

**22 July 2019**  
**[86–19]**

## **2<sup>nd</sup> Call for submissions – Application A1155**

### **2'-FL and LNnT in infant formula and other products**

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Pursuant to section 31 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), FSANZ now calls for submissions to assist FSANZ's consideration of the draft food regulatory measure it has prepared arising from 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.

For information about making a submission, visit the FSANZ website at [information for submitters](#).

All submissions on applications and proposals will be published on our website. We will not publish material that we accept as confidential, but will record that such information is held. In-confidence submissions may be subject to release under the provisions of the *Freedom of Information Act 1991*. Submissions will be published as soon as possible after the end of the public comment period. Where large numbers of documents are involved, FSANZ will make these available on CD, rather than on the website.

Under section 114 of the FSANZ Act, some information provided to FSANZ cannot be disclosed. More information about the disclosure of confidential commercial information is available on the FSANZ website at [information for submitters](#).

Submissions should be made in writing; be marked clearly with the word 'Submission' and quote the correct project number and name. While FSANZ accepts submissions in hard copy to our offices, it is more convenient to receive submissions electronically through the FSANZ website via the link on [documents for public comment](#). You can also email your submission directly to [submissions@foodstandards.gov.au](mailto:submissions@foodstandards.gov.au).

There is no need to send a hard copy of your submission if you have submitted it by email or via the FSANZ website. FSANZ endeavours to formally acknowledge receipt of submissions within 3 business days.

### **DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 2 September 2019**

Submissions received after this date will not be considered unless an extension had been given before the closing date. Extensions will only be granted due to extraordinary circumstances during the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.

Questions about making submissions or the application process can be sent to [standards.management@foodstandards.gov.au](mailto:standards.management@foodstandards.gov.au).

Hard copy submissions may be sent to one of the following addresses:

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# Table of contents

<b>EXECUTIVE SUMMARY .....</b>	<b>2</b>
<b>1 INTRODUCTION.....</b>	<b>4</b>
1.1 THE APPLICANT.....	4
1.2 THE APPLICATION .....	4
1.3 THE CURRENT STANDARDS .....	4
1.3.1 <i>Australia and New Zealand</i> .....	4
1.3.2 <i>International regulations</i> .....	6
1.4 REASONS FOR ACCEPTING APPLICATION.....	8
1.5 PROCEDURE FOR ASSESSMENT .....	8
<b>2 SUMMARY OF THE ASSESSMENT.....</b>	<b>8</b>
2.1 SUMMARY OF ISSUES RAISED IN SUBMISSIONS.....	8
2.2 SAFETY, TECHNICAL AND HEALTH EFFECTS ASSESSMENT .....	22
2.2.1 <i>Safety and technical assessment</i> .....	22
2.2.2 <i>Health effects assessment</i> .....	23
2.3 RISK MANAGEMENT .....	24
2.3.1 <i>Health effects</i> .....	25
2.3.2 <i>Permitted use</i> .....	26
2.3.3 <i>Maximum use levels and units expression</i> .....	27
2.3.4 <i>Prohibition of use with existing oligosaccharide permissions</i> .....	29
2.3.5 <i>Labelling</i> .....	30
2.3.6 <i>Specifications for 2'-FL and LNnT</i> .....	34
2.3.7 <i>Exclusivity</i> .....	34
2.3.8 <i>Risk management conclusion</i> .....	34
2.4 RISK COMMUNICATION.....	35
2.4.1 <i>Consultation</i> .....	35
2.4.2 <i>World Trade Organization (WTO)</i> .....	36
2.5 FSANZ ACT ASSESSMENT REQUIREMENTS .....	36
2.5.1 <i>Section 29</i> .....	36
2.5.2 <i>Subsection 18(1)</i> .....	38
2.5.3 <i>Subsection 18(2) considerations</i> .....	38
<b>3 DRAFT VARIATION .....</b>	<b>39</b>
<b>4 REFERENCES.....</b>	<b>39</b>
ATTACHMENT A – DRAFT VARIATION TO THE AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE.....	42
ATTACHMENT B – DRAFT EXPLANATORY STATEMENT.....	48
ATTACHMENT C – UNITS BASIS FOR EXPRESSING MAXIMUM PERMITTED AMOUNTS .....	52

## Supporting documents

The [following documents](#)<sup>1</sup> which informed the assessment of this Application are available on the FSANZ website:

- SD1 Safety, technical and health effects assessment
- SD2 Assessment against Ministerial Policy Guidelines

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<sup>1</sup> <http://www.foodstandards.gov.au/code/applications/Pages/A1155-2'-FL-and-LNnT-in-infant-formula-and-other-products-.aspx>

## Executive summary

FSANZ has assessed an application from Glycom A/S 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 and formulated supplementary foods for young children (FSFYC). Permission is 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); and for exclusive use of this permission for 15 months after gazettal.

2'-FL and LNnT are non-digestible oligosaccharides found naturally in human milk. The applicant's 2'-FL and LNnT are produced by microbial fermentation using genetically modified (GM) production strains. These oligosaccharides are chemically and structurally identical to those in human milk.

FSANZ has assessed whether the proposed addition meets its objectives under section 18 of the FSANZ Act. In doing so, we have given regard to relevant Ministerial Policy Guidelines.

FSANZ's safety and technical assessment 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 levels requested, or at higher levels of 2'-FL consistent with average levels in mature human milk.

FSANZ also assessed evidence of the favourable health effects stated in the application, for the purpose of the proposed compositional permission. FSANZ concluded that the requested addition of 2'-FL alone or with LNnT has the potential to confer beneficial health outcomes in infants and young children. The available evidence supports the biological and mechanistic plausibility of 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 health effects may be enhanced as concentrations of 2'-FL are increased.

On 22 November 2018, FSANZ sought submissions on its preliminary position in the 1<sup>st</sup> Call for Submissions (CFS) report. Twelve submissions were received. FSANZ also subsequently conducted targeted consultation with jurisdictions and the applicant to discuss issues raised in submissions.

After assessing the application, and considering comments on the 1st CFS and targeted consultation, FSANZ has prepared a draft variation to permit the voluntary addition of 2'-FL alone or combined with LNnT to infant formula products and FSFYC. FSANZ now seeks comments on the draft variation.

The draft variation is based on the regulatory approaches summarised in the following list. Some of the approaches have been amended since the 1<sup>st</sup> CFS (where indicated) following consideration of submissions:

- Permit a maximum level of 2.4 g/L for 2'-FL alone; or 2'-FL and LNnT combined (with a maximum of 0.6 g/L LNnT). For consistency with existing permissions in the Code, these levels are expressed in mg/100 kJ or g/serving as listed below. FSANZ has made a slight correction since the 1<sup>st</sup> CFS to the converted level for 2'-FL alone and 2'-FL and LNnT combined for FSFYC (from 0.56 to 0.55 g/serving).

Infant formula products:

- 2'-FL alone – maximum of 96 mg/100 kJ
- 2'-FL and LNnT combined – maximum of 96 mg/100 kJ of 2'-FL and LNnT combined which contains not more than 24 mg/100 kJ of LNnT

FSFYC:

- 2'-FL alone – maximum of 0.55 g/serving
  - 2'-FL and LNnT combined – maximum of 0.55 g/serving of 2'-FL and LNnT combined which contains not more than 0.14 g/serving of LNnT
- Prohibit the use of 2'-FL alone or with LNnT with already permitted galacto-oligosaccharides (GOS) and inulin-type fructans (ITF).

*Proposed amended regulatory measures since the 1<sup>st</sup> CFS:*

- Prohibit terms such as 'human milk identical oligosaccharide' or 'HiMO' (or similar words or abbreviations) on infant formula products and FSFYC. This new approach is consistent with the policy guideline for infant formula products and prevents consumers being misled or confused about the use of such terminology on FSFYC.
- Apply generic ingredient labelling requirements, rather than prescribed ingredient names previously proposed, consistent with the general approach in the Code.
- Permit 2'-FL and LNnT to be *used as a nutritive substance* and as *food produced using gene technology* as previously proposed, however, permission is now linked to the specific gene-donor information rather than the final GM production strains.
- Apply exclusive permission for a period of 15 months, linked to the applicant's brand name, commencing on the date of gazettal of the variation.
- Prescribe specifications for 2'-FL and LNnT as previously proposed, but without the applicant's specific methods of analysis.

FSANZ considers the relevant ministerial policy guideline for infant formula products, which refers to the need to link health effects to specific health outcomes with appropriate evidence, has been adequately addressed. 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. This accords with the policy to use breastmilk as the primary reference for the composition of infant formula and follow-on formula.
- The policy leaves open the interpretation of the level of appropriate evidence required to demonstrate specific health outcomes.
- Evidence demonstrated biological and mechanistic plausibility of the health effects and supported a link to potential beneficial health outcomes. FSANZ considers the available evidence is appropriate for the purpose of compositional permission, noting the addition is safe and comparable to human milk.
- Although suggested by some submitters, FSANZ has not applied the health claims substantiation framework for the purpose of assessing the proposed compositional permission. The applicant has not applied for a permitted health claim for FSFYC in the Code and infant formula products are prohibited from making claims. Health claims made on FSFYC must comply with the requirements in Standard 1.2.7 which are intended to prevent misleading or deceptive claims on food labels.

FSANZ recognises the proposed addition to FSFYC may not strongly align with the intended purpose of this food category as referred to in the relevant policy guideline for special purpose foods. However, the proposed addition is safe and provides potential beneficial health outcomes in toddlers.

The proposed permission supports international consistency and trade opportunities, as 2'-FL and LNnT are permitted for use in infant formula products and FSFYC in overseas markets (including the EU and USA). It also allows alternative options to existing GOS and ITF permitted at higher levels, providing industry with innovation opportunities.

# 1 Introduction

## 1.1 The applicant

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

## 1.2 The application

The application is seeking 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<sup>2</sup> and formulated supplementary foods for young children (FSFYC)<sup>3</sup>. 2'-FL and LNnT are oligosaccharides found naturally in human milk. The application is specifically for 2'-FL and LNnT produced by microbial fermentation from genetically modified (GM) *Escherichia coli* (*E.coli*) strains. The applicant claims these oligosaccharides produced by microbial fermentation are structurally and chemically identical to 2'-FL and LNnT found in human milk.

Permission is 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<sup>4</sup>. The application states these requested levels are within the ranges of 2'-FL and LNnT found naturally in mature human milk. The applicant's stated purpose is 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 of human milk relating to microorganisms in the gastrointestinal system: anti-infective effect against pathogens; bifidogenic effect; immune modulation, improved intestinal barrier function and alleviation of allergic responses.

The application is seeking to include 2'-FL and LNnT as novel foods in the table to S25—2 of Schedule 25 (Permitted novel foods) and also notes 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 has also requested exclusive permission for their brand of 2'-FL and LNnT for a period of 15 months after gazettal.

## 1.3 The current standards

### 1.3.1 Australia and New Zealand

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

#### *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*.

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<sup>2</sup> 'Infant formula products' used throughout this report captures infant formula, follow-on formula and infant formula products for special dietary use.

<sup>3</sup> Toddler milk is the main type of FSFYC currently available.

<sup>4</sup> Specified in Table D.1-1 of the application dossier.

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* 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.

#### *Infant formula products*

Standard 2.9.1 and Schedule 29 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).

#### *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.

#### *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 1.2.8 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).

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 1.5.2—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.

#### *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.

### **1.3.1.1 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](#).

### **1.3.1.2 Proposals P1028 and P1024**

FSANZ is currently reviewing the regulation of infant formula under [Proposal P1028 – Infant Formula](#). The purpose of this proposal is to revise and clarify standards relating to infant formula and infant formula products for special dietary use comprising category definitions, composition, labelling and representation of products.

FSANZ is also currently reviewing the regulation of nutritive substances and novel foods under [Proposal P1024 – Revision of the Regulation of Nutritive Substances & Novel Foods](#). The purpose of this proposal is to develop an alternative framework for the regulation of nutritive substances and novel foods in the Code.

No issues under review in P1028 or P1024 affect FSANZ's assessment of this application.

## **1.3.2 International regulations**

2'-FL and LNnT produced by microbial fermentation (denoted as 'micro' in the following sections) and by chemical synthesis (denoted as 'chem') are permitted for use in infant formula products and FSFYC in various countries overseas.

### **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<sup>5</sup> (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<sup>6</sup>.

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<sup>5</sup> '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 6<sup>th</sup> month on and for young children (12-36 months)*.

<sup>6</sup> For further information, search on the [Codex Alimentarius website](#) (accessed 25 October 2018).

### 1.3.2.2 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<sup>7</sup> 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.
- 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 as listed below:

- 2'-FL<sub>micro</sub> and LNnT<sub>micro</sub> sourced from GM strain *E.coli* K-12 (based on the applicant's and other 2'-FL manufacturers'<sup>8</sup> specifications)
- 2'-FL<sub>micro</sub> sourced from GM strain *E.coli* BL21 (based on another manufacturer, Jennewein Biotechnologie GmbH approval (EU 2017b)).

At the time of our assessment for the 1<sup>st</sup> CFS, the 2'-FL specification sourced from GM strain *E.coli* K-12 above was based on the applicant's product specification only. New EU regulations have since come into force which modified this specification to a more generic one based on equivalence notifications to the EU Commission from other manufacturers (EU 2018, MEB 2017a, b), and further amendment requests by Glycom (EU 2019).

### 1.3.2.3 United States

The United States Food and Drug Administration (USFDA) issued 'no questions'<sup>9</sup> responses to the applicant's self-assessed Generally Recognized as Safe (GRAS) notifications for 2'-FL<sub>chem & micro</sub> 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<sub>micro</sub> 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 and Dupont).

'No questions' responses were also issued for the applicant's LNnT<sub>chem & micro</sub> (GRAS GRN 547 and 659). The maximum intended use level of LNnT in term infant formula and toddler formula's is 0.6 g/L.

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<sup>7</sup> 'Infant formula', 'follow-on formula', 'foods for special medical purposes' and 'young children' are defined in [Regulation \(EU\) No 609/2013](#) (accessed 17 September 2018).

<sup>8</sup> FrieslandCampina Nederland BV (FrieslandCampina) and DuPont Nutrition & Biosciences ApS (Dupont)

<sup>9</sup> 'No questions' response means the USFDA does not question the basis for the notifier's GRAS conclusion (USFDA 2016b).

#### **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<sub>micro</sub> (up to 1.2 g/L) and LNnT<sub>micro</sub> (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.

#### **1.3.2.5 Israel**

2'-FL<sub>micro</sub> and LNnT<sub>micro</sub> 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.

### **1.4 Reasons for accepting application**

The application was accepted for assessment because:

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

### **1.5 Procedure for assessment**

The application is being assessed under the Major procedure<sup>10</sup>.

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.

## **2 Summary of the assessment**

### **2.1 Summary of issues raised in submissions**

A total of 12 submissions were received to the 1<sup>st</sup> CFS, five from jurisdictions and seven from industry (including one late industry submitter).

Industry submitters supported the proposed voluntary addition of 2'-FL alone or with LNnT to infant formula products and FSFYC.

Many of the jurisdiction submitters raised concerns about the proposed addition to infant formula products and FSFYC.

The following table summarises the issues raised in submissions and FSANZ's response.

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<sup>10</sup> The Major procedure is used when the variation of the food regulatory measure being considered involves a significant change to the scope of the measure and is of significant technical and scientific complexity.

**Table 1: Summary of issues**

Issue	Raised by	FSANZ response
<p><b>Beneficial health effects</b></p> <p>Addition to infant formula products is not consistent with the Ministerial Policy Guideline for the Regulation of Infant Formula Products in relation to ‘substantiated beneficial role’ and ‘appropriate evidence’ (specific policy principle j). The evidence provided for the bifidogenic effect and anti-infective effect against invasive <i>Campylobacter jejuni</i> (<i>C. jejuni</i>), based on a plausible relationship, is insufficient to meet the policy requirements.</p>	<p>DHHS &amp; DJPR Vic NSWFA QLD Health SA Health</p>	<p>In assessing the proposed voluntary addition of 2'-FL and LNnT to 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 <i>had regard to</i> 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.</p> <p>FSANZ has concluded that the proposed addition is safe and supported by appropriate evidence in providing potential beneficial health outcomes in infants (see section 2.3.1), and considers the policy guideline has been adequately addressed (see our assessment against each specific policy principle in SD2).</p> <p>FSANZ has applied particular caution in this assessment (as referred to in specific policy principle j), noting:</p> <ul style="list-style-type: none"> <li>- The proposed voluntary addition is safe.</li> <li>- 2'-FL and LNnT are present in human milk which is referred to as the primary reference for determining the composition of infant formula and follow-on formula (specific policy principle h).</li> <li>- The maximum levels proposed are within the range of concentrations present in mature human milk, as referred to as the reference in specific policy principles (h and j).</li> <li>- The policy indicates a beneficial role is ‘substantiated’ where there is ‘appropriate evidence’ to link physiological, biochemical or functional effects to specific health outcomes. The guideline leaves open the interpretation of the strength, type and quality of evidence required as ‘appropriate evidence’.</li> <li>- Evidence demonstrated biological and mechanistic plausibility of the identified health effects and supported a link to potential beneficial health outcomes.</li> <li>- ‘Health effects’ and ‘beneficial health outcomes’ is used in this report in the context of assessing compositional permission, and not for the purpose of substantiating a food-health relationship in relation to making a health claim (see section 2.2).</li> </ul>

Issue	Raised by	FSANZ response
		<p>- 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.</p> <p>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).</p>
<p>Concerned about quality and certainty of evidence compared to that required for health claims substantiation (Proposal P293 – Nutrition, Health and Related Claims). Notes ‘substantiation’ in health claims context may not be perceived to mean that expressed in the Ministerial Policy Guideline for the Regulation of Infant Formula Products, but does not consider the evidence meets the threshold for ‘substantiate’ as defined in the Macquarie dictionary.</p>	<p>NSWFA</p>	<p>FSANZ’s assessment of this application is for the purpose of permitting the voluntary addition of 2’-FL and LNnT to infant formula products as requested by the applicant. The health claims substantiation framework has a very different purpose of preventing misleading or deceptive claims to be made about foods on their labels (i.e. it is not used for the purpose of permitting addition of ingredients). Claims on infant formula products are prohibited in the Code and any nutrition content or health claims made on FSFYC must meet the requirements of Standard 1.2.7.</p> <p>In having regard to all high order policy principles, FSANZ does not consider that the strength, quality and type of evidence required to substantiate a health claim on food labels is appropriate to apply to this application for voluntary compositional permission.</p> <p>As discussed in the response above, FSANZ considers the evidence is appropriate for the proposed compositional permission, and the infant formula policy guideline has been adequately addressed. We have applied particular caution in this assessment (as per specific policy principle (j)), noting the proposed addition is safe and is comparable to the natural presence of 2’-FL and LNnT in human milk.</p>
<p>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.</p>	<p>QLD Health NSWFA</p>	<p>FSANZ’s position with respect to making a health claim regarding ‘gut health’ as referenced in P293 has not changed. The Ministerial 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.</p> <p>In assessing this application, FSANZ considered specific health effects stated in the application, for the purpose of permitting voluntary addition to</p>

Issue	Raised by	FSANZ response
		<p>infant formula products and FSFYC. 'Health effects' is used in this context for assessing compositional permission, and not for the purpose of substantiating a food-health relationship in relation to making a health claim (see section 2.2).</p> <p>The application is not seeking to add a food-health relationship to Schedule 4 for FSFYC, for either a general level or a high level health claim, and evidence has not been provided to support this. As noted above, FSANZ has not assessed the application for the purpose of permitting a new food-health relationship for health claims in the Code.</p>
<p>Recommends FSANZ form an independent scientific expert group to review and provide advice regarding the status of prebiotics and probiotics intestinal microflora effects as beneficial health effects for classification in the Code; and review other countries' assessment criteria in this regard.</p>	<p>QLD Health</p>	<p>A general review about prebiotics and probiotics and other countries' assessment criteria is out of scope and is much broader than the specific health effects assessed for this application for the purpose of voluntary compositional permission.</p>
<p>A number of specific issues were raised 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.</p>	<p>DHHS &amp; DJPR Vic SA Health QLD Health</p>	<p>FSANZ assessed all available information for the anti-infective and bifidogenic effects, including an additional clinical study of 2'-FL and LNnT in obese children (5-12 years old) provided by the applicant since the 1<sup>st</sup> CFS (see SD1, section 4.2.3 <i>Human studies with 2'-FL and/or LNnT</i>).</p> <p>FSANZ has concluded that 2'-FL binding to invasive <i>C. jejuni</i> strains and subsequently inhibiting their attachment and growth, is biologically and mechanistically plausible and thereby has an anti-infective effect. The evidence also supports the biological and mechanistic plausibility 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 (see section 2.2.2).</p> <p>FSANZ acknowledges that additional clinical trials would provide further evidence and give greater confidence to any conclusions from the assessment. However, as discussed in SD1 (section 4), it is difficult to definitively and reproducibly demonstrate causality of a health effect associated with a substrate targeted at modulating gut microflora. FSANZ therefore considers the evidence supporting the anti-infective and bifidogenic effects is appropriate for the purpose of the proposed voluntary permission.</p>

Issue	Raised by	FSANZ response
Further clarity is requested on the effective dose of 2'-FL and LNnT required to provide for the bifidogenic and anti-infective effects. Suggests further information is requested from the applicant on this matter.	NSWFA	<p>FSANZ has assessed all information provided by the applicant, and conducted our own independent literature search. As discussed in SD1, FSANZ is not able to establish a dose response for the anti-infective and bifidogenic effects. No further information is available from the applicant on this matter.</p> <p>Based on the evidence assessed, FSANZ considers these health effects could occur at the levels requested by the applicant, and may be enhanced as concentrations of 2'-FL are increased (see sections 2.2.2 and 2.3.1). FSANZ has also considered levels in human milk, estimated dietary intakes and international permissions, to determine the proposed maximum levels for 2'-FL alone and combined with LNnT (see further in section 2.3.3).</p>
Addition of selected human milk identical oligosaccharides (HiMOs) to infant formula products does not consider the role, and possible interactive properties, of many other human milk oligosaccharides (HMOs) in human milk.	DHHS & DJPR Vic SA Health	FSANZ has assessed the addition of 2'-FL and LNnT to infant formula products as requested in the application. FSANZ is satisfied that the proposed voluntary addition is safe. Consideration of other HMOs is not within the scope of this application.
<b>Addition to FSFYC</b>		
<p>Concerns raised about the addition to FSFYC:</p> <ul style="list-style-type: none"> <li>• Addition to FSFYC is inconsistent with the Ministerial Policy Guideline on the Intent of Part 2.9 – Special Purpose Foods regarding the 'intended purpose' of this food category.</li> <li>• There is no clear nutritional need for addition to FSFYC.</li> <li>• GOS and ITF permissions for FSFYC were granted prior to the Ministerial Policy Guideline.</li> <li>• There is no clinical evidence to substantiate the addition of these substances to FSFYC specifically.</li> <li>• Suggest further information is sought from the applicant on this matter.</li> </ul>	DHHS & DJPR Vic SA Health NSWFA	<p>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 <i>had regard</i> 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.</p> <p>FSANZ acknowledges that the proposed addition to FSFYC may not strongly align with the policy guideline regarding the 'intended purpose' of this food category. However, as discussed in section 2.3.1.4, the addition is safe and may provide potential beneficial health outcomes for toddlers.</p> <p>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. These health effects for toddlers were inferred from infant and adult studies where evidence is available.</p>

Issue	Raised by	FSANZ response
		<p>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) permitted for use in FSFYC at higher levels (see sections 2.5.1.1 and 2.5.3).</p> <p>Although the policy guideline did not apply when GOS and ITF were permitted for use in the Code, these oligosaccharides are currently permitted for safe use in FSFYC. Permitting alternative options to these oligosaccharides provides industry with innovation opportunities.</p>
<b>Used as a nutritive substance</b>		
Supports approval as <i>used as a nutritive substance</i> .	Glycom, Nestle, NSWFA	Noted.
<p>Approval of 2'-FL and LNnT to be <i>used as a nutritive substance</i> is inconsistent with other oligosaccharides GOS and ITF, noting:</p> <ul style="list-style-type: none"> <li>• This could create regulatory confusion and complexity.</li> <li>• The same labelling provisions should apply for all these oligosaccharide substances.</li> <li>• Do GOS and ITF therefore also need to be considered as nutritive substances?</li> <li>• Issue could be considered within scope of P1024 and P1028.</li> </ul>	Fonterra, INC, NZFGC, NZMPI	<p>Making changes to the specific regulatory approach for GOS and ITF is outside the scope of this application.</p> <p>Under Proposal P306 (Addition of Inulin/FOS &amp; GOS to food), FSANZ specifically excluded ITF (termed 'inulin-derived substances' at the time) from the definition of <i>used as a nutritive substance</i> (then defined as 'nutritive substances') because it was already added to some general foods. GOS was also excluded under P1025 (Code Revision) for clarity. This approach provided regulatory certainty for manufacturers who were using ITF and GOS in general foods (i.e. they did not require express permission in the Code). Classifying ITF or GOS to be <i>used as a nutritive substance</i> would render all foods that contained these substances as non-compliant until approved.</p> <p>For special purpose foods, FSANZ included express permissions for the use of ITF and GOS in infant formula products, foods for infants and FSFYC, to make clear that express permission was still needed for these types of foods. The regulatory certainty of this approach was not dependent on deeming ITF or GOS to be <i>used as a nutritive substance</i>.</p> <p>For A1155, specifically approving 2'-FL and LNnT to be <i>used as a nutritive substance</i> (in Schedule 29) means that any extension of use for these substances in other special purpose or general foods would require express permission (in accordance with section 1.1.1—10(6) of the Code). There is no need to apply a special circumstance as done for ITF and GOS to allow for use in general foods.</p>

Issue	Raised by	FSANZ response
		<p>Regarding labelling provisions, any substance <i>used as a nutritive substance</i> in infant formula products is required to be declared in the nutrition information statement (section 2.9.1— 21(1)(iii)) in a similar manner that GOS and ITF are required to be declared (section 2.9.1— 21(1)(iv)). For FSFYC, general nutrition information labelling requirements (Standard 1.2.8) would equally apply to 2'-FL, LNnT, GOS and ITF. The specific issue of ingredient names for 2'-FL and LNnT is discussed further below in this table and in section 2.3.5.1.</p> <p>The definition and regulation of <i>used as a nutritive substance</i> is currently being reviewed under Proposals P1024 and P1028. Any potential changes made under these proposals will take account of existing permissions in the Code.</p>
<p>Seeks clarification on whether 2'-FL and LNnT whose physiological impact is indirect (i.e. via bifidogenic effect) and which are not directly absorbed or metabolised by humans, can be considered nutritive substances for the purposes of addition and Standard 1.2.7 and Schedule 4 (Nutrition, health and related claims) of the Code.</p>	<p>QLD Health</p>	<p>A definition for <i>used as a nutritive substance</i> (not 'nutritive substance') is currently provided in section 1.1.2—12 of the Code which refers to addition to food to 'achieve a nutritional purpose' (which is not defined). There is no requirement in the Code for a substance to be absorbed or metabolised to be <i>used as a nutritive substance</i>. This is also the case for the purposes of the definitions in Standard 1.2.7.</p> <p>FSANZ notes that some types of dietary fibre, which are metabolised by the gut microbiome, are generally understood to be, and classified as, a nutrient (e.g. in Nutrient Reference Values). This scenario also applies to 2'-FL and LNnT oligosaccharides.</p>
<p>Recommends FSANZ form an expert scientific and regulatory group to review and clearly delineate the status of prebiotics as nutritive substances for classification in the Code, and review other countries' assessment criteria in this regard.</p>	<p>QLD Health</p>	<p>A general review of prebiotics, or other countries' assessment criteria in this regard, is not within the scope of this application.</p>
<p>Recommends FSANZ review its criteria for definition of – and associated claims as - <i>nutritive substances</i> and <i>nutritive purposes</i> with a goal of potentially revising the Code definition to clarify and delineate criteria qualifying substances as same. Seeks information as to whether this is part of P1024.</p>	<p>QLD Health</p>	<p>Such a review is out-of-scope for this application. The current definition and regulation of <i>used as a nutritive substance</i> is currently being reviewed under Proposals P1024 and P1028.</p> <p>Claims made about foods are regulated by Standard 1.2.7 and associated Schedules. 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.</p>

Issue	Raised by	FSANZ response
<b>Proposed maximum levels</b>		
Supports maximum use levels proposed for 2'-FL alone and combined with LNnT.	INC, Glycom, Nestle, NZFGC, Abbott, NZMPI	Noted.
Although would prefer the levels to be based on g/L units as used internationally, can support the units of measure proposed (mg/100 kJ and g/serving)	INC, Nestle	Noted.
<p>Does not support proposed higher maximum use level for 2'-FL alone or combined with LNnT; reasons provided include:</p> <ul style="list-style-type: none"> <li>• Literature (Plaza-Diaz et al 2018) states there is a lack of evidence to support the proposed combination.</li> <li>• There are no studies at the higher level in the target populations (infant and young children).</li> <li>• There is no history of use in Australia and NZ of microbially produced 2'-FL and LNnT.</li> <li>• GOS permissions were determined prior to introduction of the Regulation of Infant Formula Products Ministerial Policy Guideline.</li> <li>• 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.</li> </ul>	SA Health DHHS & DJPR Vic	<p>FSANZ notes the paper by Plaza-Diaz et al (2018) does not raise concerns as to the safety of 2'-FL and LNnT. The proposed higher level of 2'-FL, alone or in combination with LNnT, does not raise public health and safety concerns based on the following evidence as discussed in SD1:</p> <ul style="list-style-type: none"> <li>- 2'-FL<sub>micro</sub> and LNnT<sub>micro</sub> respectively are structurally and chemically identical to 2'-FL and LNnT present in human milk, and the proposed concentrations to be added to infant formula products are within the range of concentrations found in mature human milk. This provides a history of safe human use.</li> <li>- Intestinal absorption of 2'-FL and LNnT is limited and a large proportion of these substances passes to the large intestine, where they are fermented by the intestinal microbiota or excreted intact in the faeces.</li> <li>- No adverse effects were observed at high doses in subchronic studies with 2'-FL or LNnT in juvenile rats, or in studies with 2'-FL in neonatal piglets.</li> <li>- 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.</li> <li>- Taken together, the evidence on chemical identity and concentration range in human milk, limited absorption and lack of effects at high doses in suitable animal models of an appropriate age and in infants is sufficient to conclude with reasonable certainty that 2'-FL or LNnT will not cause harm in infants.</li> </ul> <p>The policy guideline for infant formula products refers to breastmilk as the primary reference for determining the composition of infant formula and follow-on formula; and to take account of levels of comparable substances in breastmilk (specific policy principles h and j). As discussed in section 2.3.3, the proposed higher level of 2'-FL provides dietary intakes similar to those of 3 and 9 month old breastfed infants.</p>

Issue	Raised by	FSANZ response
		<p>Although the relevant policy guidelines did not apply when GOS was permitted in the Code, these oligosaccharides are currently permitted for safe use in infant formula products and FSFYC at levels several times higher than those proposed (see section 2.3.3).</p> <p>The proposed higher maximum level also provides for a more efficient and internationally competitive food industry, noting higher levels of 2'-FL, up to that proposed, are permitted for use internationally (e.g. in the US) (see section 2.3.3).</p>
<b>Labelling issues</b>		
To retain consistency with section 2.9.1—21(1)(a)(iv), recommends 2'-FL and LNnT be subject to same nutrition declaration requirements as ITF and GOS.	QLD Health	The addition of 2'-FL and LNnT would trigger a mandatory declaration in the nutrition information statement in accordance with section 2.9.1—21(1)(iii) (see section 2.3.5.3). This declaration is similar to the requirements for ITF and GOS in section 2.9.1—21(1)(a)(iv) - i.e. expressed in weight/100 mL.
Further labelling restrictions are required to prevent reference to 'human milk identical', 'human milk oligosaccharides' or abbreviations (or words of similar effect) on infant formula products.	DHHS & DJPR Vic NSWFA SA Health	In response to submitter comments, FSANZ is now proposing to specifically prohibit reference to 'human milk identical oligosaccharide', 'human milk oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) on infant formula products as discussed in section 2.3.5.2.
<p>Additional labelling measures are required to prohibit reference to 'human milk' equivalency (e.g. 'human milk identical' or 'HMO' abbreviation) on the label of FSFYC. Submitters noted:</p> <ul style="list-style-type: none"> <li>• Prescribed ingredients names do not prevent the use of such terms elsewhere on FSFYC.</li> <li>• This approach is a logical extension of policy for infant formula products.</li> <li>• Codex is currently discussing a new food standard for toddler milks which will shape global and national regulation.</li> </ul>	NZMPI QLD Health NSWFA DHHS & DJPR Vic SA Health	In addition to infant formula products as discussed above, FSANZ is now also proposing to specifically prohibit reference to 'human milk identical oligosaccharide', 'human milk' oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) on FSFYC (see further discussion in section 2.3.5.2).
Concerned about the likelihood for cross promotion of infant formula through 'line marketing' from FSFYC, which would negate any associated restrictions on labelling and reference to human identical milk for infant formula.	DHHS & DJPR Vic SA Health	<p>The broader issue of line marketing is out of scope.</p> <p>Prohibiting the terms 'human milk oligosaccharide', 'human milk identical oligosaccharide' and abbreviations 'HiMO' or 'HMO' or similar, for infant formula products and FSFYC, would constitute a limited restriction in relation to the potential for cross promotion.</p>

Issue	Raised by	FSANZ response
FSANZ should consider a prohibition on terms such as 'human milk identical' more generally for foods for other purposes (e.g. sports supplements).	QLD Health	Extending the proposed prohibition to other foods is beyond the scope of this application.
Does not support prescribing use of ingredient names '2-fucosyllactose' and 'lacto-N-neotetraose', relying on section 1.2.4—4 instead noting this is consistent with the general approach in the Code and other oligosaccharides GOS and ITF.	NZFGC, Fonterra, INC, Nestle	<p>FSANZ has reconsidered the approach to prescribe ingredient names and is now of the view that generic ingredient naming requirements should apply, consistent with the general approach in the Code. See further discussion in section 2.3.5.1.</p> <p>However, as discussed above, suppliers would be prohibited from using the terms 'human milk oligosaccharide', 'human milk identical' oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) anywhere on the label of infant formula products and FSFYC.</p>
Supports prescribing ingredient names for ingredient list declaration.	NZMPI DHHS & DJPR Vic QLD Health NSWFA SA Health	See above response.
Prescribing ingredient names would preclude the use of acronyms (2'-FL and LNnT) in the nutrition information panel (NIP).	INC	The proposed revised approach in which the ingredient names are not prescribed would also mean that the use of their acronyms is not prohibited.
Disagrees with FSANZ's view that terms 'human identical milk oligosaccharides' or 'HiMO' is prohibited under 2.9.1 – 24; or considers that this terminology should be able to be used. This terminology is technically correct, is used internationally, and is helpful to consumers.	NZFGC, INC, Nestle	Noted, see approach above to specifically prohibit such terms.
<p>Proposed additions to Schedule 4:</p> <ul style="list-style-type: none"> <li>Advocates a pre-approved listing in Schedule 4 for any substantiated food-health relationships to underpin any health claims that may appear on FSFYC products containing 2'-FL and LNnT, to provide national consistency and clarity on permissible claims.</li> <li>Advocates a listing in Schedule 4 for any permissible nutrition content claims (e.g. contains 'HMO' or contains 'X g of human milk oligosaccharides') that may arise.</li> </ul>	NSWFA	<p>The applicant has not sought to add a food-health relationship to Schedule 4 for FSFYC, for either a general level health or a high level health claim.</p> <p>The proposed prohibition of terms 'human milk identical oligosaccharide', 'human milk' oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) on FSFYC would mean a nutrition content claim or health claim using this terminology could not be made.</p> <p>FSANZ notes that listing a pre-approved claim in Schedule 4 does not preclude additional self-substantiated claims.</p>

Issue	Raised by	FSANZ response
		A voluntary nutrition content claim about 2'-FL or LNnT on the label of FSFYC would be subject to the requirements in Standard 1.2.7—13 (Nutrition content claims about properties of food not in section S4—3) and nutrition information requirements in Standard 1.2.8 (the latter includes the requirement for a declaration in the NIP).
<p>Seeks clarity about the nature of claims that could be made:</p> <ul style="list-style-type: none"> <li>• Considers the evidence provided for the anti-infective and bifidogenic effects are not satisfactory to permit health claims (for FSFYC).</li> <li>• Requests clarification on whether a health claim concerning the anti-infective effect against <i>C.jejuni</i> is a therapeutic claim or a permissible high level health claim (HLHC).</li> <li>• Queries the status of declaration of presence of 2'-FL and LNnT in FSFYC that do not bear a claim regulated by Standard 1.2.7 of the Code but make a claim according to the definition of claim under Standard 1.1.2 of the Code. Any claim made should trigger a declaration in the NIP.</li> </ul>	NSWFA QLD Health	<p>The evidence provided supports permission to add 2'-FL and LNnT to infant formula and FSFYC. The applicant has not sought to add a food-health relationship to Schedule 4 for FSFYC, for either a general level health or a high level health claim (noting infant formula products are prohibited from making claims).</p> <p>In relation to FSFYC, the existing prohibition for therapeutic claims and provisions for high level health claims (including preapproval) will apply.</p> <p>As the terms 'human milk identical oligosaccharide', 'human milk' oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) would be prohibited, these terms could not be used for the purpose of making labelling claims.</p> <p>A voluntary nutrition content claim about 2'-FL or LNnT on the label of FSFYC would be subject to the claim requirements in Standard 1.2.7 and nutrition information requirements in Standard 1.2.8 (the latter includes the requirement for a declaration in the NIP).</p>
FSANZ should seek advice from the ACCC on the possibility of consumers being misled about the source of HMO that may be added to FSFYC. Any labelling claims on products concerning these substances should not create a misleading impression that the FSFYC is somehow related to human milk.	NSWFA	FSANZ is now proposing a revised approach to prohibit the terms 'human milk identical oligosaccharide', 'human milk' oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) on both infant formula products and FSFYC. See further discussion in section 2.3.5.2.
The general prohibition on health claims for infant formula and indications of human breast milk equivalency should extend to follow-on and FSFYC.	QLD Health	<p>Follow-on formula (and infant formula) is prohibited from making health claims in Standard 2.9.1.</p> <p>The issue of whether the claims prohibition should extend to FSFYC is broader than what can be addressed in A1155. FSANZ notes there are other substances already permitted to be added to FSFYC, for which nutrition content and health claims can be made (subject to meeting the requirements in Standard 1.2.7).</p>

Issue	Raised by	FSANZ response
Code amendments for composition and labelling of infant formula and FSFYC should align with the <i>WHO International Code of Marketing of Breastmilk Substitutes</i> .	QLD Health	<p>The WHO Code only relates to marketing and not composition.</p> <p>The existing labelling requirements and specific prohibition of terms such as ‘human milk identical oligosaccharide’ for infant formula products support the WHO Code (see also specific policy principle (k) in SD2). FSFYC are not considered breastmilk substitutes in Australia and New Zealand. Aligning with the WHO Code for FSFYC is therefore beyond the scope of this application.</p>
<b>Implications of P1024 &amp; P1028</b>		
FSANZ should consider delaying a decision on this application until the outcomes of P1024 and P2018 are known. Alternatively, this application could be reviewed with respect to stakeholder input received to date on P1024 and P1028.	QLD Health	<p>FSANZ does not consider a deferral of the application is justified and is progressing the application in accordance with the FSANZ Act. Considerations under Proposals P1024 and P1028 are still in progress. Any potential changes made under these Proposals will take account of existing permissions in the Code.</p>
<b>Food produced using gene technology</b>		
<p>Does not support approval of 2'-FL and LNnT as <i>food produced using gene technology</i>, and should instead be regulated as novel foods, noting:</p> <ul style="list-style-type: none"> <li>• 2'-FL and LNnT meet the definition of non-traditional foods.</li> <li>• The substances are highly purified and equivalent to same molecules from different sources.</li> <li>• 2'-FL and LNnT are substantially different to GM plants currently listed in Schedule 26.</li> <li>• The substances are regulated as novel foods internationally (e.g. EU and US).</li> <li>• The proposed approach may introduce a barrier to trade.</li> </ul>	Glycom, INC, NZFGC, Nestle	<p>As discussed in section 1.3.1, express permission must be provided in the Code for any <i>food produced using gene technology</i> 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). 2'-FL and LNnT are <i>food produced using gene technology</i> as they are derived from an organism modified by gene technology.</p> <p>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). 2'-FL and LNnT are not food additives or processing aids and must therefore be listed in Schedule 26 to comply with the requirements of the Code. As discussed in section 2.3.2, FSANZ proposes to add a new, separate table in Schedule 26, to clearly delineate 2'-FL and LNnT of microbial origin from the existing approvals of plant origin. This approach does not change existing pre-market assessment and approval requirements, or the existing approvals of plant origin.</p> <p>FSANZ acknowledges that the Code operates differently to the regulatory framework for GM/novel foods in overseas regulations such as the EU and US. However, 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</p>

Issue	Raised by	FSANZ response
		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.
Suggests approval is based on a platform strain (identified as RO-1 in SD1), rather than the specific production strains proposed. This will facilitate innovation at production strain variant level without any impact to the genes being expressed to produce 2'-FL/LNnT. Also suggests the platform strain be located with the specification in Schedule 3.	Glycom, Nestle	In the 1 <sup>st</sup> CFS, FSANZ proposed linking approval of the oligosaccharides to the final production strains (SCR6 and MP576). As further discussed in section 2.3.2, FSANZ is now proposing to link approval of 2'-FL and LNnT to the gene-gene donor information specific to the production of the oligosaccharides, rather than specific production strains. This approach allows some flexibility to the production strain within a limited pool of gene-gene donor pairs specific to the production of the oligosaccharides which has been assessed by FSANZ. Any further optimisation beyond these donor pairs would require a new application for assessment. As discussed in the response above, approval as <i>food produced using gene technology</i> is required in Schedule 26, not Schedule 3.
Does not support approval of 2'-FL based on specific GM production strain; should instead be based on the production host <i>E.coli</i> K-12. This will support an efficient, internationally competitive food industry, noting 2'-FL is approved internationally from different sub-strains.	BASF	FSANZ has conducted a GM safety assessment for the source organisms and gene-gene donor combinations specific to this application. As discussed above and in section 2.3.2, FSANZ proposes to link approval to the specific gene-gene donor information as assessed by FSANZ. 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.
As proposed amendment represents first addition of GM microorganism-derived food to infant formula products and FSFYC, suggests FSANZ prepare an associated public communications strategy.	QLD Health	Noted. FSANZ has prepared a communication strategy for this application (see section 2.4.1).
<b>Exclusive permission</b>		
Exclusivity is required under novel food provisions (Standard 1.5.1)	Glycom, NZFGC	There is no limitation in the Code or FSANZ Act for exclusivity to be provided only under the novel food standard. FSANZ proposes to provide 15 months exclusivity from the date of gazettal for the applicant's brand of 2'-FL and LNnT in Schedule 26 of the Code (see section 2.3.7).
Approval of 2'-FL and LNnT linked to the specific production strains would provide unlimited exclusivity far beyond the requested 15 month exclusivity period.	BASF	See responses to above issues regarding change to GM drafting approach and exclusivity.

Issue	Raised by	FSANZ response
<b>Specifications</b>		
Does not support methods of analysis (MOA) in specifications as this would limit future method improvements.	BASF, Fonterra, Glycom, INC, Nestle, NZFGC, Abbott (late)	The two tables provided in the application for 2'-FL and LNnT product specifications included a method for each parameter, which was information that assisted in FSANZ's assessment. The 1 <sup>st</sup> CFS broadly proposed that the specification provided in the application would be inserted into the Code. Consistent with other specifications in the Code (Schedule 3), FSANZ does not propose to include the applicant's stated MOA's in the specifications (see also section 2.3.6).
Suggests the specifications are consistent with those recently incorporated in the EU regulation (EU 2018), which now provides a generic specification based on <i>E.coli</i> K-12 to cover different manufacturers' specifications.	BASF, Fonterra, INC, NZFGC, Abbott (late)	<p>Australia and New Zealand regulations do not provide a substantial equivalence notification system as provided in the EU and used as the basis for the EU 2018 specification amendment. FSANZ notes that since the 1<sup>st</sup> CFS submission period closed, a further amendment to the EU 2'-FL specification has come into force (EU 2019) as further discussed in section 1.3.2.2.</p> <p>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). As also noted above, FSANZ proposes linking approval to the specific gene-gene donor information, not the generic <i>E.coli</i> 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.</p>
<b>Prohibited use with GOS/ITF</b>		
Should not prohibit combinations of GOS/ITF with 2'-FL/LNnT in infant formula products and FSFYC: <ul style="list-style-type: none"> <li>- This is not consistent with the data for some combinations of GOS/scFOS with 2'-FL.</li> <li>- This is not consistent with international permissions.</li> <li>- Suggests limit of 8 g/L could be set for combined use of 2'-FL/LNnT with existing GOS and ITF.</li> </ul>	Fonterra, Abbott (late)	<p>As further discussed in section 2.3.4, the applicant has not sought to use 2'-FL alone or with LNnT, in any combination with existing ITF and GOS permissions. Appropriate evidence has not been specifically provided in the application 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.</p> <p>An application process exists for industry who wish to seek to amend the Code to allow such combinations, with appropriate supporting evidence.</p>
Supports this prohibition within the scope of this application, but is not opposed to future permitted combined use with appropriate scientific evidence.	Nestle	Noted.

## 2.2 Safety, technical and health effects assessment

The safety, technical and health effects assessment (see SD1) comprised:

- (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 the intake resulting from the addition of 2'-FL and LNnT to infant formula products and FSFYC
- (iv) an assessment of the health effects stated by the applicant.

Regarding point (iv) above, FSANZ's assessment of the favourable health effects stated in the application was for the purpose of the requested compositional permission. The term 'health effect(s)' used throughout this report is therefore in the context of our assessment for compositional permission, and not for the purpose of establishing a relationship between a food or property of food and a *health effect* in relation to making a health claim (as used in Standard 1.2.7 of the Code).

Subsequent to public release of the 1<sup>st</sup> CFS, the applicant provided an unpublished report on interim results of a clinical study of 2'-FL and LNnT in 5-12 year old obese children. SD1 has been amended to incorporate assessment of this report in both our safety and health effects assessments (see sections 3.2.6 and 4.2.3 *Human studies with 2'-FL and/or LNnT* in SD1). These new data, contained in the interim report, do not amend FSANZ's overall safety and health effects conclusions discussed in the following sections.

### 2.2.1 Safety and technical assessment

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.

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.

A few changes were made to the SD1 released with the 1<sup>st</sup> CFS. In section 3.1.1 *History of use: Gene donor organisms*, changes were made to reflect the re-evaluation of confidential commercial information by FSANZ, acknowledging information that is in the public domain. Two minor changes were also made to the enzyme names used in the LNnT production strain to be more consistent with how these enzymes are referenced in the literature.

Based on an assessment of the available toxicological and clinical evidence for 2'-FL and LNnT, it was concluded that there were 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 the levels requested by the applicant and at the estimated levels of dietary intake based on 2.4 g/L of 2'-FL and 0.6 g/L of LNnT. Since the applicant's 2'-FL and LNnT are structurally and chemically identical to the forms of these substances present in human milk, no differences in pharmacokinetics between naturally occurring and manufactured forms of 2'-FL and LNnT are expected. Overall, the available data indicated that intestinal absorption is limited, and a significant proportion of human milk oligosaccharides (HMOs) including 2'-FL and LNnT reach the large intestine where they are fermented by the microbiota or excreted unchanged in the faeces.

Both 2'-FL and LNnT produced by microbial fermentation were not genotoxic in *in vitro* bacterial mutagenicity assays or in *in vitro* micronucleus assays in human lymphocytes. No adverse effects were observed in subchronic oral toxicity studies with 2'-FL or LNnT in juvenile rats at doses up to 5000 mg/kg bw/day. In human studies, infant formula supplemented with 2'-FL and LNnT was well tolerated with age-appropriate increases in body weight and other growth measures, and no significant increases in adverse events. 2'-FL and LNnT were also well tolerated in studies with obese children aged 5-12 years and healthy adults.

The assessment of effect on infant growth concluded that the addition of 2'-FL, alone or in combination with LNnT, to infant formula products (at the levels requested) has no effect on growth. Also, based on a lack of adverse effects on growth in the clinical studies reviewed and the limited gastrointestinal absorption of 2'-FL and LNnT, there is no evidence to indicate a nutritional concern at the concentrations of these oligosaccharides that are typically observed in human milk.

The concentration of 2'-FL in infant formula / follow-on formula / FSFYC considered in the dietary intake assessment was 2.4 g/L (rather than 1.2 g/L as requested) as this level is similar to the mean concentration in mature human milk (2.4–3.0 g/L for 2'-FL secretors, which represents approximately 80% of women worldwide). This is about one fifth of the total concentration of oligosaccharides present in mature human milk (10–15 g/L). 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).

The applicant's requested maximum of 0.6 g/L LNnT in infant formula products and FSFYC was considered in the dietary intake assessment. The mean concentration of LNnT in mature human milk is 0.28–0.31 g/L, noting all human milk contains LNnT. The estimated dietary intake of LNnT is therefore higher than that for 3 month and 9 month old breastfed infants due to the requested concentration being higher than the mean concentration in human milk. However, the use level of 0.6 g/L is within the range of LNnT concentrations in mature human milk (0.09–1.08 g/L). Estimated mean intakes of LNnT from FSFYC for 12-month-old infants and 2–3 year old children are similar to or lower than those for younger formula-fed infants (<12 months).

Overall, 2'-FL and LNnT are naturally present in human milk in a range of concentrations and ratios, providing a history of safe human exposure to these substances for breastfed infants. FSANZ concludes 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 the requested levels, or at higher estimated levels of dietary intakes based on 2.4 g/L 2'-FL.

### **2.2.2 Health effects assessment**

The assessment of anti-infective effect concluded that the addition of 2'-FL to infant formula products and FSFYC may be detrimental to attachment and growth of invasive *Campylobacter jejuni* (*C. jejuni*) infection through binding inhibition. The biological and mechanistic plausibility of this health effect is supported by evidence from an *in vivo* murine model demonstrating decreased disease severity in animals fed 5 g/L 2'-FL, binding studies demonstrating a specific interaction between invasive *C. jejuni* strains and 2'-FL, and *in vitro* studies demonstrating *C. jejuni* binding inhibition in multiple cell lines. Evidence from a human study showing a decreased incidence of *Campylobacter* associated diarrhoea in infants of mothers with a higher proportion of 2'-FL in their milk provides additional supporting evidence. Based on the evidence assessed, FSANZ considers that this health effect could occur at the level of 2'-FL requested, although the extent of the effect in infants and toddlers at this level cannot be determined. The evidence for a health effect of 2'-FL and LNnT

protecting against other pathogens and toxins is inconclusive and is primarily limited to *in vitro* inhibition studies with no specific mechanism of inhibition identified. A single human infant trial study provided limited evidence of a decreased rate of bronchitis and lower respiratory tract infection in infants fed formula supplemented with 2'-FL and LNnT. However, the reproducibility of this finding in multiple populations has not been demonstrated and is therefore inconclusive.

The assessment of bifidogenic effect concluded that the ability of *Bifidobacterium* spp. to metabolise 2'-FL and LNnT is variable within and between species and that a bifidogenic effect is biologically and mechanistically plausible if the *Bifidobacterium* strains present in the infant and toddler colon are able to metabolise 2'-FL or LNnT. A single study, published as abstracts, demonstrated that infants fed formula supplemented with 2'-FL and LNnT at levels similar to those requested, had a gut microbiome at 3 months of age that more closely resembled that of breastfed infants and with a higher relative abundance of *Bifidobacterium* spp. compared to infants fed unsupplemented formula. As the reproducibility of this study has not been demonstrated in other populations the results are inconclusive. However, the biological plausibility of a bifidogenic effect occurring due to the requested addition of 2'-FL alone or with LNnT is further supported by a single clinical feeding trial for adults that showed a shift in the gut microflora to a higher relative abundance of bifidobacteria in a dose dependent manner following supplementation with either 2'-FL or LNnT alone or in combination at a 2:1 ratio of 2'-FL:LNnT.

The assessment of immune modulation and improved barrier function concluded that there is insufficient evidence to support the assertion that infant formula supplemented with 2'-FL alone or with LNnT will have an immune modulating effect or improve barrier function in infants and toddlers. The evidence to support these proposed health effects are largely based on *in vitro* studies and are not well supported by *in vivo* animal models or infant feeding studies. Of clinical significance in the assessment of food allergies, the available evidence demonstrates that 2'-FL does not prevent the production of allergen-specific IgE-immunoglobulins after sensitisation has occurred, and therefore 2'-FL does not protect against anaphylaxis.

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, although direct and consistent evidence of association in infants and toddlers, as demonstrated by well-designed randomised control trials, are lacking. In reaching this conclusion, FSANZ has taken into consideration the complexity of definitively and reproducibly demonstrating a health effect for a substrate targeted at modulating gut microflora. Evidence from an *in vitro* laboratory study for anti-infective effect and an adult study for bifidogenic effect, 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. 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. However, a safe and nutritious substitute for human milk is needed for infants who are not breastfed. As infants and young children (i.e. 'toddlers') are vulnerable population groups, infant formula products and FSFYC are regulated by prescriptive provisions for the composition and labelling of these products. Any changes to the composition of these products must be established as safe prior to being permitted.

FSANZ has had regard to the requirements of the FSANZ Act (see section 2.5) in developing the proposed regulatory measure. Since the safety, technical and health effects assessment (SD1) concluded that there are no public health and safety concerns associated with the

addition of 2'-FL alone or with LNnT in a wide range of ratios and at levels up to 2.4 g/L 2'-FL to infant formula products and FSFYC, FSANZ also had regard to matters covered in the following two Ministerial Policy Guidelines (see SD2):

- Regulation of infant formula products<sup>11</sup>
- Intent of Part 2.9 – Special purpose foods of the Code<sup>12</sup>

The infant formula policy guideline refers to the need to demonstrate a link between physiological, biochemical or functional effects to specific health outcomes for formula-fed infants with appropriate evidence, and to use human milk as the primary reference for determining the composition of infant formula and follow-on formula. The intent of Part 2.9 policy guideline refers to the need for the proposed change to be consistent with the intended purpose of the food.

### **2.3.1 Health effects**

FSANZ has assessed each of the favourable health effects of 2'-FL and LNnT stated in the application: anti-infective effect; bifidogenic effect; and immune modulation, improved intestinal barrier function and alleviation of allergic responses.

#### **2.3.1.1 Anti-infective effect**

The current available evidence for 2'-FL supports the biological and mechanistic plausibility of an inhibitory effect against invasive *C. jejuni* infection in infants and toddlers. Human and animal studies provided evidence which linked this effect to a potential beneficial health outcome of decreased severity or incidence of invasive *Campylobacter* associated diarrhoea. *In vitro* binding studies and inhibition assays showed a specific interaction between invasive *C. jejuni* strains and 2'-FL. As discussed in section 2.2.2, FSANZ considers the anti-infective effect could occur at the requested level of 2'-FL, although the extent of the effect cannot be determined. As observed in an *in vitro* study, it is possible that higher concentrations of 2'-FL could enhance the anti-infective effect. No studies were provided which demonstrated an anti-infective effect of LNnT against invasive *C. jejuni* infection.

As discussed in section 2.2.2, the current available evidence for the stated health effects of 2'-FL or LNnT against other pathogens and toxins identified in the application, or for decreased rates of bronchitis or respiratory tract infection in infants, is inconclusive. These stated health effects are therefore not supported by the evidence.

#### **2.3.1.2 Bifidogenic effect**

For the purposes of this assessment, as discussed in the SD1 report, we have defined bifidogenic effect as the proliferation and increase in the relative abundance of bifidobacteria in the intestinal microflora. FSANZ has previously recognised (under Proposal P306 and Application A1055) that the dominance of *Bifidobacterium* in the intestinal microflora is generally considered to be beneficial to the host.

The current available evidence supports the biological and mechanistic plausibility of a bifidogenic effect at the requested levels of addition of 2'-FL alone or with LNnT, providing the *Bifidobacterium* which metabolise these oligosaccharides are present in the infant or toddler gut. The biological and mechanistic plausibility of a bifidogenic effect occurring in infants and toddlers is based on the combination of evidence from *in vitro* studies and human studies in infants and adults (noting that evidence suggests that the gut microflora of toddlers is progressively more similar to that of adults than infants). FSANZ notes that the adult study

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<sup>11</sup> [Policy guideline on infant formula products](#) (accessed 25 September 2018)

<sup>12</sup> [Policy guideline on intent of Part 2.9](#) (accessed 25 September 2018).

showed a dose dependent relationship for a bifidogenic effect, in which higher levels of 2'-FL and/or LNnT were associated with a higher relative abundance of bifidobacteria.

### **2.3.1.3 Immune modulation, intestinal barrier function and allergic response**

As discussed in section 2.2.2, 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. These stated health effects are therefore not supported by the evidence.

### **2.3.1.4 Health effects conclusion**

#### *Infant formula products*

FSANZ concludes that the requested addition of 2'-FL alone or combined with LNnT to infant formula products is safe and supported by appropriate evidence in providing potential beneficial health outcomes in infants, noting the anti-infective and bifidogenic effects may be enhanced as concentrations of 2'-FL (or LNnT in the case of the bifidogenic effect only) are increased. In reaching this conclusion, FSANZ notes that 2'-FL and LNnT occur naturally in human milk, and approval of these substances would provide alternative options to existing oligosaccharides permitted for voluntary use in infant formula products, which are not present in human milk (ITF) or only present in trace amounts (GOS). The requested addition is also consistent with the Code's defined purpose for infant formula products and the relevant Ministerial Policy Guideline (see SD2), and supports international consistency and trade opportunities (see section 2.5.1.1).

FSANZ's approach is to permit the addition of 2'-FL alone or combined with LNnT to infant formula products. Consideration of the proposed levels of use in infant formula products is discussed in section 2.3.3.1 below.

#### *FSFYC*

FSANZ concludes that the requested addition of 2'-FL alone or combined with LNnT in FSFYC is safe and supported by appropriate evidence in providing potential beneficial health outcomes in toddlers, noting the anti-infective and bifidogenic effects may be enhanced as concentrations of 2'-FL (or LNnT in the case of the bifidogenic effect only) are increased. Although the addition of these substances may not have strong alignment with the Code's definition of FSFYC, the addition is safe and may provide beneficial health outcomes in toddlers. The addition also supports international consistency and trade opportunities, and provides alternative options to existing oligosaccharides (GOS and ITF) permitted for use in FSFYC providing product innovation opportunities (see section 2.5.1.1).

FSANZ's approach is to permit the addition of 2'-FL alone or combined with LNnT to FSFYC. Consideration of the proposed levels of use in FSFYC is discussed in section 2.3.3.2 below.

### **2.3.2 Permitted use**

In permitting 2'-FL and LNnT as proposed above, express permission would be provided for both 2'-FL and LNnT to be *used as a nutritive substance* (i.e. in Schedule 29) and as *food produced using gene technology* (i.e. in Schedule 26) (as discussed in section 1.3.1).

At 1<sup>st</sup> CFS, FSANZ had proposed linking approval of 2'-FL and LNnT to the applicant's specific GM production strains *E.coli* SCR6 and *E.coli* MP572, respectively. However, after

considering industry submissions, FSANZ now proposes to link permission to the following gene-gene donor information specific to the production of the oligosaccharides:

- 2'-FL derived from *E.coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*
- LNnT derived from *E.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*.

This approach is consistent with how production microorganisms are typically listed in the Code (e.g. in the case of enzyme processing aid approvals in Schedule 18). There are no public health and safety concerns associated with this approach.

FSANZ also proposes amending Schedule 26 to add a new, separate table for *food produced using gene technology of microbial origin*, which lists 2'-FL and LNnT from the permitted source as listed above. Consequently, an amendment to the existing table in Schedule 26 would be made to clarify the existing list of approvals are of plant origin (i.e. *food produced using gene technology of plant origin*). This approach clearly delineates the different sources of permitted GM foods (i.e. plant origin and microbial origin), similar to the existing approach used in S18—4 of the Code which lists permitted enzymes in separate tables for plant, animal and microbial origin. The proposed changes to Schedule 26 do not change the requirements for pre-market assessment and approval of GM foods, or alter the existing approvals of plant origin.

The applicable GM labelling requirements are discussed in section 2.3.5.5 below.

FSANZ's approach is to permit both 2'-FL and LNnT to be *used as a nutritive substance*, and as *food produced using gene technology* linked to the gene-gene information specific to the production of the oligosaccharides, for use in infant formula products and FSFYC.

### **2.3.3 Maximum use levels and units expression**

FSANZ has considered the maximum requested levels of 2'-FL and LNnT in the context of the safety, technical and health effects assessment, including estimated dietary intakes and naturally occurring levels in human milk, and other relevant matters as discussed in the following sections.

#### **2.3.3.1 Infant formula products**

As the safety, technical and health effects assessment concluded that there are no public health and safety concerns associated with the addition of 2'-FL alone or with LNnT to infant formula products at the requested levels, or at higher estimated levels of dietary intakes based on 2.4 g/L 2'-FL, FSANZ has also considered the levels of use in relation to potential beneficial health outcomes, international regulations and existing permissions for other non-digestible oligosaccharides.

As discussed in section 2.3.1.1, higher levels of 2'-FL could potentially enhance the effect of this substance against invasive *C. jejuni* infection in infants (and toddlers). As noted in section 2.2.1, a level of use double that requested (i.e. 2.4 g/L rather than 1.2 g/L) in infant formula and follow-on formula provides dietary intakes of 2'-FL similar to 3 and 9 month old breastfed infants.

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 for use 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.

Regarding the combined use of 2'-FL and LNnT, as discussed in SD1, where 2'-FL and LNnT occur together naturally in human milk (in the majority of women) there is shown to be a wide variation in the ratio of 2'-FL to LNnT present from about 1:1 to greater than 10:1. FSANZ therefore considers that a maximum combined total of 2.4 g/L for 2'-FL and LNnT in any ratio, is safe and suitable for addition to infant formula products. This proposed combined total is 33% higher than the amount requested (i.e. from 1.8 g/L to 2.4 g/L). This approach differs from the applicant's request for separate maxima of 1.2 g/L 2'-FL or 1.8 g/L combined but has the advantage of setting the same overall total for one or both requested substances. This same approach was adopted for GOS and ITF. When used in combination, the requested maximum of 0.6 g/L LNnT is proposed to be permitted, noting this is within the range naturally present in mature human milk and is consistent with international permissions.

As discussed in section 2.3.1.4, approval of 2'-FL and LNnT would provide alternative options to existing oligosaccharides permitted for use in infant formula products. FSANZ notes that a maximum of 2.4 g/L for 2'-FL alone and for 2'-FL and LNnT combined, is around three times lower than the maximum amount currently permitted for GOS alone or combined with ITF (i.e. based on 8 g/L), and lower than the maximum permitted for ITF (i.e. based on 3 g/L). 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).

FSANZ also proposes prohibiting the use of existing GOS and ITF permissions in combination with 2'-FL and LNnT, as further discussed in section 2.3.4. As such, there would be no cumulative increase to the total oligosaccharide load consumed by infants.

Based on the available evidence, including comparative levels in human milk and other relevant matters considered above, FSANZ proposes to permit a maximum of 2.4 g/L of 2'-FL alone in infant formula products; and a total maximum of 2.4 g/L for 2'-FL and LNnT combined, with no more than 0.6 g/L of LNnT. For consistency with existing permissions for the addition of substances to infant formula products in the Code, FSANZ has converted the maximum levels to mg/100 kJ units as set out below (further discussion about this approach is provided in Attachment C).

These maximum permitted amounts capture both naturally-occurring and added 2'-FL and LNnT. Noting that the concentration of naturally occurring 2'-FL and LNnT in cow's or goat's milk is low or not present (see SD1), the amounts present in infant formula products and FSFYC would primarily be based on added 2'-FL and LNnT.

A minimum permitted amount is not proposed as this was not requested in the application and has not been determined by FSANZ.

FSANZ's approach is to permit the following maximum levels for addition to infant formula products:

- If only 2'-FL added – not more than 96 mg/100 kJ of 2'-FL
- If both 2'-FL and LNnT added – 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.

### 2.3.3.2 FSFYC

To provide a consistent regulatory approach across infant formula products and FSFYC, FSANZ also considered a maximum permitted level of 2.4 g/L of 2'-FL alone in FSFYC; and a total maximum of 2.4 g/L of 2'-FL and LNnT combined, with no more than 0.6 g/L of LNnT.

As discussed in section 2.2.1, there are no public health and safety concerns for FSFYC at the estimated levels of dietary intake based on 2.4 g/L of 2'-FL or 0.6 g/L of LNnT. Although not directly comparable, FSANZ notes that the estimated intakes for 2'-FL or LNnT from FSFYC in toddlers are less than the intakes for the more vulnerable 3 month old infants who are exclusively formula-fed, and for whom intakes based on 2.4 g/L of 2'-FL or 0.6 g/L of LNnT are safe.

As discussed for infant formula products above, higher levels of 2'-FL could potentially enhance the effect of 2'-FL against invasive *C. jejuni* infection in toddlers. There is also some evidence that higher levels of 2'-FL and/or LNnT could increase the abundance of bifidobacteria in the gut microflora as discussed in section 2.3.1.2.

Also similar to infant formula products, a maximum of 2.4 g/L of 2'-FL (rather than 1.2 g/L) would promote greater compatibility with international permissions for FSFYC. A maximum of 2.4 g/L for 2'-FL alone and for 2'-FL and LNnT combined, is also lower than the total level currently permitted for GOS or ITF in FSFYC (i.e. based on 8 g/L). A maximum of 0.6 g/L of LNnT is consistent with international FSFYC permissions.

FSANZ therefore proposes permitting a maximum of 2.4 g/L for 2'-FL alone in FSFYC; and a total maximum of 2.4 g/L for 2'-FL and LNnT combined, with no more than 0.6 g/L of LNnT. For consistency with existing permissions for the addition of substances to FSFYC in the Code, FSANZ has converted these maximum permitted amounts to g/serving units as set out below (further discussion about this approach is provided in Attachment C). A slight correction to the converted level for 2'-FL alone and for 2'-FL and LNnT combined has been made since the 1<sup>st</sup> CFS (i.e. amended from 0.56 to 0.55 g/serving). The maximum amounts capture both naturally-occurring and added 2'-FL and LNnT.

A minimum permitted amount is not proposed as this was not requested in the application and has not been determined by FSANZ.

FSANZ's approach is to permit the following maximum levels for addition to FSFYC:

- If only 2'-FL added – not more than 0.55 g/serving
- 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.

### 2.3.4 Prohibition of use with existing oligosaccharide permissions

FSANZ notes that the applicant is not seeking use of the proposed permissions for 2'-FL and LNnT together with existing permissions for GOS and ITF in infant formula products or FSFYC. We have, however, considered the available evidence for this potential combined use. As discussed in SD1, no adverse effects were reported in infant studies which tested formula supplemented with 2'-FL in combination with scFOS (a permitted ITF) or GOS. However, the maximum amounts of scFOS or GOS permitted in the Code were not tested in these studies. Additionally, no evidence was provided which investigated the use of 2'-FL combined with both GOS and scFOS (i.e. GOS and ITF are currently permitted to be used in combination in infant formula products in the Code). As such, the tolerance of infants to this total combination of added oligosaccharides could not be determined, noting also that this combination does not occur naturally in human milk.

Based on the available evidence, and given the combined use of the proposed and existing permissions is not requested, FSANZ proposes prohibiting the use of 2'-FL and LNnT in combination with existing GOS and ITF permissions.

FSANZ's approach is to prohibit the addition 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).

## **2.3.5 Labelling**

### **2.3.5.1 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 1<sup>st</sup> CFS, 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 1<sup>st</sup> CFS, FSANZ has reconsidered the approach to prescribe ingredient names and is now of the view that generic ingredient naming requirements should apply, consistent with the general approach in the Code. There is no prescription in the Code for the naming other ingredients (including nutritive substances) currently permitted to be added to infant formula products and FSFYC. The revised approach will provide 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 is suggested by the applicant).

FSANZ has addressed concerns about the use of terms such as 'human milk identical oligosaccharide' or 'HiMO' by proposing a specific prohibition as discussed below in section 2.3.5.2.

### **2.3.5.2 Prohibited representations**

After considering submissions to the 1<sup>st</sup> CFS, FSANZ is now proposing to specifically prohibit reference to 'human milk identical oligosaccharide', 'human milk oligosaccharide', 'HiMO' or 'HMO' (or words or abbreviations of similar effect) on infant formula products and FSFYC.

#### *Infant formula products*

Although the intent of section 2.9.1—24 (Prohibited representations) is to prevent the use of such terms in the statement of ingredients or nutrition information statement (noting representations elsewhere on the label are already prohibited) on infant formula products, FSANZ considers a specific prohibition would communicate more clearly that such

terminology is inconsistent with specific policy principle I of the Ministerial Policy Guideline on the Regulation of Infant Formula Products.

FSANZ's approach is to specifically prohibit the following terms on the label of infant formula products:

- 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.

#### *Formulated supplementary foods for young children*

In regard to FSFYC, FSANZ considers terms such as 'human milk identical oligosaccharide' would be confusing to caregivers if they are present on FSFYC labels and not on infant formula products. Further, the presence of such terms could mislead consumers. FSFYC (or 'toddler milks') are not considered breastmilk substitutes in Australia and New Zealand, however, there is a risk that this terminology may suggest FSFYC are intended for 'infants', which is contrary to the infant formula policy guideline.

Research commissioned by FSANZ (Malek et al. 2019) suggests some caregivers interpret references to breastmilk on infant formula products as an indication those particular products are closer in composition to breastmilk than other brands. Research conducted with advertisements for toddler milk products has found similar responses to references to breastmilk. In one of the studies reviewed, three of four respondents who saw a claim about prebiotics 'found naturally in breastmilk' next to a statement concerning the importance of breastfeeding, believed the advertisement suggested an equivalence between 'formula' and breastmilk' (Berry, Jones & Iverson, 2010).

This concern is relevant to FSFYC because Australian research suggests that when caregivers are shown toddler milk advertisements they believe they are also advertising infant formula products (Berry, Jones & Iverson, 2010, 2011, 2012). This is partly due to their similar packaging and common branding. The implication of this is that where a toddler milk product carries a reference to human milk, it is possible caregivers may infer infant formula and follow on formula within the same brand range are closer in composition to breastmilk than other products. Furthermore, it is possible that caregivers who believe an infant formula product is closer in composition to breastmilk may be more likely to use infant formula in place of or in addition to breastfeeding (Malek et al. 2019).

Another 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. An Australian study (Berry, Jones & Iverson, 2012) investigated whether parents perceive toddler milk advertising as also promoting infant formula. In the study, 439 Australian parents were asked to recall if they had seen an advertisement for 'formula' and, if so, whether the advertisement originated from a retailer or from elsewhere. Ninety three percent of respondents indicated they had seen an advertisement that was not from a retailer. Two thirds of respondents reported they had seen a formula product suitable for use from birth advertised. Around two thirds of respondents who only reported seeing non-retail formula advertisements (i.e. did not report seeing retail formula advertisements) believed they had seen an advertisement for infant formula. As manufacturers in Australia have agreed not to advertise infant formula products to caregivers, the authors concluded the caregivers must have actually been seeing advertisements for toddler milk products. However, they were recalling these as advertisements for infant formula products.

In the same study, respondents were asked to indicate which, if any, of seven claims<sup>13</sup> they had seen in relation to the product they saw advertised (Berry, Jones & Iverson, 2012). The seven claims were variations of claims that appeared in toddler milk advertising in 2007. More than 90% of the respondents who reported having seen an infant formula advert in the past also reported having seen at least one of the seven claims (which are not permissible on infant formula). Twenty seven percent of respondents reported they had seen a formula advertisement claiming the product 'is like breastmilk'. These findings provide further evidence that caregivers confuse advertising for toddler milks with advertising for infant formula. Again, this is likely due to similar packaging and styling of brand lines. The findings of this study suggest references to terms such as 'human milk identical oligosaccharide' on toddler milks could influence caregivers' perceptions of infant formula products. In particular, they may believe infant formula products in the same product range are closer in composition to breastmilk than other products.

Noting that section 2.9.1—24 states that *the word 'humanised' or 'maternalised' or any word or words having the same or similar effect and information relating to the nutritional content of human milk* are prohibited on infant formula product labels, FSANZ considers the presence of terms such as 'human milk identical oligosaccharide' on FSFYC could imply substantive equivalence with breastmilk.

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 breastmilk. With the exception of the research by Malek et al. (2019), the research described above is limited to Australia. However, FSANZ considers New Zealand caregivers are likely to respond in a similar way to references to human milk as Australian caregivers.

FSANZ's approach is to specifically prohibit the following terms on the label of 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.

### **2.3.5.3 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 FSANZ proposes to permit both 2'-FL and LNnT to be *used as a nutritive substance* in infant formula products, when they are used, they must be declared in the nutrition information statement.

For FSFYC, the existing general requirements in Standard 1.2.8 – Nutrition information requirements would 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.

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<sup>13</sup> Seven claims included: is like breast milk, is convenient, makes babies healthy/happy, improves brain development/contains nutrients such as Omega 3, iron or probiotics, ensures proper growth and development.

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's preferred approach in which the ingredient names are not prescribed (see section 2.3.5.1) would mean that the use of acronyms (e.g. 2'-FL or LNnT) is not prohibited on infant formula products or FSFYC. However, manufacturers would 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).

#### **2.3.5.4 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.

This regulatory approach is consistent with the Ministerial Policy Guidelines on Nutrition, Health and Related Claims<sup>14</sup> and the Regulation of Infant Formula Products (specific policy principle n, see SD2).

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

In contrast, there is no prohibition in the Code for nutrition content or health claims to be made about FSFYC. Existing claim requirements and conditions set out in Standard 1.2.7 and Schedule 4 – Nutrition, health and related claims would therefore apply to FSFYC. This is consistent with the current approach for other permitted substances (e.g. lutein, GOS) that may be added voluntarily to FSFYC.

However, noting the preferred approach in section 2.3.5.2, terms such as 'human milk identical oligosaccharide' or abbreviations such as 'HiMO' would be prohibited, meaning they could not be used in the wording of a nutrition content or health claim for FSFYC.

#### **2.3.5.5 Labelling as 'genetically modified'**

As discussed in the safety, technical and health effects assessment (SD1), 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' would apply in accordance with section 1.5.2—4 of Standard 1.5.2.

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<sup>14</sup> [Policy guideline on Nutrition, Health and Related Claims](#) (accessed 25 September 2018)

### 2.3.6 Specifications for 2'-FL and LNnT

At 1<sup>st</sup> CFS, FSANZ broadly proposed that, since no specifications currently exist for 2'-FL or LNnT in Schedule 3, the specifications provided in the application would be inserted into the Code. Following consideration of submissions to the 1<sup>st</sup> CFS, FSANZ confirms that it does not propose to include the applicant's specific methods of analysis in the specifications in the Code (Schedule 3). This approach is consistent with other specifications in the Code which do not list methods of analysis.

The proposed specifications are essentially identical to those approved in the EU and US at the time of FSANZ's assessment (as discussed in SD1), and are captured by the current EU specifications which have come into force since the 1<sup>st</sup> CFS publication (see section 1.3.2.2).

FSANZ's approach is to set specifications for 2'-FL and LNnT in the Code using those provided by the applicant (without specifying the methods of analysis).

### 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<sup>15</sup> on the basis that they, and their business partners, have invested significantly in the technology development and safety studies.

At 1<sup>st</sup> CFS, FSANZ noted the previously proposed approval of 2'-FL and LNnT linked to the applicant's specific GM production strains may provide exclusive permission to the applicant, without the need for a specific brand name. As discussed in section 2.3.2, FSANZ now proposes linking permission to the gene-gene donor information specific to the production of the oligosaccharides. As this new approach does not inherently provide exclusivity to the applicant, FSANZ proposes to provide 15 months exclusivity from the date of gazettal, linked to the applicant's brand of 2'-FL and LNnT. This exclusive permission will be set out in Schedule 26 of the Code. Following the 15 month period, the permission would 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.

FSANZ's approach is to provide 15 months exclusivity from the date of gazettal for the applicant's brand of 2'-FL and LNnT.

### 2.3.8 Risk management conclusion

Having considered all aspects of the assessment against the statutory requirements, including relevant Ministerial Policy Guidelines, FSANZ has prepared a draft variation to permit the voluntary addition of 2'-FL alone, and 2'-FL and LNnT combined, to infant formula products and FSFYC.

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<sup>15</sup> Brand name GlyCare.

The draft variation is based on the proposed regulatory measures summarised in the following list.

### **Summary of FSANZ's proposed regulatory measures**

- Permit both 2'-FL and LNnT to be *used as a nutritive substance*, and 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.
- Set a maximum permitted use level of 2.4 g/L for 2'-FL alone; and a total maximum level of 2.4 g/L for 2'-FL and LNnT combined with no more than 0.6 g/L of LNnT. For consistency with existing voluntary permissions for infant formula products and FSFYC, these levels are expressed in mg/100 kJ and g/serving as follows:

Infant formula products:

- If only 2'-FL added – not more than 96 mg/100 kJ of 2'-FL
- If both 2'-FL and LNnT added – 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.

FSFYC:

- If only 2'-FL added – not more than 0.55 g/serving
- 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.

- 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 of 2'-FL and LNnT.

The details supporting this recommendation are outlined in the following sections. The draft variation reflecting this option is at Attachment A. The draft explanatory statement for the variation is in Attachment B.

## **2.4 Risk communication**

### **2.4.1 Consultation**

Consultation is a key part of FSANZ's standards development process.

FSANZ has developed a communication strategy for this application. Subscribers and interested parties have been notified about this 2<sup>nd</sup> CFS 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 1<sup>st</sup> CFS from 22 November 2018 – 17 January 2019. Twelve submissions were received. The issues raised in submissions are addressed in section 2.1.

FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application. All comments are valued and contribute to the rigour of our assessment. Comments received will be taken into account when developing any draft variation(s) for approval by the FSANZ Board.

If the draft variation to the Code is approved by the FSANZ Board, that decision will be notified to the Australia and New Zealand Ministerial Forum on Food Regulation. If the Board's decision is not subject to a request for a review, the applicant and stakeholders, including the public, will be notified of the gazettal of the variation to the Code in the national press and on the FSANZ website.

#### **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 1<sup>st</sup> 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 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**

When assessing this application and the subsequent development of food regulatory measures, FSANZ has had regard to the following matters in section 29 of the FSANZ Act:

#### **2.5.1 Section 29**

##### **2.5.1.1 Consideration of costs and benefits**

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 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 1<sup>st</sup> 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 1<sup>st</sup> 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 draft 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. 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 the biological and mechanistic plausibility of a bifidogenic effect from the proposed use of 2'-FL alone or combined with LNnT, providing the bifidobacterium strains which metabolise these oligosaccharides are present. 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 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. 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, which 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 has completed a safety, technical and health effects assessment (SD1) 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 the requested levels, or at higher estimated levels of dietary intakes based on 2.4 g/L 2'-FL.

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

Current labelling requirements would apply to 2'-FL and LNnT when added to infant formula or FSFYC, as discussed in section 2.3.5, 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, would apply to 2'-FL and LNnT when added to infant formula or FSFYC. Further, 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 breastmilk (see section 2.3.5.2).

### **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 best available scientific evidence to assess this application. The applicant submitted a dossier of scientific studies as part of its application. Other relevant information including scientific literature was also used in assessing the application. In light of issues raised in submissions, 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. An additional clinical study provided by the applicant has been assessed by FSANZ in SD1.

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

The applicant's 2'-FL and LNnT are permitted for use overseas, including in the US and EU. Permitting 2'-FL and LNnT as proposed by FSANZ will promote greater compatibility between domestic and overseas food standards for infant formula products and FSFYC.

- **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

FSANZ considers these policy guidelines have been adequately addressed. Our assessment against the policy guidelines is provided at SD2.

### **3 Draft variation**

The draft variation to the Code is at Attachment A and is intended to take effect on gazettal.

A draft 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.

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## **Attachments**

- A. Draft variation to the *Australia New Zealand Food Standards Code*
- B. Draft Explanatory Statement
- C. Units basis for expressing maximum permitted amounts

## Attachment A – Draft variation 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
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[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
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[4.2] inserting in the table to subsection S3—2(2) in alphabetical order

lacto-N-neotetraose	section S3—41
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[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— $\alpha$ -L-fucopyranosyl-(1→2)- $\beta$ -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— $\beta$ -D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy- $\beta$ -D-glucopyranosyl-(1→3)- $\beta$ -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**

<b>Substance</b>	<b>Source</b>	<b>Conditions of use</b>
<b>1 2'-O-fucosyllactose</b>	(a) <i>Escherichia coli</i> K-12 containing the gene for alpha-1,2-fucosyltransferase from <i>Helicobacter pylori</i>	<ol style="list-style-type: none"> <li>1. May only be added to infant formula products and to formulated supplementary food for young children.</li> <li>2. During the exclusive use period, may only be sold under the brand GlyCare.</li> <li>3. For the purposes of condition 2 above, <b>exclusive use period</b> means the period commencing on the date of gazettal of the <i>Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation</i> and ending 15 months after that date.</li> </ol>
<b>2 Lacto-N-neotetraose</b>	(a) <i>Escherichia coli</i> K-12 containing the gene for beta-1,3-N-acetylglucosaminyltransferase from <i>Neisseria meningitides</i> and the gene for beta-1,4-galactosyltransferase from <i>Helicobacter pylori</i>	<ol style="list-style-type: none"> <li>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.</li> <li>2. During the exclusive use period, may only be sold under the brand GlyCare.</li> <li>3. For the purposes of condition 2 above, <b>exclusive use period</b> means the period commencing on the date of gazettal of the <i>Food Standards (Application A1155 – 2'-FL and LNnT in infant formula and other products) Variation</i> and ending 15 months after that date.</li> </ol>

[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**

<b>Column 1</b>	<b>Column 2</b>	<b>Column 3</b>	<b>Column 4</b>
<i>Substance</i>	<i>Permitted forms</i>	<i>Minimum amount per 100 kJ</i>	<i>Maximum amount per 100 kJ</i>
2'-O-fucosyllactose permitted for use by Standard 1.5.2	2'-O-fucosyllactose		96 mg
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

<b>Column 1</b>	<b>Column 2</b>	<b>Column 3</b>	<b>Column 4</b>
<i>Substance</i>	<i>Permitted forms</i>	<i>Minimum amount per 100 kJ</i>	<i>Maximum amount per 100 kJ</i>
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 <i>Tagetes erecta L.</i>	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**

<b>Column 1</b>	<b>Column 2</b>	<b>Column 3</b>
<i>Substance</i>	<i>Permitted form</i>	<i>Maximum amount per serving</i>
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 <i>Tagetes erecta L.</i>	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 seeks 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 prepared a draft variation to the Code.

### **2. Purpose**

The Authority has prepared a draft variation 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 will include two rounds of public comment following an assessment and the preparation of a draft Standard and associated assessment summaries (this being the second consultation round).

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.

## 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.

### *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 will only be 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)) will be permitted for use in infant formula products. The permission in section 29—5 also lists permitted forms, and will require 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 – Units basis for expressing maximum permitted amounts

### 1 Infant formula products

Existing compositional requirements for infant formula products regulated in Standard 2.9.1 and Schedule 29 of the Code are primarily based on mg/100 kJ units. For consistency with existing provisions, FSANZ proposes to base the maximum amounts of 2'-FL and LNnT permitted for use in infant formula products on mg/100 kJ units as follows:

- If only 2'-FL added – not more than 96 mg/100 kJ of 2'-FL
- If both 2'-FL and LNnT added – not more than 96 mg/100 kJ of 2'-FL and LNnT combined, of which contains no more than 24 mg/100 kJ of LNnT.

The minimum energy content of 2500 kJ/L currently permitted for infant formula and follow-on formula in the Code (section 2.9.1—9) was used to convert the proposed g/L amounts (i.e. 2.4 g/L of 2'-FL alone; and 2.4 g/L of 2'-FL and LNnT combined, with no more than 0.6 g/L LNnT) to mg/100 kJ.

This approach based on mg/100 kJ would mean that the actual amount of 2'-FL and LNnT in infant formula products could vary depending on the energy content of the formula. In particular, a formula with a higher energy content per 100 mL may contain more 2'-FL, or more 2'-FL and LNnT, than a formula with a lower energy content. However, where a formula has a higher energy content, less formula would need to be consumed to meet infant energy requirements. Conversely, more would need to be consumed to meet infant energy requirements for a formula with a lower energy content. As such, the respective dietary intakes for 2'-FL and LNnT would be similar for formulas with varying energy contents as the amount of formula consumed is regulated by infant energy needs.

FSANZ's dietary intake assessment (SD1) estimated the respective dietary intakes of 2'-FL and LNnT from infant formula and follow-on formula (for infants aged 3 and 9 months respectively), using the proposed amounts in mg/100 kJ units listed above. As discussed in section 2.2.1, the estimated intake of 2'-FL was similar to the intakes from 3 and 9 month old breastfed infants. Although the estimated intake of LNnT was higher than those for 3 and 9 month old breastfed infants (based on the mean concentration present in human milk), the proposed maximum use level is within the range of concentrations naturally present in human milk (i.e. 0.09 – 1.08 g/L). Additionally, the highest P90 intakes estimated for 2'-FL and LNnT respectively, were well below the no observable adverse effect level (NOAEL) identified by FSANZ in SD1 (i.e. 7-fold lower for 2'-FL, and 30-fold lower for LNnT, for 3 month old infants).

Based on the conclusions of FSANZ's safety, technical and health assessment, and noting the range of 2'-FL and LNnT concentrations naturally present in human milk, FSANZ considers that the proposed maximum permitted amounts based on mg/100 kJ are unlikely to pose a risk to infant health.

## 2. Formulated supplementary foods for young children

Existing permissions in Division 4 of Standard 2.9.3 and Schedule 29 for the addition of substances to FSFYC are on a per serving basis. For consistency with existing permissions, FSANZ proposes to base the maximum amounts of 2'-FL and LNnT permitted for use in FSFYC on g/serving units as follows:

- If only 2'-FL added – not more than 0.55 g/serving
- 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.

A 230 mL serve size was used for the conversion from the proposed maximum g/L amounts to g/serving. According to the applicant, and an online search of FSFYC products by FSANZ, this is the largest serve size currently used in the Australia and New Zealand FSFYC market. FSANZ has corrected the converted amount for 2'-FL alone and 2'-FL and LNnT combined since the 1<sup>st</sup> CFS (i.e. corrected from 0.56 to 0.55 g/serving as listed above).

'Serving' is defined in Standard 1.1.2 – Definitions used throughout the Code<sup>16</sup>. The serving size is determined by the food manufacturer and must be declared in the nutrition information panel (Standard 1.2.8). The proposed permission in the Code would therefore specify the permitted amounts per serve (as listed above), but would not specify the serving size. This means that the permitted amounts per serving would be the same irrespective of the serving size (e.g. maximum of 0.55 g of 2'-FL per 115 mL serving and per 230 mL serving).

FSANZ's dietary intake assessment (SD1), estimated the respective dietary intakes of 2'-FL and LNnT from FSFYC (for 12 month old infants and 2–3 year old children) using the proposed amounts based on g/serving listed above. In the modelling, two FSFYC serving sizes were used to provide a range of estimated intakes (i.e. smallest serve of 115 mL and largest serve of 230 mL as currently available in the Australia and New Zealand market). The smaller FSFYC serving size resulted in higher intakes of 2'-FL and LNnT respectively, as more servings would need to be consumed to meet the energy needs of an older infant and young child.

As discussed in section 2.3.3.2 of this report, the estimated intakes from FSFYC are similar to or less than the respective intakes of 2'-FL and LNnT for 3 month old infants who are exclusively formula-fed and are a more vulnerable population group. The highest P90 intakes of 2'-FL and LNnT from FSFYC are also well below the NOAEL's identified by FSANZ in SD1 (i.e. 12-fold lower for 2'-FL, and 50-fold lower for LNnT, for 12 month old infants).

As there are no safety concerns identified with the proposed addition of 2'-FL and LNnT to FSFYC, FSANZ considers that the maximum levels based on g/serving are unlikely to pose a risk to the health of young children.

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<sup>16</sup> *Serving* means an amount of the food which constitutes one normal serving when prepared according to manufacturer's directions or when the food requires no further preparation before consumption, and in the case of a formulated meal replacement is equivalent to one meal.