10 October 2023
266-23

Call for submissions – Application A1277

2′-FL from GM *Escherichia coli* K-12 (gene donor: *Helicobacter enhydrae*) in infant formula products

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Food Standards Australia New Zealand (FSANZ) has assessed an application made by Inbiose N.V. to amend the Australia New Zealand Food Standards Code to permit a new genetically modified strain of *Escherichia coli* K-12 for the production of 2′-fucosyllactose as a nutritive substance in infant formula products and has prepared a draft food regulatory measure. Pursuant to section 31 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), FSANZ now calls for submissions to assist consideration of the draft food regulatory measure.

For information about making a submission, visit the FSANZ website at current calls for public comment and how to make a submission.

All submissions on applications and proposals will be published on our website. We will not publish material that we accept as confidential. In-confidence submissions may be subject to release under the provisions of the *Freedom of Information Act 1982*. Submissions will be published as soon as possible after the end of the submission period.

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

For information on how FSANZ manages personal information when you make a submission, see FSANZ's Privacy Policy.

Submissions should be made in writing; be marked clearly with the word 'Submission'. You also need to include the correct application or proposal number and name. Electronic submissions can be made by emailing your submission to submissions@foodstandards.gov.au. FSANZ also accepts submissions in hard copy to our Australia and/or New Zealand offices.

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

DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 21 November 2023

Submissions received after this date will not be considered unless an extension had been given before the closing date. Extensions will only be granted due to extraordinary circumstances during the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.
Questions about making a submission or application and proposal processes can be sent to standards.management@foodstandards.gov.au.

Submissions in hard copy may be sent to the following addresses:

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Supporting documents

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

SD1 Risk and technical assessment – Application A1277

Executive summary

Food Standards Australia New Zealand (FSANZ) has assessed an application made by Inbiose N.V. to amend the Australia New Zealand Food Standards Code (the Code) to permit 2′-fucosyllactose (2′-FL) derived from a genetically modified (GM) strain of *Escherichia coli (E. coli)* K-12 to be used as a nutritive substance in infant formula products.

The Code already permits the voluntary addition of 2′-FL to be used as a nutritive substance and as a food produced using gene technology in infant formula products. However, the Code does not currently permit 2′-FL produced from genetically modified *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae (H. enhydrae).* The application therefore seeks to amend Schedule 26 to permit this alternative GM source organism for the production of 2′-FL.

The applicant has also requested an exclusive use permission under the brand name '2′-FL-Inbiose' for a period of 15 months after gazettal.

Overall, FSANZ's safety assessment concluded there are no public health and safety concerns associated with the addition of 2′-FL synthesised from the applicant's source organism to infant formula products at the proposed use levels. The applicant's 2′-FL is chemically and structurally identical to the naturally occurring substance present in human milk. It is also chemically and structurally identical to 2′-FL already assessed and permitted by FSANZ. Given this, the associated health benefits from the addition of 2′-FL to infant formula products for infants remain the same: (1) an anti-pathogenic effect; (2) immunomodulation and (3) development of the gut microbiome through supporting growth of *Bifidobacteria* spp.

FSANZ has prepared a draft variation to the Code to permit 2′-FL derived from *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* as a nutritive substance and food produced using gene technology to infant formula products. If approved, the draft variation would:

- amend Schedule 26 of the Code to permit the applicant's 2′-FL to be added to infant formula products subject to certain conditions, including an exclusive use period of 15 months linked to the applicant's brand name '2′-FL-Inbiose', and
- amend the current specification in Schedule 3 of the Code for 2′-FL sourced from *E. coli* K-12 (section S3—40) to include 2′-FL from *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* in the list of substances to which the specifications in section S3—40 apply.

FSANZ now seeks submissions on the draft variation (Attachment A).

1 Introduction

1.1 The applicant

The applicant, Inbiose N.V. is a Belgian company with a focus on development of specialty carbohydrates, including human identical milk oligosaccharides.

1.2 The application

On 25 May 2023, Inbiose N.V. applied to amend Schedule 26 of the Australia New Zealand Food Standards Code (the Code) to permit a new source organism for the production of 2′-fucosyllactose (2′-FL) to be added as a nutritive substance to infant formula products. The applicant's 2′-FL is produced by microbial fermentation using a genetically modified (GM) strain of *Escherichia coli* (*E. coli*) K-12. The application seeks to amend Schedule 26 to permit this alternative GM source organism for the production of 2′-FL.

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 infant formula products 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

1.3.2.1 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 applicant's 2′-FL is a *food produced using gene technology* (section 1.1.2—2) as it is derived from an organism modified using gene technology (i.e. derived from GM *E. coli* K-12). If approved, express permission for the applicant's 2′-FL is required in accordance with Standard 1.5.2 (i.e. to be listed in Schedule 26 and to comply with any corresponding conditions).

2′-FL is already permitted in the Code as a *food produced using gene technology* for use in infant formula products from microbiological origin including *E. coli* K-12 (subsection S26—3(7)), however not from *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae (H. enhydrae).*

1.3.2.2 Nutritive substances

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). The applicant's 2′-FL is *used as a nutritive substance* because its addition to food is intended to achieve specific nutritional purposes.

2′-FL is a non-digestible oligosaccharide that is a component of human milk. 2′-FL is currently permitted to be *used as a nutritive substance* in infant formula products at levels up to 96 mg/100 kJ (equivalent to 2.4 g/L) in accordance with section 2.9.1—5 (i.e. if it is listed in the table to section S29—5; and is in a permitted form at up to the maximum amount per 100 kJ specified in that table). The applicant is not requesting any changes to the existing permissions for 2′-FL in section S29—5.

1.3.3 Galacto-oligosaccharides and inulin-type fructans

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).

Section 2.9.1—7 sets out restrictions on the addition of ITF and GOS. Subsection 2.9.1—7(3) permits 2′-FL to be used in combination with ITF and/or GOS. An exclusive use period for 2′-FL in combination with ITF and/or GOS is current[1], however will expire 2 June 2024, which is prior to anticipated gazettal of this application.

1.3.4 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 lists two specifications for 2′-FL, including for 2′-FL sourced from *E. coli* K-12 (section S3—40) and 2′-FL sourced from *E. coli* BL21 (section S3—45).

1.3.5 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

[1] The exclusive use period requires that infant formula products which contain 2′-FL in combination with ITF and/or GOS may only be sold if the infant formula product 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.

an ingredient, food that is a *genetically modified food*[2] (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 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.

1.4 Regulation in other countries

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

2′-FL produced by microbial fermentation and by chemical synthesis is permitted for use in infant formula products equivalent products and many other foods in at least 37 overseas countries at a range of levels. Table 1 outlines some international permissions for 2′-FL.

It is noted that internationally, the permitted levels of 2′-FL for use in infant formula range from 1.2 g/L to 2.4 g/L. FSANZ set the existing permitted maximum levels of 2′-FL in the Code after undertaking a safety, technical and health effects assessment, including estimated dietary intakes and naturally occurring levels in human milk (FSANZ 2019; FSANZ 2021).

Table 1: International permissions for use of 2′-FL in infant formula*

Country	Max. use level (g/L)
Australia	2.4
New Zealand	2.4
United States	2.4
Canada#	1.2
Singapore	1.2
European Union (EU)	1.2
Israel	2.0
Korea	2.0
Philippines	1.2

Notes to table:
*Infant formula categories vary between countries
Permission as novel food with support for use in infant formula

Codex Alimentarius (Codex) International Food Standards do not currently exist for 2′-FL. 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.

In March 2022, Inbiose N.V. submitted a GRAS notice to the Food and Drug Administration

[2] 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*).

(FDA) for approval in the USA for 2′-FL manufactured with *E. coli* K-12 MG1655 INB-2FL_03 (GRAS Notice No 1091)[3], which is the production host being assessed under this current application.

The FDA has responded with 'no questions' to an earlier production host of *E. coli* K-12 MG1655 INB000846 (GRN No 897)[4] from the applicant. The specification of the latest submission is equivalent to the 2′-FL approved in GRN 897.

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* (FSANZ Act);
- it related to a matter that warranted the variation of a food regulatory measure.

1.6 Procedure for assessment

The application is being assessed under the General Procedure.

2 Summary of the assessment

2.1 Risk assessment

The Code already permits 2′-FL from different source organisms for addition to infant formula products. The maximum permitted level is 96 mg/100 kJ, equivalent to 2.4 g/L. FSANZ has previously determined that there are no safety concerns associated with the addition of 2′-FL to infant formula products at concentrations up to 2.4 g/L. The primary purpose of the present assessment is therefore to assess the safety of 2′-FL produced by the new production strain.

The applicant's 2′-FL is chemically and structurally identical to the naturally occurring substance present in human milk. It is also chemically and structurally identical to 2′-FL previously assessed and permitted by FSANZ, therefore does not raise any safety concerns.

The *E. coli* K-12 host organism has a long history of use for the production of recombinant proteins and other products, and poses no risks to humans. No safety concerns arising from the gene donors were identified. Characterisation of the GM production strain confirmed that all introduced genes were both genetically stable and functional.

On the basis of the data provided, no potential safety concerns were identified in the assessment of the 2′-FL production strain *E. coli* K-12. Based on previous FSANZ assessments of 2′-FL and the toxicological assessment in the present application, it was concluded that there are no public health and safety concerns associated with 2′-FL produced from the new GM source organism that is the subject of this application.

The nutrition assessment concluded that, based on the available evidence, the addition of 2′-FL to infant formula products is unlikely to pose a risk to the normal growth of infants.

[3]GRN No.1091: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=GRASNotices&id=1091&sort=GRN_No&order=DESC&startrow=1&type=basic&se

[4] GRN No. 897: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=GRASNotices&id=897&sort=GRN_No&order=DESC&startrow=1&type=basic&sea

Based on these previous microbiological assessments, given the identical chemical structure and that the applicant has not requested any change in the maximum permitted level of 2′-FL added to infant formula products, the associated health benefits from the addition of 2′-FL to infant formula products for infants remain the same: (1) an anti-pathogenic effect; (2) immunomodulation and (3) development of the gut microbiome through supporting growth of *Bifidobacteria* spp.

The safety assessment concluded there are no public health and safety concerns associated with the addition of 2′-FL synthesised from a new source organism to infant formula products at the proposed use levels.

2.2 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.

2.2.1 Proposed regulatory approval

FSANZ is proposing to list *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* in the table to subsection S26—3(7).

Application A1277 requested an amendment to the Code to provide a permission for 2′-FL produced from *E. coli* K-12 strain MG1655 INB-2FL_03 containing the gene alpha-1,2 fucosyltransferase. Such a permission, if granted, would be specific to strain MG1655 INB-2FL_03 only, and would not reference the species of the gene donor organism (i.e. *H. enhydrae*).

The draft variation prepared by FSANZ instead provides a permission for 2′-FL from *E. coli* K12 containing the gene alpha-1,2-fucosyltransferase from *H. enhydrae*, without specifying the strain of *E. coli* K12. This approach will provide greater flexibility in terms of strain improvement and avoid the need for new applications to be lodged to provide permissions for new strains of *E. coli* K12.

The approach is also consistent with current permissions in the Code for 2′-FL which specify the gene insertion alpha-1,2-fucosyltransferase, and the gene donor organism. Given the applicant's 2′-FL is proposed to be permitted as a *food produced using gene technology,* and noting the applicant has not requested any changes to current permissions in the Code for 2′-FL, FSANZ considers that, if the draft variation is approved, the applicant's 2′-FL would meet requirements under Standard 2.9.1 and Schedule 29 to be *used as a nutritive substance* with a maximum amount of 96 mg/100 kJ in infant formula products.

2.2.2 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. The applicant's 2′-FL meets the requirements of the current specification for 2′-FL sourced from *E. coli* K-12, i.e. S3—40 (refer Section 2.1.1 of SD1). The draft variation amends the entry in S3—40 to include *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* as a permitted source organism.

2.2.3 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 has requested an exclusive use permission for their specific brand of 2′-FL. FSANZ is proposing to provide the applicant with a 15 month exclusive use permission for the permitted forms of 2′-FL commencing on the date of gazettal of the draft variation (if approved).

If the draft variation is approved, this means that, during that 15 month period, the permission would apply exclusively to those substances under the brand name '2′-FL-Inbiose' in accordance with the Code.

Once the 15 month period ends, the exclusive use permission would revert to a general permission, meaning that anyone may use the permitted forms of 2′-FL 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.

2.2.4 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[5], 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 Lacto-N-neotetraose (LNnT) in the normal growth and development of infants. This 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.

2.2.5 Labelling

2.2.5.1 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 products must contain a statement of ingredients. Should manufacturers choose to add the applicant's 2′-FL alone or combined with LNnT to an infant formula product, then the 2′-FL must be declared as an ingredient 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

[5] Communiqué of outcomes from the Australia and New Zealand Ministerial Forum on Food Regulation meeting held on 27 November 2020

a generic ingredient name if one is specified in Schedule 10 *Generic names of ingredients and conditions for their use*. These ingredient naming requirements would apply to the applicant's 2′-FL, enabling industry to have flexibility in how they declare these ingredients (for example, using the name '2′-fucosyllactose'). However, note that existing prohibited representations in paragraphs 2.9.1—24(1)(ca) and (cb) would also apply to the ingredient name (refer to section 2.2.5.3 below).

2.2.5.2 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. Therefore, the applicant's 2′-FL would need to be declared in the NIS when it is voluntarily added to an infant formula product.

2.2.5.3 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 applicant's 2′-FL would be subject to these provisions regarding prohibited representations.

2.2.5.4 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 would apply to the applicant's 2′-FL.

2.2.5.5 Labelling as 'genetically modified'

As discussed in section 2.3 of SD1, the applicant's 2′-FL is highly unlikely to contain novel protein or novel DNA due to the purification step used in its production. 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 the 2′-FL ingredient as 'genetically modified' would apply in accordance with section 1.5.2—4.

2.2.6 Risk management conclusion

Having considered and weighed all aspects of the assessment against the statutory requirements and current permissions for 2′-FL in the Code, FSANZ is proposing to approve a draft variation to the Code to permit the voluntary addition of 2′-FL from *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* to infant formula products.

If the draft variation is approved, the applicant's 2′-FL would be subject to relevant requirements and conditions in the Code, which include the following:

- It may be added alone or in combination to infant formula products with LNnT up to a maximum level of 2.4 g/L for 2′-FL, as consumed.
- Once the current exclusive use period ends, it may be added to infant formula products in combination with ITF and/or GOS.
- The existing prohibition for the use of the words 'human milk identical oligosaccharide' or 'human milk oligosaccharide', and abbreviations 'HMO', 'HiMO' or any word or words or abbreviations having the same or similar effect, would apply to infant formula products that contain the applicant's 2′-FL.
- An exclusive permission to use 2′-FL produced using *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *H. enhydrae* would apply for a period of 15 months, linked to the applicant's brand name '2′-FL-Inbiose', commencing on the date of gazettal of the approved draft variation.
- It would have to comply with the existing specification in section S3—40 for 2′-FL sourced from *E. coli* K-12.

2.3 Risk communication

2.3.1 Consultation

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

FSANZ developed and applied a standard communication strategy to this application. All calls for submissions are notified via the FSANZ Notification Circular, media release, through FSANZ's social media channels and Food Standards News.

Subscribers and interested parties are also notified about the availability of reports for public comment. The draft variation will be considered for approval by the FSANZ Board taking into account all public comments received on this call for submissions.

The applicant and individuals and organisations that make submissions on this application will be notified at each stage of the assessment.

2.3.2 World Trade Organization (WTO)

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

There are relevant overseas standards and amending the Code to permit the voluntary addition of the applicant's 2′-FL to infant formula products is unlikely to have a significant effect on international trade as this substance is already permitted in similar products in some countries overseas. Therefore, a notification to the WTO under Australia's and New Zealand's obligations under the WTO Technical Barriers to Trade or Application of Sanitary and Phytosanitary Measures Agreement was not considered necessary.

2.4 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:

2.4.1 Section 29

2.4.1.1 Consideration of costs and benefits

Changes have been made to the Impact Analysis requirements by the Office of Impact Analysis (OIA) [6]. 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 and GM. This is because applications relating to permitting the use of nutritive substances and GM 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.

FSANZ, however, has given consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act considerations. The FSANZ Act requires FSANZ to have regard to whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the community, government or industry that would arise from the proposed measure (paragraph 29 (2)(a)).

The purpose of this consideration is to determine if the community, government, and industry as a whole is likely to benefit, on balance, from a move from the status quo (where status quo is rejecting the application). This analysis considers permitting the new source organism for the production of 2′-FL to be added as a nutritive substance to infant formula products.

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 permitting the use of the nutritive substance.

FSANZ's conclusions regarding the costs and benefits of the proposed measure are set out below. However, information received from the Call for Submissions may result in FSANZ arriving at a different outcome.

Cost and benefits of permitting the nutritive substance

The food industry may benefit from this application being approved. Use of the nutritive substance would be voluntary if approved, and therefore industry will only use the nutritive substance where a commercial net benefit exists for them. This application will align Australia and New Zealand with the USA and the European Union and has the potential to enhance international trade in respect of both the import and export of infant formula products.

There is not expected to be any significant costs for consumers and there could in fact be savings in the longer term if production costs are reduced and these are in part or in full passed on to them. Consumers may benefit from the availability of foods containing 2′-FL, a beneficial human milk oligosaccharide.

There is not expected to be any significant impacts for governments.

Conclusions from cost benefit considerations

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

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting a new source organism for the production of 2′-FL to be added as a nutritive substance to infant formula products, most likely outweigh the associated costs

2.4.1.2 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.

2.4.1.3 Any relevant New Zealand standards

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

2.4.1.4 Any other relevant matters

Other relevant matters are considered below.

2.4.2 Subsection 18(1)

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

2.4.2.1 Protection of public health and safety

FSANZ completed a safety and risk assessment (SD1) which is summarised in Section 2.1 of this report. Previous assessments found no safety concerns associated with the addition of 2′-FL to infant formula products. New information provided did not change this conclusion.

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

Current labelling requirements discussed in section 2.2.5 would apply to the applicant's 2′-FL when added to infant formula products and would provide information to enable consumers to make an informed choice.

2.4.2.3 The prevention of misleading or deceptive conduct

Current labelling requirements, including prohibited representations described in section 2.2.5.3, which aim to prevent misleading or deceptive conduct, would apply to the applicant's 2′-FL when added to infant formula products.

2.4.3 Subsection 18(2) considerations

FSANZ has also had regard to:

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

FSANZ used the risk analysis framework and considered the best available evidence to reach its conclusions on the safety, technical and beneficial health outcomes of the applicant's 2′-FL.

- **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. 2′-FL is permitted in infant formula products equivalent products; and several other foods across various countries around the world.

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

The proposed permission would support an internationally competitive food industry in relation to the addition of 2′-FL to infant formula products, and is consistent with existing permissions in the Code for 2′-FL.

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

No issues were identified for this application relevant to this objective.

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

As part of A1277, FSANZ has had regard to both high order and specific policy principles in the following Ministerial Policy Guidelines for the Regulation of Infant Formula Products.

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

Noting the food technology aspects, safety, associated health benefits, and nutritional impact assessed in SD1 and Section 2.1 of this Report, FSANZ considers these Policy Guidelines have been met.

3 Draft variation

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

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

4 References

Codex Alimentarius (2017) Standard for Follow-Up Formula. (CXS/156, adopted in 1987. Amendment: 1989, 2011 and 2017. Rome, Italy: Codex Alimentarius Commission. Available at: https://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B156-1987%252FCXS_156e.pdf

Codex Alimentarius (2020) Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants. (CXS 72, adopted in 1981. Amendment: 1983, 1985, 1987, 2011, 2015, 2016 and 2020, Revision: 2007). Rome, Italy: Codex Alimentarius Commission. Available at: https://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B72-1981%252FCXS_072e.pdf

FSANZ (2008) First Review Report Proposal P306 Addition of Inulin/FOS and GOS to food. Food Standards Australia New Zealand, Canberra, Australia. https://www.foodstandards.gov.au/code/applications/Documents/A1155%20Review%20Report.pdf

FSANZ (2013) A1055: Short-chain fructo-oligosaccharides. Supporting Document 1. Risk and technical assessment (at approval). Food Standards Australia New Zealand, Canberra, Australia.
https://www.foodstandards.gov.au/code/applications/Documents/A1055%20Addition%20of%20scFOS%20AppR%20SD1%20Risk%20Assess.pdf

FSANZ (2019) Application A1155 - 2′-FL and LNnT in infant formula and other products. Supporting Document 1 at Second Call for Submissions. Report prepared by Food Standards Australia New Zealand, Canberra.
www.foodstandards.gov.au/code/applications/Documents/A1155_SD1_Risk%20assessment%20-%202nd%20CFS.pdf

FSANZ (2021) Application A1190 - 2′-FL and LNnT in infant formula and other products. Supporting Document 1 at Approval. Risk and safety assessment. Report prepared by Food Standards Australia New Zealand, Canberra.
https://www.foodstandards.gov.au/code/applications/Documents/A1190_SD1%20at%20Approval.pdf

Attachments

A. Draft variation to the Australia New Zealand Food Standards Code
B. Draft Explanatory Statement

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

Food Standards (Application A1277 – 2′-FL from GM *Escherichia coli* K-12 (gene donor: *Helicobacter enhydrae*) 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 A1277 – 2'-FL from GM* Escherichia coli *K-12 (gene donor:* Helicobacter enhydrae*) 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

Schedule 3—Identity and purity

[1] Section S3—40

Omit "either *Helicobacter pylori* or", substitute "either *Helicobacter enhydrae*, *Helicobacter pylori*, or"

Schedule 26—Food produced using gene technology

[2] Subsection S26—3(7) (table item 1)

Insert:

	(d) *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand 2′-FL-Inbiose. 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 A1277 – 2'-FL from GM* Escherichia coli *K-12 (gene donor:* Helicobacter enhydrae*) in infant formula products) Variation* and ending 15 months after that date.

Attachment B – Draft Explanatory Statement

DRAFT EXPLANATORY STATEMENT

Food Standards Australia New Zealand Act 1991

Food Standards (Application A1277 – 2′-FL from GM *Escherichia coli* K-12 (gene donor: *Helicobacter enhydrae*) 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 A1277 which seeks to amend the Code to permit 2′-fucosyllactose (2′-FL) derived from a genetically modified (GM) strain of *Escherichia coli* K12 to be used in infant formula products. The application also seeks a 15 month exclusive use permission.The Authority considered the application in accordance with Division 1 of Part 3 and has prepared a draft variation - the *Food Standards (Application A1277 - 2′-FL from GM* Escherichia coli *K-12 (gene donor:* Helicobacter enhydrae*) in infant formula products) Variation*.

2. Variation will be a legislative instrument

If approved, the draft variation would be a legislative instrument for the purposes of the *Legislation Act 2003* (see section 94 of the FSANZ Act) and be publicly available on the Federal Register of Legislation (www.legislation.gov.au).

If approved, this instrument would not be 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 Food Ministers Meeting (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 prepared a draft variation to the Code to:

- Amend Schedule 26 of the Code to permit 2′-FL produced from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae*, to be used as a nutritive substance and food produced using gene technology in infant formula products subject to certain conditions, including an exclusive use period of 15 months linked to the applicant's brand name '2′-FL-Inbiose'.
- Amend the current specification in Schedule 3 of the Code for 2′-FL sourced from *Escherichia coli* K-12 (section S3—40) to include 2′-FL from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae* in the list of substances to which the specifications in section S3—40 apply.

4. Documents incorporated by reference

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

However, if approved, the draft variation would 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) Combined Compendium of Food Additive Specifications (FAO JECFA Monographs 26 (2021)); the United States Pharmacopeial Convention (2022) Food Chemicals Codex (13th 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 A1277 will include one round of public consultation following an assessment and the preparation of a draft variation and associated assessment summaries. A call for submissions (including the draft variation) will be open for a six-week period.

Changes have been made to the Impact Analysis requirements by the Office of Impact Analysis (OIA)[7]. 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 and genetically modified food. This is because applications relating to permitting the use of nutritive substances and genetically modified food 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

[7] Formerly known as the Office of Best Practice Regulation (OBPR)

If approved, this instrument would be exempt from the requirements for a statement of compatibility with human rights as it would be a non-disallowable instrument under section 44 of the *Legislation Act 2003*.

7. Variation

Clause 1 of the draft variation provides that the name of the variation is the *Food Standards (Application A1277 – 2′-FL from GM* Escherichia coli *K-12 (gene donor:* Helicobacter enhydrae*) in infant formula products) Variation*.

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

Clause 3 of the draft variation provides that the variation will commence on the date of gazettal of the instrument.

Item [1] of the Schedule to the draft variation would amend 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)).
In particular, item [1] would amend section S3—40 (for 2′-FL sourced from *Escherichia coli* K-12) by including 2′-FL from *Escherichia coli* K-12 containing the gene for alpha-1,2 fucosyltransferase from *Helicobacter enhydrae* in the list of substances to which the specifications in section S3—40 apply.

Item [2] of the Schedule to the draft variation would amend Schedule 26 of the Code.

Schedule 26 relates to food produced using gene technology. 2′-FL sourced from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae* 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.

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 [2] would amend item 1 of that table (2′-FL) by inserting new paragraph (d) into the column headed ‘Source’. New paragraph (d) would refer to:

‘*Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae*’.

Associated conditions of use for 2′-FL from this new source would be set out in column 3 of the table 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 2′-FL-Inbiose; and

3. for the purposes of condition 2, exclusive use period means the period commencing on the date of gazettal of the *Food Standards (A1277 - 2′-FL from GM* Escherichia coli *K-12 (gene donor:* Helicobacter enhydrae*) in infant formula products) Variation* and ending 15 months after that date.

Condition 2 would mean that 2′-FL sourced from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae* may only be sold under the brand '2′-FL-Inbiose' during the exclusive use period. 'Exclusive use period' would be defined in condition 3 as the period commencing on gazettal of the draft variation and ending 15 months after that date.

If the draft variation is approved, the effect of the amendment in item [2] would be to permit the use of the substance, 2′-FL from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae* as a food produced using gene technology, subject to the above conditions of use for the substance.

Once the exclusive use period ends, the permission would revert to a general permission, meaning that the proposed permission would then permit the sale of 2′-FL sourced from *Escherichia coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter enhydrae* under any brand.

The proposed amendments made by item [2] would not make any substantive change to *existing* permissions and to other requirements in the Code relating to food produced using gene technology.