26 November 2024
319-24

Call for submissions – Application A1308

A1308 - 2′-FL from GM *Escherichia coli* W in infant formula products

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Food Standards Australia New Zealand (FSANZ) has assessed an application made by Kyowa Hakko Bio Co., Ltd to amend the Australia New Zealand Food Standards Code to permit the use of 2′-fucosyllactose produced from a genetically modified *Escherichia coli* W 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.

Submissions on this application need to be made through the Consultation Hub (https://consultations.foodstandards.gov.au/).

All submissions on applications and proposals will be published on the Consultation Hub. 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 following consultation and before the next stage in the statutory assessment process.

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 Making a submission.

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

FSANZ also accepts submissions in hard copy to our Australia and/or New Zealand offices. There is no need to send an email or hard copy of your submission if you have submitted it through the FSANZ Consultation Hub.

DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 24 December 2024

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.

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

The following document which informed the assessment of this application is available on the A1308 page on the FSANZ website:

SD1 Risk and technical assessment – Application A1308

Executive summary

Food Standards Australia New Zealand (FSANZ) has assessed an application made by Kyowa Hakko Bio Co., Ltd to amend the Australia New Zealand Food Standards Code (the Code) to permit 2′-fucosyllactose (2′-FL) produced from genetically modified (GM) *Escherichia coli (E. coli)* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae (H. mustelae)* to be used as a nutritive substance in infant formula products.

The Code already permits 2′-FL from other GM sources to be used as a nutritive substance in infant formula products. However, the Code does not currently permit the use of 2′-FL produced from GM *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* for that purpose.

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

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 levels up to the current maximum permitted amount in the Code. 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 by FSANZ and permitted in the Code. 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.

For reasons set out in this report, FSANZ has prepared a draft variation to the Code to permit the use of 2′-FL produced from a GM source i.e. *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* as a nutritive substance in infant formula products in accordance with the Code. If approved, the draft variation would:

- amend Schedule 26 of the Code to permit the applicant's 2′-FL to be used as a nutritive substance 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 Kyowa', and
- insert a new specification for the applicant's 2′-FL into Schedule 3 of the Code, with which the applicant's 2′-FL would have to comply when used as a nutritive substance in infant formula products (or sold for such use).

The proposed permission would be subject to existing labelling requirements.

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

1 Introduction

1.1 The Applicant

The applicant, Kyowa Hakko Bio Co., Ltd is a manufacturer of biotechnology and fermentation products. The applicant brings to market chemical substances produced via fermentation technologies.

1.2 The Application

On 29 June 2024, Kyowa Hakko Bio Co., Ltd applied to amend Standard 2.9.1 and Schedules 3, 26 and 29 of the Australia New Zealand Food Standards Code (the Code) to permit a new genetically modified (GM) source organism *Escherichia coli* W (*E. coli* W) containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae (H. mustelae)* for the production of 2′-fucosyllactose (2′-FL) to be used as a nutritive substance in infant formula products.

1.3 The current Code requirements

Australian 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

Revised regulation of infant formula products came into effect on 13 September 2024 and applies in Australia only. New Zealand opted out of this regulation under *Annex D of The Agreement between the Government of Australia and the Government of New Zealand Concerning a Joint Food Standards System*. Therefore, the permission for addition of this 2′-FL, if approved, would apply in Australia only as per the Code as currently in force.

Infant formula products in Australia are regulated by Standard 2.9.1 which sets out specific 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)
- special medical purpose product for infants (from birth).

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*.

2′-FL produced from various sources is already permitted in the Code as a *food produced using gene technology of microbiological origin* for use in infant formula products, however not from *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae.*

The applicant's 2′-FL is a *food produced using gene technology* (section 1.1.2—2) as it is produced from an organism modified using gene technology i.e. produced from GM *E. coli* W. Consequently, express permission for the applicant's 2′-FL would be required in accordance with paragraph 1.5.2—3(a) (i.e. to be listed in Schedule 26 and to comply with any corresponding conditions).

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 would be *used as a nutritive substance* for the purposes of the Code because its use in infant formula products 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—9 (i.e. if, among other things, it is listed in the tables to sections S29—7 and S29—8 and is in a permitted form at up to the maximum amount per 100 kJ specified in that table). The tables to sections S29—7 and S29—8 list 2′-fucosyllactose *permitted for use by Standard 1.5.2* (see section 1.3.2.1 of this report above).

The applicant is not requesting any changes to the existing permissions for 2′-FL in sections S29—7 and S29—8.

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. The application provided a proposed specification for the applicant's 2′-FL for this purpose.

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.

Division 3 of Standard 1.2.3 sets out the requirements for mandatory declarations of certain foods and their derivatives when they are present in a food for sale.

Standard 1.2.4 generally requires food products to be labelled with a statement of ingredients and provides requirements for ingredient names.

Standard 1.2.7 sets out the requirements and conditions for voluntary nutrition, health and related 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*[1] (GM food).

Standard 2.9.1 sets out the specific requirements for declaring nutrition information and includes provisions for prohibited representations on infant formula product labels.

[1] 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*).

1.4 Regulation in other countries

In developing food regulatory measures, Food Standards Australia New Zealand (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. permitted amount (g/L)
Australia	2.4
New Zealand	2.4
United States	2.4
Canada#	1.2
Singapore	2.4
European Union (EU)	1.2
Israel	2.0
Korea	1.1
Philippines	1.2

Notes to table:
* Infant formula categories vary between countries
# Permission as a 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 for Older Infants and Product for Young Children' (Codex Alimentarius 2023) contain provisions for 'optional ingredients' which are applicable to 2′-FL.

In the United States (US), Kyowa Hakko Bio Co., Ltd has received a letter of 'no questions' from the US Food and Drug Administration (FDA) regarding the Generally Recognised as Safe (GRAS) status of their 2′-FL produced by fermentation using a modified strain of *E. coli* W (GRAS Notice (GRN) 1051) (U.S. FDA 2023a).

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 several source organisms to be used as a nutritive substance in infant formula products. The maximum permitted amount of 2′-FL in infant formula products is 96 mg/100 kJ, equivalent to 2.4 g/L. The 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, produced by a microbial fermentation method of production, 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.

The *E. coli* W host organism has a long history of use for the production of recombinant proteins and other products, and is unlikely to pose a risk to humans. No safety concerns arising from the gene donor were identified. Characterisation of the GM production strain confirmed that the introduced alpha-1,2-fucosyltransferase gene is both genetically stable and functional.

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. Newly available information did not indicate a reason to change this conclusion.

No treatment-related adverse effects were found in a 90-day oral toxicity study of the applicant's 2′-FL in rats. The NOAEL in this study was 2000 mg/kg bw/day, the highest dose tested. The applicant's 2′-FL was not genotoxic *in vitro* or *in vivo*.

The dietary intake assessment compared the estimated dietary intake of 2′-FL from infant and follow-on formula to that of mature human milk for 3- and 9-month-old infants. As there is no requested change to the current permitted amount of 2′-FL in infant formula products, no extension of use, and no data suggesting a higher concentration in human milk since the most recent FSANZ assessment, estimated dietary intakes of 2′-FL from previous FSANZ assessments were used in this current assessment. These data showed that estimated mean and 90th percentile dietary intakes of 2′-FL at the maximum permitted amount in the Code from infant formula products fall within the range of estimated dietary intakes from mature human milk.

FSANZ has previously concluded that based on the available evidence the addition of 2′-FL to infant formula products is unlikely to pose a risk to normal growth of infants at levels typically found in human milk. No new relevant studies were identified for this assessment and therefore FSANZ maintains this conclusion.

Overall the safety assessment concluded there are no public health and safety concerns associated with the addition of 2′-FL from the new source organism to infant formula products at the maximum permitted amount in the Code.

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* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* as a source of 2′-FL in the table to subsection S26—3(7).

Application A1308 requested an amendment to the Code to provide a permission for 2′-FL produced from GM *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* to be used as a nutritive substance in infant formula products.

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, for reasons set out at sections 1.3.2.1 and 1.3.2.2 of this report, FSANZ considers that, if the draft variation is approved, the applicant's 2′-FL would meet the 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 that a substance that is *used as a nutritive substance* must comply with any relevant specification set out in Schedule 3. The draft variation would insert a new specification relating specifically to the applicant's 2′-FL sourced from *E. coli* W, with which this 2′-FL would have to comply when used as a nutritive substance in infant formula products (or sold for such use).

2.2.3 Exclusivity

An applicant may request exclusive permission to use and sell a food (including a substance) for a certain period of time to recognise the investment made in developing that food, 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 this 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 Kyowa' 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 human identical milk oligosaccharides (HiMOs) in the normal growth and development of infants.

At the request of Food Ministers[2], 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.

2.2.5 Labelling

Division 3 of Standard 2.9.1 provides specific labelling requirements for infant formula and follow-on formula. Labelling requirements that apply to Special Medical Purpose Products for infants (SMPPi) are set out in Division 4 of this standard. FSANZ refers to the relevant requirements below that would apply to the applicants' 2′-FL if it was added to an infant formula product.

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 or follow-on formula must contain a statement of ingredients. Should manufacturers choose to add the applicant's 2′-FL to infant formula or follow-on formula in accordance with the Code, then the 2′-FL would have to be declared in the statement of ingredients.

Generic ingredient labelling provisions in section 1.2.4—4 require ingredients to be identified using: a name by which they are commonly known; 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. A generic ingredient name for 2′-FL has not been specified. 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—28(1)(e) and (f) would also apply to the ingredient name (refer to section 2.2.5.3 below).

Section 2.9.1—51 sets the requirement for information relating to ingredients in SMPPi. This section specifies that ingredient information may be provided on the label of a SMPPi in a statement of ingredients (in accordance with the Code as mentioned immediately above), or ingredient information that complies with either the EU or US regulations. These regulatory labelling requirements are intended to facilitate the importation of highly specialised SMPPi that are manufactured in low volumes in Europe and in the United States. Therefore, for the use of the applicant's 2′-FL in SMPPi, the ingredient naming requirements of the Code or the EU or US could apply.

2.2.5.2 Mandatory nutrition information

Section 2.9.1—24 regulates the declaration of nutrition information in a Nutrition Information Statement (NIS) on the label of a package of infant formula or follow-on formula. The NIS is a single statement that must be in the form of a table, as indicated in section 2.9.1—25 and in accordance with section S29—10.

Subparagraph 2.9.1—24(3)(e)(i) requires any substance used as a nutritive substance to be declared in the NIS. Therefore, the applicant's 2′-FL would need to be declared in the NIS when it is used voluntarily in infant formula or follow-on formula. Subsection 2.9.1—25(3) requires the declaration to be made under the heading 'Additional' in the NIS, using the format specified in section 29—10.

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

Paragraph 2.9.1—53(1)(c) requires the declaration of a substance used as a nutritive substance expressed per given amount of the product and that has been added to the SMPPi to achieve its intended medical purpose. Should manufacturers choose to add the applicant's 2′-FL, then this provision would apply. However, there are no formatting requirements for this nutrition information, as labelling provisions for SMPPi are generally more flexible compared to infant formula and follow-on formula to ensure the importation of SMPPi is not impeded.

2.2.5.3 Prohibited representations and prohibited claims

Paragraph 2.9.1—28(1)(e) prohibits the use of the words 'human milk oligosaccharide', 'human identical milk oligosaccharide' or any word or words having the same or similar effect on the label of a package of infant formula or follow-on formula. In addition, paragraph 2.9.1—28(1)(f) prohibits the use of the abbreviations 'HMO' or 'HiMO' or any abbreviation having the same or similar effect. The prohibition on these words and abbreviations also applies to SMPPi as a result of paragraphs 2.9.1—45(c) and (d).

Paragraph 2.9.1—28(1)(i) prohibits information relating to the presence of a nutritive substance except for a reference in a statement of ingredients or in a NIS on the label of a package of infant formula or follow-on formula.

For SMPPi, subsection 2.9.1—46 sets out an explicit prohibition for nutrition content, health claims and claims which represent the product for therapeutic use. This prohibition would apply in relation to the use of the applicant's 2′-FL in SMPPi.

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. This provision would apply to infant formula products that contain the applicant's 2′-FL.

2.2.5.5 Labelling as 'genetically modified'

Based on previous FSANZ assessments of 2'FL, it is considered highly unlikely that the applicant's 2′-FL would 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 this 2′-FL as an ingredient. 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, including relevant Ministerial Policy Guidelines and current permissions for 2′-FL in the Code, FSANZ has decided to prepare a draft variation to the Code to permit the use of 2′-FL from *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* as a nutritive substance in 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 with Lacto-N-neotetraose (LNnT), or in combination with inulin-type fructans (ITF) and/or galacto-oligosaccharides (GOS) to infant formula products up to a maximum level of 2.4 g/L for 2′-FL, as consumed.
- The existing prohibition for the use of the words 'human identical milk 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 use permission to use 2′-FL produced using *E. coli* W containing the gene for alpha-1,2-fucosyltransferase from *H. mustelae* would apply for a period of 15 months, linked to the applicant's brand name '2′-FL Kyowa', commencing on the date of gazettal of the approved draft variation.
- Schedule 3 of the Code would set a specific specification for the applicant's 2′-FL, with which it must comply when used as a nutritive substance in infant formula products (or sold for such use).

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 and Food Standards News.

The process by which FSANZ approaches standards development matters is open, accountable, consultative and transparent. Public submissions are called to obtain the views of interested parties on the draft variation.

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 is obliged to notify WTO members where proposed mandatory regulatory measures are not substantially the same as existing international standards and the proposed measure may have a significant effect on trade.

There are no relevant international standards and amending the Code to permit the use of the applicant's 2′-FL as a nutritive substance in 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 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

Background

Changes have been made to the Impact Analysis requirements by the Office of Impact Analysis (OIA)[3]. 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 OIA Reference: OIA23-06224.

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 draft variation concerned 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 the status quo is rejecting the application). This analysis considers the costs and benefits of permitting the proposed use of the applicant's 2′-FL as a nutritive substance in 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 proposed use of the applicant's 2′-FL as a nutritive substance in infant formula products.

Consumers

The permission to add the applicant's 2′-FL to infant formula products would apply in Australia only (see section 1.3.1).

FSANZ's risk assessment concludes no safety concerns from the addition of the applicant's 2′-FL to infant formula products at the proposed maximum permitted amounts.

Consumers in Australia may benefit from a larger range and supply of infant formula products for sale that contain the applicant's 2′-FL in one or more infant formula products for sale.

A new source for an already permitted ingredient, 2′-FL may also lead to overall price reductions in infant formula products containing 2′-FL for consumers. That is if industry passes on any cost efficiencies gained from using 2′-FL from this new source (the applicant's 2′-FL). In the longer term it may also become a more common ingredient that no longer draws any price premium which will provide increased value to all consumers.

The role of granting an exclusive use permission is to encourage industry innovation and allow applicants to achieve commercial rewards through higher returns on their investment. Any commercial reward from this application's exclusive use period could come at the expense of consumers in the short-term, through other businesses not being able to compete to supply the applicant's 2′-FL at lower prices during the exclusivity period. However, without

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

this incentive this innovation may not have taken place. It is assumed that the greater incentive to innovate will lead to greater benefits in the medium to long term for consumers, because innovation encourages more products to come to market that may benefit consumers.

Industry

The permission to add the applicant's 2′-FL to infant formula products would apply in Australia only, however non-Australian manufacturers (including those in New Zealand) may be able to use the permission to manufacture products for sale in Australia (where various other conditions on exporting infant formula products to Australia are met).

Industry may benefit from increased choice of sources for 2′-FL permitted to be used as nutritive substances in infant formula products for sale. That may reduce costs of sourcing 2′-FL. Industry may voluntarily use 2′-FL from this new source or buy and sell infant formula products containing 2′-FL from this new source, where they believe a commercial net benefit exists for them.

Given the applicant's 2′-FL is already approved in some overseas countries, approving the applicant's 2′-FL would favour trade and any growth of overseas markets for exports of Australian infant formula products. The proposed permission may also support innovation in infant formula products.

Producers of infant formula products in Australia, may however face greater competition in the domestic infant formula products market from overseas-based producers that can also supply Australia with infant formula products containing the applicant's 2′-FL. Any such impacts to domestic producers are assumed to be outweighed by benefits to consumers from greater industry competition.

Granting an exclusive use permission as proposed would prevent other businesses from producing 2′-FL from this additional source in the short-term. There may also be short-term restrictions on numbers of businesses that can access the applicant's 2′-FL, relative to if the exclusive use period had not been granted. However, the granting of exclusive use permission does not preclude any other company from applying to amend the Code in relation to the same food or ingredient. Therefore, the market for this additional source of 2′-FL could be opened during the 15 months' exclusivity for any other companies willing to make an application.

Government

The approval of this application may result in a small but likely inconsequential cost to Australian governments in terms of an addition to the current range of 2′-FL from various sources which are monitored for compliance.

Conclusion

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting the applicant's 2′-FL as proposed, are likely to 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

New Zealand opted out of Standard 2.9.1 under *Annex D of The Agreement between the Government of Australia and the Government of New Zealand Concerning a Joint Food Standards System.*

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 use of 2′-FL in 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 outlined in section 2.2.5 of this report would apply to infant formula products containing the applicant's 2′-FL, 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 infant formula products containing the applicant's 2′-FL.

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[4] and considered the best available scientific 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 equivalent products; and several other foods across various countries around the world.

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

[4] Risk analysis and assessment | Food Standards Australia New Zealand

The proposed permission would support an internationally competitive food industry in relation to the use of 2′-FL as a nutritive substance in 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 A1308, 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 (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

Codex Alimentarius (2023) Standard for Follow-up formula for Older Infants and Product for Young Children. (CXS/156, adopted in 1987. Amendment: 1989, 2011, 2017, Revision: 2023. Rome, Italy: Codex Alimentarius Commission. 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

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/sites/default/files/food-standards-code/proposals/Documents/P306%20FOS%20_%20GOS%20FRR%20FINAL.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/sites/default/files/food-standards-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. https://www.foodstandards.gov.au/sites/default/files/food-standards-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/sites/default/files/food-standards-code/applications/Documents/A1190_SD1%20at%20Approval.pdf

U.S. FDA (2023a). Agency Response Letter GRAS Notice No. GRN 1051 [2′-fucosyllactose, Tokyo, Japan: Kyowa Hakka Bio Co., Ltd.] Silver Spring (MD): U.S. Food and Drug Administration (U.S FDA), Center for Food Safety and Applied Nutrition (CFSAN), Office of Food Additive Safety. Available at : https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=1051 [Nov. 21, 2023 – FDA response – no questions]

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 A1308 – 2′-FL from GM *Escherichia coli W* 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 A1308 – 2'-FL from GM* Escherichia coli W *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] Subsection S3—2(2) (table, after the table item dealing with 2′-fucosyllactose and difucosyllactose sourced from *Escherichia coli* K-12)

Insert:

2′-fucosyllactose sourced from *Escherichia coli* W	section S3—52

[2] After section S3—51

Insert:

S3—52 Specification for 2′-fucosyllactose sourced from *Escherichia coli W*

For 2′-fucosyllactose (2′-FL) sourced from *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae*, the specifications are the following:

(a) chemical name—α-L-fucopyranosyl-(1→2)-β-D-galactopyranosyl-(1→4)-D-glucopyranose;
(b) chemical formula—$C_{18}H_{32}O_{15}$;
(c) molecular weight—488.44 g/mol;
(d) CAS number—41263-94-9;
(e) description—white to off-white powder;
(f) 2′-FL—not less than 82% (water free);
(g) D-lactose—not more than 5.0% (water free);
(h) L-fucose—not more than 1.0% (water free);
(i) fucosylgalactose—not more than 3.0% (water free);
(j) difucosyllactose (difucosyl-d-lactose)—not more than 3.0% (water free);
(k) glucose and galactose—not more than 1.0% (water free);
(l) water—not more than 9.0%;
(m) ash, sulphated—not more than 0.5%;
(n) residual proteins—not more than 0.01%;
(o) lead—not more than 0.1 mg/kg;
(p) arsenic—not more than 0.1 mg/kg;
(q) cadmium—not more than 0.1 mg/kg;
(r) mercury—not more than 0.1 mg/kg;
(s) microbiological:
    (i) aerobic mesophilic bacteria total count—not more than 1,000 cfu/g;
    (ii) yeasts and moulds—not more than 100 cfu/g;
    (iii) *Enterobacteriaceae*—absent in 10 g;
    (iv) residual endotoxins—not more than 10 EU/g.

Schedule 26—Food produced using gene technology

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

Insert:

(f)	*Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae*	1. May only be added to infant formula products. 2. During the exclusive use period, may only be sold under the brand 2′-FL Kyowa. 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 A1308 - 2′-FL from GM* Escherichia coli W *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 A1308 – 2'-FL from GM* Escherichia coli *W 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 A1308 which seeks to amend the Code to permit the use of 2′-fucosyllactose (2′-FL) produced from genetically modified *Escherichia coli* W to be used as a nutritive substance 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 A1308 – 2'-FL from GM* Escherichia coli *W in infant formula products) Variation* (the draft 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.

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 the draft variation to:

- Amend Schedule 26 of the Code to permit 2′-FL produced from a new genetically modified source, *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae*, to be used as a nutritive substance in infant formula products subject to certain conditions, including an exclusive use permission for a period of 15 months linked to the applicant's brand name '2′-FL Kyowa'.
- Insert a new specification for this 2′-FL into Schedule 3 with which this 2′-FL would have to comply when used as a nutritive substance in infant formula products (or sold for such use).

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 A1308 will include one round of public consultation following an assessment and the preparation of a draft variation and associated assessment summary. A call for submissions (including the draft variation) will be open for a seven-week period.

Changes have been made to the Impact Analysis requirements by the Office of Impact Analysis (OIA)[5]. 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 applications relating to nutritive substances OIA Reference: OIA23-06224. 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 draft variation concerned 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

If approved, this instrument would be 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*.

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

7. Variation

Clause 1 of the draft variation provides that the name of the variation is the *Food Standards (Application A1308 - 2′-FL from GM* Escherichia coli *W 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.

Items [1] and [2] 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 when added to food in accordance with the Code or sold for use in food. Specifications include those set out in provisions which are listed in the table to subsection S3—2(2) (see paragraph S3—2(1)(a)).

Item [1] would insert into columns 1 and 2 of the table to subsection S3—2(2), in alphabetical order, new references to '2′-fucosyllactose sourced from *Escherichia Coli* W' and 'section S3—52' respectively. These new references relate to the new provision that would be inserted by item [2] below.

Item [2] would insert a new section S3—52 which sets out the specifications relating specifically to 2′-fucosyllactose sourced from *Escherichia coli W*, the new substance sought to be permitted by the applicant.

Consequently, the proposed permission for 2′-fucosyllactose sourced from *Escherichia coli* W to be used as a nutritive substance in infant formula products (or sold for such use) would be subject to the requirement in section 1.1.1—15 that the substance must comply with these specifications.

Item [3] 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* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae* is a food produced using gene technology (as defined in subsection 1.1.2—2(3) of the Code) because it is produced 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 [3] would amend item 1 of that table (2′-FL) by inserting new paragraph (f) into the column headed 'Source'. New paragraph (f) would refer to:

'*Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae*.

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 Kyowa; and;
3. for the purposes of condition 2, exclusive use period means the period commencing on the date of gazettal of the *Food Standards (A1308 - 2′-FL from GM* Escherichia Coli *W in infant formula products) Variation* and ending 15 months after that date.

Condition 2 would mean that 2′-FL sourced from *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae* may only be sold under the brand 2′-FL Kyowa 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 [3] would be to permit the use of the substance, 2′-FL from *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae* 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 and use of 2′-FL sourced from *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae* under any brand.

The proposed amendments made by item [3] would not make any substantive change to *existing* permissions and to other requirements in the Code relating to food produced using gene technology.

If the draft variation is approved, the effect of the amendment in item [3] would also be to permit 2′-FL from *Escherichia coli* W containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter mustelae* to be used as a nutritive substance in infant formula products.

This is because subsection 2.9.1—5(1) and section S29—5 permit a '2′-fucosyllactose permitted for use by Standard 1.5.2' to be used as a nutritive substance in infant formula products at an amount no greater than 96 mg/100 kJ.