INFANT NUTRITION COUNCIL
AUSTRALIA & NEW ZEALAND

19 August 2022

INC SUBMISSION ON CALL FOR SUBMISSIONS – APPLICATION A1251: 2'-FL COMBINED WITH GALACTO-OLIGOSACCHARIDES AND/OR INULIN-TYPE FRUCTANS IN INFANT FORMULA PRODUCTS

This submission has been prepared by the Infant Nutrition Council (INC). The INC represents manufacturers, marketers and suppliers of infant formula and toddler milk dinks (formulated supplementary foods for young children) and, is the key industry stakeholder in the advancement of infant nutrition representing over 95% of the volume manufactured and marketed in in Australia and New Zealand.
INC aims to:

1. Improve infant nutrition by supporting the public health goals for the protection and promotion of breastfeeding and, when needed, infant formula as the only suitable alternative; and
2. Represent the infant formula product and toddler milk drink industry in Australia and New Zealand.

INC is a responsible group that voluntarily restricts its marketing practices for infant formula products to support government policies for the protection and promotion of breastfeeding.

INC believes that breastfeeding is the normal way to feed infants as it has numerous benefits for both mothers and babies. When an infant is not given breast milk the only suitable and safe alternative is a scientifically developed infant formula product. For these infants, infant formula is the sole source of nutrition for around the first 6 months. It is important that scientific advances in infant nutrition are captured and incorporated into these products to ensure the best possible outcome for infants who do not receive breast milk.

We welcome the opportunity to provide written comment to Food Standards Australia New Zealand (FSANZ) in response to the *Call for Submissions – Application A1251: 2'-FL combined with galacto-oligosaccharides and/or inulin-type fructans in infant formula products.*

Yours sincerely

EXECUTIVE SUMMARY

1. After lactose and fat, the third main solid component in human milk is neutral and acid oligo- (and poly) saccharides. Neutral oligosaccharides such as 2'-FL are the predominant oligosaccharides in human milk.

2. Inulin and oligofructoses have been assessed as safe and regulated as unstandardised foods for almost 30 years. 'Unstandardised foods' such as inulin-type fructans, fructo-oligosaccharides and substances normally consumed as foods are taken not to be nutritive substances.

3. FSANZ concluded from its overall *risk and technical assessment* (safety, toxicological and microbiological assessments and dietary and nutrition assessments) that consumption of infant formula containing a combination of 2′-FL GOS and/or ITF was safe and well tolerated.

4. In light of existing permissions and labelling requirements, no additional labelling requirements were proposed, a position INC agrees with. INC nonetheless continues of the view that the prohibition on the use of the term, 'human identical milk oligosaccharides' or HiMO, is counter to building consumer confidence in, and understanding of, labelling information.

5. We note FSANZ is committed to reviewing new evidence on the beneficial role of 2′-FL (alone, or in combination with LNnT) in the normal growth and development of infants. INC is wholly supportive of FSANZ's ongoing work in this area.

6. Harmonisation with international standards, that are based on relevant science and scientific expert opinion, is essential to allow the manufacture and availability of these types of products for consumers in Australia and New Zealand and for export. As well, the alignment of regulations with international standards encourages consideration of future investments in innovation in Australia and New Zealand. Alignment will result after the 15 month exclusivity period.

7. INC has no comments to make on the exclusivity of this particular Application. We are, however, seeking clarity and consideration around the current and future scope of the application of exclusivity in the broader food supply.

8. To date, an exclusive capturable commercial benefit has been applied by way of proposal to novel foods and as part of a category-specific application (infant formula) to nutritive substances. The current category-specific application for an exclusive period of use is for a branded food that contains a previously approved nutritive substance and unstandardised foods (GOS and/or ITF).

9. INC is concerned that the scope of "exclusive capturable commercial benefit" is being expanded by applications on a case-by-case basis rather than in a more transparent and regularised way. Without this, the broader food industry is unaware of the opportunity to comment on various implementation pathways of the concept of exclusivity.

10. INC is supportive of the concept of exclusive capturable commercial benefit and fully recognises the value that this has to deliver on investment for the food industry and for innovation. We are concerned, however, at the ad hoc way in which the concept appears to be implemented and suggest a more consistent approach be applied in order to ensure visibility for the broader food industry.

DETAILED COMMENTS

The application

11. Nutricia and Chr. Hansen A/S ("**Hansen**") have applied to Food Standards Australia New Zealand ("**FSANZ**") to amend the Australia New Zealand Food Standards Code ("**the Food Standards Code**") to permit 2'-fucosyllactose ("**2'-FL**") to be added to infant formula products in combination with galacto-oligosaccharides ("**GOS**") and/or inulin-type fructans ("**ITF**"). Nutricia and Hansen have also requested an exclusive use permission for a period of 15 months for their combination of 2′-FL with GOS and/or ITF.

Content of human milk

12. After lactose and fat, the third main solid component in human milk is neutral and acid oligo- (and poly) saccharides. The structure of about 200 human milk oligosaccharides has been identified and many more are present, at least in small quantities. These oligosaccharides occur in concentrations between 10-15 g/L in mature breast milk and up to 20 g/L in colostrum (Kunz et al. 2000 and Thurl et al. 2017). Neutral oligosaccharides such as 2'-FL are the predominant oligosaccharides in human milk and the permitted addition in infant formula products is in line with Policy Principle (h) relating to composition in the Policy Guideline on *Regulation of Infant Formula Products*.

13. As the most prevalent of the HMOs found in human breast milk, 2'-FL is reported to have a role in the gut and immune system of infants (Lewis et al. 2015, Morrow et al. 2004 and Siziba et al. 2021), reduce the risk for lower respiratory tract illnesses through a protective effect on mucosal barrier function (Sprenger et al. 2019) and an immunomodulation role in prevention of allergic diseases in early life (Zuurveld et al. 2020).

14. Inulin and oligofructoses have been assessed as safe and regulated as unstandardised foods since 1993 in Australia (National Food Authority) and 1995 in New Zealand (Ministry of Health). 'Unstandardised foods' can be added to any food that does not have specific compositional requirements. From Standard 1.1.2, inulin-type fructans, fructo-oligosaccharides and substances normally consumed as foods are taken not to be nutritive substances.

International status

15. FSANZ states in the CFS that 2′-FL as individual ingredients are permitted in similar products without prohibition of the combination, or with the combination expressly permitted, in some countries overseas. Harmonisation with international standards, that are based on relevant science and scientific expert opinion, is essential to allow the manufacture and availability of these types of products for consumers in Australia and New Zealand and for export.

Risk and Safety Assessment

16. As noted, inulin and oligofructose have been assessed as safe and regulated as unstandardised foods since the mid 1990s. As also noted, there are already permissions to add 2′-FL to infant formula products in the Food Standards Code. The source and specifications of the Chr. Hansen 2′-FL derived from *Escherichia coli* (*E. coli*) BL-21 (Application A1190) to be added to infant formula products to a maximum level of 2.4 g/L appears in the Food Standards Code.

17. FSANZ's ***toxicology assessment*** noted there were no safety concerns associated with
    - the addition of 2′-FL to infant formula products at concentrations up to 2.4 g/L (it is within the range of naturally occurring levels in human milk from the majority of women (0.6 – 7.8 g/L))
    - the addition of a total level of 8 g/L of ITF and/or GOS, alone or in combination at any ratio, to infant formula products

- the addition of various combinations of 2′-FL and ITF and/or GOS.

18. FSANZ's ***microbiological assessment*** noted that a literature review covering the period 2008–2021 confirmed that there were no microbiological safety concerns from the addition of GOS and/or ITF to infant formula products. FSANZ assessments of applications for 2'-FL identified no microbiological safety concerns from its addition to infant formula products. Clinical studies to date of various combinations of 2′-FL with GOS and/or ITF have not indicated any microbiological safety concerns.

19. FSANZ's ***nutritional assessment*** concluded the addition of 2′-FL to infant formula was not expected to affect the growth profiles of infants and there was no evidence to indicate a nutritional concern at concentrations that were typically observed in human milk. Similarly, the addition of GOS and/or ITF alone or combined, at any ratio in infant formula products was unlikely to pose a risk to young infants. One multi-centre (Belgium, Hungary, Poland, Spain and Ukraine) study involving almost 200 infants has indicated that equivalence in daily weight gain from baseline to 17 weeks in infants receiving test and control formula was achieved. From all these, FSANZ has concluded that, based on the available evidence, no difference in growth is likely to occur in infants fed formula that contains 2′-FL and GOS and/or ITF at previously permitted levels.

20. FSANZ's **dietary intake assessment** concluded that, based on the maximum permitted concentration levels in the Food Standards Code, the estimated mean and P90 intakes of 2′-FL combined with GOS and/or ITF from infant formula and follow-on formula range between 5 and 17 g/day and that these intakes are less than the estimated mean and P90 intakes of human milk oligosaccharides from human milk.

21. FSANZ's **health effects assessment** considered anti-pathogenic and bifidogenic effects and concluded that there was no evidence that implied any antagonistic effects between the individual components. FSANZ did note that the evidence was insufficient to draw conclusions on how the magnitude of the effects due to the combination of 2′-FL and GOS and/or ITF compares to the effects of the individual components.

22. FSANZ concluded from its overall ***risk and technical assessment*** that consumption of infant formula containing a combination of 2′-FL GOS and/or ITF was safe and well tolerated.

Risk Management

23. On **labelling**, in light of existing permissions and labelling requirements whereby ingredients must be declared and nutrition information provided and certain representations are prohibited, no additional labelling requirements were proposed, a position INC agrees with.

24. Nonetheless, INC continues of the view that the prohibition on the use of the term, 'human identical milk oligosaccharides' or HiMO, is counter to building consumer confidence in, and understanding of, labelling information. The prohibition ignores the existing protections in the Food Standards Code and other legislation in New Zealand and Australia such as the *Fair Trading Act 1987* and the Australian Consumer Laws in the *Competition and Consumer Act 2010* concerning truthfulness of the description of ingredients by manufacturers. INC notes these terms and abbreviations are permitted to be used on labels under other internationally recognised standards.

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

25. We note FSANZ is committed to reviewing any new evidence on the beneficial role of 2′-FL (alone, or in combination with LNnT) in the normal growth and development of infants. INC is actively supporting this review and the gathering and analysis of relevant

evidence. This Application, as with other pertinent applications, adds to this body of knowledge.

Investment in innovation

26. Alignment of regulations to permit ingredients that are safe and permitted internationally encourages consideration of future investments in innovation in Australia and New Zealand. Both countries gain consideration of future investments in innovation if regulations continue to align. Without such investment we stand to lose the public health benefits of such innovation and consign our infants to less than optimal foods in the future.

Trade impacts

27. In 15 months (after the exclusivity period), Australia and New Zealand will be aligned with other jurisdictions where these ingredients are approved both individually and in combination.

Food industry impacts

28. INC has no comments to make on the exclusivity of this particular Application. We are, however, seeking clarity and consideration around the current and future scope of the application of exclusivity in the broader food supply.

29. In June 2022, FSANZ published a statement *Exclusivity of use for novel foods and nutritive substances* which states that:

    "Applicants requesting approval of a novel food or nutritive substance may also apply for a period of 'exclusive' use to apply to a brand or class of food for up to 15 months."

30. INC notes that exclusivity of use for novel foods has been in place since 2007 and was, at that time, subject to a specific proposal and consultation in *Proposal P305: Permission for exclusivity of use of novel foods*. This arose from requests from the Food Regulation Standing Committee ("**FRSC"**) and the Australia and New Zealand Food Regulation Ministerial Council (now the Food Ministers Meeting). FSANZ was requested to consider the capacity for including a specific provision for exclusivity of use for novel foods in Standard 1.5.1 – Novel Foods of the Food Standards Code. FSANZ was also requested to consider that an exclusive permission, if granted, should be limited to a period of 15 months, after which any exclusive approvals would revert to generic approvals within the Novel Foods Standard. A note is now included in Standard 1.5.1 Novel Foods that states:

    "Novel foods are added to the table to section S25—2 by variations to the Code. When added for the first time, the conditions may include some that apply to the novel food only during the first 15 months after gazettal of the variation."

31. This provides clarity for users of the Food Standards Code about the implementation of the capacity for exclusive permissions for novel food products and prospective 15-month time limits on exclusive permissions.

32. We are aware that Section 8 in the *FSANZ Act 1991* provides that:

    "an exclusive capturable commercial benefit is conferred upon a person who applies for the development of a food regulatory measure or the variation of a food regulatory measure under section 22".

33. To date, an exclusive capturable commercial benefit has been applied by way of proposal to novel foods and as part of category-specific application (infant formula) to nutritive substances. The current category-specific application for an exclusive period of use is for a branded food (manufactured by Nutricia Australia Pty. Ltd) that contains a previously approved nutritive substance (2′-fucosyllactose sourced from *Escherichia coli* BL21 containing the gene for alpha-1,2-fucosyltransferase from *Escherichia coli* O126) and

unstandardised foods (GOS and/or ITF). The approved 2'-FL is currently subject to a 15 month exclusivity period which concludes in 2023.

34. INC is concerned that the scope of "exclusive capturable commercial benefit" is being expanded by applications on a case-by-case basis rather than in a more transparent and regularised way so that the entire food industry is aware of, and has opportunity to comment on, various implementation pathways of the concept of exclusivity. For example, future combinations of foods (not necessarily novel foods or nutritive substances) could be subject to exclusivity through an application.

35. For example, exclusivity of use for nutritive substances was introduced in 2020 with the finalisation of Application A1155. There was no proposal to consider exclusivity for nutritive substances as there had been for novel foods. Consequently, others in the broader food industry without an interest in infant formula had no awareness of the opportunity to comment on exclusivity for nutritive substances.

36. To be clear, INC is supportive of the concept of exclusive capturable commercial benefit and fully recognises the value that this has to deliver on investment for the food industry and for innovation. We are concerned, however, at the ad hoc way in which the concept appears to be implemented and suggest a more consistent approach be applied in order to ensure visibility for the broader food industry.

Drafting – Variation to Standard

37. INC agrees with the FSANZ draft variation to the Food Standards Code to permit 2'-FL in combination with GOS and/or ITF in infant formula products and that it is appropriate.

References

Kunz C, Rudloff S, Baier W, Klein N, Strobel S. 2000 Oligosaccharides in human milk: structural, functional, and metabolic aspects". *Annual Review of Nutrition*; 20:699-722, 2000. DOI:10.1146/annurev.nutr.20.1.699

Lewis ZT, Totten SM, Smilowitz J, PopovicM, Parker E, Lemay DG, van Tassell ML, Miller MJ, Jin Y-S, German JB, Lebrilla CB, Mills DA. (2015) Maternal fucosyltransferase 2 status affects the gut bifidobacterial communities of breastfed infants. *Microbiome* 3, 13 (2015). https://doi.org/10.1186/s40168-015-0071-z

Morrow AL, Ruiz-Palacios GM, Altaye M, Jiang X Guerrero-ML, Meinzen-Derr J, Farkas T,-Chaturvedi P, Pickering LK, Newburg DS (2004) Human milk oligosaccharides are associated with protection against diarrhea in breast-fed infants. *The Journal of Pediatrics,* 145(3):297-303. DOI:10.1016/j.jpeds.2004.04.054

Sprenger N, Binia A, Austin S. (2019) *Human milk oligosaccharides: Factors affecting their composition and their physiological significance*. Nestlé Nutrition Institute, 2019. https://www.nestlenutrition-institute.org/resources/publication-series/publications/article/details/nniw90-human-milk-composition-clinical-benefits-and-future-opportunities/human-milk-oligosaccharides-factors-affecting-their-composition-and-their-physiological-significance

Siziba LP, Mank M, Stahl B, Gonsalves J, Blijenberg B, Rothenbacher D, Genueit J (2021) Human milk oligosaccharide profiles over 12 months of lactation: the m SPATZ Health Study. *Nutrients*, 13(6), 1973. https://doi.org/10.3390/nu13061973

Thurl S, Munzert M, Boehm G, Mathews C, Stahl B (2017) Systematic review of concentrations of oligosaccharides in human milk. *Nutrition Review;* 75(11):920-933. DOI: 10.1093/nutrit/nux044.

Zuurveld M, van Witzenburg NP, Garssen J, Folkerts G, Stahl B, Van't Land B, Willemsen LEM. Immunomodulation in human milk oligosaccharides: the potential role in prevention of allergic diseases. *Frontier Immunology*; 2020 11:801. DOI: 10.3389/fimmu.2020.00801.