25 September 2023
263-23

Approval Report – Application A1265

A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products

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Food Standards Australia New Zealand (FSANZ) has assessed an application made by Glycom A/S to amend the Australia New Zealand Food Standards Code to permit the voluntary addition of 2'-fucosyllactose (2'-FL) and difucosyllactose (DFL) (2'-FL/DFL), lacto-N-tetraose (LNT), 6'-sialyllactose (6'-SL) sodium salt and/or 3'-sialyllactose (3'-SL) sodium salt as nutritive substances in infant formula products.

On 8 June 2023, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received ten submissions.

FSANZ approved the draft variation with amendments on 13 September 2023. The Food Ministers' Meeting was notified of FSANZ's decision on 25 September 2023.

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

Table of contents

Supporting document

The following document which informed the assessment of this application is available on the FSANZ website:

SD1 Risk assessment - Risk, technical and benefit assessment (at Approval)

Executive summary

Food Standards Australia New Zealand (FSANZ) assessed Application A1265 made by Glycom A/S (the Applicant) to amend the Australia New Zealand Food Standards Code (the Code) to permit the voluntary addition of four human-identical milk oligosaccharide products for use as nutritive substances in infant formula products[1]. The substances are produced by microbial fermentation using a genetically modified strain of *Escherichia coli* K-12. The substances and their proposed maximum permitted amounts are:

- a mixture of 2'-fucosyllactose (2'-FL) and difucosyllactose (DFL) (2'-FL/DFL) (96 mg/100 kJ);
- lacto-N-tetraose (LNT) (32 mg/100 kJ);
- 6'-sialyllactose (6'-SL) sodium salt (16 mg/100 kJ); and
- 3'-sialyllactose (3'-SL) sodium salt (8 mg/100 kJ).

The applicant also requested an exclusive use permission for their brand of each substance for a period of 15 months after gazettal.

FSANZ's safety and technical assessment concluded that there are no public health and safety concerns associated with adding the substances to infant formula products at the levels requested, which are comparable to levels in human milk and are chemically and structurally identical to the naturally occurring forms.

In accordance with the relevant Ministerial Policy Guidelines[2], FSANZ's assessment of beneficial health effects and intended purpose concluded that the use of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, individually or in combination in infant formula products, would have a beneficial outcome for infants and align with the equivalent role of these substances in human milk. The weight of evidence supports health effects of 2'-FL/DFL, LNT, 6'-SL and 3'-SL added to infant formula products through an increase in the abundance of *Bifidobacterium* spp. in the infant gut microbiota, anti-pathogenic effects, inflammatory suppression and facilitation of appropriate immune responses and antigenic memory.

Following assessment and the preparation of a draft variation, FSANZ called for submissions regarding the draft variation from 8 June 2023 to 7 July 2023. Ten submissions were received, all of which FSANZ had regard to (see Section 2.1 of this report for details of submissions made).

Based on the information above and on other relevant considerations set out in this report, FSANZ has approved the draft variation proposed following assessment with amendments. The effect of the approved draft variation is that the voluntary addition of 2'-FL/DFL, LNT, 6'-SL and 3'-SL to be used as a nutritive substance and as food produced using gene technology in infant formula products will be permitted in accordance with the Code. The approved draft variation will:

- amend Schedule 29 of the Code to permit the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL to be used in infant formula products, either alone or in combination, as a nutritive substance up to a specified maximum permitted amount;
- amend Schedule 26 of the Code to permit the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, as substances derived from a new genetically modified microbial source, to be

[1] Includes infant formula, follow-on formula and infant formula products for special dietary purposes.

[2] Policy guideline on infant formula products and Policy guideline on intent of Part 2.9 of the Food Standards Code - special purpose foods.

added to infant formula products subject to certain conditions, including an exclusive use period of 15 months for the applicant's brand of each substance;

- amend Schedule 3 of the Code to include identity and purity specifications for the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL; and
- remove the current prohibition in Standard 2.9.1 on the use of galacto-oligosaccharides and/or inulin-type fructans with lacto-N-neotetraose.

1 Introduction

1.1 The applicant

The applicant, Glycom A/S, is a Danish food ingredient manufacturer who specialises in the development, synthesis and commercialisation of human-identical milk oligosaccharide[3] (HiMO) substances.

1.2 The application

Glycom A/S sought to amend the Australia New Zealand Food Standards Code (the Code) to permit the voluntary addition of four HiMO products for use as nutritive substances in infant formula products[4]. The substances are produced by microbial fermentation using a genetically modified strain of *Escherichia coli* K-12. The substances and their proposed maximum permitted amounts are:

- a mixture of 2'-fucosyllactose (2'-FL) and difucosyllactose (DFL) (2'-FL/DFL) (96 mg/100 kJ);
- lacto-N-tetraose (LNT) (32 mg/100 kJ);
- 6'-sialyllactose (6'-SL) sodium salt (16 mg/100 kJ); and
- 3'-sialyllactose (3'-SL) sodium salt (8 mg/100 kJ).

2'-FL/DFL, LNT, 6'-SL and 3'-SL are non-digestible oligosaccharides that are components of human milk. The applicant applied to add its 2'-FL/DFL, LNT, 6'-SL and 3'-SL, individually or in combination, as nutritive substances to infant formula products. The substances are not expressly permitted by the Code for use as nutritive substances, and as per paragraph 1.1.1—10(6)(b) of Standard 1.1.1, required pre-market assessment.

1.3 The current Code requirements

Australian and New Zealand food laws require food for sale to comply with relevant provisions in the Code. The provisions relevant to this application are summarised below.

1.3.1 Infant formula products

The composition and labelling of IFP is regulated in Standard 2.9.1 and Schedule 29. They set out specific compositional and labelling requirements for the following infant formula products:

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

1.3.2 Permitted use

Food produced using gene technology

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*. The four substances are

[3] The term “HiMO” is used in this Approval Report to refer generically to human-identical milk oligosaccharides when relevant. It is not intended to indicate or infer that the term is appropriate or approved to be used in labelling infant formula products.

[4] Includes infant formula, follow-on formula and infant formula products for special dietary purposes.

each considered a *food produced using gene technology* (section 1.1.2—2) having been derived from an organism modified using gene technology (i.e. derived from genetically modified (GM) *E.coli* strains). Express permission for 2'-FL/DFL, LNT, 6'-SL and 3'-SL produced using *Escherichia coli (E.coli)* K-12 is required in accordance with Standard 1.5.2 (i.e. to be listed in Schedule 26 and to comply with any corresponding conditions).

Nutritive substances

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* (as defined in section 1.1.2—12).

FSANZ considered the four substances to be nutritive substances because their addition to food is intended to achieve specific nutritional purposes (as per the stated definition of a nutritive substance in section 1.1.2—12 of the Code). Therefore, an express permission for 2'-FL/DFL, LNT, 6'-SL and 3'-SL to be *used as a nutritive substance* is required in section S29—5 in addition to the permission as *food produced using gene technology* above.

1.3.3 Identity and purity

Section 1.1.1—15 requires that a substance that is *used as a nutritive substance* must comply with any relevant identity and purity specification set out in Schedule 3. Schedule 3 currently only lists two specifications for HiMO: 2'-FL and lacto-N-neotetraose (LNnT). 2'-FL has been assessed in applications A1155, A1190 and A1233 (FSANZ 2019; FSANZ 2021a; FSANZ 2022). ApplicationA1155 assessed permitting both 2′-FL and LNnT in infant formula products[5] and other products.

1.3.4 Labelling requirements

Subsection 1.1.1—10(8) requires that food for sale must comply with all relevant labelling requirements in the Code for that food.

Section 1.2.4—2 requires food products to be labelled with a statement of ingredients. Section 1.2.4—4 requires ingredients to be declared using: a name by which they are commonly known; a name that describes their true nature; or a generic ingredient name if one is specified in Schedule 10.

Standard 1.2.7 sets out the requirements and conditions for voluntary nutrition content and health claims made about food. Paragraph 1.2.7—4(b) states a nutrition content claim or health claim must not 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*[6] (GM food).

Subparagraph 2.9.1—21(1)(a)(iii) of Standard 2.9.1 requires the average amount of any substance used as a nutritive substance permitted by Standard 2.9.1 to be declared in the nutrition information statement (NIS), expressed in weight/100 mL. Paragraphs 2.9.1—24(1)(ca) and (cb) prohibit the use of: the words ‘human milk oligosaccharide’, ‘human milk

[5] Application A1155 assessed the voluntary addition of 2′-FL and LNnT to infant formula products and formulated supplementary food for young children (FSFYC). Only permission for infant formula products was approved.

[6] Section 1.5.2—4(5) defines ***genetically modified food*** to mean a ‘*food produced using gene technology that
a) contains novel DNA or novel protein; or
b) is listed in Section S26—3 as subject to the condition that its labelling must comply with this section’ (*that being section 1.5.2—4*).

identical oligosaccharide'; the abbreviations 'HMO' or 'HiMO'; or any words and abbreviations having the same or similar effect. Paragraph 2.9.1—24(1)(f) prohibits a reference to the presence of a nutrient or substance that may be used as a nutritive substance, except for a reference in: a statement relating to lactose under subsection 2.9.1—14(6); a statement of ingredients; or in the NIS.

1.3.5 Current oligosaccharide permissions and restrictions

2'-FL and LNnT are permitted to be *used as a nutritive substance* in infant formula products in accordance with section 2.9.1—5, with forms permitted for use being listed in the table to section S29—5. All 2'-FL and LNnT currently permitted by the Code are chemically and structurally identical to those found in human milk.

In conjunction with the Schedule 29 permissions, subsection S26—3(7) permits 2′-FL and LNnT as *foods produced using gene technology of microbial origin* with microbial sources and conditions as listed. This includes the applicant's 2'-FL produced by microbial fermentation from genetically modified (GM) *E coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*. However, the Code does not currently permit 2'-FL as a mixture with DFL.

Schedule 3 provides specifications for the permitted oligosaccharides.

Section 2.9.1—7 of the Code regulates the addition of galacto-oligosaccharides (GOS) and inulin-type fructans (ITF) (both are defined in subsection 1.1.2—2(3)) to infant formula products (see section 2.9.1—7). GOS and ITF 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). ITF are not present in human milk and GOS is found only in trace amounts (FSANZ 2008).

For infant formula products, section 2.9.1—7 sets out restrictions on the addition of ITF and GOS.

- Subsection 2.9.1—7(1) 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.
- Subsection 2.9.1—7(2) prohibits the use of ITF and/or GOS in infant formula products with lacto-N-neotetraose (LNnT)[7]. Subsection 2.9.1—7(3) permits 2′-FL to be used in combination with ITF and/or GOS[8].

1.4 International standards

In developing food regulatory measures, FSANZ must have regard to the promotion of consistency between domestic and international food standards.

Internationally, 2'-FL/DFL, LNT, 6'-SL and 3'-SL, produced through microbial fermentation

[7] Recent Application A1251 removed this prohibition from applying to 2'-FL.

[8] An exclusive use period is current for this permission and requires that infant formula products which contains 2′-FL in combination with ITF and/or GOS may only be sold if the infant formula products is the prescribed infant formula product manufactured by Nutricia Australia Pty. Ltd. Exclusive use period means the period commencing on the date of gazettal of the *Food Standards (Application A1251 – 2'-FL combined with galactooligosaccharides and/or inulin-type fructans in infant formula products) Variation* and ending 15 months after that date.

and by chemical synthesis, are permitted for use in infant formula equivalent products and a number of general foods at a range of levels and in combination with other oligosaccharides.

Codex Alimentarius (Codex) International Food Standards do not currently exist for 2'-FL/DFL, LNT, 6'-SL nor 3'-SL. However, the Codex Standards for 'Infant Formula and Formulas for Special Medical Purposes Intended for Infants' (Codex Alimentarius 2020) and for 'Follow-Up Formula' (Codex Alimentarius 2017) contain provisions for 'optional ingredients' which are applicable to 2'-FL/DFL, LNT, 6'-SL and 3'-SL.

2'-FL produced by microbial fermentation and by chemical synthesis are permitted for use in infant formula products and/or formulated supplementary foods for young children (also known as 'toddler milks') in at least 37 overseas countries including the United States, Canada, Singapore, the European Union (EU), Israel, Korea and the Philippines.

In the EU, the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL are authorised as novel food ingredients for foods including infant formula and follow on formula (EU 2019, 2020, 2021a,b).

In the UK, the applicant's 2'-FL/DFL and LNT are authorised for use as novel food ingredients for foods including infant formula and follow on formula under retained EU law, and 6'-SL and 3'-SL have been authorised for use as novel food ingredients for foods including infant formula and follow on formula under:

- The Novel Foods (Authorisations) and Smoke Flavourings (Modification of Authorisations) (England) Scotland, Wales) Regulations 2022;
- The Novel Foods (Authorisations) and Smoke Flavourings (Modification of Authorisations) (Scotland) Regulations 2022; and
- The Novel Foods (Authorisations) and Smoke Flavourings (Modification of Authorisations) (Wales) Regulations 2022.

The applicant's 2'-FL/DFL, LNT, 6'-SL, and 3'-SL in infant formula and other products have been notified as GRAS (Generally Recognised as Safe) in the United States, with a US Food and Drug Administration (FDA) no questions letter (U.S. FDA, 2019a,b, 2020a,b).

In Singapore, 2'-FL/DFL, LNT, 6'-SL and 3'-SL have been authorised for use by the Singapore Food Agency (SFA). Permitted conditions of use of 2'-FL/DFL and LNT in infant formula were gazetted in the most recent amendment of the Food Regulations (SSO 2021), while 6'-SL and 3'-SL will be included in the next planned amendment of the Food Regulations (approval letters were provided to FSANZ in-confidence).

In Israel, the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL are permitted as novel foods for which provisions are laid down in New Food Directives from the National Food Service Guidelines List (Israel MOH, 2022 a, b, c, d).

In Brazil, the applicant's LNT, 6'-SL and 3'-SL have been authorised for use by the Brazilian Health Regulatory Agency (approval letters provided in-confidence).

FSANZ notes that another manufacturer of HiMO substances has recently gained EU approval for LNT, 3-fucosyllactose (3-FL), 6'-SL and 3'-SL to be used in infant formula products and other foods.[9]

[9] Infant formula HMOs get EU novel food approval (foodprocessing.com.au)

1.5 Reasons for accepting application

The Application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act); and
- it related to a matter that warranted the variation of a food regulatory measure.

1.6 Procedure for assessment

The application was assessed under the General Procedure.

1.7 Decision

The draft variation as proposed following assessment was approved with amendments. The amendments to the draft variation were minor and reflect what was requested by the applicant. The amendments are listed below in Section 1.7.1 and Table 2 provides additional explanation.

The approved draft variation, as varied after consideration of submissions, is at Attachment A. The approved draft variation takes effect on Gazettal.

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

The draft variation on which submissions were sought is at Attachment C.

1.7.1 Summary of amendments to the draft variation

S3—47 (f),(g), and (h): add "(water free)"
(i): remove "FL", amend typographical error (capital "N" to lower case), and add "(water free)"

S3—48 (f) and (g): add "(water free)"
(j): correct *para*-lacto-N-hexaose to *para*-lacto-N-hexaose-2

S3—49 Amend 6′-sialyllactose sodium salt (6′-SL) to 6′-sialyllactose (6′-SL) sodium salt
(f): add "sodium salt" and "(water free)"
(g): add "(water free)"

S3—50 Amend 3′-sialyllactose sodium salt (3′-SL) to 3′-sialyllactose (3′-SL) sodium salt
(f): add "sodium salt" and "(water free)"
(g): add "(water free)"

Subsection S26—3(7) (table)
Correct typographical error in the right column: for each entry should say "For the purposes of condition 2 above."

2 Summary of the findings

2.1 Summary of issues raised in submissions

FSANZ called for submissions on the draft variation to the Code from 8 June 2023 to 7 July 2023. Ten submissions were received, five from government agencies and five from industry (Table 1). All submitters supported the voluntary permission to add 2'-FL/DFL, LNT, 6'-SL

and 3'-SL produced by a microbial fermentation method to infant formula products at the permitted amounts. Several issues were raised in relation to the combined use of oligosaccharides in infant formula products, the application of ministerial policy guidelines, the specifications and the granting of an exclusive use permission.

The key issues raised in submissions and how they have been addressed is provided in Table 2.

Table 1: List of submitters

Submitter	Abbreviation	Submitter type
Australian Food & Grocery Council	AFGC	Industry
Glycom A/S	Glycom	Industry
Infant Nutrition Council Australia & New Zealand	INC	Industry
Nestlé Australia Ltd; Nestlé New Zealand Limited	Nestlé	Industry
New South Wales Food Authority	NSWFA	Jurisdiction
New Zealand Food & Grocery Council	NZFGC	Industry
New Zealand Food Safety – Haumaru Kai Aotearoa	NZFS	Jurisdiction
Tasmania Department of Health	TasDoH	Jurisdiction
Victorian Department of Health; Victorian Department of Jobs, Precincts and Regions	VicDoH	Jurisdiction
WA Department of Health	WADoH	Jurisdiction

Table 2: Summary of issues raised in submissions

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
Safety, nutrition and benefit assessment (SD1)		
Request further information on the cumulative safety assessment, particularly the level of safety of total oligosaccharide content that will be permitted under this application. In addition, the departments seek further information from FSANZ on the considerations required to set a maximum total amount for total added oligosaccharides.	VicDoH	The safety assessment considered the addition of four oligosaccharides both alone and in combination to infant formula products at maximum use levels. The maximum amount for each of the oligosaccharides assessed is consistent with the concentration of identical counterparts naturally present in human milk. FSANZ did not identify any safety concern from the addition of oligosaccharides in combination in infant formula, nor the need to set a maximum level for total oligosaccharides noting that the maximum amounts of each HiMO are consistent with levels in human milk (see Section 2.3.6). As discussed in Section 2.3.1, the combined amount of HiMO based on existing permissions in the Code (including this application) is less than the lower limit of total human milk oligosaccharides (HMO) reported in mature human milk (0.34 – 0.51 g/100 kJ). It is unlikely that additional permissions requested in this application, or in future applications would exceed the concentration of HMOs in human milk. FSANZ could consider setting additional limits for total added oligosaccharide to infant formula products in future applications, if found to be warranted by an evidence based risk assessment. FSANZ's safety assessments to date have not identified any safety concern to support this approach.
Longer term studies are required to determine effect of HiMOs on nutrition and safety outcomes and it is *naïve to consider that an identical intake level of substrate in infant formula as observed in human milk does not by itself ensure safety and suitability (Carlson, Schipper et al. 2021).*	WADoH	FSANZ conducted a comprehensive risk assessment covering toxicological and nutritional considerations and used the best available evidence. In addition, FSANZ took into consideration the growing body of scientific studies and expert opinion showing the beneficial effects of human milk oligosaccharides on infant health. FSANZ notes the cited paper but also considers that it does not specifically relate to safety of HiMOs in infant health. FSANZ's toxicological safety assessment was based on a weight of evidence approach taking into account the following information: - 2'-FL, DFL, LNT, 6'-SL and 3'-SL are identical to 2'-FL, DFL, LNT, 6'-SL and 3'-SL present in human milk and the proposed concentrations to be added to infant formula products are within the range of concentrations found in human

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
		milk. This provides a history of safe use. - Intestinal absorption of HMOs is very limited. A large proportion of these substances passes to the large intestine, where they are fermented by intestinal microbiota or excreted intact in the faeces. - The substances are not genotoxic. - No adverse effects were observed at high doses in subchronic toxicity studies in neonatal animals. - In a human clinical study, infant formula containing the HiMOs was safe, well tolerated and did not affect growth. - Taken together, the evidence on chemical identity and concentrations in human milk, limited absorption, lack of adverse effects in infants and in neonatal animal models of an appropriate age for assessing safety of the target population is sufficient to conclude with reasonable certainty that 2'-FL, DFL, LNT, 6'-SL and 3'-SL will not cause harm in infants.
The evidence appears to include a number of clinical trials, only one of these assessed the health effects; the remainder reported only on safety, tolerance, and infant growth. The submitter queried if this is enough evidence to substantiate beneficial role in normal growth and development. Concerned about extending permissions for the addition of HiMOs or the combination of HiMOs with other ingredients to infant formula products if it does not provide a beneficial role in normal growth and development.	TasDoH	FSANZ notes there is a key study on the health benefits of the addition of the combination of four HiMOs and there are constraints on conducting relevant clinical trials. However, the beneficial health assessment is extensive, including evidence for functional roles of these HMOs in human milk, as well as the four HiMO products added singly or in combination to infant formula. FSANZ further considered available information on the role of the microbiome in infant gut-health and beyond. There is evidence (SD1; Section 5) of the applicant's HMOs impacting the development of the gut microbiome by supporting the growth of specific beneficial bacteria (e.g. *Bifidobacterium* spp.), inhibiting the growth of common bacterial pathogens and supporting the development of a functional immune system. Although the evidence is spread over a number of studies there is sufficient supporting data that addition of specific HMOs to infant formula does result in the formation of a gut microbiome that more closely aligns to that of a breastfed infant, providing a benefit greater than unsupplemented infant formula products. FSANZ also notes that the Application A1251 assessment of *in vitro* and animal studies of combinations of HiMO and GOS and/or ITF are consistent with beneficial health effects observed for the individual components and provided

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
		some indication of the mechanisms involved. FSANZ recognises that this is an active research area. Since completion of FSANZ's assessment, a recent publication by Holst et al 2023 (published after the completion of FSANZ's assessment) provides further evidence of the beneficial impact on the composition of the gut microbiome of addition of the applicant's HMOs to infant formula. This is part of the same clinical trial published by Parschat 2021 (SD1: Section 4.3) where they investigated the impact on infant growth parameters. Another recent review of published studies of the functional effects of HMOs in both breast and formula fed infants found the evidence to date supports a variety of physiologic functions for HMOs that are beneficial to infant development (Dinleyici et al 2023).
Agrees that the available evidence indicates that infants achieve normal growth when they are fed HiMOs at the levels normally present in human milk but suggest the wording of the conclusions (section 4.6) be modified in light of the relatively small number of directly relevant studies.	NZFS	FSANZ agrees with this comment. SD1 (section 4.6) has been amended in line with the submitter's comment. Section 4.6 now concludes "Based on the small number of directly relevant studies, the nutrition assessment concludes that the HiMO blend added to infant formula products is unlikely to pose a risk to the normal growth of infants."
Clarify summary of findings for Cohen et al (2022); unclear whether or not there were statistically significant differences in daily body weight gain, though it is clear that any differences were not clinically significant (i.e. within the margin of ±3 g/day).	NZFS	The sentence on the findings from Cohen et al. in SD1, section 4.3.3 has been clarified.
Permitted levels		
Unclear why a higher level of a mixture of 2'-FL/DFL compared to EFSA proposed levels. EFSA has permitted the combination of these substances at 1.6 g/L in infant formula however FSANZ is proposing to permit to a maximum of 2.4 g/L.	NSWFA	The applicant requested 2'-FL/DFL at a proposed maximum level of 96 mg/100 kJ (2.4 g/L) for use in infant formula products. The safety assessment indicated no concerns with addition of the applicant's 2'-FL/DFL to infant formula products at the highest permitted use level of 2.4 g/L, which is within the range found in human milk. The maximum permitted amount of 2'-FL/DFL is consistent with the existing permission in the Code for 2'-FL derived from *E.coli* K-12 to infant formula products to a maximum level of 96 mg/100 kJ or 2.4 g/L (i.e. 2'-FL alone or in combination with LNnT). Noting that 2'-FL and DFL are structurally and

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
		biologically closely related since DFL is metabolically obtained from 2'-FL by the addition of a second fucose unit ('fucosylation').
Use of GOS and/or ITF in combination with HiMOs in infant formula products		
Does not support permissions for use of GOS and/or ITF in combination with 2'-FL/DFL, LNT, 6'-SL and/or 3'-SL and removing the prohibition of LNnT combined with GOS and/or ITF without specific risk assessment evidence for this approach.	NSWFA	In Application A1251 FSANZ concluded, based on the best available scientific evidence that 2'-FL, in combination with GOS and/or ITF does not pose a public health and safety risk. For the current application, FSANZ notes that: • Intestinal absorption of HMOs, GOS and/or ITF is very limited, with the majority passing to the large intestine where they are fermented by the intestinal microbiota or excreted intact in the faeces. Data previously reviewed by FSANZ indicates that GOS and ITF are fermented to a similar or greater extent to HMOs. • No adverse effects have been observed in toxicity studies with these substances at high doses that exceed the estimated dietary intakes for infants consuming infant formula products containing them at the maximum permitted amounts. • Clinical studies with these substances also found no adverse effects. No further evidence demonstrating safety risks was provided in these submissions. Given the limited absorption of HMOs, GOS and/or ITF, the absence of any identifiable hazard, as well as the history of safe human exposure to these substances (via human milk or infant formula), FSANZ is satisfied there are no public health and safety concerns with the combination of ITF and/or GOS in infant formula products with 2'-FL/DFL, LNT, 6'-SL, 3'-SL and/or LNnT at current permitted maximum use amounts. See section 2.3.4 for further discussion.
Concerns about the combined use of HiMOs with GOS and/or ITF extends the permitted maximum levels of oligosaccharides without further evidence of safety.	TasDoH VicDoH	
Supports the removal the current prohibition on addition to infant formula products of GOS and/or ITF in combination with LNnT	INC Glycom Nestle NZFGC	FSANZ notes this support.

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
	NZFS	
Labelling		
Proposes prescribing names for all substances permitted in the nutrition information statement (NIS) to improve product comparability and inform purchase decisions. Considers standardising the names of human milk oligosaccharides (HiMOs) that appear in the NIS is important to avoid doubt that their listing may constitute prohibited representations, or nutrition content or health claims.	NSWFA	Under Proposal P1028 - Infant formula, FSANZ is proposing to standardise the NIS to provide consistency in the formatting and most terminology used. Standardisation includes grouping nutrients and substances under the subheadings 'Vitamins', 'Minerals' and 'Additional' to enable caregivers to make easier product comparisons and assist their understanding so they can make informed choices (see subsection 2.9.1—26(2) and the table to section S29—10 of the draft variation in Attachment A to the P1028 2nd CFS). FSANZ does not consider it is necessary to standardise names for HiMOs in the NIS because: • it is consistent with the approach taken for declaring other nutritive substances when voluntarily added to infant formula and other special purpose foods. • the mandatory requirement for HiMOs to be declared in the NIS is intended to enable caregivers to make an informed choice and being mandatory, it does not constitute a claim (as defined in subsection 1.1.2—2(3)). • Standard 2.9.1 provides a restriction on how HiMOs are named, specifically a prohibition on the use of HiMO terminology.
Opposes the current prohibition on use of the words 'human milk identical oligosaccharide', 'human milk oligosaccharide', and abbreviations 'HMO', 'HiMO', or any word, words or abbreviations having the same or similar effect.	AFGC INC NZFGC	FSANZ is aware of the views on this issue as they have been raised previously (see submissions to Applications A1155, A1190, A1233 and A1251). See FSANZ's response provided in Table 1 to section 2.1 in the Approval Report for A1190 2′-FL in infant formula and other products.
Supports the current labelling prohibitions against: • the word 'humanised' or 'maternalised' or any word or words having the same or similar effect; • the words 'human milk oligosaccharide', 'human milk identical oligosaccharide' or any word or words having	NSWFA NZFS TasDoH	

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
the same or similar effect; • the abbreviations 'HMO' or HiMO' or any abbreviation having the same or similar effect; • information on the nutritional content of human milk.		
Expression of maximum permitted use levels		
Recommends that maximum permitted use levels are expressed on a HiMO basis rather than on an ingredient basis noting the following: • The purity of active HiMOs varies across batches, products and manufacturers. When expressed on an ingredient basis this can result in different maximum amounts of the active HiMO. • This is consistent with estimate dietary intake assessments which assume 100% purity of the active HiMOs in the final HiMO ingredient. • In clinical trials, doses are expressed on a pure HiMO basis, analytically measured in the final test formula. • Other authorities, including the US and the EU consider maximum permitted use levels of HiMOs to be expressed on a HiMO basis.	Glycom	The purpose of a Schedule 3 specification is to set minimum standards relating to a particular substance's purity and identity to ensure the safe use of that substance. FSANZ has assessed the safety of the substances requested in this application against the specification provided. There is no minimum amount set for the requested HiMOs (there is no evidence base on which set to set mandatory minimums). As such, a batch or product variation that results in an amount that is less than the maximum permitted amount is not a compliance matter. The Code specifies all nutrients in infant formula products on the basis of mass per 100 kJ. Deviation from this for these substances is not considered warranted and potentially creates inconsistency in the Code.
Sialyllactose abbreviations		
Recommends that the "6'-SL" and "3'-SL" abbreviations do not include the sodium salt, as follows: • 6'-sialylactose (6'-SL) sodium salt • 3'-sialylactose (3'-SL) sodium salt	Glycom	FSANZ notes the submitter's comments and agrees. Where applicable in the Approval Report (including SD1) and the approved draft variation, 6'-sialylactose sodium salt (6'-SL) has been amended to read 6'-sialylactose (6'-SL) sodium salt and 3'-sialylactose sodium salt (3'-SL) has been amended to read 3'-sialylactose (3'-SL) sodium salt.
LNnT listing as individual permission		

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
In line with other permissions for addition of HiMOs to infant formula products, proposes that the Code is amended to permit use of LNnT alone or in combination with HiMOs other than 2'-FL; i.e. remove current restriction that LNnT must be used in combination with 2'-FL.	Glycom Nestle	Removal of the restriction that LNnT must be used in combination with 2'-FL has not been assessed in this application. The restriction originates from Application A1155 where the permission for LNnT as a single HiMO was not requested by that applicant nor was it assessed. Removal of the restriction effectively establishes a new permission for LNnT which would require pre-market assessment as with any nutritive substance added to infant formula products.
Exclusivity		
Submitter(s) support exclusive capturable commercial benefit which recognises the value that this has to deliver on investment for the food industry and for innovation. Industry submitters also seek clarity and consideration around the current and future scope of the application of exclusivity in the broader food supply and its implementation.	AFGC INC NZFS Nestle	FSANZ notes these comments. See also section 2.3.9 of this report and the FSANZ website: Exclusivity of use for novel foods and nutritive substances (foodstandards.gov.au)
The submitter agrees it is consistent with previous nutritive substances approved to be added to infant formula products and therefore equitable to extend exclusive permission. However they are concerned by the granting of exclusive use permissions for substances that are demonstrated to benefit infant health and development outcomes.	VicDoH	FSANZ notes these comments. As discussed in this Report, the Ministerial Policy Guideline on *Regulation of Infant Formula Products* sets out that composition of infant formula must be safe, suitable for the intended use and strive to achieve normal growth and development compared to a healthy full term exclusively breastfed infant – as measured by appropriate physiological, biochemical and/or functional effects. FSANZ's assessment of the stated beneficial effects is for the purpose of the requested voluntary compositional permission. FSANZ's first order priority was to ensure there are no public health and safety risks in accordance with subsection 18(1) of the FSANZ Act. In having regard to all high order policy principles, FSANZ considers that the strength, quality and type of evidence assessed in this application is appropriate for voluntary compositional permission. FSANZ's deliberations and the granting of a limited exclusive use period is a separate secondary consideration. The granting of an exclusive use permission does not preclude anyone else from applying for permission to add their HiMOs to IFP, including within the 15 month exclusive permission period. Further, the approved variation relates to an ingredient that IFP manufacturers

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
		may purchase. The variation does not apply any restrictions on who may purchase the applicant's HiMOs during the 15 month exclusive use period.
Five year review of benefit of HiMOs in infant formula products		
Submitter(s) supports and/or comments on FSANZ's five-year review of new evidence on the beneficial role of HiMOs in the normal growth and development of infants.	AFGC INC NZFGC	As part of the Application A1155, the Food Ministers[10] agreed that within five years of gazettal (March 2021), the permission for voluntary addition of 2'-FL and LNnT would be reviewed by FSANZ to determine whether there is sufficient evidence for a *'substantiated beneficial role in the normal growth and development of infants, or a technological role'*. FSANZ aims to complete this review by March 2026. The process will include consultation with a range of stakeholders including experts, industry and government agencies and will be independently peer reviewed. At this time, the scope of the review will meet the Ministerial request from Application A1155.
Considers appropriate to include all HiMOs (individually and in combination) in scope of the five-year review of HiMO's (including 2′-FL and LNnT) and requests clarity from FSANZ as to the process, scope and outcomes of the 5-year review in the approval report for A1265.	NSWFA TasDoH VicDoH	
Regard for the Policy Guideline		
Lack of application of the Ministerial Policy Guideline on the Regulation of Infant Formula Products and alerts FSANZ to the April 4, 2023 FMM and the consensus for the convening of *a FRSC working group to examine the evidence required to substantiate whether an infant formula product has a beneficial role in the normal growth and development of infants including considering the cumulative effects*.	WADoH	FSANZ notes this comment. FSANZ had regard to the Ministerial Policy Guideline in its assessment, as required by the FSANZ Act. For the reasons stated in this report, FSANZ considers that the Guideline has been met. See, for example, Section 2.5.3. FSANZ was aware that, on 4 April 2023, the Food Ministers' Meeting recommended that FRSC should examine and, if necessary, clarify the evidence required to substantiate whether an infant formula product has a beneficial role in the normal growth and development of infants including considering the cumulative effects.[11] However, FSANZ understands that work is yet to progress. FSANZ's evidence based assessment is that addition of the substances to infant formula products - as proposed - will have a beneficial role or outcome. That assessment included consideration of total oligosaccharide amounts and cumulative effect of oligosaccharides added to infant formula products (see

[10] Australia and New Zealand Ministerial Forum on Food Regulation Communiqué 27 November 2020
[11] Communiqué of outcomes from the Food Ministers' Meeting held on 4 April 2023

Submitter comment	Raised by	FSANZ response (including any amendments to drafting)
		section 2.3.6).
Timeframes		
Concerns that the application was presented at a time of competing priorities and that the final outcomes of P1028, and/or the convening of the FRSC working group had not been finalised prior to consultation on this application.	WADoH	FSANZ notes this comment. FSANZ completed the assessment of this application in accordance with the requirements of the FSANZ Act and Australian administrative law.
Amendments to specifications		
Request that the term 'water-free' be added against a number of the purity criteria as proposed and requested in the application for the different specifications proposed for each of the specifications, ie S3—47, S3—48, S3—49 and S3—50. This is because the water content for each batch can vary so it is more appropriate to define the purity on the dried water free state. A small number of minor edits and corrections were noted within the specifications.	Glycom	FSANZ agrees that the term 'water-free' should be added against certain purity criteria and has amended the draft variation accordingly (see Section 1.7.1). This is consistent with other specifications for HiMOs in Schedule 3.
Suggested that the most appropriate analytical method to determine residual protein analysis is the Bradford assay as alternative methods such as Kjeldahl method based on nitrogen content is not suitable. Therefore it is suggested this method be indicated in the specifications HiMOs.	Glycom	FSANZ does not agree that methods of analyses should be stated in specifications set out in Schedule 3. The preference is to allow experienced analysts to determine the most appropriate method to use. This also allows future proofing of the entries.
The preference is not to include sodium salt within the abbreviation of "6'-SL" and "3'-SL" for reasons explained and discussed earlier in the report. The preference is to therefore use the terms "6'-SL, sodium salt" and "3'-SL, sodium salt". This approach is also relevant for listing within the specifications for S3—49 and S3—50 and so requires some amendments.	Glycom	FSANZ notes and agrees with the approach for listing the abbreviations and has made the minor amendments to the specifications (see Section 1.7.1).

2.2 Risk assessment

FSANZ has undertaken an assessment of the food technology aspects, safety, nutritional impact and beneficial health effects of the addition of 2'-FL/DFL, LNT, 6'-SL and 3'-SL to infant formula products.

Information reviewed in the food technology assessment demonstrated the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL were chemically and structurally identical to the naturally occurring forms of these substances in human milk. The substances were shown to be stable in infant formula products with an adequate shelf-life. Multi-batch analyses showed the oligosaccharides can be consistently produced to meet their proposed specifications.

The *E. coli* K-12 host organism has a long history of use for the production of recombinant proteins and poses no risks to humans. Analyses of the gene donors also confirmed there are no safety concerns. The production strains were genetically and phenotypically stable.

Mean estimated dietary intakes of 2'-FL, DFL, LNT, 6'-SL and 3'-SL from infant formula products were comparable to mean estimated dietary intakes from mature human milk. High (90th percentile) estimated dietary intakes from infant formula products did not exceed estimated dietary intakes from mature human milk at high consumption and high concentration levels, except for DFL when assuming a representative maximum composition of 25% in the proposed 2'-FL/DFL mixture. The maximum composition of 25% for DFL is the most conservative concentration, and is markedly higher compared to the mean composition from analysis provided by the applicant (12%). Based on the mean analysed concentration of DFL, the estimated mean intakes, which are more reflective of longer term intakes, from infant formula products are similar to that from human milk.

Based on the available toxicological and clinical data, also considering the dietary intake assessment, it was concluded that there were no public health and safety concerns associated with the addition of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL to infant formula products at the proposed use amounts. No microbiological safety concerns were identified.

Post-marketing surveillance data have also found no safety concerns following consumption of infant formula containing a combination of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL.

The weight of evidence supports health benefits of HiMOs added to infant formula products through an increase in the abundance of *Bifidobacterium* spp. in the infant gut microbiota, anti-pathogenic effects, inflammatory suppression and facilitating appropriate immune responses and antigenic memory. The inclusion of a wider range of HiMOs to infant formula products enables the microbiota profile to more closely resemble that of breastfed infants.

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 when breastfeeding is not possible. As infants are a vulnerable population group, infant formula products are regulated by prescriptive provisions for composition and labelling. Any changes to the composition of these products must be established as safe prior to being permitted.

2.3.1 Risk management options

The risk management options available to FSANZ after assessment are to:

- approve the draft variation proposed following assessment; or
- approve that draft variation subject to such amendments as FSANZ considers necessary; or
- reject that draft variation.

FSANZ had regard to the requirements of the FSANZ Act (see Section 2.5 below) in developing the proposed regulatory measure. For the reasons set out in this report, FSANZ has amended the draft variation proposed following assessment and approved the amended draft variation to permit the use of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL as nutritive substances in infant formula products, subject to certain conditions and in accordance with the Code.

Further details on the permission and associated conditions are provided below.

2.3.2 Use as a nutritive substance in infant formula products

There are more than 200 human milk oligosaccharides (HMOs) in human milk and a large accumulating body of evidence demonstrating their role in the normal growth and development of infants, in particular to aid in the maturation of the infant microbiota. In human milk, 10 individual HMOs make up over 70% of total HMO concentration (Soyyılmaz et al. 2021). Recent innovation has seen the synthesis of these primary oligosaccharides biochemically identical to HMOs, such as those requested by the applicant.

The safety, technical and health effects assessment (SD1) concluded that there are no public health and safety concerns associated with the addition of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL in infant formula products at the maximum permitted levels, which are comparable to that of human milk.

FSANZ's assessment of potential health effects of 2'-FL/DFL, LNT, 6'-SL and 3'-SL was consistent with assessments undertaken previously for the same types of substances. In previous applications (A1155, A1190 and A1233). FSANZ considered the weight of available evidence when assessing the beneficial role of 2'-FL and LNnT in the normal growth and development of infants.

While data from well-controlled human studies are considered of greatest value, ethical constraints limit their availability when considering health outcomes from interventions in infants and children. In the absence of this data, and in order to fully consider benefit, evidence from non-human studies is used to add weight to the determination of a substance's role, particularly in understanding the mode of action and biological plausibility. In assessing a link between the relevant physiological, biochemical or functional effects of a substance in infant formula and specific health effects in infants, FSANZ deems it appropriate to consider an evidence base that includes animal studies, *in vitro* evidence and relevant observational and/or epidemiological studies. FSANZ refers to the assessment from the Independent Expert Advisory Group (IEAG) undertaken under Application A1155, who concluded that there are many different factors in the microbiome which influence infant health, and that it is not possible to determine a linear effect from the presence of one substance in human milk and a specific health outcome (FSANZ 2020). Referring also to Section 2.2 above, development of a microbiota profile closer to that of breastfed infants is supported by inclusion of a wider range of HiMOs.

The nutritional purpose for adding 2'-FL/DFL, LNT, 6'-SL and 3'-SL to infant formula products is to create products that better reflect the oligosaccharide profile of human milk. A demonstrable health outcome in conjunction with bringing the composition of infant formula

products closer to that of human milk is aligned with the definitions of infant formula and follow-on formula in the Code and reflects the primary purpose of consumption in supporting the development of infants that cannot be breastfed. In line with specific policy principle (j)[12], FSANZ has considered these requirements in assessing each of the beneficial health effects of the applicant's substances stated in the application: anti-pathogenic effect; bifidogenic effect; and immunomodulation.

Based on FSANZ's assessment of beneficial health effects and role in normal growth and development, and taking a weight of evidence approach, FSANZ concludes that the use of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, individually or in combination, would have a beneficial outcome.

2.3.3 Permission in the Code

In permitting the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, express permission is provided for each of 2'-FL/DFL, LNT, 6'-SL and 3'-SL to be *used as a nutritive substance* and as *food produced using gene technology* (as discussed in section 1.3.2), noting that no public health and safety concerns have been identified for these substances, individually or in combination, derived from the applicant's GM production strains.

2'-FL and DFL are two distinct fucosylated HMOs that are always found together in human milk. They are structurally and biologically closely related since DFL is metabolically obtained from 2'-FL by the addition of a second fucose unit ("fucosylation"). In this application, 2'-FL and DFL are produced in the same fermentation and are isolated together to produce the 2'-FL/DFL mixture. For this reason the permission for 2'-FL/DFL is listed as a single entity.

Listing 2'-FL/DFL, LNT, 6'-SL and 3'-SL, as individual permissions in section S29—5 is consistent with how 2'-FL and 2'-FL/LNnT are currently listed in the Code, with permission for the GM organism in accordance with Standard 1.5.2. Single entry permissions allows for more efficient assessments of future applications for HiMO-type ingredients. FSANZ considers the approach to list oligosaccharides as individual permissions as minimum effective regulation.

The approved permissions also support international consistency and a competitive food industry (high order policy principles 2(b) and (c)[11]), providing trade opportunities. In countries where permissions exist (e.g. Singapore, EU, United States), the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL are permitted as single ingredients in infant formula products (refer Section 1.4).

2.3.4 Use with GOS and ITF

GOS and ITF have been permitted for addition to infant formula products since the gazettal of Proposal P306 in 2008, to emulate the effects of HMO and strive to achieve as closely as possible the normal growth and development of infants, consistent with specific policy principles (d), (e) and (h) of the ministerial policy guideline on *Regulation of Infant Formula Products*. As noted in Section 1.3.5 above, ITF is not present in human milk, and GOS only in trace amounts. At the time of approval of P306, ITF and GOS were the only available form of non-digestible oligosaccharides.

In Application A1155, based on the available evidence, and given the combined use of the proposed and existing permissions was not requested, FSANZ decided to prohibit the combination of 2'-FL alone or with LNnT in combination with GOS and/or ITF in infant

[12] Policy guideline on infant formula products.

formula products. At that time, it was considered that an application with appropriate supporting evidence would have been required to allow consideration of such oligosaccharide combinations.

More recently under Application A1251, FSANZ assessed the combination of 2'-FL, GOS and ITF substances in infant formula products. FSANZ's risk and technical assessment identified no public health and safety concerns with the combination of 2′-FL with GOS and/or ITF in infant formula products at current permitted maximum use amounts (FSANZ 2022a). Taking into account the A1251 assessment, FSANZ is not prohibiting the use of GOS and/or ITF in combination with 2'-FL/DFL, LNT, 6'-SL and/or 3'-SL.

Human milk oligosaccharides present in human milk play an important role in the normal growth and development of infants, in particular to mature the infant microbiota. Recent innovation has seen the synthesis of oligosaccharides biochemically identical to HMOs, such as those assessed in this application, and can be seen as a positive development for infant health. This technology, however, remains expensive and if used as the sole source of oligosaccharides in infant formula products, could raise infant formula products prices to be prohibitive to consumers. While the technology is in development to become more efficient and affordable, the evidence supports that the combination of HiMOs with GOS and/or ITF in infant formula products presents no safety, tolerance or growth concerns, and can benefit formula-fed infants.

2.3.5 Removal of the prohibition on the use of ITF and/or GOS with LNnT

The approved draft variation prepared by FSANZ removes the current prohibition imposed by subsection 2.9.1—7(2) on the use of ITF and/or GOS in infant formula products with LNnT. Removal of the prohibition was not requested by the applicant. LNnT is a HMO and is permitted to be added to infant formula products at concentrations consistent with human milk. LNnT has no known chemical or biological characteristics different from other permitted HiMOs that would lead to adverse outcomes in infants. Consistent with FSANZ's assessment under this application and the previous assessment removing the prohibition for 2'-FL with ITF and/or GOS (see Application A1251), FSANZ is satisfied that there are no public health and safety concerns with the combination of ITF and/or GOS in infant formula products with LNnT at current permitted maximum use amounts. FSANZ considers this amendment reflects the scientific evidence, provides regulatory clarity and also allows for greater flexibility in combinations of oligosaccharides in infant formula products.

2.3.6 Total oligosaccharide amounts and cumulative effect

The approved draft variation adds permissions for four new oligosaccharides to infant formula products. These are permitted to be added either as single ingredients (2'-FL/DFL, LNT, 6'-SL and 3'-SL) or as a mixture (see Table 3). The maximum amounts for each are consistent with the concentrations of these individual oligosaccharides in human milk (refer to Section 4.5 of SD1). In terms of the total amount of HMOs to be added, the combined maximum amount of 2'-FL or 2'-FL/LNnT or 2'-FL/DFL, LNT, 6'-SL and 3'-SL would total 0.15 g/100 kJ added to infant formula products. This amount is less than the lower limit of average total oligosaccharide concentration reported in mature human milk (10 – 15 g/L or 0.34 – 0.51 g/100 kJ[13]), as reported by Zhang et al. (2021). As the oligosaccharides listed in Table 3 represent the most abundant HMOs in mature human milk (Soyyilmaz et al. 2021), it is unlikely that the additional permissions in this application, or in future applications, would exceed concentrations in human milk.

[13] Amount in g/100 kJ is calculated using the energy density reported in AUSNUT (FSANZ 2016): 286 kJ/100 g = 297 kJ/100 mL based on the specific gravity of human milk of 1.04 g/mL.

Including the maximum amount permitted for ITF and GOS would equal 0.55 g/100 kJ of total added oligosaccharides. However, as noted above, the technology to produce HMOs remains expensive but as biochemically identical HMOs become more available, ITF and GOS will become unnecessary in infant formula products. In future applications, FSANZ can consider setting a maximum amount for total added oligosaccharides, if warranted. At this time, such a measure is (1) not supported by FSANZ safety assessments conducted to date and (2) potentially places Australia and New Zealand out of step with international regulations.

Based on the permissions listed in Table 3, total added oligosaccharides would be a small fraction of the total carbohydrate content. Total carbohydrate content is calculated by difference based on the prescribed range of fat and protein, and the energy density. The calculated carbohydrate range in infant formula expressed as a percentage of the energy density is 36 – 52%. The calculated amount of oligosaccharides expressed as a percentage of the energy density would be 1.2% for HiMOs only, and 4.4% if ITF and GOS are included, which is a fraction of the total range of carbohydrate content.

These calculations demonstrate that the potential cumulative increase to the total oligosaccharide load consumed by infants is aligned with human milk, poses no safety or public health risks, and complies with longstanding total carbohydrate permissions. Details of the above calculations are provided at Appendix 1.

Table 3: Summary of infant formula products oligosaccharide permissions including those proposed in this application

Oligosaccharide	Maximum amount (mg/100 kJ)	Amount expressed as %Energy
2'-FL or 2'-FL/LNnT or 2'-FL/DFL	96	0.8
LNT	32	0.3
6'-SL	16	0.1
3'-SL	8	0.1
Total HiMO	152	1.2
ITF	110	0.9
GOS	290	2.3
Total oligosaccharides	552	4.4

2.3.7 Specification

Section 1.1.1—15 requires *a substance that is used as a nutritive substance* must comply with any relevant specification set out in Schedule 3. Since no published specifications currently exist for 2'-FL/DFL, LNT, 6'-SL and 3'-SL in Schedule 3, proposed specifications were provided by the applicant. The proposed specifications do not raise any safety concerns and are considered appropriate for substances added to infant formula products.

The specification parameters provided by the applicant are shown in Tables 1 to 4 of SD1. These specifications, with amendments as noted in Section 1.7 of this Approval Report, are included in the approved draft variation at Attachment A.

2.3.8 Labelling

2.3.8.1 Statement of ingredients

Standard 1.2.4 requires food for sale to be labelled with a statement of ingredients unless exempt. The label on a package of infant formula product must contain a statement of ingredients. Should manufacturers choose to add 2'-FL/DFL, LNT, 6'-SL and 3'-SL individually or in combination, then these substances must 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; 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*.

The existing generic ingredient labelling requirements will apply to the permitted forms of 2'-FL/DFL, LNT, 6'-SL and 3'-SL, enabling industry to have flexibility in how they declare these ingredients (for example, using the names ‘2′-fucosyllactose’ and ‘6'-sialyllactose sodium salt’). Noting however the existing prohibited representations in paragraphs 2.9.1—24(1)(ca) and (cb) (refer to section 2.2.8.3 below) will also apply.

2.3.8.2 Mandatory nutrition information

Section 2.9.1—21 regulates the declaration of nutrition information in a nutrition information statement (NIS) on the label of infant formula products. The NIS is a single statement and may be in the form of a table, as indicated in section S29—10 *Guidelines for Infant Formula Products*.

Subparagraph 2.9.1—21(1)(a)(iii) requires the average amount of any substance used as a nutritive substance permitted by the Standard to be declared in the NIS. The substances 2'-FL/DFL, LNT, 6'-SL and 3'-SL will need to be declared in the NIS when they are voluntarily added to an infant formula products.

2.3.8.3 Prohibited representations

Paragraph 2.9.1—24(1)(ca) prohibits the use of the words ‘human milk oligosaccharide’, ‘human milk identical oligosaccharide’ or any word or words having the same or similar effect. In addition, paragraph 2.9.1—24(1)(cb) prohibits the use of the abbreviations ‘HMO’ or ‘HiMO’ or any abbreviation having the same or similar effect. The words and abbreviations in these provisions cannot be used anywhere on the label of a package of infant formula products. The substances 2'-FL/DFL, LNT, 6'-SL and 3'-SL will be subject to these provisions regarding prohibited representations.

2.3.8.4 Voluntary representations

Paragraph 1.2.7—4(b) states that a nutrition content or health claim must not be made about an infant formula product. Paragraph 2.9.1—24(1)(f) also prohibits a reference to the presence of a nutrient or substance that may be used as a nutritive substance, except for a reference in: a statement relating to lactose under subsection 2.9.1—14(6), a statement of ingredients, or in the NIS. These existing prohibitions for nutrition content and health claims for infant formula products will apply to the substances 2'-FL/DFL, LNT, 6'-SL and 3'-SL.

2.3.8.5 Labelling as 'genetically modified'

As discussed in section 2.3 of SD1, the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL 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 or novel DNA will be present in an infant formula product that contains these substances as ingredients. However, where novel protein or novel DNA is present, the requirement to label 2'-FL/DFL, LNT, 6'-SL and 3'-SL as 'genetically modified' will apply in accordance with section 1.5.2—4.

2.3.9 Exclusivity

An applicant may request exclusive permission to use and sell a nutritive substance for a period of up to 15 months to recognise the investment made in developing that nutritive substance and the need to achieve return on this investment, thereby supporting innovation.

The applicant requested an exclusive use permission for their specific brand of 2'-FL/DFL, LNT, 6'-SL and 3'-SL, alone or in combination in infant formula products, on the basis that there has been significant research and investment by the applicant into the development of these highly refined products obtained via proprietary manufacturing processes.

The applicant is provided with a 15 month exclusive use permission for the permitted forms of 2'-FL/DFL, LNT, 6'-SL and 3'-SL, commencing on the date of gazettal of the approved draft variation.

This means that, during that 15 month period, the permission will apply exclusively to those substances under the brand names "GlyCare™ 2FL/DFL 8001, GlyCare™ LNT 8001, GlyCare™ 6SL 9001, and GlyCare™ 3SL 9001" in accordance with the Code.

Once the 15 month period ends, the exclusive use permission will revert to a general permission, meaning that anyone may use the permitted forms of 2'-FL/DFL, LNT, 6'-SL and 3'-SL in accordance with the Code.

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

2.3.10 The five-year review for 2'-FL and LNnT in infant formula products

FSANZ is committed to reviewing any new evidence on the beneficial role of HiMOs in the normal growth and development of infants.

At the request of Food Ministers, FSANZ will carry out a five-year review (to be completed by March 2026) of the initial permission gazetted under Application A1155. This will review the evidence of a substantiated beneficial role of 2′-FL and LNnT in the normal growth and development of infants. The process will include consultation with a range of stakeholders including experts, industry and government agencies, and will be independently peer reviewed. Details on the review process, including stakeholder input will be made available on the FSANZ website.

2.3.11 Risk Management conclusion

FSANZ has considered the maximum amounts requested for 2'-FL/DFL, LNT, 6'-SL and 3'-SL in the context of the safety, technical, nutrition and health effects assessment. This included estimated dietary intakes and naturally occurring levels in human milk, potential beneficial health effects and alignment with international regulations. Based on this assessment which found no public health and safety concerns with the requested permissions, FSANZ has approved a draft variation to the Code to permit the voluntary addition of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, meeting the applicant's specifications, to infant formula products. Permitting these substances individually supports the principle of minimum effective regulation and minimisation of technical barriers to trade.

The addition of the permitted forms of 2'-FL/DFL, LNT, 6'-SL and 3'-SL to infant formula products will be subject to relevant existing requirements and conditions in the Code, and include the following amendments:

- amend Schedule 29 of the Code to permit 2'-FL/DFL, LNT, 6'-SL and 3'-SL, which are permitted for use by Standard 1.5.2, to be used in infant formula products, either alone or in combination, as nutritive substances up to a specified maximum permitted amount;
- amend Schedule 26 of the Code to permit the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL, as substances derived from a new genetically modified microbial source, to be added to infant formula products subject to certain conditions, including an exclusive use period of 15 months for the applicant's brand of each substance;
- amend Schedule 3 of the Code to include identity and purity specifications for the permitted forms of 2'-FL/DFL, LNT, 6'-SL and 3'-SL; and
- remove the current prohibition in Standard 2.9.1 on the use of galacto-oligosaccharides and/or inulin-type fructans with lacto-N-neotetraose.

The approved draft variation is at Attachment A. The 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 developed and applied a standard communication strategy to this application. The call for submissions was notified via the FSANZ Notification Circular, media release, FSANZ's social media channels and Food Standards News.

A public consultation paper called for submissions on FSANZ's assessment and on a draft variation from 8 June 2023 to 7 July 2023. FSANZ received 10 submissions. FSANZ had regard to all submissions received for this application as part of its assessment.

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.

2.5 FSANZ Act assessment requirements

When assessing this Application and the subsequent development of a food regulatory measure, 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

Prior to changes to the Impact Analysis requirements by the Office of Impact Analysis (OIA)[14], the OIA advised FSANZ that a Regulatory Impact Statement was not required for applications like this relating to nutritive substances. This is because applications relating to nutritive substances that have been determined to be safe are considered to be minor and deregulatory in nature as their use will be voluntary if the application is approved.

FSANZ, however, has considered the costs and benefits that could arise from the proposed measure for the purposes of meeting FSANZ Act considerations. The FSANZ Act requires FSANZ to have regard to whether the direct and indirect benefits that would arise from a food regulatory measure developed or varied as a result of the application would outweigh the costs to the community, government or industry that would arise from the development or variation of that food regulatory measure.

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 (where the status quo is rejecting the application).

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 potential positives and negatives of moving away from the status quo by approving this application.

Impacts on infant formula consumers

Consumers may benefit from improved health outcomes. The link between the permitted 2'-FL/DFL, LNT, 6'-SL and 3'-SL, alone or in combination, and improved health outcomes for infants is discussed earlier in this document.

Caregiver understanding and behaviour is not expected to be significantly impacted. A literature review of studies between 2003 and 2019 undertaken by FSANZ to inform Proposal P1028 highlighted that caregivers often lack knowledge about the contents of ingredient lists and nutritional information statements, particularly what different nutrients are and the benefits they have. Many caregivers report not reading the ingredients list, often because they do not understand what the ingredients are (FSANZ 2022b).

On balance, FSANZ considers it unlikely that a significant proportion of consumers will notice the additional ingredients and alter their purchasing behaviour as a result.

Impact on industry

Industry may benefit from increased choice of ingredients for domestically sold and imported

[14] Regulatory Impact Analysis Guide for Ministers' Meetings and National Standard Setting Bodies | The Office of Impact Analysis (pmc.gov.au)

infant formula products. Industry will voluntarily use alone or in combination the permitted 2'-FL/DFL, LNT, 6'-SL and 3'-SL or buy and sell infant formula products containing either, where they believe a commercial benefit exists for them to do so.

Given addition of the applicant's 2'-FL/DFL, LNT, 6'-SL and 3'-SL in infant formula products is already approved in some overseas countries (see Section 1.4), granting the permission requested by the application would favour trade and any growth of overseas markets for domestic infant formula products exporters. Approving the requested permission may also promote and support imports from other countries.

The proposed exclusivity period creates an additional incentive to industry to innovate.

Impact on governments of Australia and New Zealand

The approval of this application may result in a small but likely inconsequential cost to government from an additional combination of infant formula products ingredients that is monitored for compliance with individual ingredient maximum limits. That assumes an increase in infant formula products containing 2'-FL/DFL, LNT, 6'-SL and 3'-SL.

Conclusion

FSANZ's assessment at the call for submissions was that the direct and indirect benefits that would arise from permitting the use of 2'-FL/DFL, LNT, 6'-SL and 3'-SL, from specified sources, in infant formula products most likely outweigh the associated costs. No further information was received during the consultation process that changed that assessment

2.5.1.2 Other measures

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

2.5.1.3 Any relevant New Zealand standards

The relevant standards apply in both Australia and New Zealand. There are no relevant New Zealand only Standards.

2.5.1.4 Any other relevant matters

Other relevant matters are considered below.

2.5.2. Subsection 18(1)

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

2.5.2.1 Protection of public health and safety

FSANZ completed a safety and risk assessment (SD1) which is summarised in Section 2.1 of this report. The assessment concluded that there are no public health and safety concerns from the addition of applicant's 2′-FL/DFL, LNT, 6′-SL or 3′-SL at the proposed amounts. Additionally, the weight of evidence supports beneficial health effects of HiMOs added to infant formula products.

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

Current labelling requirements discussed in Section 2.2.8 will apply to the permitted 2'-FL/DFL, LNT, 6'-SL, and 3'-SL when added to infant formula products and will provide information to enable consumers to make an informed choice.

2.5.2.3 The prevention of misleading or deceptive conduct

Current labelling requirements, including prohibited representations which aim to prevent misleading or deceptive conduct, will apply to infant formula products containing the permitted 2'-FL/DFL, LNT, 6'-SL, and 3'-SL, either individually or in combination (see Section 2.3.8 above).

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**

Using risk analysis, FSANZ considered the best available evidence to reach its conclusions on the safety, technical, nutrition and beneficial health effects of the addition of the permitted 2'-FL/DFL, LNT, 6'-SL, and 3'-SL in infant formula products.

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

FSANZ considered the promotion of consistency between domestic and international food standards and the desirability of an efficient and internationally competitive food industry. HiMOs including those requested in this application are permitted for addition to equivalent infant formula products in other overseas jurisdictions. The permission will promote consistency between domestic and a number of international food standards. See also Section 1.4 of this report.

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

The permissions would support an internationally competitive food industry in relation to the addition of the permitted 2'-FL/DFL, LNT, 6'-SL, and 3'-SL to infant formula products.

Additionally, removing the existing prohibition for the use of ITF and/or GOS with LNnT in infant formula products and not applying the prohibition to the permitted 2'-FL/DFL, LNT, 6'-SL, and 3'-SL aligns with the Code permissions for 2′-FL as an individual ingredient and will support an internationally competitive food industry.

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

No negative impact is anticipated on fair trading.

- **any written policy guidelines formulated by the Food Ministers' Meeting**

FSANZ has had regard to both high order and specific policy principles in relevant Ministerial Policy Guidelines. Two Ministerial Policy Guidelines specifically applied to this application:

- Regulation of Infant Formula Products
- Intent of Part 2.9 of the Food Standards Code –Special Purpose Foods.

Noting the food technology aspects, safety, nutritional impact and beneficial health effects assessed in SD1 and Section 2.3.2 of this report, FSANZ considers these Policy Guidelines have been met.

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Appendix 1: Calculation of cumulative oligosaccharide amounts

The table below was reproduced from EC SCF (2003) which reported the calculated carbohydrate content of infant formula based on protein and fat content.

Macronutrient amounts in Standard 2.9.1 - as proposed in Proposal P1028 2nd Call for Submissions (CFS):

	Minimum	**Maximum**
Energy	2510 kJ/L	2930 kJ/L
Protein	0.43 g/100 kJ	0.72 g/100 kJ
Fat	1.1 g/100 kJ	1.4 g/100 kJ
CHO	By difference	By difference

Protein and fat amounts (minimum and maximum) are calculated as a percentage of the energy density (at maximum and minimum permitted energy) based on Atwater factors[15]: 1 g fat = 37 kJ, 1 g carbohydrate (CHO) = 17 kJ, 1 g protein = 17 kJ.

For each minimum and maximum, total carbohydrate expressed as percentage of energy density was derived from 100 – (%Energy $_{fat}$ + %Energy $_{protein}$).

In Table 1 (Section 2.2.5), the oligosaccharide content calculated as a percentage of energy density was based on the Atwater factor for unavailable carbohydrate[1] (1 g carbohydrate = 8 kJ). This was calculated to be 1.2% for the combined HiMO permissions only, and 4.4% if ITF and GOS are included.

Macronutrient	**At Energy Minimum = 2510 kJ/L**				**At Energy Maximum = 2930 kJ/L**			
Fat	Minimum		Maximum		Minimum		Maximum	
g/100 kJ	1.1		1.4		1.1		1.4	
%Energy	40.7		51.8		40.7		51.8	
Protein	Min	Max	Min	Max	Min	Max	Min	Max
g/100 kJ	0.43	0.72	0.43	0.72	0.43	0.72	0.43	0.72
% Energy	7.3	12.2	7.3	12.2	7.3	12.2	7.3	12.2
%Energy$_{F+P}$	48	53	59	64	48	53	59	64
%Energy CHO$_{total}$	52	47	41	36	52	47	41	36
CHO$_{total}$ *g/100 kJ*	3.1	2.8	2.4	2.1	3.1	2.8	2.4	2.1

[15] FAO (2003) Food and Nutrition Paper 77: Food energy - methods of analysis and conversion factors. Report of a Technical Workshop, Rome. ISBN 92-5-105014-7

Attachments

A. Approved draft variation to the Australia New Zealand Food Standards Code

B. Explanatory Statement

C. Draft variation to the Australia New Zealand Food Standards Code (Call for Submissions)

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

Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula 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 the Delegate]

[Insert Delegate's name and position title]
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 A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula 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

Standard 2.9.1—Infant formula products

[1] Subsection 2.9.1—7(2)

Repeal the subsection.

Schedule 3—Identity and purity

[2] Subsection S3—2(2) (table)

Insert:

2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12*	section S3—47
lacto-N-tetraose sourced from *Escherichia coli* K-12	section S3—48
6′-sialyllactose sodium salt sourced from *Escherichia coli* K-12	section S3—49
3′-sialyllactose sodium salt sourced from *Escherichia coli* K-12	section S3—50

[3] After section S3—46

Insert:

S3—47 Specification for a combination of 2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12*

For a mixture of 2′-fucosyllactose (2′-FL) and difucosyllactose (DFL) sourced from *Escherichia coli K-12* containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*, the specifications are the following:

(a) chemical names:
  (i) for 2′-FL—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-D-glucopyranose;
  (ii) for DFL—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-[α-L-fucopyranosyl-(1→3)]-D-glucose;

(b) chemical formulas:
  (i) for 2′-FL—$C_{18}H_{32}O_{15}$;
  (ii) for DFL—$C_{24}H_{42}O_{19}$;

(c) molecular weights:
  (i) for 2′-FL—488.44 g/mol;
  (ii) for DFL—634.58 g/mol;

(d) CAS numbers:
  (i) for 2′-FL—41263-94-9;
  (ii) for DFL—20768-11-0;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 2′-FL—not less than 75.0% (water free);

(g) DFL—not less than 5.0% (water free);

(h) sum of 2′-FL and DFL—not less than 85.0% (water free);

(i) sum of human identical milk saccharides: 2′-FL, DFL, D-lactose, L-fucose, 3-fucosyllactose —not less than 92.0% (water free);

(j) D-lactose—not more than 10%;

(k) L-fucose—not more than 1.0%;

(l) 2'-fucosyl-D-lactulose—not more than 2.0%;

(m) pH (20°C, 5% solution)—4.0-6.0;

(n) water—not more than 6.0%;

(o) ash, sulphated—not more than 0.8%;

(p) residual protein—not more than 0.01%;

(q) lead—not more than 0.1 mg/kg;

(r) microbiological:

(i) aerobic mesophilic bacteria total count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—48 Specification for lacto-N-tetraose sourced from *Escherichia coli K-12*

For lacto-N-tetraose (LNT) sourced from *Escherichia coli K-12* containing the gene for beta-1,3-N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1.3-galactosyltransferase from *Helicobacter pylori*, the specifications are the following:

(a) chemical name—β-D-galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-glucose;

(b) chemical formula—$C_{26}H_{45}NO_{21}$;

(c) molecular weight—707.63 g/mol;

(d) CAS number—14116-68-8;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) LNT—not less than 70.0% (water free);

(g) sum of human identical milk saccharides: LNT, D-lactose, lacto-N-triose II—not less than 90.0% (water free);

(h) D-lactose—not more than 12.0%;

(i) lacto-N-triose II—not more than 10.0%;

(j) *para*-lacto-N-hexaose-2—not more than 3.5%;

(k) β-D-Galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-fructose (LNT fructose isomer)—not more than 1.0%;

(l) pH (20°C, 5% solution)—4.0-6.0;

(m) water—not more than 6.0%;

(n) residual protein—not more than 0.01%;

(o) ash, sulphated—not more than 0.5%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic bacteria total count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—49 Specification for 6′-sialyllactose sodium salt sourced from *Escherichia coli K-12*

For 6′-sialyllactose (6′-SL) sodium salt sourced from *Escherichia coli K-12* containing the gene for alpha-2,6-sialyltransferase from *Photobacterium damsela* and CMP-Neu5Ac synthetase, Neu5Ac synthetase, *N*-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*, the specifications are the following:

(a) chemical name—N-acetyl-α-D-neuraminyl-(2→6)-β-D-galactopyranosyl-(1→4)-D-glucose, sodium salt;

(b) chemical formula—$C_{23}H_{38}NO_{19}Na$;

(c) molecular weight—655.53 g/mol;

(d) CAS number—157574-76-0;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 6′-SL sodium salt—not less than 90.0% (water free);

(g) sum of human identical milk saccharides: 6′-SL sodium salt, D-lactose, sialic acid—not less than 94.0% (water free);

(h) D-lactose—not more than 5.0%;

(i) sialic acid—not more than 2.0%;

(j) sialyl-lactulose—6’- isomer—not more than 3.0%;

(k) sodium—2.5-4.5%;

(l) chloride—not more than 1.0%;

(m) pH (20°C, 5% solution)—4.5-6.0;

(n) water—not more than 6.0%;

(o) residual protein—not more than 0.01%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic total plate count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—50 Specification for 3′-sialyllactose sodium salt sourced from *Escherichia coli K-12*

For 3′-sialyllactose (3′-SL) sodium salt sourced from *Escherichia coli K-12* containing the gene for alpha-2,3-sialyltransferase from *Neisseria meningitides* and CMP-Neu5Ac synthetase, Neu5ac synthase, *N*-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*, the specifications are the following:

(a) chemical name—N-acetyl-α-D-neuraminyl-(2→3)-β-D-galactopyranosyl-(1→4)-D-glucose, sodium salt;

(b) chemical formula—$C_{23}H_{38}NO_{19}Na$;

(c) molecular weight—655.53 g/mol;

(d) CAS number—128596-80-5;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 3′-SL sodium salt—not less than 88.0% (water free);

(g) sum of human identical milk saccharides: 3′-SL sodium salt, D-lactose, sialic acid—not less than 90.0% (water free);

(h) D-lactose—not more than 5.0%;

(i) sialic acid—not more than 1.5%;

(j) sialyl-lactulose-3′-isomer—not more than 5.0%;

(k) sodium—2.5-4.5%;

(l) chloride—not more than 1.0%;

(m) pH (20°C, 5% solution)—4.5-6.0;

(n) water—not more than 8.0%;

(o) residual protein—not more than 0.01%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic total plate count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

Schedule 26—Food produced using gene technology

[4] Subsection S26—3(7) (table)

Insert:

4	**A combination of 2′-fucosyllactose and difucosyllactose**	*Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand GlyCare 2′-FL/DFL 8001. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2′-FL/DFL, LNT, 6′-SL sodium salt and 3′-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.
5	**lacto-N-tetraose**	*Escherichia coli* K-12 containing the gene for beta-1,3- N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1,3- galactosyltransferase from *Helicobacter pylori*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand GlyCare LNT8001. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2′-FL/DFL, LNT, 6′-*

			SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation and ending 15 months after that date.
6	**6′-sialyllactose sodium salt**	*Escherichia coli* K-12 containing the gene for alpha-2,6-sialyltransferase from *Photobacterium damsela* and CMP-Neu5Ac synthetase, Neu5Ac synthase, N-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand GlyCare 6SL 9001. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.
7	**3′-sialyllactose sodium salt**	*Escherichia coli* K-12 containing the gene for alpha-2,3-sialyltransferase from *Neisseria meningitides* and CMP-Neu5Ac synthetase, Neu5Ac synthase, N-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand GlyCare 3SL 9001. 3. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.

Schedule 29—Special purpose foods

[5] Section S29—5 (table)

Insert each of the following substances in alphabetical order:

3'-sialyllactose sodium salt permitted for use by Standard 1.5.2	3'-sialyllactose sodium salt	8 mg
6'-sialyllactose sodium salt permitted for use by Standard 1.5.2	6'-sialyllactose sodium salt	16 mg
A combination of 2′-fucosyllactose and difucosyllactose, permitted for use by Standard 1.5.2	2'-fucosyllactose and difucosyllactose	96 mg

lacto-N-tetraose permitted for use by Standard 1.5.2	lacto-N-tetraose	32 mg

Attachment B – Explanatory Statement

EXPLANATORY STATEMENT

Food Standards Australia New Zealand Act 1991

Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation

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.

The Authority accepted Application A1265 which sought to permit the use of four human-identical milk oligosaccharide products, each derived from a specific genetically modified *Escherichia coli* (*E.coli*) strain, as nutritive substances in infant formula products. The four products or substances are:

- a mixture of 2'-fucosyllactose (2'-FL) and difucosyllactose (DFL) (2'-FL/DFL);
- lacto-N-tetraose (LNT);
- 6'-sialyllactose (6'-SL) sodium salt; and
- 3'-sialyllactose (3'-SL) sodium salt.

The Application also sought a 15 month exclusive use permission.

The Authority assessed the Application in accordance with Division 1 of Part 3 of the FSANZ Act.

During that assessment, the Authority identified a need to amend the Code to remove the current prohibition on the addition to infant formula products of galacto-oligosaccharides and/or inulin-type fructans in combination with lacto-N-neotetraose (LNT). Removal of this prohibition was not requested in Application A1265, but was considered warranted by the Authority.

Based on that assessment, the Authority prepared a draft variation - the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation* and consulted on that draft variation.

Following consultation, the Authority has further considered the application in accordance with Division 1 of Part 3, amended the draft variation, and approved the amended draft variation (approved draft variation).

Following consideration by the Food Ministers' Meeting, section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the approved draft variation.

2. Variation is a legislative instrument

The approved draft variation is a legislative instrument for the purposes of the *Legislation Act*

2003 (see section 94 of the FSANZ Act) and is publicly available on the Federal Register of Legislation (www.legislation.gov.au).

This instrument is not subject to the disallowance or sunsetting provisions of the *Legislation Act 2003.* Subsections 44(1) and 54(1) of that Act provide that a legislative instrument is not disallowable or subject to sunsetting if the enabling legislation for the instrument (in this case, the FSANZ Act): (a) facilitates the establishment or operation of an intergovernmental scheme involving the Commonwealth and one or more States; and (b) authorises the instrument to be made for the purposes of the scheme. Regulation 11 of the *Legislation (Exemptions and other Matters) Regulation 2015* also exempts from sunsetting legislative instruments a primary purpose of which is to give effect to an international obligation of Australia.

The FSANZ Act gives effect to an intergovernmental agreement (the Food Regulation Agreement) and facilitates the establishment or operation of an intergovernmental scheme (national uniform food regulation). That Act also gives effect to Australia's obligations under an international agreement between Australia and New Zealand. For these purposes, the Act establishes the Authority to develop food standards for consideration and endorsement by the FMM. The FMM is established under the Food Regulation Agreement and the international agreement between Australia and New Zealand, and consists of New Zealand, Commonwealth and State/Territory members. If endorsed by the FMM, the food standards on gazettal and registration are incorporated into and become part of Commonwealth, State and Territory and New Zealand food laws. These standards or instruments are then administered, applied and enforced by these jurisdictions' regulators as part of those food laws.

3. Purpose

The Authority has approved the amended draft variation to the Code to:

- amend Schedule 29 of the Code to permit each of the four substances to be used in infant formula products, either alone or in combination, as a nutritive substance up to a specified maximum permitted amount;
- amend Schedule 26 of the Code to permit each of the four substances, as substances derived from a new genetically modified microbial source, to be added to infant formula products subject to certain conditions, including an exclusive use period of 15 months for the applicant's brand of each substance;
- amend Schedule 3 of the Code to include identity and purity specifications for each of the four substances; and
- remove the current prohibition in Standard 2.9.1 on the use of galacto-oligosaccharides and/or inulin-type fructans with lacto-N-neotetraose.

4. Documents incorporated by reference

The approved draft variation prepared by the Authority does not incorporate any documents by reference.

However, the approved draft variation will vary Schedule 3 of the Code which does incorporate documents by reference. Section 1.1.1—15 of the Code requires certain substances (such as substances used as nutritive substances) to comply with any relevant identity and purity specifications listed in Schedule 3.

Schedule 3 incorporates documents by reference to set specifications for various substances in the circumstances specified in that Schedule. The documents incorporated include:

- the Joint FAO/WHO Expert Committee on Food Additives (JECFA) Compendium of Food Additive Specifications (FAO/WHO 2019);

- the United States Pharmacopeial Convention (2020);
- Food Chemicals Codex (12th edition); and
- the Commission Regulation (EU) No 231/2012.

5. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of Application A1265 included one round of public consultation following an assessment and the preparation of a draft variation and associated report. Submissions were called for on 8 June 2023 for a 4-week consultation period.

Changes have been made to the Impact Analysis requirements by the Office of Impact Analysis (OIA)[14]. Impact analysis is no longer required to be finalised with the OIA. Prior to these changes the OIA advised FSANZ that a Regulatory Impact Statement was not required for the applications relating to nutritive substances. This is because applications relating to permitting the use of nutritive substances that have been determined to be safe are considered to be minor and deregulatory in nature as their use will be voluntary if the application is approved. Under the new approach, FSANZ's assessment is that a regulatory impact statement is not required for this application.

6. 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 44 of the *Legislation Act 2003*.

7. Variation

Clause 1 provides that the name of the variation is the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation*

Clause 2 provides that the Code is amended by the Schedule to the variation.

Clause 3 provides that the variation commences on the date of gazettal of the instrument.

Item [1] of the Schedule to the variation amends Standard 2.9.1 by repealing subsection 2.9.1—7(2). The effect of this amendment is to remove the current prohibition on the addition to infant formula products of galacto-oligosaccharides and/or inulin-type fructans in combination with lacto-N-neotetraose.

Items [2] and [3] of the Schedule amends Schedule 3 of the Code.

Schedule 3 contains specifications for the purposes of section 1.1.1—15 of the Code. Section 1.1.1—15 requires certain substances, e.g. substances used as nutritive substances, to comply with any relevant identity and purity specifications listed in Schedule 3. Specifications include those set out in provisions which are listed in the table to subsection S3—2(2) (see paragraph S3—2(1)(a)).

The amendments made by items [2] and [3] set – for the purposes of section 1.1.1—15 of the Code - a specification for each of the four substances listed above.

Item [2] amends the table to subsection S3—2(2) by inserting in alphabetical order new entries for:

- ‘2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12’* and a corresponding reference to new section S3—47 (see item [3] below)
- ‘lacto-N-tetraose sourced from *Escherichia coli K-12’* and a corresponding reference to new section S3—48 (see item [3] below)
- ‘6′-sialyllactose sodium salt sourced from *Escherichia coli K-12’* and a corresponding reference to new section S3—49 (see item [3] below)
- ‘3′-sialyllactose sodium salt sourced from *Escherichia coli K-12’* and a corresponding reference to new section S3—50 (see item [3] below)

Item [3] inserts new sections S3—47, S3—48, S3—49 and S3—50 into Schedule 3 in numerical order after S3—46.

New section S3—47 lists a specification for 2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12.*

New section S3—48 lists a specification for lacto-N-tetraose sourced from *Escherichia coli K-12.*

New section S3—49 l lists a specification for 6′-sialyllactose sodium salt sourced from *Escherichia coli K-12.*

New section S3—50 lists a specification for 3′-sialyllactose sodium salt sourced from *Escherichia coli K-12.*

Item [4] of the Schedule amends Schedule 26 of the Code.

Schedule 26 relates to food produced using gene technology. Each of the four substances listed above is a food produced using gene technology (as defined in subsection 1.1.2—2(3) of the Code) because it is derived from an organism modified using gene technology. That is, from a genetically modified *Escherichia coli* (*E.coli*) K-12 strain.

Paragraph 1.5.2—3(a) permits a food for sale to consist of, or have as an ingredient, a food produced using gene technology if the food produced using gene technology (other than a processing aid or food additive) is listed in Schedule 26 and complies with any corresponding conditions in that Schedule.

The table to subsection S26—3(7) lists food produced using gene technology of microbial origin. Item [4] amends that table by adding new table items 4 to 7 to provide a permission for the use of each of the four substances.

Each permission is subject to conditions of use set out in column 3. These conditions of use are as follows:

1. the substance may only be added to infant formula products;
2. during the exclusive use period, the substance may only be sold under the brand name specified by and for that permission; and
3. for the purposes of condition 2, exclusive use period means the period commencing on the date of gazettal of the variation and ending 15 months after that date.

Condition 2 means that each substance, as a permitted food produced using gene technology, may only be sold under the specified brand during the exclusive use period. ‘Exclusive use period’ is defined in condition 3 as the period commencing upon gazettal of the variation and ending 15 months after that date

Once this period ends, each permission will revert to a general permission, meaning that the proposed permission will then permit the four substances sourced from the specified genetically modified *Escherichia coli* (*E.coli*) strain to be sold under any brand.

The amendments made by item [4] do not make any substantive change to *existing* permissions and to other requirements in the Code relating to food produced using gene technology.

Item [5] of the Schedule amends Schedule 29 of the Code.

The item amends the table to section S29—5. The table lists the new substances permitted for use as nutritive substances in infant formula products. The item amends the table by inserting into that table in alphabetical order a separate new permission for each of the following:

- 3'-sialyllactose sodium salt, with a specified maximum permitted amount of 8 mg/100 kJ;
- 6'-sialyllactose sodium salt, with a specified maximum permitted amount of 16 mg/100 kJ;
- a combination of 2'-fucosyllactose and difucosyllactose, with a specified maximum permitted amount of 96 mg/100 kJ; and
- lacto-N-tetraose, with a specified maximum permitted amount of 32 mg/100 kJ.

A minimum amount is not set for each permission or substance as this was not requested in the Application and has not been determined by the Authority.

Each permission prescribes a permitted form for the permitted substance. This means that the substance must be used in that form.

Each permission is also expressly linked to these substances as permitted for use by Standard 1.5.2 (*Food produced using gene technology*). This means that only those substances derived from the relevant microbial source listed in Schedule 26 (table to subsection 26—3(7)) for that substance will be permitted for use as a nutritive substance in infant formula products.

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

Food Standards (Application A1265 – 2'FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula 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 the Delegate]

[Insert Delegate's name and position title]
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 A1265 –2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula 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

Standard 2.9.1—Infant formula products

[1] Subsection 2.9.1—7(2)

Repeal the subsection.

Schedule 3—Identity and purity

[2] Subsection S3—2(2)(table)

Insert:

2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12*	section S3—47
lacto-N-tetraose sourced from *Escherichia coli K-12*	section S3—48
6′-sialyllactose sodium salt sourced from *Escherichia coli K-12*	section S3—49
3′-sialyllactose sodium salt sourced from *Escherichia coli K-12*	section S3—50

[3] After section S3—46

Insert:

S3—47 Specification for a combination of 2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli K-12*

For a mixture of 2′-fucosyllactose (2′-FL) and difucosyllactose (DFL) sourced from *Escherichia coli K-12* containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*, the specifications are the following:

(a) chemical names:
  (i) for 2′-FL—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-D-glucopyranose;
  (ii) for DFL—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-[α-L-fucopyranosyl-(1→3)]-D-glucose;

(b) chemical formulas:
  (i) for 2′-FL—$C_{18}H_{32}O_{15}$;
  (ii) for DFL—$C_{24}H_{42}O_{19}$;

(c) molecular weights:
  (i) for 2′-FL—488.44 g/mol;
  (ii) for DFL—634.58 g/mol;

(d) CAS numbers:
  (i) for 2′-FL—41263-94-9;
  (ii) for DFL—20768-11-0;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 2′-FL—not less than 75.0%;

(g) DFL—not less than 5.0%;

(h) sum of 2′-FL and DFL—not less than 85.0%;

(i) sum of human identical milk saccharides: 2′-FL, DFL, D-lactose, L-fucose, 3-fucosyllactose FL—Not less than 92.0%;

(j) D-lactose—not more than 10%;

(k) L-fucose—not more than 1.0%;

(l) 2'-fucosyl-D-lactulose—not more than 2.0%;

(m) pH (20°C, 5% solution)—4.0-6.0;

(n) water—not more than 6.0%;

(o) ash, sulphated—not more than 0.8%;

(p) residual protein—not more than 0.01%;

(q) lead—not more than 0.1 mg/kg;

(r) microbiological:

(i) aerobic mesophilic bacteria total count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—48 Specification for lacto-N-tetraose sourced from *Escherichia coli K-12*

For lacto-N-tetraose (LNT) sourced from *Escherichia coli K-12* containing the gene for beta-1,3-N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1.3-galactosyltransferase from *Helicobacter pylori*, the specifications are the following:

(a) chemical name—β-D-galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-glucose;

(b) chemical formula—$C_{26}H_{45}NO_{21}$;

(c) molecular weight—707.63 g/mol;

(d) CAS number—14116-68-8;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) LNT—not less than 70.0%;

(g) sum of human identical milk saccharides: LNT, D-lactose, lacto-N-triose II—not less than 90.0%;

(h) D-lactose—not more than 12.0%;

(i) lacto-N-triose II—not more than 10.0%

(j) *para*-lacto-N-hexaose—not more than 3.5%;

(k) β-D-Galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-D-fructose (LNT fructose isomer)—not more than 1.0%;

(l) pH (20°C, 5% solution)—4.0-6.0;

(m) water—not more than 6.0%;

(n) residual protein—not more than 0.01%;

(o) ash, sulphated—not more than 0.5%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic bacteria total count—Not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—49 Specification for 6′-sialyllactose sodium salt sourced from *Escherichia coli K-12*

For 6′-sialyllactose sodium salt (6′-SL) sourced from *Escherichia coli K-12* containing the gene for alpha-2,6-sialyltransferase from *Photobacterium damsela* and CMP-Neu5Ac synthetase, Neu5Ac synthetase, *N*-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*, the specifications are the following:

(a) chemical name—N-acetyl-α-D-neuraminyl-(2→6)-β-D-galactopyranosyl-(1→4)-D-glucose, sodium salt;

(b) chemical formula—$C_{23}H_{38}NO_{19}Na$;

(c) molecular weight—655.53 g/mol;

(d) CAS number—157574-76-0;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 6′-SL—not less than 90.0%;

(g) sum of human identical milk saccharides: 6′-SL sodium salt, D-lactose, sialic acid—not less than 94.0%;

(h) D-lactose—not more than 5.0%;

(i) sialic acid—not more than 2.0%;

(j) sialyl-lactulose—6’- isomer—not more than 3.0%;

(k) sodium—2.5-4.5%;

(l) chloride—not more than 1.0%;

(m) pH (20°C, 5% solution)—4.5-6.0;

(n) water—not more than 6.0%;

(o) residual protein—not more than 0.01%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic total plate count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

S3—50 Specification for 3′-sialyllactose sodium salt sourced from *Escherichia coli K-12*

For 3′-sialyllactose sodium salt (3′-SL) sourced from *Escherichia coli K-12* containing the gene for alpha-2,3-sialyltransferase from *Neisseria meningitides* and CMP-Neu5Ac synthetase, Neu5ac synthase, *N*-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*, the specifications are the following:

(a) chemical name—N-acetyl-α-D-neuraminyl-(2→3)-β-D-galactopyranosyl-(1→4)-D-glucose, sodium salt;

(b) chemical formula—$C_{23}H_{38}NO_{19}Na$;

(c) molecular weight—655.53 g/mol;

(d) CAS number—128596-80-5;

(e) description—white, white to off-white, or off-white powder, agglomerates, or powder with agglomerates;

(f) 3′-SL—not less than 88.0%;

(g) sum of human identical milk saccharides: 3′-SL sodium salt, D-lactose, sialic acid—not less than 90.0%;

(h) D-lactose—not more than 5.0%;

(i) sialic acid—not more than 1.5%;

(j) sialyl-lactulose-3′-isomer—not more than 5.0%;

(k) sodium—2.5-4.5%;

(l) chloride—not more than 1.0%;

(m) pH (20°C, 5% solution)—4.5-6.0;

(n) water—not more than 8.0%;

(o) residual protein—not more than 0.01%;

(p) lead—not more than 0.1 mg/kg;

(q) microbiological:

(i) aerobic mesophilic total plate count—not more than 1,000 cfu/g;

(ii) *Enterobacteriaceae*—absent in 10 g;

(iii) yeasts—not more than 100 cfu/g;

(iv) moulds—not more than 100 cfu/g;

(v) residual endotoxins—not more than 10 EU/mg.

Schedule 26—Food produced using gene technology

[4] Subsection S26—3(7) (table)

Insert:

4	**A combination of 2′-fucosyllactose and difucosyllactose**	*Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*	4. May only be added to infant formula products. 5. During the exclusive use period, may only be sold under the brand GlyCare 2′-FL/DFL 8001. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2′-FL/DFL, LNT, 6′-SL sodium salt and 3′-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.
5	**lacto-N-tetraose**	*Escherichia coli* K-12 containing the gene for beta-1,3- N-acetylglucosaminyltransferase from *Neisseria meningitides* and the gene for beta-1,3-galactosyltransferase from *Helicobacter pylori*	4. May only be added to infant formula products. 5. During the exclusive use period, may only be sold under the brand GlyCare LNT8001. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2′-FL/DFL, LNT, 6′-*

			SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation and ending 15 months after that date.
6	**6′-sialyllactose sodium salt**	*Escherichia coli* K-12 containing the gene for alpha-2,6-sialyltransferase from *Photobacterium damsela* and CMP-Neu5Ac synthetase, Neu5Ac synthase, N-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*	4. May only be added to infant formula products. 5. During the exclusive use period, may only be sold under the brand GlyCare 6SL 9001. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.
7	**3′-sialyllactose sodium salt**	*Escherichia coli* K-12 containing the gene for alpha-2,3-sialyltransferase from *Neisseria meningitides* and CMP-Neu5Ac synthetase, Neu5Ac synthase, N-acetylglucosamine-6-phosphatase epimerase from *Campylobacter jejuni*	4. May only be added to infant formula products. 5. During the exclusive use period, may only be sold under the brand GlyCare 3SL 9001. 6. For the purposes of condition 2 above, **exclusive use period** means the period commencing on the date of gazettal of the *Food Standards (Application A1265 – 2'-FL/DFL, LNT, 6'-SL sodium salt and 3'-SL sodium salt as nutritive substances in infant formula products) Variation* and ending 15 months after that date.

Schedule 29—Special purpose foods

[5] Section S29—5 (table)

Insert each of the following substances in alphabetical order:

3'-sialyllactose sodium salt permitted for use by Standard 1.5.2	3'-sialyllactose sodium salt	8 mg
6'-sialyllactose sodium salt permitted for use by Standard 1.5.2	6'-sialyllactose sodium salt	16 mg

A combination of 2′-fucosyllactose and difucosyllactose, permitted for use by Standard 1.5.2	2'-fucosyllactose and difucosyllactose	96 mg
lacto-N-tetraose permitted for use by Standard 1.5.2	lacto-N-tetraose	32 mg