels while others do not. The different frameworks for nutrition content and health claims for infant formula and other products for young children are also relevant. Some countries permit claims on infant formula and FSFYC products, some that permit claims on follow-on formula and FYFYC, and others only for FSFYC.

Table 1: International permissions for use of 2'FI and LNnT

Country	2'FI		LNnT	
	Max use level IF	Max use level Toddler milks	Max use level IF	Max use level Toddler milks
United States	2.4 g/L	2.4 g/L	0.6 g/L	0.6 g/L
Canada[#]	1.2 g/L	1.2 g/L	-	-
Singapore	1.2 g/L	1.2 g/L	0.6 g/L	0.6 g/L
EU	1.2 g/L^	1.2 g/L^	0.6 g/L	0.6 g/L
Israel	2 g/L*	2 g/L*-	0.6 g/L	0.6 g/L
Korea	2 g/L	-	-	-
Philippines	1.2 g/L	-	-	-

Notes to table:
^ alone or in combination with LNnT
# permission as novel food no clear permission for use in IF
* when used alone, 1.2 max when used in combination with LNnT

An international influence in the labelling and advertising of infant formula is the International Code of Marketing of Breast-milk Substitutes (WHO 1981), commonly known as the WHO Code. The WHO Code was adopted in 1981 and recommends various requirements and restrictions for the marketing and distribution of breast milk substitutes for industry and health care workers. Various national authorities have implemented the WHO Code within their respective jurisdictions. The labelling differences discussed below are influenced by whether countries are signatories to the WHO Code. Most countries that are signatories restrict the claims and representations that are allowed on the label and/or advertising to align with the WHO Code. For example, in Canada, infant formula cannot be compared with breast-milk, and highlighting an ingredient in infant formula as a key component of breast milk is considered misleading. In the USA, some types of claims are permitted to be used in infant formula labelling. Singapore has recently introduced a similar restriction on statements that any ingredient is sourced/obtained from or similar to breast milk. Table 2 summarises some of the differences between countries in relation to infant formula labelling requirements and restrictions.

Table 2a: Labelling framework for infant formula in selected countries or regions

Country	WHO Code signatory	IFP labelling			
		Nutrition and Health claims generally permitted? Specific health claim approved for 2'-FL or LNnT?	Prohibition on terms like 'humanised'	Prohibition on comparisons to breast milk	Specified name of ingredient?
AU & NZ	✓	✗ ✗ No specific health claim approved	✓	✓	✓
United States	✗	✓ Nutrient claims in specified conditions Structure function claims permitted ✗ No specific health claim approved	✗	✗	✗
Canada	✓	✓ Limited number of nutrient content claims, to highlight differences in formulas not to suggest superiority It is inappropriate and misleading to use nutrient content claims to suggest that one infant formula is superior to another based on its nutrient content ✗ No specific health claim approved	✗	✓ No references to breast milk	✗
European Union	N/A	✓ Some permitted for products + 6 months – with conditions and approval ✗ No specific health claim approved	✓	✓	✓

Country	WHO Code signatory	IFP labelling			
		Nutrition and Health claims generally permitted? **Specific health claim approved for 2'-FL or LNnT?**	**Prohibition on terms like 'humanised'**	**Prohibition on comparisons to breast milk**	**Specified name of ingredient?**
Singapore	✓	✗ Can make ingredient claims but using correct scientific name or acronym (e.g. GOS, DHA) Cannot imply that the formula is enriched, fortified or is an excellent source in any way ✗ No specific health claim approved .	✓	✓	✓ Correct scientific name or acronym
Hong Kong	✓	Some nutrient claims and health claims ✗ No specific health clam approved	✓	✓	Names or abbreviations that are commonly known to consumers are considered acceptable in nutrition labelling

Table 2b: Labelling framework for FSFYC/toddler milks in selected countries or regions

Country	Regulates products for young children as 'breast milk substitutes'	Current FSFYC labelling			
		Nutrition and Health claims generally permitted? **Specific health claim approved for 2'-FL or LNnT?**	**Prohibition on terms like 'humanised'**	**Prohibition on comparisons to breast milk**	**Specified name of ingredient?**
AU & NZ	✗	✓ ✗ No specific health claim approved	✗	✗	✓

Country	Regulates products for young children as 'breast milk substitutes'	Current FSFYC labelling			
		Nutrition and Health claims generally permitted? Specific health claim approved for 2'-FL or LNnT?	Prohibition on terms like 'humanised'	Prohibition on comparisons to breast milk	Specified name of ingredient?
United States	✘	✓ Nutrient claims in specified conditions Structure function claims permitted ✘ No specific health claim approved	✘	✘	-
Canada	✓	✓ Limited number of nutrient content claims, to highlight differences in formulas not to suggest superiority It is inappropriate and misleading to use nutrient content claims to suggest that one infant formula is superior to another based on its nutrient content ✘ No specific health claim approved	✘	✓ No references to breast milk	-

Country	Regulates products for young children as 'breast milk substitutes'	Current FSFYC labelling			
		Nutrition and Health claims generally permitted? Specific health claim approved for 2'-FL or LNnT?	Prohibition on terms like 'humanised'	Prohibition on comparisons to breast milk	Specified name of ingredient?
European Union	✗	✓ ✗ No specific health claim approved	✓	✓	The novel food regulation specifies a prescribed name for both 2'Fl and LNnT
Singapore	✓	✓ ingredient claims using correct scientific name or acronym (e.g. GOS, DHA) but cannot imply that the formula is enriched, fortified or is an excellent source in any way. ✓Approved health effect claims - claims must not in anyway, relate to infants ✗No specific health claim approved	✓	✓	✗ Must use correct scientific name
Hong Kong	✓	✓ Some nutrient claims and health claims ✗No specific health claim approved	✓	✓	✗ Names or abbreviations that are commonly known to consumers are considered acceptable in nutrition labelling

1.3.2.1 Codex standards

The current Codex Alimentarius Standards for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (Codex Standard 72-1981) and for Follow-up Formula[5] (Codex Standard 156-1987), do not contain specific provisions for 2′-FL or LNnT. However, the standards contain provisions for 'optional ingredients' which would apply to the addition of substances such as 2′-FL and LNnT. FSANZ notes that the Follow-up Formula Standard is currently being reviewed by Codex[6]. The standards for infants include labelling requirements which align with principles of the WHO Code.

1.3.2.2 United States of America

The United States Food and Drug Administration (USFDA) issued 'no questions'[7] responses to the applicant's self-assessed Generally Recognized as Safe (GRAS) notifications for 2′-$FL_{chem\ \&\ micro}$ for use in various general and special purpose foods (USFDA 2015a, 2016a). The maximum intended use level in 'term infant formula' and 'toddler formula' (terms used in the US) is 2.4 g/L. The USFDA also issued 'no questions' responses to applications of other 2′-FL_{micro} manufacturers who use different GM production strains (Jennewein (USFDA 2015b), FrieslandCampina (USFDA 2018a) and Dupont (USFDA 2018b)). The maximum intended use levels for term infant formula and toddler formula is 2 g/L (Jennewein) and 2.4 g/L (FrieslandCampina; Dupont).

'No questions' responses were also issued for the applicant's LNnT (produced by chemical synthesis - GRAS GRN 547 and produced microbial fermentationGRAS GRN 659). The maximum intended use level of LNnT in term infant formula and toddler formula's is 0.6 g/L.

The US Code of Federal Regulations (CFR) permits some nutrient content claims on infant formula with conditions. The FDA Regulations allow statements describing the percentage of the vitamin or mineral in the product in relation to RDIs (US FDA 2016). There are also processes for a company to petition for new nutrient content claims, synonymous terms and the use of an implied claim in a brand name (21 CFR 101.69 - Petitions for nutrient content claims); misleading claims are not permitted. Health claims can also be made on infant formula subject to being permitted under the CFR. Structure and function claims are also permitted to be used on infant formula subject to conditions. There is no prescribed term for 2′-FL or LNnT.

1.3.2.3 European Union

2′-FL and LNnT are permitted as novel foods in the European Union (EU) for use in a range of general foods (e.g. milk-based products, cereal bars, bread and pasta products) and special purpose foods (EU 2017a). The relevant requirements for infant formula products and milk-based drinks for young children[8] are:

- For infant formula and follow-on formula, a maximum level of 1.2 g/L of 2′-FL alone or in combination with up to 0.6 g/L of LNnT at a ratio of 2:1 in the final ready-to-use product.

[5] 'Follow-up Formula' is currently defined by Codex as *a food intended for use as a liquid part of the weaning diet for the infant from the 6th month on and for young children* (12-36 months).
[6] For further information, search on the Codex Alimentarius website (accessed 23 September 2019).
[7] 'No questions' response means the USFDA does not question the basis for the notifier's GRAS conclusion (USFDA 2016b).
[8] 'Infant formula', 'follow-on formula', 'foods for special medical purposes' and 'young children' are defined in Regulation (EU) No 609/2013 (accessed 23 September 2019).

- For milk-based drinks for young children, a maximum of 1.2 g/L of 2′-FL alone, or 0.6 g/L of LNnT alone, or 1.2 g/L 2′-FL in combination with up to 0.6 g/L LNnT at a ratio of 2:1 in the final ready-to-use product.
- For foods for special medical purposes which includes such foods for infants, the maximum level used must be in accordance with the particular nutritional requirements of the persons for whom the products are intended.

Specifications are currently prescribed in the EU for 2′-FL and LNnT. These have recently been modified to be generic based on several equivalence notifications to the EU Commission from manufacturers (EU 2018, MEB 2017a, b).

The novel food permissions in Commission Implementing Regulation (EU) 2018/1023 designates that labelling of the foodstuffs containing 2′-FL and LNnT need to use the terms '2′-fucosyllactose' and 'Lacto-N-neotetraose'.

Point 3 of Article 13 of Commission Directive 2006/141/EC states that "The use of the terms 'humanised', 'maternalised', 'adapted', or similar terms shall be prohibited." The incoming EU Directive on Nutrition and Health Claims (Regulation (EU) 2016/127) prohibits nutrition and health claims on infant formula. This comes into effect in 2020 and 2021.

1.3.2.4 Singapore

The Agri-Food & Veterinary Authority (now known as the Singapore Food Agency) granted permission for the applicant's 2′-FL_{micro} (up to 1.2 g/L) and $LNnT_{micro}$ (up to 0.6 g/L) in infant formula and follow-on formula (Singapore 2018). According to the application, their use in 'growing-up milks' (12 to 36 months) is also permitted.

Singapore has recently reviewed the labelling regulations for infant formula. There is a prohibition on the use of health claims on infant formula. Companies can make ingredient claims but only using correct scientific name or acronym (for example GOS or DHA), but claims must not imply that the infant formula is enriched, fortified or is an excellent source of a nutrient in any way. The regulations also include a restriction on the use of the terms 'humanised', 'maternalised', 'or similar term as well as comparisons to breast milk. Guidance documents for industry on labelling provide the following specific examples: "{name of ingredient} sourced/obtained from breast milk", or "{name of ingredient} similar to breast milk"

1.3.2.5 Israel

2′-FL_{micro} and $LNnT_{micro}$ are authorised for use in infant formulas, follow-on formula and toddler formulas (Israel MOH 2017, 2019). A maximum level of 2 g/L 2′-FL alone, or 0.6 g/L LNnT alone, is permitted in the final ready-to-use product. Where LNnT is added in combination with 2′-FL, the permitted maximum levels are 0.6 g/L LNnT and 1.2 g/L 2′-FL at a ratio of 1:2 in the final product. The labelling restrictions for infant formula products are unclear.

1.4 Reasons for accepting Application

The Application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2)
- it warranted the variation of a food regulatory measure.

1.5 Procedure for assessment

The application was assessed under the Major procedure. FSANZ extended the consideration period for the application by 6 months under subsection 109(4) of the *Food Standards Australia New Zealand Act 1991*. We determined that it was not practicable to consider the application within the 12 month consideration period (for a Major procedure) due to its complexity.

1.6 Decision

The draft variation as proposed following assessment was approved with one amendment. The amendment was required to correct a typographical error. The variation takes effect on gazettal. The approved draft variation is at Attachment A.

The related explanatory statement is at Attachment B. An explanatory statement is required to accompany an instrument if it is lodged on the Federal Register of Legislation.

2 Summary of the findings

2.1 Summary of issues raised in submissions

Twenty-one submissions were received: 6 from jurisdictions, 1 from a healthcare professional organisation, 1 from a consumer group and 13 from industry and industry groups. Submissions can be accessed on the FSANZ website here http://www.foodstandards.gov.au/code/applications/Pages/A1155–2'-FL-and-LNnT-in-infant-formula-and-other-products-.aspx.

Twelve submissions supported the addition of the ingredients to infant formula products and formulated supplementary foods for young children. Several issues were raised in relation to the labelling restrictions and prohibition of use with existing GOS and ITF (as noted in Tables 3a, b, and c). Five Australian jurisdictions did not support the addition of the oligosaccharides to infant formula products or FSFYC. Industry supported the permission but raised concerns related to the labelling restrictions. The following tables summarise the issues raised in submissions and FSANZ's response.

Table 3a: Summary of issues: safety, evidence and approach to support addition

Issue	Raised by	FSANZ response
FSANZ Approach		
FSANZ has not adequately addressed the concerns raised by Jurisdictions at 1st CFS	WA DoH	FSANZ has carefully weighed and considered the concerns raised by all submitters. We consider that the issues raised in response to the 1st CFS were given due regard in the development of the approach to the 2nd CFS. The proposed level is safe, aligns with higher levels used internationally and will expedite assessment of future similar applications. The assessment had regard to two policy guidelines. The labelling prohibition was introduced in response to concerns raised by stakeholders including the Jurisdictions.
Addition to infant formula products is not consistent with the *Ministerial Policy Guideline for the Regulation of Infant Formula Products* as reliable evidence has not been provided to support beneficial effects.	Vic Govt, WA DoH, NSWFA, SA Health	FSANZ's consideration of the Ministerial Policy Guidelines is at SD2. FSANZ has applied particular caution in this assessment (as referred to in the policy guideline), noting: • The proposed addition is safe. • 2′-FL and LNnT are present in human milk at the levels proposed which accords with the policy to use breast milk as the primary reference for the composition of infant formula and follow-on formula. • Evidence demonstrates biological and mechanistic plausibility of the health effects and supports a link to potential beneficial health outcomes. • FSANZ considers the best available evidence is appropriate for the purpose of compositional permission, noting the addition is safe and comparable to human milk.
Concerned about the level of evidence that FSANZ considers sufficient in this application. In particular, FSANZ has used the premise that 'possible' or 'plausible' effects is all that is required to meet the scientific evidence criteria of a 'substantiated beneficial role in the normal growth and development of infants'.	WA DoH, QLD Health	The term 'plausible' (as used in the assessment reports) is a conclusion about 'causality' of the physiological, biochemical and/or functional effects to produce any favourable health effects. Biological plausibility is a key component of establishing a cause-and-effect relationship between a biological factor and a particular outcome. As discussed in SD2, the policy guideline sets out that composition of infant formula must be safe, suitable for the intended use and strive

Issue	Raised by	FSANZ response
The Policy Guideline refers to a 'substantiated beneficial role in the normal growth and development of infants or children' – a plausible benefit is not synonymous with a substantiated benefit. Also concerned that FSANZ' approval sets a concerning precedent regarding criteria for permitting the addition of substances to infant formula in the future.		to achieve normal growth and development compared to a healthy full term exclusively breastfed infant – as measured by appropriate physiological, biochemical and/or functional effects. FSANZ has considered the assessment strives to achieve the physiological, functional and health effects of breastfed infants. The assessment considers that the available evidence demonstrates relevant physiological, and functional effects in infants. FSANZ's assessment of the stated health effects is for the purpose of the requested voluntary compositional permission. FSANZ's first order priority was to ensure there are no public health and safety risks in accordance with subsection 18(1) of the FSANZ Act. In having regard to all high order policy principles, FSANZ considers that the strength, quality and type of evidence assessed in this application is appropriate for voluntary compositional permission.
Does not consider evidence provided to date to be sufficient to provide a substantiated health outcome and requests that FSANZ convene the Independent Expert Scientific Group proposed by the Ministerial Policy Guideline for Infant Formula Products.	NSWFA, WA DoH, QLD Health	Based on submissions, FSANZ sought advice on our assessment of anti-pathogenic and bifidogenic effects from an expert microbiologist, Associate Professor Andrew Holmes[9]. Professor Holmes noted the approach and conclusions reached by FSANZ were appropriate and reasonable. He also commented that FSANZ had taken a particularly cautious approach to our assessment of bifidogenic effect, noting the effect could be greater in infants who are predisposed to respond to the addition of these oligosaccharides in infant formula. FSANZ also sought advice of FSANZ Fellow Professor Seppo Salminen[10] on the assessment who supported the approach and conclusions of the assessment. On the basis of these two independent expert opinions, FSANZ considers this fulfils the policy guidance regarding an independent scientific group for this application, noting we used a risk analysis approach and applied particular caution in reaching our conclusions.

[9] Associate Professor Holmes specialises in the relationship between nutrition, gut microbiome and health and is the Microbiome Project node leader in the Charles Perkins Centre, and Co-leader of the Food for Health theme of the Centre for Advanced Food Enginomics at the University of Sydney.
10 Professor Salminen is the Director of Functional Foods Forum and Professor Health Biosciences, University of Turku, Finland and Visiting Professor, Food

Issue	Raised by	FSANZ response
Believes there is an absence of clarity on how FSANZ assessed weight of evidence	SA Health	As always FSANZ used an internationally accepted risk analysis framework in our decision making. The risk assessment component included: (i) a food technology assessment of 2′-FL and LNnT; (ii) a safety assessment to identify potential adverse effects associated with 2′-FL and LNnT; (iii) a dietary intake assessment to estimate the total dietary intake of 2′-FL and LNnT for breastfed infants and intake resulting from the addition of 2′-FL and LNnT to infant formula products and FSFYC; and (iv) an assessment of the stated health effects. The conclusions of the assessments were made taking into account all of evidence. In assessing a link between the relevant physiological, biochemical or functional effects and specific health effects FSANZ will consider an evidence base including animal studies, *in vitro* evidence as well as relevant observational or epidemiological studies. To clarify our assessment process we have summarised the approach and the relevant evidence considered in reaching our conclusions in section 2.2.1, 2.2.2 and 2.2.3.

and Health, University of Life Sciences (BOKU), Vienna, Austria. Professor Salminen has a particular interest in food toxicology, probiotics, novel food risk assessment and health claims and has served on the EFSA Panel on Dietetic Products, Nutrition and Allergies NDA for these topics.

Issue	Raised by	FSANZ response
Beneficial health effects		
Recommends FSANZ form an independent scientific expert group to review and provide advice to commensurately define criteria for substantiating a bifidogenic effect in terms of microbial and human physiological criteria. ' This could include broader delineation of the status of prebiotics as nutritive substances for classification in the Code. This includes general criteria related to human normal flora indicative of an impact on same, i.e. increase/decrease in total population of an organism/class of organisms, their relative proportion of the total microbial population, or both as beneficial health effects for classification in the Code; and review other countries' assessment criteria in this regard (EU, US, Canada).	QLD Health	A general review of the effects of prebiotics and probiotics and other countries' assessment criteria is much broader than the specific beneficial health effects assessed for this application for the purpose of voluntary permitted use and is out of scope.
Supports FSANZ determination that the beneficial immune modulation, intestinal barrier and allergic mediation health effects are not supported by the evidence.	QLD Health	Noted
The evidence provided for the bifidogenic effect and anti-infective effect against invasive *Campylobacter jejuni*, based on a plausible relationship, is insufficient to meet the policy requirements**.** There is insufficient evidence of positive or negative effects on formula-fed infants.	NSWFA	As discussed above, biological plausibility is a key component of establishing a cause-and-effect relationship. FSANZ concluded the evidence strongly demonstrates that 2′-FL binds to invasive *C. jejuni* strains and subsequently inhibits their attachment and growth. The evidence from in vitro studies showed a specific binding mechanism whereby 2'FL mimics the intestinal binding site of invasive campylobacter and inhibits binding. Appropriate animal studies demonstrated that this mechanism inhibits pathogen binding to intestinal epithelial cells and prevents subsequent progression of invasive disease. Animal studies are more appropriate for assessing this effect as pathogen challenge studies in infants are not possible. Human studies were used as supporting evidence, where a study reported higher incidence of Campylobacter diarrhoea in infants whose mother's milk contains low levels of 2'-FL. FSANZ considers it to be self-evident that any reduction in severity of an invasive *C.*

Issue	Raised by	FSANZ response
		jejuni infection would be beneficial to an infant. The evidence also demonstrates a mechanism and the likelihood of a bifidogenic effect from the proposed use of 2′-FL alone or with LNnT, if the bifidobacterium strains which metabolise these oligosaccharides are present in the gut. The complexity of demonstrating effect size in clinical trial is discussed below. FSANZ concludes the evidence substantiates the pathogen binding mechanism (anti-infective) and bifidogenic effects. And therefore considers the evidence is appropriate for the purpose of the proposed voluntary permission.
Concern that citing an anti-infective effect against the binding of *Campylobacter jejuni* may be implying that such infection should be interpreted as normal in the development of infants. Considers a health outcome of this nature to be related to a high level health claim (serious disease) or a therapeutic or prophylactic effect or claim (prevention of a serious disease).	NSWFA	As noted, the evidence demonstrated a specific binding mechanism for 2'-FL and invasive strains of *C. jejuni* in cell culture studies. These results were corroborated in animal challenge studies where disease severity from invasive *C. jejuni* infection was markedly reduced in animals fed 2'-FL. As noted in SD1 breastfeeding exclusively from 3–6 months is associated with a significant reduction in gastrointestinal tract infections. Given Camplyobacter infections are one of the most causes of gastrointestinal disease[11], particulaly in children under 5 years of age[12] ,FSANZ considers it to be self-evident that any reduction in severity of an invasive infection with C. *jejuni* is beneficial to infants and young children. A reduction in GI infections in formula-fed to rates similar of breastfed infants would align with intention of the ministerial policy guidelines (specific policy principles d & e). No claims are permitted on infant formula. Although the health effects could be the subject of a health or therapeutic claim, it is the description of the impact (eg reduced risk *c.f.* prevention) that affects its regulatory status. The Applicant did not apply for a permitted health claim for FSFYC. FSANZ considers that this assessment could not be used as the basis of a health claim, since asessment of any

[11] https://www.health.nsw.gov.au/Infectious/factsheets/Pages/campylobacteriosis.aspx
[12] https://www2.health.vic.gov.au/public-health/infectious-diseases/disease-information-advice/campylobacter

Issue	Raised by	FSANZ response
		health claim was not part of FSANZ's consideration of this application. A high level health claim on FSFYC products would have to be approved through a separate application and would have to meet the requirements of Standard 1.2.7.
Concerns about the quality, applicability and certainty of the current evidence to support the anti-infective and bifidogenic effects. Further clinical trials are required to substantiate these health benefits.	Vic Govt, SA Health	Noted. Refer to the comments above regarding the applicability and certainty of the evidence base. FSANZ considers it is neither feasible nor ethical to conduct human clinical trials in infants to demonstrate the protective effects in reducing severity of invasive *C. jejuni* infection. We have relied on appropriate animal models. As discussed in SD1 and section 2.2.3.1 the composition of the microbiota depends on a range of factors. Breastfed infants are typically referred to in the scientific literature as the reference standard for the normal healthy development of gut microflora in infants. Breastfed infants typically have a a higher relative abundance of bifidobacteria compared to formula-fed infants. There are also a number of complexities and difficulty of measuring outcomes of dietary interventions to modulate the intestinal microbiota, thus clinical trials are not the most appropriate evidence base. Our assessment established the evidence for a mechanism or mode of action underpinning the bifidogenic effect with in vitro studies. We then assessed evidence from studies assessing microbiota development of breastfed and formula-fed infants showing presence of fucosylated oligosaccharides has a bifidogenic effect and shifts microbiota composition to be more similar to breastfed infants. Clinical trial evidence showed that formula supplemented with 2'FL and LNnT was both bifidogenic and also resulted in a shift to a intestinal microflora composition that more closely resembled that of the breastfed infants.
There is a lack of certainty for the bifidogenic effect as a result of supplementing infant formula with 2'-FL and	NSWFA, Vic Govt	As discussed in section 4.2.1 of SD1 to the 2nd CFS, individuals' (infants, children and adults) intestinal microbial ecosystems all vary.

Issue	Raised by	FSANZ response
LNnT. The evidence base does not enable the extent of the effect and relies on human milk studies. Rather than producing a general bifidogenic effect, the evidence suggests the effect of human milk oligosaccharides in breast milk is to encourage only certain types of *Bifidobacteria*		A range of *Bifidobacterium* species has been identified in infant and adult faecal samples. In infants there are differences in the microflora of infants fed human milk vs infant formula. The evidence does show differences in how some *Bifidobacteria* species utilise human milk oligosaccharides. Depending on individual intestinal microbial ecosystems, some infants will respond positively to 2'FL and LNnT supplementation (responders) and others will not (non-responders). Due to these complexities and the difficulty of differentiating between responders and non-responders at the commencement of a clinical trial, FSANZ considers that the evidence assessed and the conclusions reached for the purpose of voluntary addition of 2'FL and LNnT to infant formula and FYSYC is appropriate and reasonable. Also that the available evidence supports that 2'FL and LNnT supplementation of infant formula and FSFYC may lead to an increase in bifidobacteria abundance and short chain fatty acid production.

Issue	Raised by	FSANZ response
Addition to infant formula		
Support approval to voluntarily add at the proposed levels on the basis that • human milk composition should be the primary reference for the composition of infant formula products. • oligosaccharides are a major component of human milk and are present in higher amounts than protein, and 2'FL and LNnT are two of the most abundant HMOs present in human milk. • they have been shown to be safe • these oligosaccharides are already available in infant formulas in many other countries including the USA and across Europe where the evidence around the addition of these two HMOs has also been discussed and reviewed.	Royal Australian College of Physicians (RACP), Infant Nutrition Council (INC), Glycom, NZ Food and Grocery Council (NZFGC), Australian Food and Grocery Council (AFGC), Danone, Fonterra, Dairy Goat Coop (DGC), Friesland Campina Ingredients, Dairy Companies Association of New Zealand (DCANZ)	Noted

Issue	Raised by	FSANZ response
Do not support the permission for voluntary addition 2′-FL and LNnT in infant formula and FSFYC, as the Applicant has not provided sufficient evidence to support a beneficial health outcome for the purposes of compliance with the *Ministerial Policy Guideline for Infant Formula Products.* Also consider the evidence is insufficient to substantiate general level helath claims and nutrition content claims on FSFYC irrespective of permissions for health claims.	QLD Health	FSANZ notes the views of QLD Health about ***compliance*** with the policy guideline. As discussed in section 2.5.2 and 2.5.3 in this report, the FSANZ Act outlines three objectives for the Authority in developing food regulatory measures. The Act also outlines other matters to which the Authority must have regard. In the assessment FSANZ has ***had regard*** (i.e. given genuine consideration) to the relevant policy guidelines in accordance with subsection 18(2) of the Act, as well as best available evidence, international consistency and industry trade and competition. The assessment was not undertaken for the purpose of assessing a food-health relationship for either a general level health or a high level health claim. On this basis FSANZ considers that this assessment could not be used as the basis of a health claim, since asessment of any health claim, including claims of a preventive nature, was not part of FSANZ's consideration of this application. In relation to FSFYC, the existing prohibition on therapeutic claims and provisions for high level health claims (including preapproval) will apply.
Supports approval and the approach to not specify a minimum amount on the basis that minimum levels should only be specified for mandatory substances; also consistent with international permissions.	Nestle	Noted.
Minimum permitted amounts – other substances are required to have a minimum quantity of the active ingredient.	NSWFA	A minimum permitted amount was not requested in the application and has not been determined by FSANZ. As noted in the safety, technical and health effect assessment the naturally occurring human milk oligosaccharide concentrations vary in lactating women. In addition, ingredients which are intended to modulate gut microflora may result in variable outcomes in individuals due to the unique microbial ecology of individuals and a variety of host and environmental factors. For these reasons setting a minimum effective 'dose' isn't an appropriate approach. This is consistent with the permissions overseas.

Issue	Raised by	FSANZ response
Addition to FSFYC		
Do not support the addition to FSFYC - is not consistent with the Ministerial Policy Guideline on the Intent of Part 2.9 – Special Purpose Foods regarding the 'intended purpose' of this food category. - does not consider current information sufficient to adequately define the nutritional benefit provided by these substances to toddlers. - FSFYC are designed to supplement children's (age 1 – 3 years) diet that are inadequate in energy and nutrients.	SA Health, NSWFA, WA DoH, Vic Govt	In assessing the proposed addition of 2′-FL and LNnT to FSFYC, FSANZ's first order priority was to ensure there are no public health and safety risks in accordance with subsection 18(1) of the FSANZ Act. FSANZ has also *had regard* to the relevant policy guideline in accordance with subsection 18(2) of the Act, as well as best available science, international consistency and industry trade and competition. The voluntary addition of 2′-FL and LNnT to FSFYC is safe. In addition the evidence demonstrates that both favourable effects (bifidogenic effect and pathogen binding effect) are valid for both infants and young children. As noted above Camplyobacter infections are one of the most common causes of gastrointestinal disease[13], in children under 5 years of age[14]. Thus, permitting the addition of 2'-FL and LNnT is consistent with the applicant's first two stated purposes. Although the policy guideline did not exist when GOS and ITF were permitted for use in the Code, these oligosaccharides are currently permitted for safe use in FSFYC at higher levels than proposed for A1155. Permitting alternative options to these oligosaccharides supports industry innovation. The proposed addition also supports international consistency and a competitive food industry (in accordance with high order policy principles 2(b) and (c)), and provides alternative options to ITF and GOS currently permitted at higher levels in FSFYC.
Safety		
Supports FSANZ conclusion re public health and safety and noted these conclusions are consistent with international assessment conclusions	New Zealand Food Safety, Abbott Nutrition, Nestle, BASF,	Noted
FSANZ has not demonstrated sufficiently the protection of public health and safety at the proposed levels.	Vic Govt	FSANZ conducted a comprehensive risk assessment according to internationally accepted methods and principles for the risk assessment of chemical substances in foods.

Issue	Raised by	FSANZ response
		The assessment included a literature review and identification of additional studies not provided by the applicant, critical assessments of the studies provided by the applicant, and a comprehensive dietary exposure assessment for Australian and New Zealand consumers. 2'-FL and LNnT have also been assessed as safe and suitable for use in IF & FSFYC by many regulatory bodies across the world including at the levels proposed. They are permitted to be added to IF & FSFYC (as well as a number of other foods) in at least 37 other countries. The proposed concentrations to be added to infant formula products are within the range of concentrations found in mature human milk. The levels approved by FSANZ are also consistent with the range approved in various countries overseas in the last 3–4 years.
Consider that the long term safety of HMO is unknown	Breast Feeding Advocacy Australia	Noted. Refer to comments above and to section 2.2 below.
Proposed maximum level		
Supports maximum use levels proposed for 2′-FL alone and combined with LNnT noting still significantly lower than human milk and other oligosaccharides permitted for addition	Nestle	Noted
The amount and composition of human milk oligosaccharides varies over the course of lactation, therefore, in the absence of additional trials, it is unknown if the maximum levels proposed are comparable to the range present in mature human milk, at any one time nor across an infant's feeding lifespan. Given the availability of products containing 2'-FL and LNnT overseas, there is opportunity to demonstrate the safety of these products, through future high quality research.	SA Health	Tables 3.13 and 3.14 (page 63) in section 3.4.1 of SD1 to the 2nd CFS, provides a summary of the range of 2'-FL and LNnT in human milk for 10–60 days partum and 60+ days post-partum**.** The data for 2'FL show a mean level of 2.4 g/L in milk collected 60+ days postpartum (with a range of 1.0–3.6 g/L). For LNnT the mean at 60+ days post-partum was 0.28 g/L (range 0.04–1.08 g/L). FSANZ considers that the use of products overseas for the last few years contributes to the evidence of a history of safe use.

[13] https://www.health.nsw.gov.au/Infectious/factsheets/Pages/campylobacteriosis.aspx
[14] https://www2.health.vic.gov.au/public-health/infectious-diseases/disease-information-advice/campylobacter

Issue	Raised by	FSANZ response
FSANZ has not sufficiently demonstrated the protection of public health and safety for the target population at the proposed levels. Do not consider there is sufficient justification for the maximum limit for 2'-FL level based on what has been tested in the toxicity and feeding studies. FSANZ has theorised that the higher maximum levels are safe, but evidence to demonstrate this position has not been provided. The proposed maximum appears to be justified primarily on a trade basis, given the US allows a higher 2'-FL level.	WA DoH, QLD Health	Refer to section 2.2. No adverse effects were observed at high doses in subchronic studies with 2'-FL or LNnT in juvenile rats (doses up to 5000 mg/kg bw/day), or in studies with 2'-FL in neonatal piglets at concentrations in formula of up to 2 g/L. These studies include histopathological analyses, which cannot be evaluated in clinical studies in human infants. The higher maximum use level was also assessed in light of several companies' interest in applying for their proprietary brand of one or both oligosaccharides, based on overseas approvals up to 2.4 g/L. FSANZ's assessment of the safety and health effects up to this maximum level in A1155, if approved, would mean that subsequent applications[15] would be less complex to assess consistent with the Ministerial priority to maintain an agile food regulatory system.

[15] A1190: 2'FI in infant formula products and FSFYC at 2g/L; PA1197: 2'FL in infant formula products, infant food, and FSFYC at 2.4 g/L/ (withdrawn)

Issue	Raised by	FSANZ response
Does not support proposed maximum use level for 2′-FL alone or combined with LNnT; reasons provided include: • There is no history of use in Australia and New Zealand of microbially produced 2′-FL and LNnT. • Extrapolation of human milk and breastfed infant health data to determine safety introduces some uncertainty which is not aligned with the specific policy principle that infant formula regulation should recognise the physiological vulnerability of infants.	SA Health, WA DoH	Refer to section 2.2. FSANZ has concluded that there are no safety concerns associated with the use of 2′-FL and LNnT at the proposed levels. Clinical studies in formula-fed infants and appropriate toxicological studies in experimental animals, including studies in neonatal animals, were available to support the safety of these substances. This is consistent with the approvals in several overseas markets. FSANZ further notes that 2′-FL and LNnT are structurally and chemically identical to the oligosaccharides in human milk. The proposed concentrations to be added to infant formula products are within the range of concentrations found in mature human milk. A study comparing breastfed infants with those consuming infant formula supplemented with 2′-FL_{chem} found no evidence to suggest that absorption of 2′-FL_{chem} from formula is significantly different to that of 2′-FL in human milk. Studies in rats found no adverse effects at high doses, confirming the lack of toxicity of 2'-FL. As noted above the assessment for a higher maximum use level means that subsequent applications[16] would be less complex to assess consistent with the Ministerial priority to maintain an agile food regulatory system. Based on all of the above FSANZ considers that the presence of 2′-FL and LNnT in human milk at the levels found in human milk provides evidence of safe use in human populations.

[16] A1190: 2'FI in infant formula products and FSFYC at 2g/L; PA1197: 2'FL in infant formula products, infant food, and FSFYC at 2.4 g/ L (withdrawn)

Issue	Raised by	FSANZ response
FSANZ states that the addition of 2'-FL alone or combined with LNnT is supported by appropriate evidence regarding safe levels of consumption. However the literature (Plaza-Diaz et al 2018) states there is a lack of evidence to support the proposed combination of 2'-FL and LNnT.	SA Health	FSANZ notes that the paper from Plaza-Diaz et al (2018) does not raise concerns as to the safety of 2′-FL and LNnT. The authors conclude the three studies investigating 2′-FL and LNnT found consumption of "*infant formula during the first 6 months of age was safe, well-tolerated, and supports age-appropriate growth….may provide immune benefits….shifts stool microbiota and metabolic signatures of infants born at term closer to that of breastfed infants"*
Would prefer the levels to be based on g/L units as used internationally, but can support the units of measure proposed (mg/100 kJ and g/serving)	Nestle	Noted
Prohibition on use with GOS/ITF		
Should not prohibit combinations of GOS/ITF with 2′-FL/LNnT in infant formula products and FSFYC: • This is not consistent with the data for some combinations of GOS/scFOS with 2′-FL. • This is not consistent with international permissions. • Suggests limit of 8 g/L could be set for combined use of 2′-FL/LNnT with existing GOS and ITF. Prohibition on use with other oligosaccharides limits trade with overseas markets	Fonterra, Friesland Campina Ingredients, Abbott Nutrition, Danone	As outlined in the 2nd CFS, the applicant has not sought to use 2′-FL and LNnT, in any combination with existing ITF and GOS permissions. Thus FSANZ has not assessed evidence to support the combined use of existing GOS and ITF permissions with 2′-FL/LNnT (noting also scFOS is only one form of ITF), or a limit of 8 g/L for total combined use suggested in submissions. An application process exists for industry who wish to seek to amend the Code to allow such combinations, with appropriate supporting evidence.
Supports the prohibition within the scope of this application, but is not opposed to future permitted combined use with appropriate scientific evidence.	Nestle, Glycom	Noted
2'FL occurs naturally in goat milk. Concerned that the drafting can be interpreted to mean if 2'FL is detected in goat milk formula which has GOS and ITF it would be non-compliant.	DGC	The drafting in both Standard 2.9.1 and Standard 2.9.3 specifies the prohibition of 2'FL and LNnT with GOS and ITN is linked to the *addition* of added 2′-O-fucosyllactose; or a combination of 2′-O-fucosyllactose and lacto-N-neotetraose.

Table 3b: Labelling and other issues

Issue	Raised by	FSANZ response
Generic approach vs prescribed name		
Supports FSANZ's decision to apply generic ingredient labelling requirements, rather than as proposed in the 1st CFS.	INC, NZFS, NZFGC, AFGC	Noted
Prohibition on use of terms human milk oligosaccharide, HMO, HMiO, HiMO etc.		
While there is support for the prohibition of use of the terms, have concerns that the change from FSANZ prescribing the ingredient names between 1st & 2nd CFS will enable use of generic term oligosaccharide. This could mean that any trademarks and implied claims in trademarks could be lodged on the generic terms. The change means that any claims or trademarks related to specific health outcomes associated with 2'-FL and LNnT as specific substances could be linked 'oligosaccharides' not the specific substance and will not be clearly visible to the consumer.	NSWFA, QLD Health	As discussed in section 2.3.4, the change of approach at 2nd CFS to the generic labelling requirements (from prescription of the ingredient names '2'-fucosyllactose' and 'lacto-N-neotetraose') was in response to submitter concerns. The change provides some flexibility in labelling and is consistent with the generic labelling requirements of the Code. The change will enable the use of the full chemical name, the acronyms 2'FL and LNnT and the generic term oligosaccharide. This also aligns with the EU approach. However if any health or nutrition content claims are to be made on FSFYC about 2'FL and LNnT, the claim conditions, (including substantiation requirements in Schedule 6, for general level health claims) must be met for claims about 'oligosaccharides', '2'-fucosyllactose' and 'lacto-N-neotetraose'. FSANZ notes that Schedule 6 requires a description of the food or propoerty of the food which needs to be linked to the supporting evidence base. As noted below The issue of trade marks is out of scope for this application. Refer to discussion in section 2.3.4.5.

Issue	Raised by	FSANZ response
Do not support labelling prohibition because the approach taken by FSANZ is inadequate and not evidence based.	INC, NZFGC, AFGC, DCANZ	FSANZ's decisions are based on the best available evidence, noting there is often limited consumer research evidence available relating to infant formula and FSFYC. In this case FSANZ has considered the Australian evidence, which is further supported by international research as discussed in section 2.3.4.
Could support the labelling restrictions (if an appropriate evidence base can be established to permit the use of these oligosaccharides).	Vic Govt, WA DoH, NSWFA	Noted
Do not support the labelling restrictions for the following reasons: • These terms reflect the common name and true nature of the ingredient • They are structurally identical to the oligosaccharides (2'FL and LNnT) in human milk and should be able to be listed as such. • The terms have been used by the scientific community for 20+ years. • The prohibition is inconsistent with existing conditions for other oligosaccharides which are labelled in accordance to Standards 1.2.4, 1.2.8 and relevant product standards 2.9.1 and 2.9.3. • There are already existing prohibitions in Std 2.9.1 • These terms are currently used on product labels in both the EU and the USA, where regulations allow for the use of these terms on label.	Glycom, Abbott, INC, DGC, Nestle	The terms '2'-fucosyllactose' and 'lacto-N-neotetraose' reflect the true nature of the ingredients and pose no conflict with current Code prohibitions. FSANZ notes terms such as 'oligosaccharides', which are part of the ingredient name desired by industry, would not be prohibited. The proposed requirements for 2'-FL and LNnT differ to existing conditions for other oligosaccharides (inulin type fructans and GOS), as the latter are not present in breast milk (not 'human milk oligosaccharides') and terminology referring to human milk contravenes policy guidance and Code requirements. FSANZ notes there are diverging stakeholder views about whether existing prohibitions in section 2.9.1—24 are sufficient. Given the uncertainty, FSANZ considers the specific prohibition provides clarity. FSANZ notes there are different permissions and restrictions for labelling in different countries. Refer to section 1.3.2 regarding international permissions.

Issue	Raised by	FSANZ response
Propose an approach consistent with the First Review Report for Proposal P306 for all oligosaccharides: “use the terms inulin-derived substances and GOS to clarify the compositional permissions, 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.”	Danone	Refer to response above. However, FSANZ considers it inappropriate to apply the same labelling approach to 2′-FL and LNnT, given these substances are present in breast milk and there are Code requirements prohibiting such representations in infant formula products. Further, the rationale for prohibiting specific terminology on FSFYC labels is described in section 2.3.4.3.
There is a need for the consumer to understand the ‘common name’ and true nature of the ingredient. Allowing the substances to be labelled as ‘human milk identical’ aligns with the requirements set out in ‘High Order Policy principle 1(b) in the Policy Guidelines on Regulation of Infant Formula Products’. 2′-FL and LNnT are more complex structures compared to the linear structures of plant based oligosaccharides (FOS and GOS) thus they should be clearly differentiated.	Nestle	Refer to the response above.
FSANZ’s approach ignores other consumer-related legislation such as Fair Trading Act 1987 and Australian Competition and Consumer Act 2010.	INC, NZFGC, DCANZ	In addition to Food Standards Code requirements, all domestic and imported food for sale in Australia and New Zealand is subject to consumer legislation which requires that labels do not misinform through false, misleading or deceptive representations. FSANZ considers that 2′-O-fucosyllactose (2′-FL) and Lacto-N-neotetraose (LNnT) are the accurate names for these specific oligosaccharides.
Propose FSANZ removes the restriction and sets a voluntary requirement for labels to include a reference that these ingredients are ‘Not sourced from human milk’.	Nestle	FSANZ considers that caregivers may find the presence of a statement ‘not sourced from human milk’ in association with ‘human milk identical oligosaccharides’ to be confusing. Caregivers may perceive this statement applies to other ingredients in the product, or may question whether other ingredients are in fact sourced from human milk.

Issue	Raised by	FSANZ response
The consumer research to justify the prohibition relies on very limited consumer sample populations, labours the consumer impact, is limited to a small number of papers which reflect author conclusions and inferences rather than explicit data.	INC, NZFGC	Refer to section 2.3.4.3.
The restrictions on use of these terms do not promote consistency with international markets; has the potential to create trade barriers. *Export* Competitiveness with other global products in relation to cross-border e-commerce (CBEC) with China. Constraining labelling for Australian and New Zealand products that are not applied to other foreign products, could mean trade will not compete with the developments that other countries permit. In the longer term, there will be a sustained impact on expanding trade and recognition of products from Australian and New Zealand origin. *Import* Raises conflicts in labelling requirements elsewhere that will influence/restrict the importation, and thus the availability, of innovative nutritious products for infants and young children in Australia and New Zealand.	DGC, AFGC, INC, Danone, NZFGC	As noted in sections 1.3.2.2 to 1.3.2.5, there is no consistency in the labelling requirements or restrictions relating to these oligosaccharides across countries. This is related to the policy framework around claims in different countries. FSANZ's approach is consistent with the EU regulation which specifies the use of the terms '2'-fucosyllactose' and 'Lacto-N-neotetraose' (Commission Implementing Decision (EU) 2017/2470). FSANZ notes that many companies already have to label products for specific markets.
Labelling restrictions are not appropriate for FSFYC – as claims for FSFYC are regulated by Standard 1.2.7	AFGC, INC, Nestle, NZFGC	The approach does not prohibit claims on FSFYC, however it does place some restrictions on the voluntary information that can be used on FSFYC. This is consistent with current approaches in the Code.
Concerned that the trademarked ingredient name is an implied health claim and that trademarks are exempt from the health claims standard.	NSWFA	The issue of trade marks is out of scope for this application. Refer to discussion in section 2.3.4.5. FSANZ has held discussions with IP Australia regarding the prohibition on nutrition content claims and health claims on infant formula.

Issue	Raised by	FSANZ response
There is a need to fully investigate future proofing these proposed prohibitions, such as how to deal with potential impact of trademarking	WA DoH, VIC	Trademarks are outside the scope of the Code. See comment above.
The FSANZ approach stifles innovation, impacting competition in both countries.	DGC, AFGC, INC, Danone, NZFGC	Noted.
FSANZ should consider a prohibition on terms such as 'human milk identical' more generally for foods for other purposes (e.g. sports supplements).	NZFS	Extending the proposed prohibition to other foods is beyond the scope of this application.
Not opposed to the approach proposed by FSANZ to specifically prohibits the words or abbreviations or words having same or similar effect on the label of IFP. NZFS is of the view that in this context the prohibition on the word humanised etc means making something more human, by giving human character Note Std 2.9.1-24: prohibited representations states humanised materialised words or any words to that effect and info re the nutritional content of human milk – consider that this already prohibits the use of term on the label of IFP.	NZFS	Noted.

Issue	Raised by	FSANZ response
Claims		
FSANZ did not support listing of 'gut health' in Proposal P293 as an approved substantiated health effect from probiotics and prebiotics. Requests clarification as to FSANZ's current position regarding this issue.	QLD Health	FSANZs position with respect to making a health claim regarding 'gut health' as referenced in P293 has not changed. The Policy Guideline on Nutrition, Health and Related Claims states that claims must communicate a specific, rather than a broad, benefit. 'Gut health' is multifactorial and not considered to be specific. The assessment of A1155, considered a bifidogenic effect and associated change in stool to be specific health effects. FSANZ considers that this assessment could not be used as the basis of a health claim, since asessment of any health claim, including claims of a preventive nature, was not part of FSANZ's consideration of this application.
Standard 1.2.7 prohibits claims in all foods that "refer to the prevention, diagnosis, cure or alleviation of a disease, disorder or condition;" Considers that the Applicant's anti-infective claim with respect to prevention of campylobacteriosis a high-level health claim due to a claim of a therapeutic and/or prophylactic effect against an infectious disease. There is a risk a consumer may erroneously rely on products containing these substances as, in-effect, substitutes/supplements to antimicrobials, i.e. antibiotics.	QLD Health	The applicant has not sought to add a food-health relationship to Schedule 4, for either a general level health or a high level health claim. In relation to FSFYC, the existing prohibition for therapeutic claims and provisions for high level health claims (including preapproval) will apply.
Recommend the general prohibition on health claims should also apply to FSFYC	QLD Health	Expansion of the health claims framework and regulation is outside of the scope of Application A1155.

Issue	Raised by	FSANZ response
Other issues		
Considers there will be practical and resource difficulties enforcing potential industry complaints regarding comparative beneficial nutrient content claims on FSFYC during the proposed exclusivity period. Such complaints would require allocatation of limited resources to undertake compliance and potential enforcement actions in the absence of a definitive established Code Schedule 4 food-health relationship.	QLD Health	Noted.
FSFYC is an unnecessary product, not recommended by health care professionals and carry misleading claims.	Breast feeding Australia Advocacy Facebook group	Noted.
Concern that availability and marketing of infant formula is negatively impacting breast feeding rates resulting in negative cognitive and health outcomes. FSANZ should reconsider the labelling and marketing restrictions to ensure the health and wellbeing of mothers and their infants is protected.	Breast feeding Australia Advocacy Facebook group	The Food Standards Code covers the labelling of infant formula products and FSFYC. The marketing and distribution of breast milk substitutes for industry are overseen by two voluntary agreements: • the Australian Marketing in Australia of Infant Formulas: Manufacturers and Importers Agreement (the MAIF Agreement), and • the New Zealand Infant Nutrition Council Code of Practice for the Marketing of Infant Formula (CoPMIF). These non-regulatory agreements specify restrictions for the marketing and distribution of breast milk substitutes for industry, including restrictions on products being advertised or otherwise promoted to the public.
The applicant's trademarked name is a an implied health claim. This in addition to the ability of FSFYC to make claims presents a risk of cross promotion. This makes it difficult for consumers to make informed choices between a FSFYC in which a health claim may be made, and an infant formula under the same trade name for which health claims are prohibited.	QLD Health	Refer to section 2.3.4.5. This is outside the scope of this application.

Table 3c: Drafting related issues

Issue	Raised by	FSANZ response
Permission as a food produced using gene technology		
Does not support approval of 2′-FL and LNnT as food produced using gene technology, should instead be regulated as novel foods, noting: • 2′-FL and LNnT meet the definition of non-traditional foods. • The substances are highly purified and equivalent to same molecules from different sources. • 2′-FL and LNnT are substantially different to GM plants currently listed in Schedule 26. • The substances are regulated as novel foods internationally (e.g. EU and US). • The proposed approach may introduce a barrier to trade.	Glycom, INC, NZFGC, Nestle	As noted at 2nd CFS, the Code operates differently to the regulatory framework for GM/novel foods in overseas regulations such as the EU and US. According to the definitions in the Code 2′-FL and LNnT are *food produced using gene technology* as they are derived from an organism modified by gene technology. An express permission must be provided in the Code for any *food produced using gene technology* to be sold, or used as an ingredient in a food for sale, in Australia and New Zealand (in accordance with section 1.1.1—10). Section 1.5.2—3 requires that a permitted food produced using gene technology is listed in Schedule 26, or is a substance permitted for use as a food additive (by Standard 1.3.1) or processing aid (by Standard 1.3.3). As 2′-FL and LNnT are not food additives or processing aids they must therefore be listed in Schedule 26 to comply with the requirements of the Code. Food for sale in Australia and New Zealand must meet the requirements of the Code. Regardless of approval as GM food in Australia and New Zealand, or as novel food overseas, the substances would be permitted to be used as ingredients in infant formula products and FSFYC which would support trade (noting, as discussed in section 2.3.5.5, it is highly unlikely that novel protein will be present in the final food in regard to GM labelling requirements). FSANZ therefore considers that the proposed permission is unlikely to negatively impact trade as noted in section 2.4.2.
Requests change to proposed approach for the approval. Proposes options to be consistent with safety assessment data: • linking the exact production strains OR • linking the approval to the derivative of host strain	Glycom	FSANZ is confident that the proposed drafting is consistent with our safety assessment. As the production strains SCR6 and MP572 have been superseded and are no longer used for commercial production. If the approval is linked to the specific strains named in the applications, the use of newer strains would require a new

Issue	Raised by	FSANZ response
used OR • linking to specific amino acid sequences		application to FSANZ. Linking the approval to *E. coli* K-12 maintains consistency with how other microbially-derived products are listed in the Code. Sub-species or strains are generally not listed unless necessary from a public health & safety perspective. FSANZ understands that some proteins have isoforms with differing amino acid sequences. If a food producer chooses to use a potentially different isoform of a protein from the same gene donor, the onus is on the producer to determine whether the different isoform meets the requirements in the Code. Linking approvals to specific amino acid sequences introduces unnecessary complexity and prescription into the drafted approval and is not justified from a safety perspective.
Suggest the drafting in Schedule 26 clearly states that the approved 2'-FL and LNnT will not contain the source organism	Glycom	Schedule 3 outlines the identity and purity of the approved 2'-FL and LNnT. It is the responsibility of the food business to ensure any use of the permitted substance complies with all requirements of the Code. In the Code, the absence or presence of novel DNA or novel protein determines whether the ingredient would need to be declared and is a factor determined by the food manufacturer not FSANZ.
Specifications		
Support removal of the methods of analysis (MOA) from the specifications.	BASF, Fonterra, Glycom, INC	Noted
Support the approach to link permission to the gene-gene-donor information and not to the production strain as the latter approach would provide exclusive permission to the applicant, without the need for a specific brand name	BASF	Noted
Do not support a generic specification	Glycom	Noted
Suggests generic specifications to be consistent with the recent updated version in the EU regulation as the *E.coli* K-12 specification covers different manufacturers' specifications.	BASF, Fonterra, INC, DGC, NZFGC, Nestle	Australia and New Zealand regulations do not provide a substantial equivalence notification system as per the EU regulations, noting the 2018 EU specification amendment is based on this approach. As FSANZ's assessment was based on the specifications provided in the application, these are the specifications proposed for insertion in Schedule 3 (without MOA's as discussed in the response above).

Issue	Raised by	FSANZ response
		As also noted above, FSANZ proposes linking approval to the specific gene-gene donor information, not the generic *E.coli* K-12 host. An application process exists for other companies to seek amendments to the Code for 2′-FL or LNnT based on their gene-gene donor information and relevant specifications (or to seek a generic specification), providing appropriate evidence and justification.
Exclusive permission		
Supports the exclusivity permissions. Approach is justified by the significant investment required to develop the ingredients.	Glycom A/S	Noted
Support the exclusivity permission but suggest it is better located in schedule 3 or a preceding clause in schedule 26	Nestle	FSANZ considers those suggestions are impractical for the Code.
Do not support exclusivity. Understand the intention of granting exclusivity with regard to the importance of data protection and/or first to market advantage to ensure commercial advantage for the first applicant. However as many companies produce these products across many different markets should not be considered 'novel' any longer.	BASF	Noted. 2′-FL or LNnT have been permited for 'use as a nutritive substance' not as novel foods.

2.2 Risk assessment

The majority of the safety, technical and health effects assessment report (SD1 at 2nd CFS) was not amended following the 2nd CFS. However following consideration of the submissions, FSANZ sought advice on our assessment from an expert microbiologist, Associate Professor Andrew Holmes[17]. Professor Holmes noted the approach and conclusions reached by FSANZ relating to the anti-pathogenic and bifidogenic effects were appropriate and reasonable. FSANZ also sought advice of FSANZ Fellow Professor Seppo Salminen on the assessment approach; he supported the approach and conclusions of the assessment. On this basis the health effects assessment has been summarised in SD1 to this approval report. The whole assessment is summarised in the following sections.

2.2.1 FSANZ's approach to the assessment of evidence

FSANZ has conducted a comprehensive assessment following the internationally recognised risk analysis framework. The assessment was based on the best available scientific evidence as legislatively required. The safety and composition of substances to be added to infant formula products is assessed with a particular focus on the target population and the intended special purpose of the food. Specific data relevant to the particular population group are required, including safety studies involving the exposure of very young animals.

FSANZ undertakes a safety assessment using the detailed study reports, where possible, of all animal and human toxicity studies related to the substance under consideration. In assessing the quality of individual studies, including epidemiological studies, FSANZ assesses various elements of the study design and method. These include: the purpose of the study; appropriateness of the study design for the purpose; appropriateness of the instruments used to measure the outcome variables of interest; the duration of the study; and the appropriateness of the statistical analyses undertaken.

For the assessment of many toxicological endpoints, a weight of evidence approach is necessary, utilising the data from all the available studies in which the same or functionally related fluids, cells, tissues or organs have been studied. Similar findings across different studies and evidence of dose-response relationships give added weight to the hazard characterisation.

Assessment of nutritional safety, tolerance and the efficacy also relies on a weight of evidence approach. While infant studies are required, evidence from non-human studies adds weight to the determination of a substance's role, particularly in understanding the mode of action and biological plausibility.

For the current assessment for both safety and favourable health effects, FSANZ considered a body of evidence including *in vitro* studies, animal studies including those in neonatal animals, and human studies including clinical trials. While FSANZ considers that the information submitted by the applicant met the requirements set out in the Application Handbook, a literature review was also undertaken and identified additional studies.

A comprehensive dietary exposure assessment for Australian and New Zealand consumers was undertaken that employed conservative assumptions (i.e. that the maximum permitted level would be present in all products) and gave overestimates of likely exposure. FSANZ also reviewed the assessments by other agencies and the information provided to other

[17] Associate Professor Holmes specialises in the relationship between nutrition, gut microbiome and health and is the Microbiome Project node leader in the Charles Perkins Centre, and Co-leader of the Food for Health theme of the Centre for Advanced Food Enginomics at the University of Sydney.

agencies overseas. The evidence reviewed is consistent with that used in overseas assessments.

2.2.2 Safety and technical assessment

The GM safety assessment concluded that no public health and safety concerns are identified for 2′-FL and LNnT derived from genetically modified *E. coli* K-12, production strains SCR6 and MP572, respectively.

The food technology assessment concluded that the applicant's 2′-FL and LNnT are chemically and structurally identical to the naturally occurring oligosaccharides in human milk and to chemically synthesised oligosaccharides, using appropriate methods of analysis. The shelf-life and specifications are appropriate for addition to infant formula products and FSFYC.

FSANZ considers there is sufficient evidence demonstrating that intakes of 2'-FL at levels up to 2.4 g/L alone or in combination with LNnT do not pose a risk to infant and young child health and safety. In reaching this conclusion FSANZ has taken a 'weight of evidence' approach that considered a range of appropriate evidence including:

- Glycom's 2'-FL and LNnT are chemically and structurally identical to the naturally occurring substances in human milk.

- Intestinal absorption of 2′-FL and LNnT is limited, and a large proportion of these substances passes to the large intestine, where it is fermented by the intestinal microbiota or excreted intact in the faeces.

- The proposed concentrations to be added to infant formula products are within the range of concentrations found in mature human milk (refer to figure 1). This is about one fifth of the total concentration of oligosaccharides present in mature human milk (10–15 g/L). This provides an appropriate history of safe human use in the target populations.

- The estimated dietary intake of 2′-FL based on 2.4 g/L is similar to 2′-FL intakes for 3 and 9 month old breastfed infants.

- Estimated mean intakes of 2′-FL from FSFYC based on 2.4 g/L for 12 month old infants and 2-3 year old children, are similar to or less than those for younger formula-fed and breast-fed infants (<12 months).

- No adverse effects were observed at high doses in subchronic studies with 2'-FL or LNnT in juvenile rats (doses up to 5000 mg/kg bw/day), or in studies with 2'-FL in neonatal piglets at concentrations in formula of up to 2 g/L. These studies include histopathological analyses, which cannot be evaluated in clinical studies in human infants.

- Clinical studies with 2'-FL at concentrations up to 1.2 g/L, either alone or in combination with LNnT, GOS or scFOS, also found no adverse effects. None of these studies found a difference in growth compared to a control formula.

- FSANZ is unaware of any reports of adverse events associated with the use of 2′-FL and LNnT in countries in which it is approved.

Taken together, the evidence on: chemical and structural equivalence; comparable

concentration ranges in human milk; the limited absorption; the lack of adverse effects at high doses in animal models of an appropriate age and in human infants, is sufficient to conclude that there are no public health and safety concerns associated with the addition of 2'-FL alone or in combination with LNnT at the proposed concentrations (up to 2.4 g/L of 2'-FL and up to 0.6 g/L of LNnT).

2.2.3 Assessment of health effects

2.2.3.1 Bifidogenic effect

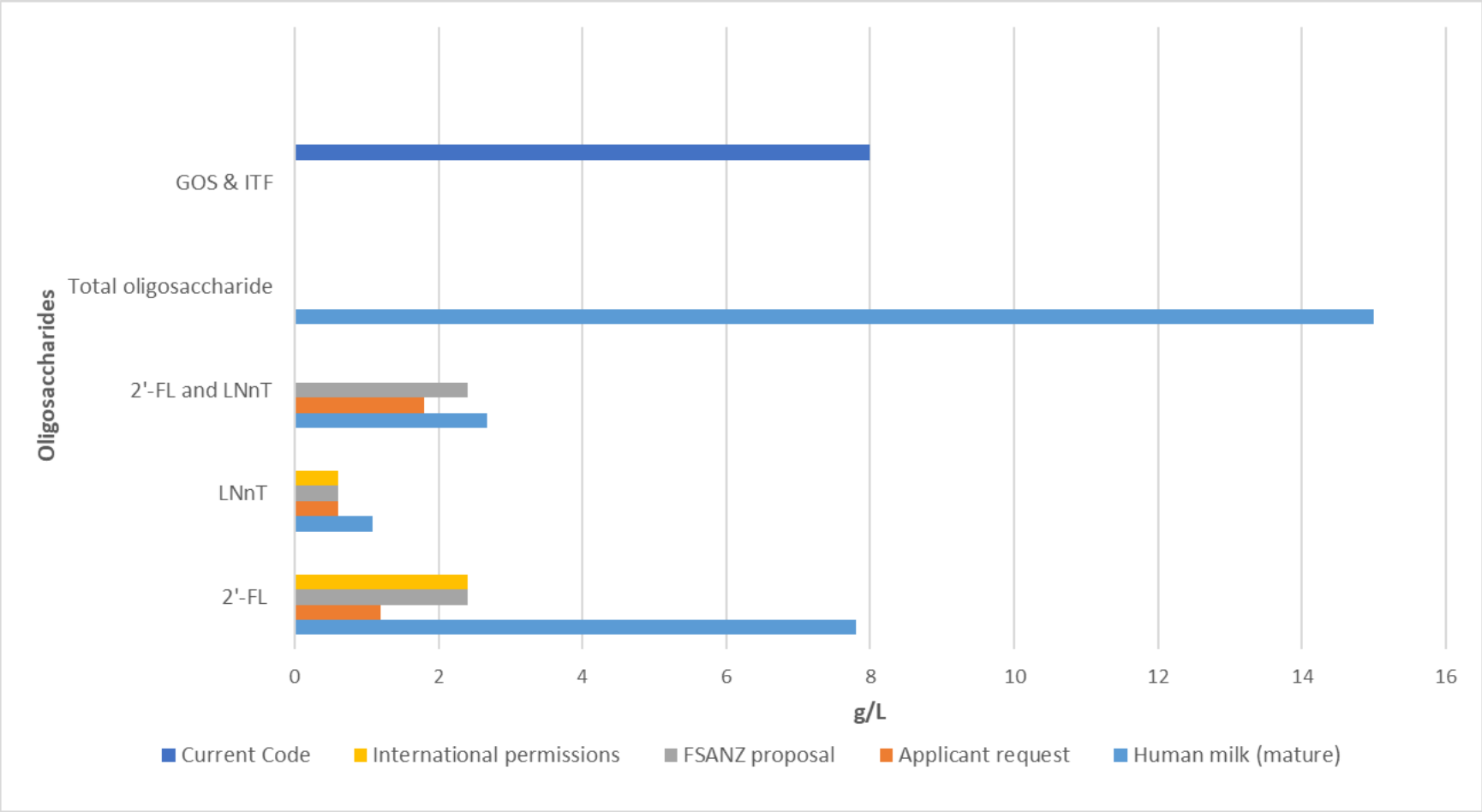
The composition of the microbiota depends on a range of factors including delivery method (vaginal vs caesarean), diet (breast vs infant formula), geographical origin, familial environment, diseases and the use of antibiotics (Bezirtzoglou et al. 2011; Milani et al. 2017).

It is not possible to define a universal standard for a healthy intestinal microbiota, however the composition of exclusively breastfed infants is generally the accepted reference standard for the normal, healthy development of an infant's gut microbiota. Studies have found that the composition of the gut microflora of breastfed infants are more homogeneous and are generally dominated by bifidobacteria compared to formula-fed infants (Bezirtzoglou et al. 2011). The EFSA states that the oligosaccharides of human milk are one of the principal growth factors for bifidobacteria in the infant gut and are responsible for the composition of the gut microbiota found in breastfed infants (EFSA 2014).

FSANZ assessed a body of evidence (refer to SD1 at 2nd CFS) to reach a conclusion that the bifidogenic effect in infants and toddlers is likely to occur and that there is a substantiated beneficial role in growth and development. This assessment followed several steps which included: consideration of the microflora development in breastfed infants and formula-fed infants, *in vitro* studies of bacterial growth and utilisation of 2′-FL and LNnT as well as studies of the microflora development in breastfed and formula-fed infants and an infant clinical trial. As summarised in Table 4, the assessment approach first sought to establish the evidence for a mechanism or mode of action underpinning the bifidogenic effect. This was established in *in vitro* studies showing that bifidobacteria are able to metabolise 2'FL and LNnT giving them a selective growth advantage. The next step assessed evidence from studies which examined microbiota development of breastfed and formula-fed infants. This showed that the presence of fucosylated oligosaccharides, including 2'-FL, in the infant diet has a bifidogenic effect and that the microbiota composition is more diverse in formula-fed infants compared to breastfed infants. Clinical trial evidence was also examined which compared breastfed infants with infants fed unsupplemented formula and formula supplemented with 2'FL and LNnT. This showed that formula supplemented with 2'FL and LNnT was both bifidogenic and also resulted in a shift to a intestinal microflora composition that more closely resembled that of the breastfed infants.

The evidence assessed by FSANZ from in vitro and human studies demonstrates the likelihood of formula supplemented with 2'-FL and LNnT having a bifidogenic effect in humans, including in infants and toddlers.

Figure 1: Comparison of oligosaccharide levels in regulation and human milk



Notes to figure:
Human milk levels based on Table 3.13 and 3.14 in SD1 at 2nd CFS.

Table 4: Summary of the evidence base for bifidogenic effect

Type of studies	Key studies	Main findings	Why this is important
In vitro bacterial growth/utilisation studies on 2'-FL and LNnT	Asakuma et al. (2011) Bunesova et al. (2016) Garrido et al. (2015) Garrido et al. (2016) Ruiz-Moyano et al. (2013) Yu et al. (2013a) Yu et al. (2013b)	These studies show that bifidobacteria and a limited number of other bacteria that are typically a component of the infant microflora, such as *Bacteroides* spp., have the ability to metabolise 2'-FL or LNnT, whereas other bacteria such as *E. coli*, are unable to utilise 2'-FL for growth.	These studies demonstrate the metabolic mechanism that underpins the bifidogenic effect associated with 2'-FL and LNnT and that bifidobacteria have a selective growth advantage when 2'-FL and LNnT are present.
Microflora composition in infants	Bezirtzoglou et al. (2011) Tannock et al. (2013) Lewis et al. (2015) Smith-Brown et al. (2016)	These studies show that fucosylated oligosaccharides present in human milk, including 2'-FL, have a bifidogenic effect and that formula-fed infants not only have a lower relative abundance of bifidobacteria but also a faecal microflora that is more diverse.	These studies corroborate the *in vitro* studies in demonstrating the growth advantage afforded to bifidobacteria when fucosylated oligosaccharides, including 2'-FL, are present in the infant diet. Thereby supporting the biological plausibility of 2'-FL having a bifidogenic effect.
Clinical studies in infants	Puccio et al (2017) Alliet et al. (2016) Steenhout et al. (2016)	This study provides evidence that the addition of 2′-FL and LNnT to infant formula products influences the infant gut microflora to more closely resemble that of breastfed infants and with a higher relative abundance of bifidobacteria compared to infants fed unsupplemented formula.	This study provides evidence further supporting the biological plausibility of 2'-FL and LNnT supplementation having a bifidogenic effect and an infant gut microflora composition and metabolic profile that more closely resembles breastfed infants.
Study in adults	Elison et al. (2016)	Supplementation of an adult study population with either 2'-FL or LNnT or a combination of both HMOs resulted in an increased relative abundance of *Bifidobacterium* an *Actinobcter* in a dose dependant manner.	This study provides further evidence supporting the biological plausibility of 2'-FL and LNnT supplementation having a bifidogenic effect and that the effect is not restricted to infant populations and likely dose dependant.

2.2.3.2 Pathogen binding effect

In full-term infants, breastfeeding exclusively from 3-6 months of age and partially thereafter, has been associated with a significant reduction in infections of the gastrointestinal tract of infants (Kramer et al. 2001; Kramer et al. 2003; Duijts et al. 2010; Tarrant et al. 2010). Oligosaccharides in human milk are one of the components attributed to this protective effect (Lawrence and Pane 2007; Cacho and Lawrence 2017).

The evidence assessed by FSANZ demonstrated a specific binding mechanism for 2'-FL and invasive strains of *Campylobacter jejuni*. Two key studies submitted by the Applicant and assessed by FSANZ underpin this conclusion. The first study by Ruiz-Palacios et al. (2003) is important because it demonstrated that the intestinal binding site for invasive strains of *C. jejuni* is structurally similar to 2'-FL and that incubation of 2'-FL with invasive *C. jejuni* prevents it binding to this site. This study demonstrated the specific inhibitory mechanism that underpins the anti-pathogenic effect.

Secondly, an animal study by Yu et al. (2016) corroborated the results observed by Ruiz-Palacios et al. (2003). In a mouse infection model, Yu et al. (2016) demonstrated a marked decrease in disease severity and invasiveness by feeding mice with 2'-FL either 3 days before or concurrently with invasive *C. jejuni* challenge. This study is important because the addition of 2'-FL to the diet of mice reduced binding of *C. jejuni* to the intestinal cells of infected mice and subsequently reduced invasion and spread to other bodily sites such as the spleen and mesenteric lymph nodes.

Taken together, these two studies show the mechanism by which pathogen inhibition occurs and the biological plausibility of a similar inhibitory effect being observed in infants fed formula supplemented with 2'-FL.

It is neither feasible or ethical to conduct human clinical trials in infants to demonstrate the protective effects of 2'-FL in reducing severity of invasive *C. jejuni* infection. FSANZ therefore relied on cell culture and animal studies to reach the conclusion that there is an inhibitory effect against invasive *C. jejuni* infection. FSANZ considers this approach to be appropriate and reasonable and considers it to be self-evident that any reduction in severity of an invasive *C. jejuni* infection would be beneficial to the infant.

2.2.3.3 Immune modulation, intestinal barrier function and allergic response

The current available evidence for the stated immune modulating effect, improved intestinal barrier function, and protective effects against allergic responses for 2′-FL and LNnT is insufficient. For the immune modulation effect there was some evidence for 2′-FL which supported the proposed effects, however the clinical significance of the data was inconclusive. These stated health effects are therefore not supported by the evidence. For the role in protection against allergies there was not strong evidence to support the protective effect of HMOs, such as 2′-FL, in preventing development of allergies in infants and children.

2.2.3.4 Applicability of the findings to infants and young children

FSANZ undertook assessments to determine whether the proposed health effects of adding 2′-FL and/or LNnT to infant formula products and FSFYC are supported by evidence. The available clinical studies were mainly conducted in infants, as well as one in young children (up to 24 months) and one adult study.

Thus as a part of the assessment, FSANZ considered whether the evidence would apply across the infant and young child age range. No evidence indicated that the proposed effects would be limited to a particular age group of infants or toddlers. Overall, FSANZ concludes that the bifidogenic effect and anti-infective effect against invasive *C. jejuni* are biologically plausible and the assessed evidence supports a mechanism for these effects. FSANZ also considered evidence from *in vitro* laboratory studies for anti-infective effect and an adult study for bifidogenic effect, which indicates that these health effects may be enhanced as concentrations of 2′-FL (or LNnT in the case of the bifidogenic effect only) are increased. The conclusions reached for each proposed health effect in infants are therefore applicable to all the infant formula products and FSFYC to which this application applies.

2.2.4 Risk assessment summary

There are no public health and safety concerns associated with adding the applicant's 2′-FL and LNnT to infant formula products and FSFYC at the levels permitted which are consistent with average levels in mature human milk. The evidence supports the proposed compositional permission. FSANZ concluded that the requested addition of 2′-FL alone or with LNnT demonstrates a favourable health effect and has the potential to confer beneficial health outcomes in infants and young children. The available evidence demonstrates a mechanism for an pathogen binding with an anti-infective effect against invasive *Campylobacter jejuni* infection and a bifidogenic effect (an increase in the relative abundance of bifidobacteria in the intestinal microflora). Other less direct evidence indicates these favourable health effects may be enhanced as concentrations of 2′-FL are increased.

Evidence to support the health effects of improved barrier function, immune modulation and alleviation of allergic responses are inconclusive.

2.3 Risk management

Breastfeeding is the recommended way to feed infants. As infants are a vulnerable population group, a safe and nutritious substitute is necessary when breastfeeding is not possible. Any changes to the composition of infant formula products must be established as safe and suitable prior to being permitted.

2.3.1 FSANZ's approach and consideration of the policy guidelines

FSANZ's decision requires consideration of the higher and lower objectives of the FSANZ Act (section 18(10 and 18(2)) as discussed in section 2.5, which includes the relevant ministerial policy guidelines (SD2), and issues raised and considered at the 2nd Call for Submissions. As outlined in Supporting Document 2 FSANZ has given regard to both relevant policy guidelines as part of the assessment process.

Policy Guideline on the Regulation of Infant Formula Products

FSANZ's first order priority was to ensure there are no public health and safety risks in accordance with subsection 18(1) of the FSANZ Act. FSANZ has also had regard to the relevant policy guideline in accordance with subsection 18(2) of the Act, as well as best available evidence, international consistency and industry trade and competition.

In keeping with the ministerial policy guideline (SD2), FSANZ considers that the proposed voluntary addition of 2′-FL and LNnT is consistent with current national nutrition polices and guidelines for infant feeding. As 2′-FL and LNnT are naturally occurring in human milk, and the levels proposed are within the range found in human milk, there is a history of safe intake by breastfed infants.

The safety, technical and health effects assessment, including an assessment on infant growth, concluded that there are no public health and safety concerns associated with the addition of 2′-FL alone or with LNnT at the levels requested, or at higher levels up to 2.4 g/L to infant formula products (includes infant formula, follow-on formula and infant formula for special dietary use).

FSANZ considers the assessment of relevant physiological, biochemical or functional effect(s) in infants fed an infant formula product can be considered within the context of safety and favourable health effects. Given it is not always possible to attribute a particular outcome or health effect to specific factors in human milk or an ingredient in infant formula, comparison of outcomes in healthy breastfed infants is considered an internationally accepted approach (IOM, 2004; Ryan & Hay 2016). In addition, evidence from non-human studies adds weight to the determination of a substance's role, particularly in understanding the mode of action and biological plausibility. In assessing a link between the relevant physiological, biochemical or functional effects and specific health outcomes it is appropriate to consider an evidence base including animal studies, *in vitro* evidence and relevant observational or epidemiological studies.

As discussed in SD2, the first policy guideline sets out that "composition of infant formula must be safe, suitable for the intended use and strive to achieve normal growth and development compared to a healthy full term exclusively breastfed infant – as measured by appropriate physiological, biochemical and/or functional effects". FSANZ's assessment of the bifidogenic effect has considered the differences between formula-fed and breastfed infants in relation to gut and stool microflora. As bifidobacteria are generally recognised as benefical to infants because they produce short chain fatty acids from HMOs and these short chain fatty acids have a role in the development and maintenance of healthy intestinal cells. The assessment thus looked for modes of action and biological plausibility for the proposed effects. Biological plausibility is a key component of establishing a cause-and-effect relationship. In vitro studies of bacterial growth/utilisation on 2'-FL and LNnT were used in combination with infant studies to reach a conclusion that the gut and stool microflora of formula-fed infants can be shifted closer to those of breastfed infants when formula contains 2'FL and LNnT. Due to the complexities and difficulty of measuring outcomes of dietary interventions to modulate the intestinal microbiota, FSANZ considers that the approach taken, the evidence assessed and the conclusions reached are appropriate and reasonable.

FSANZ has concluded that the evidence demonstrates a specific binding mechanism for 2'-FL and invasive strains of C. jejuni in cell culture studies. These results were corroborated in animal challenge studies where disease severity from invasive C. jejuni infection was markedly reduced in animals fed 2'-FL. Animal studies are more appropriate for assessing this effect as pathogen challenge studies in infants are not possible. As noted in SD1 breastfeeding exclusively from 3–6 months is associated with a significant reduction in gastrointestinal tract infections. Camplyobacter infections are one of the most common causes of gastrointestinal disease, particulaly in children under 5 years of age. FSANZ considers it to be self-evident that any reduction in severity of an invasive infection with C. jejuni is beneficial to infants and young children. A reduction in GI infections in formula-fed infants to rates similar in breastfed infants would align with the intention of the ministerial policy guidelines (specific policy principles d & e).

Evidence reviewed by FSANZ has demonstrated physiological and functional effects that can be favourable to infants and young children, consistent with the oligosaccharide fraction of human milk. FSANZ considers the evidence assessed is appropriate for the purpose of the proposed voluntary compositional permission, noting the proposed addition is safe and comparable to human milk.

FSANZ *had regard* to the Infant Formula Food policy guideline in accordance with subsection 18(2) of the Act, as well as the other objectives of the FSANZ Act (best available scientific evidence, international consistency and industry trade and competition). FSANZ considers that the strength, quality and type of evidence assessed in this application is appropriate for voluntary compositional permission.

Intent of Part 2.9 – Special Purpose Foods of the Code

FSANZ has also *had regard* to the Special Purpose Food policy guideline in accordance with subsection 18(2) of the Act, as well as best available science, international consistency and industry trade and competition.

FSANZ acknowledges that FSFYC are intended to supplement young children's diets when food intakes may be inadequate. The literature indicates that the diet in early childhood influences the continuing establishment of the gut microbiota (Mohammadkahah et al 2018; Robertson et al 2019). Oligosaccharides (as GOS & ITF) are already permitted in FSFYC and FSANZ's assessment concluded that 2'FL and LNnT having a bifidogenic effects and a pathogen inhibitory affect are biologically plausible, both of which can provide beneficial health outcomes for young children (as for infants). FSANZ has assessed all available information provided by the applicant and from our own independent literature search, and did not identify evidence that would indicate the assessed anti-infective and bifidogenic effects would be limited to a particular age group of infants or toddlers.

As 2'FL and LNnT are permitted in this food in a number of other countries, the proposed permission also supports international consistency and a competitive food industry (high order policy principles 2(b) and (c)), providing trade opportunities; and provides alternative options to existing oligosaccharides (GOS and ITF) which introduces innovation opportunities for Australian and New Zealand industry.

2.3.2 Maximum use levels and units expression

The maximum levels of 2′-FL and LNnT were based on adequate consideration of the safety, technical and health effects assessment, including estimated dietary intakes and naturally occurring levels in human milk.

Internationally, the permitted levels of 2′-FL for use in infant formula and follow-on formula range from 1.2 g/L to 2.4 g/L. Approving a higher level of 2.4 g/L of 2′-FL alone or with 0.6 mg/L LNnT in Australia and New Zealand would therefore provide greater compatibility with a greater range of overseas food standards and allow for a more efficient and internationally competitive food industry given the high level of international interest in these substances.

The higher maximum use level was also assessed in light of several companies' interest in applying for their proprietary brand of one or both oligosaccharides, based on overseas approvals up to 2.4 g/L. FSANZ's assessment of the safety and health effects up to this maximum level means that, if A1155 were approved, subsequent applications[18] would reduce in scope to an assessment of the safety of the method of production and product

[18] A1190: 2'FI in infant formula products and FSFYC at 2g/L; PA1197: 2'FL in infant formula products, infant food, and FSFYC at 2.4 g/L (withdrawn)

specification. This would simplify future assessments consistent with the Ministerial priority to maintain an agile food regulatory system..

We also note that a maximum of 2.4 g/L is significantly lower than the total concentration of oligosaccharides present in mature human milk (i.e. 10–15 g/L). This enables future consideration of alternative oligosaccharides. The prohibition of use in combination with GOS and ITF means these are an alternative and there is no cumulative increase to the total oligosaccharide load consumed by infants.

2.3.3 Minimum levels

A minimum permitted amount was not requested in the application and has not been determined by FSANZ. FSANZ also considers that ingredients which are intended to modulate gut microflora may result in variable outcomes in individuals due to the unique microbial ecology of individuals and a variety of host and environmental factors. For these reasons setting a minimum effective 'dose' isn't an appropriate approach. This is consistent with the permissions overseas.

2.3.4 Labelling

2.3.4.1 Statement of ingredients

Standard 1.2.4 – Information requirements – statement of ingredients requires food for sale to be labelled with a statement of ingredients unless exempt. The label on a package of infant formula products and FSFYC must contain a statement of ingredients. Should manufacturers choose to add 2′-FL alone or combined with LNnT to these foods, then these substances will be required to be declared in the statement of ingredients.

Generic ingredient labelling provisions in section 1.2.4—4 require ingredients to be identified using a name by which they are commonly known, or a name that describes its true nature, or a generic ingredient name if one is specified in Schedule 10 – Generic names of ingredients and conditions for their use.

At 1st Call for Submissions, FSANZ proposed prescribing ingredient names for infant formula products and FSFYC to achieve a consistent and uniform disclosure of these ingredients for both product categories. We noted that infant formula products would already be prohibited from using terms such as 'human milk identical oligosaccharide' for ingredients under section 2.9.1—24 (Prohibited representations). Following consideration of submissions to the 1st Call for Submissions, FSANZ reconsidered the approach to prescribe ingredient names and proposed that generic ingredient naming requirements apply, consistent with the general approach in the Code. The approach taken by FSANZ addresses concerns from submitters to the 1st Call for Submissions about the use of terms such as 'human milk identical oligosaccharide' or 'HiMO' by proposing a specific prohibition as discussed below in section 2.3.4.3. There is no prescription in the Code for the naming of other ingredients (including nutritive substances) currently permitted to be added to infant formula products and FSFYC. The revised approach will provide the flexibility sought by industry in how they declare these ingredients (for example, using '2-fucosyllactose' and 'lacto-N-neotetraose', which aligns with the EU approach and was originally suggested by the applicant refer to section F1 of the Application).

At 2nd Call for Submissions, submitters from industry and one jurisdiction supported the revised approach for the declaration of ingredient names. No submitters opposed this approach.

2.3.4.2 Mandatory nutrition information

For infant formula products, section 2.9.1—21 regulates the declaration of nutrition information in a nutrition information statement on the label. The nutrition information statement is a single statement and may be in the form of a table, as indicated in section S29—10 – Guidelines for infant formula products.

Paragraph 2.9.1—21(1)(iii) requires the average amount of each vitamin and mineral and any other substance *used as a nutritive substance* permitted by the standard to be declared in the nutrition information statement. As both 2′-FL and LNnT are permitted to be *used as a nutritive substance* in infant formula products, they must be declared in the nutrition information statement when they are used.

For FSFYC, the existing general requirements in Standard 1.2.8 – Nutrition information requirements apply. That is, the addition of 2′-FL alone or with LNnT to FSFYC as ingredients, would not trigger a mandatory declaration in the nutrition information panel (NIP) unless a claim requiring nutrition information (a nutrition content claim or a health claim) is made.

When a nutrition content claim is made, the property of the food that is the subject of the claim dictates how the declaration should be made in the NIP. For example, if a nutrition content claim about dietary fibre is made for 2′-FL or LNnT, the NIP must include a declaration of the presence of dietary fibre in accordance with section 1.2.8—6(5).

FSANZ has considered how 2′-FL and LNnT will be declared in the context of existing nutrition information requirements (this section) and determined ingredient names will not be prescribed (see section 2.3.4.1). This will mean that the use of acronyms (e.g. 2′-FL or LNnT) or the general term oligosaccharide are not prohibited on infant formula products or FSFYC. However, manufacturers will be prohibited from using the terms ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide’ or abbreviations of these (or words or abbreviations having the same or similar effect) when making a mandatory nutrition declaration for an infant formula product or a FSFYC (when a voluntary claim is made for the latter) (see section 2.3.4.3).

2.3.4.3 Prohibited representations

Infant formula products

The approval of 2′-FL and LNnT is on the condition that references to ‘human milk identical oligosaccharide’, ‘human milk oligosaccharide’, ‘HiMO’ or ‘HMO’ (or words or abbreviations of similar effect) on infant formula products are prohibited. These restrictions were introduced in response to concerns raised in submissions to the 1st Call for Submissions report. The permitted approach provides flexibility for declaration of ingredients and nutrition information as their full chemical name, the abbreviated chemical name/acronym or the generic term ‘oligosaccharides’ can all be used.

While the intent of section 2.9.1—24 (Prohibited representations) is to prevent the use of such terms on infant formula product labels, FSANZ considers the prohibition clearly communicates that such terminology is inconsistent with the Ministerial Policy Guideline on the Regulation of Infant Formula Products (Policy Principle (*I*)).

The restrictions:

- are consistent with the World Health Organization International Code of Marketing of Breast Milk Substitutes as implemented in Australia and New Zealand

- ensure that the products cannot be represented as an equivalent to, or better than, breast milk
- reinforce the prohibition on claims for infant formula products.

Formulated supplementary foods for young children

In the 2nd Call for Submissions, FSANZ proposed to permit the use of 2′-FL and LNnT in FSFYC on the condition that the terminology 'human milk identical oligosaccharide', 'human milk oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) is prohibited on FSFYC labels. This approach was based on consumer evidence, specifically:

- potential confusion for consumers if the terms are present on FSFYC labels but are not present on the labels of infant formula products
- the potential for consumers to be misled, whereby the presence of these terms on FSFYC labels may infer FSFYC is intended for infant consumption (FSFYC are not considered breast milk substitutes in Australia and New Zealand)
- some evidence that caregivers interpret references to breast milk on infant formula products as an indication those particular products are closer in composition to breast milk than other brands
- research suggests that when caregivers are shown toddler milk advertisements they believe they are also advertising infant formula products
- concern is that caregivers may see a reference to 'human milk identical oligosaccharide' on a toddler milk but believe they saw the phrase on an infant formula product.

FSANZ also noted that as section 2.9.1—24 prohibits terms *'humanised' or 'maternalised' or any word or words having the same or similar effect and information relating to the nutritional content of human milk* on infant formula product labels, the presence of these terms on FSFYC could imply substantive equivalence with breast milk. Identifying ingredients on FSFYC labels using such terms is highly likely to have the same effect on consumer understanding as statements or claims that refer to breast milk.

Industry submitters to the 2nd Call for Submissions expressed concern that a labelling restriction on the terms that can be used is inconsistent with the current Code approach that enables flexibility. These submitters also considered the restricted approach for 2′-FL and LNnT is setting a new policy direction. However, FSANZ notes the Code already contains examples of limitations placed on voluntary representations (for example, restrictions on representations of low alcohol, of the words 'non-intoxicating' and that a food containing alcohol is non-alcoholic). These restrictions are in place to reduce the risk of misleading consumers. When assessing 'risk' FSANZ considers the potential for risk as well as the evidence for risk in the context of the current environment, situation and relevant issues including possible effects on consumers and the community. FSANZ also notes that the approach provides flexibility as the options include use of the full chemical name, the abbreviated chemical name/acronym or the generic term 'oligosaccharides'.

Additional consumer evidence considered by FSANZ

As previously noted by FSANZ there is some research indicating caregivers may interpret references about breast milk on infant formula as suggesting those products are close in composition to breast milk (Malek et al. 2019; Parry et al 2013).

Research conducted examining advertisements for FSFYC has found similar responses concerning references to breast milk. Some consumers who saw a claim about prebiotics 'found naturally in breast milk' next to a statement concerning the importance of breastfeeding, believed the advertisement suggested an equivalence between 'formula' and breast milk (Berry, Jones & Iverson, 2010). This concern is relevant to FSFYC as the qualitative Australian research suggests when pregnant women and caregivers are shown toddler milk advertisements, they believe such adverts also advertise infant and follow-on formula products (Berry, Jones & Iverson, 2010, 2011, 2012). This is partly attributed to similar packaging and common branding across a product line, as has been noted by researchers internationally and within marketing literature (Food Standards Agency, 2010; Pomerannz et al 2018; Champeny et al 2019; Clifton, Simmons & Ahmed, 2004).

FSANZ acknowledges that there are limitations of qualitative research using focus groups. Their purpose is to understand and explain the breadth of caregiver perceptions, rather than quantify the prevalence of these perceptions and behaviours. In the case of the focus group studies discussed above, they offer insight and opportunity to explore consumer reactions to particular product labels or advertising material across a diversity of research participants. Accordingly, the focus group studies above contain heterogeneous samples allowing for greater breadth and depth of caregiver views and experiences to be collected.

The findings from qualitative studies are supported by international research. Studies in Hong Kong and Italy examining recent or expecting mothers' interpretations of toddler milk advertising found that marketed FSFYC products are perceived as being infant and follow-on formula products (Department of Hong Kong SAR Government, 2013, Cattaneo et al, 2014). Of note, in Italy where the advertisement of infant formula is strictly prohibited, only 17 out of 455 mothers reported they had never seen an advertisement for six infant formula products presented to them in a survey. Two hundred and ninety seven of the mothers who had reported seeing an advert for a formula product believed it advertised a product to be used from birth (infant formula). The finding suggests that advertising of later stage formula products may be perceived as infant formula by users of formula products.

The implication of this is that where FSFYC product labels carry references to human milk, some caregivers may infer infant formula and follow-on formula within the same brand range are closer in composition to breast milk. Furthermore, it is possible that caregivers who believe an infant formula product is closer in composition to breast milk may be more likely to use infant formula in place of, or in addition, to breastfeeding (Malek et al. 2019)

Summary

FSANZ has determined that the decision to prohibit terms such as 'human milk identical oligosaccharide' on FSFYC labels is supported by the best available consumer evidence. The approach also aligns with labelling approaches in other countries such as the EU and Singapore (refer to section 1.3.2.3). The ingredients 2′-FL and LNnT will be prohibited from the use of the terms 'human milk identical oligosaccharide', 'human milk oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) anywhere on FSFYC labels, although the general term oligosaccharide can be used.

2.3.4.4 Voluntary representations

Subsection 1.2.7—4(b) of Standard 1.2.7 states that a nutrition content claim or health claim must not be made about an infant formula product. The prohibition is also set out in section 2.9.1—24(1)(f) of Standard 2.9.1, which prohibits a reference to the presence of a nutrient or substance that may be used as a nutritive substance, except for a statement relating to lactose, a statement of ingredients or a declaration of nutrition information.

The existing prohibition for nutrition content claims and health claims for infant formula products will apply to 2′-FL and LNnT. Inclusion of these substances in the nutrition information statement will not be captured as nutrition content claims by virtue of their mandatory declaration as requirements in paragraph 2.9.1—24(1)(f) of the Code.

As noted at 2nd Call for Submissions, nutrition content claims and health claims can be made about FSFYC if they meet existing claim requirements and conditions set out in Standard 1.2.7 and Schedule 4 – Nutrition, health and related claims (for example, a nutrition content claim about 2-fucosyllactose). FSANZ notes that any health claims would either have to be applied for separately (for addition to Schedule 4), or be substantiated through a systematic review in accordance with Schedule 6.

The prohibition of terms such as 'human milk identical oligosaccharide' or abbreviations such as 'HiMO' will mean they cannot be used in the wording of a nutrition content or health claim for FSFYC. The term oligosaccharide can be used.

2.3.4.5 Trade marks

One jurisdiction submitter expressed concern that ingredient names may be trade marked to circumvent the claim requirements and claim prohibitions in the Code. Trade marks are regulated by the Australian *Trade Marks Act 1995* (Cth) and the New Zealand *Trade Marks Act 2002*; hence trade marks are out of scope of the Code. In Australia, IP Australia consider existing legislation (including Code requirements which are enabled by Food Acts) when assessing trade mark applications. The Registrar is required to examine an application for a trade mark and report on whether there are grounds under the Trade Marks Act for rejecting the trade mark. The Trade Marks Act requires a trade mark to be rejected if its use would be contrary to law. In New Zealand, IPONZ follow similar processes under the New Zealand Trade Marks Act.

2.3.4.6 Labelling as 'genetically modified'

The ingredients 2′-FL and LNnT are highly unlikely to contain novel protein or DNA due to the purification step used in the production of these oligosaccharides. It is therefore highly unlikely that novel protein will be present in an infant formula product or FSFYC that contains 2′-FL or LNnT as ingredients. However, where novel protein is present, the requirement to label 2′-FL or LNnT as 'genetically modified' will apply in accordance with section 1.5.2—4 of Standard 1.5.2.

2.3.5 Specifications for 2′-FL and LNnT

Subsection 1.1.1—15(2) of the Code requires that a substance used as a food additive (paragraph 1.1.1—15(1)(a)) must comply with a relevant specification in Schedule 3 – Identity and purity. FSANZ has set specifications for 2′-FL and LNnT in the Code using those provided by the applicant (without specifying the methods of analysis).

2.3.6 International harmonisation

The proposed permission also supports international consistency and a competitive food industry (high order policy principles 2(b) and (c)), providing trade opportunities. It also provides alternative options to existing inulin-type fructans (ITF) and galacto-oligosaccharides (GOS) permitted at higher levels in infant formula products, providing product innovation opportunities (see sections 2.5.1.1 and 2.5.3).

As there different approaches to labelling internationally, it is not possible to be completely harmonised. FSANZ considers that the restrictions on use of the terms 'human milk identical oligosaccharide' align with the approach taken in a number of countries thus supports international consistency.

2.3.7 Exclusivity

An applicant may request exclusive permission for a period of 15 months to recognise the investment made in developing the food or ingredient or nutritive substance and the need to achieve return on this investment, thereby supporting innovation. The applicant has requested exclusivity for their specific brand of 2′-FL and LNnT[19] on the basis that they, and their business partners, have invested significantly in the technology development and safety studies.

FSANZ has provided 15 months exclusivity from the date of gazettal, linked to the applicant's brand of 2′-FL and LNnT. FSANZ has conducted a GM safety assessment for the source organisms and gene-gene donor combinations specific to this application, thus the permission and exclusivity is linked to the specific gene-gene donor information as assessed by FSANZ and is located in Schedule 26. Any modifications to this gene-gene donor information would require an application for assessment and approval. This could mean that a number of 2′-FL approvals, linked to different gene-gene donor information, may be listed in Schedule 26 in the future. Following the 15 month period, the permission will revert to a general approval for the class of food.

An exclusivity permission in the Code does not, and cannot, prevent approval of second or subsequent applications either within the exclusive use period or during the progression of an application, for the use of the same food or ingredient by other food companies, providing the application process is undertaken.

2.3.8 Conclusion

FSANZ assessed the applicant's request for use of 2′-FL and LNnT in infant formula and FSFYC by assessing the evidence for safety and health effects.

FSANZ has considered all aspects of the assessment against all of the statutory requirements in accordance with Section 18 of the Act. The approach has given regard to the best available science, international consistency and industry trade and competition (high level principles in the ministerial policy guideline) as well as to the relevant policy guidelines in accordance with subsection 18(2) of the Act.

FSANZ concluded that the permission promotes consistency between domestic and international food standards and supports an efficient and internationally competitive food industry as many countries already permit the use of 2′-FL and LNnT in these products. The permission for use of 2′-FL and LNnT to be (i) *used as a nutritive substance*, and (ii) as *food produced using gene technology* for use in infant formula products and FSFYC supports international consistency and trade opportunities, and provides alternative options to existing oligosaccharides (GOS and ITF) permitted for use in FSFYC which provides product innovation opportunities.

Having considered the submissions and weighed all aspects of the assessment against all of the statutory requirements FSANZ approved a draft variation to the Code.

[19] Brand name GlyCare.

2.3.9 Summary of the regulatory measures

To permit both 2′-FL with or without LNnT to be *used as a nutritive substance*, and also as *food produced using gene technology* linked to the gene-gene donor information specific to the production of the oligosaccharides, for use in infant formula products and FSFYC

At the following maximum levels

Infant formula products:

- If only 2′-FL added – not more than 96 mg/100 kJ of 2′-FL (equivalent to 2.4 g/L)
- If both 2′-FL and LNnT added – not more than 96 mg/100 kJ of 2′-FL and LNnT combined (equivalent to 2.4 g/L), of which contains not more than 24 mg/100 kJ of LNnT (equivalent to 0.6 g/L).

FSFYC:

- If only 2′-FL added – not more than 0.55 g/serving (equivalent to 2.4 g/L)
- If both 2′-FL and LNnT added – not more than 0.55 g/serving of 2′-FL and LNnT combined, of which contains not more than 0.14 g/serving of LNnT (equivalent to 0.6 g/L).

- Prohibit the use of 2′-FL alone or with LNnT in combination with existing permissions for GOS and ITF for infant formula products and FSFYC (i.e. permissions for 2′-FL and LNnT would be used as alternatives to GOS and ITF).

- Prohibit the following terms on the label of infant formula products and FSFYC:
  - the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect
  - the abbreviations ‘HMO’ or ‘HiMO’ or any abbreviation having the same or similar effect.

- Set specifications for 2′-FL and LNnT based on the specifications provided by the applicant (without specific methods of analysis).

- Provide 15 months exclusivity from the date of gazettal of the variation for the applicant’s brand’s of 2′-FL and LNnT.

2.4 Risk communication

2.4.1 Consultation

Consultation is a key part of FSANZ’s standards development process. FSANZ developed a communication strategy for this application. Subscribers and interested parties were notified about public consultation periods via the FSANZ Notification Circular, media release and through FSANZ’s social media tools and Food Standards News.

FSANZ sought submissions to its preliminary position in the 1st CFS from 22 November 2018 – 17 January 2019. 12 submissions were received.

FSANZ sought submissions to the proposed draft variation in the 2nd CFS from 22 July 2019 – 2 September 2019. 20 submissions were received.

FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application. All comments are valued and contributed to the rigour of our assessment.

2.4.1.1 Targeted consultation

FSANZ undertook targeted consultation with the applicant and with jurisdictions in May 2019 to discuss FSANZ's preliminary position at 1st CFS and issues raised in submissions. FSANZ has considered the issues discussed in targeted consultations in its assessment.

2.4.2 World Trade Organization (WTO)

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

There are relevant overseas standards and amending the Code to permit the addition of 2′-FL alone or with LNnT to infant formula products and FSFYC as proposed is unlikely to have a significant effect on international trade as these substances are already permitted in similar products in some countries overseas. The proposed permission in the Code may provide some trade opportunities. Therefore, a notification to the WTO under Australia's and New Zealand's obligations under the WTO Technical Barriers to Trade or Application of Sanitary and Phytosanitary Measures Agreement was not considered necessary.

2.5 FSANZ Act assessment requirements

2.5.1 Section 29

2.5.1.1 Consideration of costs and benefits

The direct and indirect benefits that would arise from a food regulatory measure developed or varied as a result of the application outweigh the costs to the community, Government or industry that would arise from the development or variation of the food regulatory measure.

The Office of Best Practice Regulation (OBPR) exempted FSANZ from the need to undertake a formal Regulation Impact Statement (RIS) in relation to the regulatory change proposed in response to this application (OBPR correspondence dated 1 February 2018, reference 23349). This was due to OPBR being satisfied that the requested variation is voluntary and deregulatory and likely to have only a minor effect on consumers, businesses, and government.

FSANZ, however, has given consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act considerations.
The FSANZ Act requires FSANZ to have regard to whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the community, government or industry that would arise from the proposed measure (S29(2)(a)).

The purpose of this consideration is to determine if the community, government, and industry as a whole is likely to benefit, on balance, from a move away from the status quo. This analysis considered approving the addition of 2′-FL alone or combined with LNnT to infant formula products and FSFYC as proposed in the draft variation. A consideration of costs and benefits was included in the 1st CFS report based on the information and data held at that time. Information received from some industry stakeholders has led to the consideration of costs and benefits to be revised since the 1st CFS.

The consideration of the costs and benefits in this section is not intended to be an exhaustive, quantitative economic analysis of the proposed measures and, in fact, most of the effects that were considered cannot easily be assigned a dollar value. Rather, the

assessment seeks to highlight the likely positives and negatives of moving away from the status quo by permitting the voluntary addition of 2′-FL alone, or in combination with LNnT, to infant formula products and FSFYC as proposed in the variation.

Costs and benefits of permitting 2′-FL and LNnT as proposed

The use of 2′-FL and LNnT in infant formula products and FSFYC as proposed will not pose a health or safety risk for consumers. These substances are chemically and structurally identical to those naturally present in human milk.

The proposed permission may provide potential beneficial health outcomes for infants and toddlers. Consumers may therefore benefit from the choice of infant formula products and FSFYC containing the applicant's 2′-FL alone or with LNnT that become available.
As discussed in section 2.3.1, the evidence for 2′-FL supports the biological and mechanistic plausibility of an inhibitory effect against invasive *C. jejuni* infection. Evidence also supports a bifidogenic effect from the use of 2′-FL alone or combined with LNnT.

As the proposed permission is voluntary, industry will use 2′-FL alone or in combination with LNnT in infant formula products and FSFYC only where they believe a net benefit exists for themselves. Industry will benefit from having alternative options available to existing permitted oligosaccharides GOS and ITF providing product innovation opportunities.

The applicant's 2′-FL and LNnT is permitted for use in infant formula products and FSFYC in some overseas countries including the EU and US. The proposed permission will enable Australian and New Zealand industries to access and use ingredients that are available to their overseas competitors, which may provide trade opportunities.

FSANZ has received feedback from some industry noting that a significant portion of Australia and New Zealand's infant formula revenue is derived from exports.
In New Zealand, infant formula exports were valued at around NZ$1.1 billion in 2017/2018 (NZIER, 2018). In Australia, China is the largest dairy export market (by volume and value). In 2017/18, 'infant powder' was the top Australian dairy export to China by value (USD$325 million), with the volume of exports growing by 614% from 2013/14 to 2017/18 (Dairy Australia, 2018). CBEC (cross border e-commerce) trade into China is governed by the regulations of the market of origin. Approving the use of 2′-FL and LNnT as proposed will potentially allow Australia and New Zealand industries to better compete with overseas businesses in the CBEC Chinese market that have access to and use these ingredients. Facilitating trade opportunities may lead to flow-on economic and employment benefits to Australia and New Zealand.

The proposed permission could also result in competing imports from overseas markets into Australia and New Zealand.

Conclusion from cost benefit considerations

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting the voluntary addition of 2′-FL and LNnT in the manner proposed are likely to outweigh the associated costs.

2.5.1.2 Other measures

There are no other measures (whether available to FSANZ or not) that would be more cost-effective than a food regulatory measure developed or varied as a result of the application.

2.5.1.3 Any relevant New Zealand standards

There are no relevant New Zealand Standards.

2.5.1.4 Any other relevant matters

Other relevant matters are considered below.

2.5.2. Subsection 18(1)

FSANZ has also considered the three objectives in subsection 18(1) of the FSANZ Act during the assessment.

2.5.2.1 Protection of public health and safety

FSANZ completed a safety, technical and health effects assessment (SD1 of the 2nd CFS) which is summarised in section 2.2. The assessment concluded that there are no public health and safety concerns associated with the addition of 2′-FL alone or in combination with LNnT to infant formula products and FSFYC at dietary intakes based on 2.4 g/L 2′-FL (of which 0.6 g/L is LNnT).

2.5.2.2 The provision of adequate information relating to food to enable consumers to make informed choices

Current labelling requirements apply to 2′-FL and LNnT when added to infant formula or FSFYC, as discussed in section 2.3.4, which provides information to enable consumers make an informed choice.

2.5.2.3 The prevention of misleading or deceptive conduct

Current labelling requirements which aim to prevent misleading or deceptive conduct, apply to 2′-FL and LNnT when added to infant formula or FSFYC. In addition, a specific prohibition of terms such as ‘human milk identical oligosaccharide’ and ‘HiMO’ is intended to prevent consumers from being misled about the equivalency of infant formula products and FSFYC with breast milk (see section 2.3.4.3).

2.5.3 Subsection 18(2) considerations

FSANZ has also had regard to:

- **the need for standards to be based on risk analysis using the best available scientific evidence**

FSANZ has used the risk analysis framework and considered the best available evidence to reach its conclusion. The applicant submitted a dossier of scientific studies as part of its application. Other relevant information including scientific literature was also identified through a literature review and used in assessing the application. During the assessment the applicant was asked to provide any additional available evidence to support the application. This was to ensure the assessment was based on the best available evidence.

- **the promotion of consistency between domestic and international food standards**

FSANZ has considered the promotion of consistency between domestic and international food standards and the desirability of an efficient and internationally competitive food industry. As discussed in section 1.3.2, these oligosaccharides are permitted for use in infant formula products and formulated supplementary foods for young children in at least 37 other countries around the world at a range of levels and with different labelling requirements. FSANZ considers that the permission to add these oligosaccharides will promote consistency between domestic and international food standards. FSANZ also considers that the labelling prohibitions are consistent with the labelling requirements of a number of countries. Product imported into Australia and New Zealand is required to be compliant with the Code.

- **the desirability of an efficient and internationally competitive food industry**

The proposed permission would support an internationally competitive food industry in relation to the addition of 2′-FL and LNnT to infant formula products and FSFYC.

- **the promotion of fair trading in food**

No negative impact is anticipated on fair trading.

- **any written policy guidelines formulated by the Forum on Food Regulation**

Two Ministerial Policy Guidelines apply to this application:

- Regulation of Infant Formula Products
- Intent of Part 2.9 – Special Purpose Foods

As discussed in section 2.3.3, FSANZ considers these policy guidelines have been adequately addressed. Our assessment against the policy guidelines is also provided in SD2 at 2nd CFS.

Attachments

A. Approved draft variations to the *Australia New Zealand Food Standards Code*
B. Explanatory Statement

3 References

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Attachment A – Approved draft variations to the *Australia New Zealand Food Standards Code*

Food Standards (Application A1155 – 2′-FL and LNnT in infant formula and other products) Variation

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by Delegate]

[Insert name of Delegate]
Delegate of the Board of Food Standards Australia New Zealand

Note:

This variation will be published in the Commonwealth of Australia Gazette No. FSC XX on XX Month 20XX. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

1 Name

This instrument is the *Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation*.

2 Variation to standards in the *Australia New Zealand Food Standards Code*

The Schedule varies Standards in the *Australia New Zealand Food Standards Code*.

3 Commencement

The variation commences on the date of gazettal.

Schedule

[1] Standard 2.9.1 is varied by

[1.1] omitting section 2.9.1—7, substituting

2.9.1—7 Restriction on addition to infant formula product of inulin-type fructans and galacto-oligosaccharides

(1) If an inulin-type fructan or a galacto-oligosaccharide is added to an infant formula product, the product must contain (taking into account both the naturally-occurring and added substances) no more than:

(a) if only *inulin-type fructans are added—110 mg/100 kJ of inulin-type fructans; or

(b) if only *galacto-oligosaccharides are added—290 mg/100 kJ of galacto-oligosaccharides; or

(c) if both inulin-type fructans and galacto-oligosaccharides are added:

(i) no more than 110 mg/100 kJ of inulin-type fructans; and

(ii) no more than 290 mg/100 kJ of combined inulin-type fructans and galacto-oligosaccharides.

(2) An infant formula product to which an inulin-type fructan or a galacto-oligosaccharide is added must not contain any of the following added substances:

(a) 2′-O-fucosyllactose; or

(b) a combination of 2′-O-fucosyllactose and lacto-N-neotetraose.

[1.2] inserting after paragraph 2.9.1—24(1)(c)

(ca) the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect; or

(cb) the abbreviations ‘HMO’ or HiMO’ or any abbreviation having the same or similar effect; or

[2] Standard 2.9.3 is varied by

[2.1] inserting after subsection 2.9.3—7(2)

(2A) A substance listed in Column 1 of the table to section S29—15A may be *used as a nutritive substance in a formulated supplementary food for young children if:

(a) the substance is in a permitted form listed in Column 2 of the table; and

(b) the amount of the substance in the food (including any naturally-occurring amount) is no more than the corresponding amount listed in Column 3 of the table.

[2.2] omitting subsection 2.9.2—7(3), substituting

(3) If *inulin-type fructans or *galacto-oligosaccharides are added to a formulated supplementary food for young children:

(a) the total amount of those substances, both added and naturally occurring, must not be more than 1.6 g/serving; and

(b) the food must not contain any of the following added substances:

(i) 2′-O-fucosyllactose; or

(ii) a combination of 2′-O-fucosyllactose and lacto-N-neotetraose.

[2.3] omitting subsection 2.9.3—7(4)

[2.4] omitting subsection 2.9.3—8(6), substituting

(6) The label on a package of a formulated supplementary food for young children must not contain:

(a) the words ‘human milk oligosaccharide’ or ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect; or

(b) the abbreviations ‘HMO’ or HiMO’ or any abbreviation having the same or similar effect; or

(c) any words indicating, or any other indication, that the product contains lutein unless the total amount of lutein is no less than 30 µg/serving.

[3] **Schedule 2** is varied by inserting in the table to section S2—2, in alphabetical order

EU/mg	Endotoxin units per milligram

[4] **Schedule 3** is varied by

[4.1] inserting in the table to subsection S3—2(2) in alphabetical order

2′-O-fucosyllactose	section S3—40

[4.2] inserting in the table to subsection S3—2(2) in alphabetical order

lacto-N-neotetraose	section S3—41

[4.3] inserting after subsection S3—39

S3—40 Specification for *2′*-O-fucosyllactose

For 2′-O-fucosyllactose (2′-FL), the specifications are the following:

(a) chemical name—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-D-glucopyranose;

(b) chemical formula—$C_{18}H_{32}O_{15}$;

(c) CAS number—41263-94-9;

(d) description— white to off white powder or agglomerates;

(e) assay (water free) for sum of 2′-FL, lactose, difucosyllactose and fucose—not less than 96.0%;

(f) assay (water free) 2′-FL—not less than 94.0%;

(g) D-lactose—not more than 3.0%

(h) L-fucose—not more than 1.0%

(i) difucosyllactose—not more than 1.0%

(j) 2′-fucosyl-D-lactulose—not more than 1.0%

(k) pH (20°C, 5% solution)—3.2 to 5.0

(l) water—not more than 5.0%

(m) ash, sulphated—not more than 1.5%

(n) acetic acid (as free acid and/or sodium acetate)—not more than 1.0%

(o) residual proteins—not more than 0.01%

(p) lead—not more than 0.1 mg/kg

(q) microbiological:

(i) *salmonella*—absent in 25 g

(ii) total plate count—not more than 500 cfu/g

(iii) enterobacteriaceae—–absent in 10 g
(iv) *cronobacter (Enterobacter) sakazakii*—–absent in 10 g
(v) *listeria monocytogenes*—–absent in 25 g
(vi) *bacillus cereus*—–not more than 50 cfu/g
(vii) yeasts—–not more than 10 cfu/g
(viii) moulds—–not more than 10 cfu/g
(ix) residual endotoxins—–not more than 10 EU/mg

S3—41 Specification for lacto-N-neotetraose

For lacto-N-neotetraose (LNnT), the specifications are the following:

(a) chemical name—–β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-glucopyranose
(b) chemical formula—–$C_{26}H_{45}NO_{21}$
(c) CAS number—–13007-32-4
(d) description—–white to off white powder or agglomerates
(e) assay (water free) for sum of LNnT, lactose, lacto-N-triose II, and *para*-lacto-N-hexaose—–not less than 95.0%
(f) assay (water free) LNnT—–not less than 92.0%
(g) D-lactose—–not more than 3.0%
(h) lacto-N-triose II—–not more than 3.0%
(i) *para*-lacto-N-neohexaose—–not more than 3.0%
(j) LNnT fructose isomer—–not more than 1.0%
(k) pH (20°C, 5% solution) —–4.0 to 7.0
(l) water—–not more than 9.0%
(m) ash, sulphated—–not more than 1.5%
(n) methanol—–not more than 100 mg/kg
(o) residual proteins—–not more than 0.01%
(p) lead—–not more than 0.1 mg/kg
(q) microbiological:
  (i) *salmonella*—–absent in 25 g
  (ii) total plate count—–not more than 500 cfu/g
  (iii) enterobacteriaceae—–absent in 10 g
  (iv) *cronobacter (Enterobacter) sakazakii*—–absent in 10 g
  (v) *listeria monocytogenes*—–absent in 25 g
  (vi) *bacillus cereus*—–not more than 50 cfu/g
  (vii) yeasts—–not more than 10 cfu/g
  (viii) moulds—–not more than 10 cfu/g
  (ix) residual endotoxins—–not more than 10 EU/mg

[5] Schedule 26 is varied by

[5.1] omitting subsections S26—3(1), (2), (2A), and (3), substituting

(1) The table to subsection (4) and the table to subsection (7) list permitted food produced using gene technology.

(2) Items 1(g), 2(m), 7(e), (g) and (h), and 9(a) of the table to subsection (4) are subject to the condition that their labelling must comply with section 1.5.2—4.

Note That section requires the statement 'genetically modified'.

(2A) Products containing beta-carotene from item 6(b) of the table to subsection (4) are subject to the condition that their labelling must comply with section 1.5.2—4.

(3) Item 2(m) of the table to subsection (4) is also subject to the condition that, for the labelling provisions, unless the protein content has been removed as part of a

refining process, the information relating to *foods produced using gene technology includes a statement to the effect that the high lysine corn line LY038 has been genetically modified to contain increased levels of lysine.

[5.2] omitting the words 'gene technology' from the heading to the table to subsection (4), substituting the words' 'gene technology of plant origin'.

[5.3] inserting after the table to subsection (4)

(5) A food listed in the table to subsection (7) must comply with any corresponding conditions listed in that table.

(6) A source listed in the table to subsection (7) may contain additional copies of genes from the same strain.

(7) The table for this subsection is:

Food produced using gene technology of microbial origin

Substance	*Source*	*Conditions of use*
1 2′-O-fucosyllactose	(a) *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*	1. May only be added to infant formula products and to formulated supplementary food for young children. 2. During the exclusive use period, may only be sold under the brand GlyCare. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1155 – 2′-FL and LNnT in infant formula and other products) Variation* and ending 15 months after that date.
2 Lacto-N-neotetraose	(a) *Escherichia coli* K-12 containing the gene for beta-1,3-N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1,4-galactosyltransferase from *Helicobacter pylori*	1. May only be added to the following foods in combination with 2′-O-fucosyllactose that is permitted for use in infant formula products; and formulated supplementary food for young children. 2. During the exclusive use period, may only be sold under the brand GlyCare. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1155 – 2′-FL and LNnT in infant formula and other products) Variation* and ending 15 months after that date.

[6] **Schedule 29** is varied by

[6.1] omitting section S29—5, substituting

S29—5 Infant formula products—substances permitted as nutritive substances

For section 2.9.1—5, the table is set out below.

Infant formula products—substances permitted for use as nutritive substances

Column 1	*Column 2*	*Column 3*	*Column 4*
Substance	*Permitted forms*	*Minimum amount per 100 kJ*	*Maximum amount per 100 kJ*
2′-O-fucosyllactose permitted for use by Standard 1.5.2	2′-O-fucosyllactose		96 mg

Column 1	***Column 2***	***Column 3***	***Column 4***
Substance	*Permitted forms*	*Minimum amount per 100 kJ*	*Maximum amount per 100 kJ*
A combination of: 2′-O-fucosyllactose permitted for use by Standard 1.5.2; and lacto-N-neotetraose permitted for use by Standard 1.5.2	2′-O-fucosyllactose and lacto-N-neotetraose		96 mg which contains not more than 24 mg of lacto-N-neotetraose
Adenosine-5′-monophosphate	Adenosine-5′- monophosphate	0.14 mg	0.38 mg
L-carnitine	L-carnitine	0.21 mg	0.8 mg
Choline	Choline chloride	1.7 mg	7.1 mg
	Choline bitartrate		
Cytidine-5′-monophosphate	Cytidine-5′-monophosphate	0.22 mg	0.6 mg
Guanosine-5′-monophosphate	Guanosine-5′-monophosphate	0.04 mg	0.12 mg
	Guanosine-5′-monophosphate sodium salt		
Inosine-5′-monophosphate	Inosine-5′-monophosphate	0.08 mg	0.24 mg
	Inosine-5′-monophosphate sodium salt		
Lutein	Lutein from *Tagetes erecta L.*	1.5 µg	5 µg
Inositol	Inositol	1.0 mg	9.5 mg
Taurine	Taurine	0.8 mg	3 mg
Uridine-5′-monophosphate	Uridine-5′-monophosphate sodium salt	0.13 mg	0.42 mg

[6.2] inserting after section S29—15

S29—15A Formulated supplementary food for young children—other substances permitted as nutritive substances

For subsection 2.9.3—7(2A), the table is set out below.

Formulated supplementary food for young children—other substances permitted for use as nutritive substances

Column 1	***Column 2***	***Column 3***
Substance	*Permitted form*	*Maximum amount per serving*
2′-O-fucosyllactose permitted for use by Standard 1.5.2	2′-O-fucosyllactose	0.55 g
A combination of: 2′-O-fucosyllactose permitted for use by Standard 1.5.2; and lacto-N-neotetraose permitted for use by Standard 1.5.2	2′-O-fucosyllactose and lacto-N-neotetraose	0.55 g which contains not more than 0.14 g of lacto-N-neotetraose
Lutein	Lutein from *Tagetes erecta L.*	100 µg

Attachment B – Draft Explanatory Statement

1. Authority

Section 13 of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) provides that the functions of Food Standards Australia New Zealand (the Authority) include the development of standards and variations of standards for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

Division 1 of Part 3 of the FSANZ Act specifies that the Authority may accept applications for the development or variation of food regulatory measures, including standards. This Division also stipulates the procedure for considering an application for the development or variation of food regulatory measures.

FSANZ accepted application A1155 which sought to permit the voluntary addition of 2′-O-fucosyllactose (2′-FL) alone or in combination with Lacto-N-neotetraose (LNnT), produced by microbial fermentation, to infant formula products and formulated supplementary foods for young children (FSFYC). The Authority considered the Application in accordance with Division 1 of Part 3 and has approved a draft variation to the Code.

Following consideration by the Australia and New Zealand Ministerial Forum on Food Regulation, section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the standard or draft variation of a standard.

Section 94 of the FSANZ Act specifies that a standard, or a variation of a standard, in relation to which a notice is published under section 92 is a legislative instrument, but is not subject to parliamentary disallowance or sunsetting under the *Legislation Act 2003*.

2. Purpose

The Authority has prepared a draft variation to the Code to:

- Amend Schedule 26 to permit 2′-FL and LNnT derived from specific microbial sources for use in infant formula products and FSFYC; and to provide an exclusive use period of 15 months for the applicant's brand of 2′-FL and LNnT.
- Amend Schedule 29 to permit the same 2′-FL alone or combined with LNnT for use as nutritive substances in infant formula products and FSFYC, within specified maximum levels.
- Amend Standards 2.9.1 and 2.9.3 to prohibit certain representations (e.g. 'human milk identical oligosaccharide') on labels of infant formula products and FSFYC; and to prohibit the use of 2′-FL alone or with LNnT, in combination with existing permissions for ITF and GOS.
- Insert prescribed specifications for 2′-FL and LNnT into Schedule 3.
- Insert a new unit of measure, as used in the prescribed specifications, in Schedule 2.

3. Documents incorporated by reference

The variations to food regulatory measures do not incorporate any documents by reference.

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of application A1155 included two rounds of public comment following an assessment and the preparation of a draft variation and associated assessment summaries.

Submissions were first called for on 22 November 2018 for a six week consultation period. Submissions on a proposed draft variation were sought on 22 July 2019 for a six week consultation period.

A Regulation Impact Statement was not required because the proposed variations to Standards 2.9.1 and 2.9.3 and Schedules 2, 3, 26 and 29 are likely to have a minor impact on business and individuals (OBPR ID 23349).

5. Statement of compatibility with human rights

This instrument is exempt from the requirements for a statement of compatibility with human rights as it is a non-disallowable instrument under section 94 of the FSANZ Act.

6. Variation

Item [1]

Item [1.1] varies Standard 2.9.1 by omitting the existing section 2.9.1—7 and substituting a new subsection. The new subsection restates the permitted quantities of ITF and GOS in the current subsection, and includes a new requirement which will prohibit an infant formula product to which ITF or GOS are added, from containing 2′-FL alone, or a combination of 2′-FL and LNnT.

Item [1.2] varies Standard 2.9.1 by inserting new subparagraphs 2.9.1—24(1)(ca) and (cb). These new subparagraphs will prohibit the use of the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide (or any word or words of similar effect), and the use of abbreviations ‘HMO’ or ‘HiMO’ (or any abbreviation having the same or similar effect), on the label on a package of infant formula product (i.e. not used in associated with ‘human milk’ or ‘human milk identical’) on the label on a package of an infant formula product.

Item [2]

Item [2.1] varies Standard 2.9.3 by inserting a new subsection 2.9.3—7(2A). The effect of this new subsection is to permit substances listed in a new table in section S29—15A in Schedule 29 to be *used as a nutritive substance* in FSFYC (see Item 6.2 below), providing the substance meets the permitted form and maximum levels set in this table. 2′-FL alone, and 2′-FL and LNnT combined, are listed in the new table.

Item [2.2] varies Standard 2.9.3 by omitting the existing subsection 2.9.3—7(3) and substituting a new subsection. The new subsection restates the permitted quantity of ITF and GOS in the current subsection, and includes a new requirement which will prohibit FSFYC to which ITF or GOS are added, from containing 2′-FL alone, or a combination of 2′-FL and LNnT.

Item [2.3] varies Standard 2.9.3 by omitting subsection 2.9.3—7(4) relating to the permission for lutein to be *used as a nutritive substance.* This permission is relocated to the new table in section S29—15A in Schedule 29 (see Item [2.1] above and Item 6.2 below). This amendment does not change the existing permission and associated conditions for the use of lutein in FSFYC, it only relocates the permission.

Item [2.4] varies Standard 2.9.3 by omitting subsection 2.9.3—8(6) and substituting a new subsection. The new subsection restates the labelling restriction relating to lutein, and includes a new requirement which will prohibit use of the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide (or any word or words of similar effect), and the use of abbreviations ‘HMO’ or ‘HiMO’ (or any abbreviation having the same

or similar effect), on the label on a package of FSFYC. This amendment is not intended to prohibit the use of the term ‘oligosaccharide’ on its own (i.e. not used in associated with ‘human milk’ or ‘human milk identical’) on the label on a package of FSFYC.

Item [3]

Item [3] varies Schedule 2 to insert a new unit of measurement EU/mg (endotoxin unit per milligram), as used in the new specifications in Schedule 3 (see Item [4] below).

Item [4]

Item [4] varies Schedule 3 to insert new specifications for 2′-FL (new section S3—40) and LNnT (new section S3—41).

Item [5]

Item [5] varies Schedule 26 to insert a new table under a new subsection (7) with the heading *Food produced using gene technology of microbial origin*. This new table lists 2′-FL and LNnT from permitted microbial sources. This amendment will not amend the existing approvals currently listed in the table to subsection (4), or change the requirements for pre-market assessment and approval of GM foods. The detailed amendments made to this Schedule are discussed below.

Item [5.1] omits subsections 26—3(1), (2), (2A) and (3) and substitutes a new subsection. New subsection (1) specifies that the existing table to subsection (4) and the new table to subsection (7) lists permitted food produced using gene technology. New subsections (2), (2A) and (3) restate the existing labelling requirements, but now specify that these apply to the existing table to subsection (4).

Item [5.2] omits the words ‘gene technology’ from the heading of the existing table to subsection (4) and replaces this with the words ‘gene technology of plant origin’ (i.e. the full table heading will now be *Food produced using gene technology of plant origin*). This amendment clarifies that permissions in the existing table to subsection (4) relate to food of plant origin, to distinguish these from the new permissions for 2′-FL and LNnT which are food of microbial origin (new table to subsection (7)).

Item [5.3] inserts new subsections 26—3(5), (6) and (7). Subsection (7) inserts a new table (*Food produced using gene technology of microbial origin*) which lists 2′-FL and LNnT sourced from specific gene-gene donor information. Subsections (5) and (6) require that a food listed in this new table must comply with any corresponding conditions listed in the table, and that the source listed in the table may contain additional copies of genes from the same strain. The new table includes the condition that 2′-FL and LNnT are only permitted to be added to infant formula products and FSFYC. It also includes the condition that, during the ‘exclusive use period’, 2′-FL and LNnT from the permitted source listed may only be sold under the brand name ‘GlyCare’. ‘Exclusive use period’ is defined to be the period commencing on the date of gazettal of the variation, and ending 15 months after that date. This means that the new permission will apply exclusively to 2′-FL and LNnT as listed in Schedule 26, under the brand ‘GlyCare’. Once this period ends, the exclusive use permission will revert to a general permission, meaning that the permission will apply to all brands of 2′-FL and LNnT that meet the specific source and associated specifications in Schedule 3.

Item [6]

Item [6.1] varies Schedule 29 by omitting section 29—5 and substituting a new section to add 2′-FL, and 2′-FL combined with LNnT, in the table to this section as new substances permitted for use as nutritive substances in infant formula products. 2′-FL and LNnT listed in

this table are linked to these substances permitted for use by Standard 1.5.2 (*Food produced using gene technology*). This means that only 2′-FL and LNnT derived from the microbial sources listed in Schedule 26 (table to subsection 26—3(7)) are permitted for use in infant formula products. The permission in section 29—5 also lists permitted forms, and requires infant formula products to contain not more than 96 mg/100 kJ of 2′-FL; and not more than 96 mg/100 kJ of 2′-FL and LNnT combined (of which contains not more than 24 mg/100 kJ of LNnT). A minimum amount is not set, as this was not requested in the application and has not been determined by FSANZ.

Item [6.2] varies Schedule 29 by inserting a new section S29—15A containing a table (as referred to in subsection 2.9.3—7(2A) under Item 2.1 above). This new table lists other substances permitted for use as nutritive substances in FSFYC (i.e. substances which are additional to the vitamins and minerals currently permitted to be used as nutritive substances in FSFYC in S29—15). 2′-FL alone, and 2′-FL and LNnT combined are listed in this table, along with the existing permission for lutein (relocated from existing section 2.9.3—7(4), see Item 2.3 above). 2′-FL and LNnT listed in this table are linked to these substances permitted for use by Standard 1.5.2. This means that only 2′-FL and LNnT derived from the microbial sources listed in Schedule 26 (table to subsection 26—3(7)) will be permitted for use in FSFYC. The permission in the table in subsection S29—15A also lists permitted forms, and (in relation to 2′-FL and LNnT) will require FSFYC to contain not more than 0.55 g/serving of 2′-FL; and not more than 0.55 g/serving of 2′-FL and LNnT combined (of which contains not more than 0.14 g/serving of LNnT). A minimum amount is not set, as this was not requested in the application and has not been determined by FSANZ.

Attachment C –Draft variations to the *Australia New Zealand Food Standards Code (call for submissions)*

Food Standards (Application A1155 – 2′-FL and LNnT in infant formula and other products) Variation

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by Delegate]

[Insert name of Delegate]
Delegate of the Board of Food Standards Australia New Zealand

Note:

This variation will be published in the Commonwealth of Australia Gazette No. FSC XX on XX Month 20XX. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

1 Name

This instrument is the *Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation*.

2 Variation to standards in the *Australia New Zealand Food Standards Code*

The Schedule varies Standards in the *Australia New Zealand Food Standards Code*.

3 Commencement

The variation commences on the date of gazettal.

Schedule

[1] Standard 2.9.1 is varied by

[1.1] omitting section 2.9.1—7, substituting

2.9.1—7 Restriction on addition to infant formula product of inulin-type fructans and galacto-oligosaccharides

(1) If an inulin-type fructan or a galacto-oligosaccharide is added to an infant formula product, the product must contain (taking into account both the naturally-occurring and added substances) no more than:

(a) if only *inulin-type fructans are added—110 mg/100 kJ of inulin-type fructans; or

(b) if only *galacto-oligosaccharides are added—290 mg/100 kJ of galacto-oligosaccharides; or

(c) if both inulin-type fructans and galacto-oligosaccharides are added:

(i) no more than 110 mg/100 kJ of inulin-type fructans; and

(ii) no more than 290 mg/100 kJ of combined inulin-type fructans and galacto-oligosaccharides.

(2) An infant formula product to which an inulin-type fructan or a galacto-oligosaccharide is added must not contain any of the following added substances:

(a) 2′-O-fucosyllactose; or

(b) a combination of 2′-O-fucosyllactose and lacto-N-neotetraose.

[1.2] inserting after paragraph 2.9.1—24(1)(c)

(ca) the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect; or

(cb) the abbreviations ‘HMO’ or HiMO’ or any abbreviation having the same or similar effect; or

[2] Standard 2.9.3 is varied by

[2.1] inserting after subsection 2.9.3—7(2)

(2A) A substance listed in Column 1 of the table to section S29—15A may be *used as a nutritive substance in a formulated supplementary food for young children if:

(a) the substance is in a permitted form listed in Column 2 of the table; and

(b) the amount of the substance in the food (including any naturally-occurring amount) is no more than the corresponding amount listed in Column 3 of the table.

[2.2] omitting subsection 2.9.2—7(3), substituting

(3) If *inulin-type fructans or *galacto-oligosaccharides are added to a formulated supplementary food for young children:

(a) the total amount of those substances, both added and naturally occurring, must not be more than 1.6 g/serving; and

(b) the food must not contain any of the following added substances:

(i) 2′-O-fucosyllactose; or

(ii) a combination of 2′-O-fucosyllactose and lacto-N-neotetraose.

[2.3] omitting subsection 2.9.3—7(4)

[2.4] omitting subsection 2.9.3—8(6), substituting

(6) The label on a package of a formulated supplementary food for young children must not contain:

(a) the words ‘human milk oligosaccharide’ or ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect; or

(b) the abbreviations ‘HMO’ or HiMO’ or any abbreviation having the same or similar effect; or

(c) any words indicating, or any other indication, that the product contains lutein unless the total amount of lutein is no less than 30 µg/serving.

[3] **Schedule 2** is varied by inserting in the table to section S2—2, in alphabetical order

EU/mg	Endotoxin units per milligram

[4] **Schedule 3** is varied by

[4.1] inserting in the table to subsection S3—2(2) in alphabetical order

2′-O-fucosyllactose	section S3—40

[4.2] inserting in the table to subsection S3—2(2) in alphabetical order

lacto-N-neotetraose	section S3—41

[4.3] inserting after subsection S3—39

S3—40 Specification for *2′*-O-fucosyllactose

For 2′-O-fucosyllactose (2′-FL), the specifications are the following:

(a) chemical name—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-D-glucopyranose;

(b) chemical formula—$C_{18}H_{32}O_{15}$;

(c) CAS number—41263-94-9;

(d) description— white to off white powder or agglomerates;

(e) assay (water free) for sum of 2′-FL, lactose, difucosyllactose and fucose—not less than 96.0%;

(f) assay (water free) 2′-FL—not less than 94.0%;

(g) D-lactose—not more than 3.0%

(h) L-fucose—not more than 1.0%

(i) difucosyllactose—not more than 1.0%

(j) 2′-fucosyl-D-lactulose—not more than 1.0%

(k) pH (20°C, 5% solution)—3.2 to 5.0

(l) water—not more than 5.0%

(m) ash, sulphated—not more than 1.5%

(n) acetic acid (as free acid and/or sodium acetate)—not more than 1.0%

(o) residual proteins—not more than 0.01%

(p) lead—not more than 0.1 mg/kg

(q) microbiological:

(i) *salmonella*—absent in 25 g

(ii) total plate count—not more than 500 cfu/g

(iii) enterobacteriaceae—–absent in 10 g
(iv) *cronobacter (Enterobacter) sakazakii*—–absent in 10 g
(v) *listeria monocytogenes*—–absent in 25 g
(vi) *bacillus cereus*—–not more than 50 cfu/g
(vii) yeasts—–not more than 10 cfu/g
(viii) moulds—–not more than 10 cfu/g
(ix) residual endotoxins—–not more than 10 EU/mg

S3—41 Specification for lacto-N-neotetraose

For lacto-N-neotetraose (LNnT), the specifications are the following:

(a) chemical name—–β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-glucopyranose
(b) chemical formula—–$C_{26}H_{45}NO_{21}$
(c) CAS number—–13007-32-4
(d) description—–white to off white powder or agglomerates
(e) assay (water free) for sum of LNnT, lactose, lacto-N-triose II, and *para*-lacto-N-hexaose—–not less than 95.0%
(f) assay (water free) LNnT—–not less than 92.0%
(g) D-lactose—–not more than 3.0%
(h) lacto-N-triose II—–not more than 3.0%
(i) *para*-lacto-N-neohexaose—–not more than 3.0%
(j) LNnT fructose isomer—–not more than 1.0%
(k) pH (20°C, 5% solution) —–4.0 to 7.0
(l) water—–not more than 9.0%
(m) ash, sulphated—–not more than 1.5%
(n) methanol—–not more than 100 mg/kg
(o) residual proteins—–not more than 0.01%
(p) lead—–not more than 0.1 mg/kg
(q) microbiological:
    (i) *salmonella*—–absent in 25 g
    (ii) total plate count—–not more than 500 cfu/g
    (iii) enterobacteriaceae—–absent in 10 g
    (iv) *cronobacter (Enterobacter) sakazakii*—–absent in 10 g
    (v) *listeria monocytogenes*—–absent in 25 g
    (vi) *bacillus cereus*—–not more than 50 cfu/g
    (vii) yeasts—–not more than 10 cfu/g
    (viii) moulds—–not more than 10 cfu/g
    (ix) residual endotoxins—–not more than 10 EU/mg

[5] Schedule 26 is varied by

[5.1] omitting subsections S26—3(1), (2), (2A), and (3), substituting

(1) The table to subsection (4) and the table to subsection (7) list permitted food produced using gene technology.

(2) Items 1(g), 2(m), 7(e), (g) and (h), and 9(a) of the table to subsection (4) are subject to the condition that their labelling must comply with section 1.5.2—4.

Note That section requires the statement 'genetically modified'.

(2A) Products containing beta-carotene from item 6(b) of the table to subsection (4) are subject to the condition that their labelling must comply with section 1.5.2—4.

(3) Item 2(m) of the table to subsection (4) is also subject to the condition that, for the labelling provisions, unless the protein content has been removed as part of a

refining process, the information relating to *foods produced using gene technology includes a statement to the effect that the high lysine corn line LY038 has been genetically modified to contain increased levels of lysine.

[5.2] omitting the words ‘gene technology’ from the heading to the table to subsection (4), substituting the words’ ‘gene technology of plant origin’.

[5.3] inserting after the table to subsection (4)

(5) A food listed in the table to subsection (7) must comply with any corresponding conditions listed in that table.

(6) A source listed in the table to subsection (7) may contain additional copies of genes from the same strain.

(7) The table for this subsection is:

Food produced using gene technology of microbial origin

Substance	*Source*	*Conditions of use*
1 2′-O-fucosyllactose	(b) *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*	4. May only be added to infant formula products and to formulated supplementary food for young children. 5. During the exclusive use period, may only be sold under the brand GlyCare. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation* and ending 15 months after that date.
2 Lacto-N-neotetraose	(b) *Escherichia coli* K-12 containing the gene for beta-1,3-N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1,4-galactosyltransferase from *Helicobacter pylori*	4. May only be added to the following foods in combination with 2′-O-fucosyllactose that is permitted for use in infant formula products; and formulated supplementary food for young children. 5. During the exclusive use period, may only be sold under the brand GlyCare. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation* and ending 15 months after that date.

[6] **Schedule 29** is varied by

[6.1] omitting section S29—5, substituting

S29—5 Infant formula products—substances permitted as nutritive substances

For section 2.9.1—5, the table is set out below.

Infant formula products—substances permitted for use as nutritive substances

Column 1	*Column 2*	*Column 3*	*Column 4*
Substance	*Permitted forms*	*Minimum amount per 100 kJ*	*Maximum amount per 100 kJ*
2′-O-fucosyllactose permitted for use by Standard 1.5.2	2′-O-fucosyllactose		96 mg

Column 1	***Column 2***	***Column 3***	***Column 4***
Substance	*Permitted forms*	*Minimum amount per 100 kJ*	*Maximum amount per 100 kJ*
A combination of: 2′-O-fucosyllactose permitted for use by Standard 1.5.2; and lacto-N-neotetraose permitted for use by Standard 1.5.2	2′-O-fucosyllactose and lacto-N-neotetraose		96 mg which contains not more than 24 mg of lacto-N-neotetraose
Adenosine-5′-monophosphate	Adenosine-5′- monophosphate	0.14 mg	0.38 mg
L-carnitine	L-carnitine	0.21 mg	0.8 mg
Choline	Choline chloride	1.7 mg	7.1 mg
	Choline bitartrate		
Cytidine-5′-monophosphate	Cytidine-5′-monophosphate	0.22 mg	0.6 mg
Guanosine-5′-monophosphate	Guanosine-5′-monophosphate	0.04 mg	0.12 mg
	Guanosine-5′-monophosphate sodium salt		
Inosine-5′-monophosphate	Inosine-5′-monophosphate	0.08 mg	0.24 mg
	Inosine-5′-monophosphate sodium salt		
Lutein	Lutein from *Tagetes erecta L.*	1.5 µg	5 µg
Inositol	Inositol	1.0 mg	9.5 mg
Taurine	Taurine	0.8 mg	3 mg
Uridine-5′-monophosphate	Uridine-5′-monophosphate sodium salt	0.13 mg	0.42 mg

[6.2] inserting after section S29—15

S29—15A Formulated supplementary food for young children—other substances permitted as nutritive substances

For subsection 2.9.3—7(2A), the table is set out below.

Formulated supplementary food for young children—other substances permitted for use as nutritive substances

Column 1	***Column 2***	***Column 3***
Substance	*Permitted form*	*Maximum amount per serving*
2′-O-fucosyllactose permitted for use by Standard 1.5.2	2′-O-fucosyllactose	0.55 g
A combination of: 2′-O-fucosyllactose permitted for use by Standard 1.5.2; and lacto-N-neotetraose permitted for use by Standard 1.5.2	2′-O-fucosyllactose and lacto-N-neotetraose	0.55 g which contains not more than 0.14 g of lacto-N-neotetraose
Lutein	Lutein from *Tagetes erecta L.*	100 µg