2nd Call for submissions – Application A1155 2'-FL and LNnT in infant formula and other products

Submission by SA Health (Department for Health & Wellbeing)

2 September 2019

SA Health welcomes the opportunity to respond to this second call for submissions on the Application A1155 2'-FL and LNnT in infant formula and other products. SA Health has considered the draft variation and the amendments made since the 1st Call For Submissions (CFS).

Our comments to the 2nd CFS are as follows:

- The proposed voluntary addition of 2'-FL and LNnT to infant formula is not consistent with the Ministerial Policy Guideline: Regulation of Infant Formula Products, which requires '…*that there be a substantiated beneficial role in the normal growth and development of infants or children…..'* [1]. Further, the Global Standard for Infant Formula Composition recommends that for all formula intended for infants,…. '*nutrients and substances should be added to formulae only in amounts that serve a nutritional or other benefit.*'…. . This is especially relevant when used as a sole source of nutrition, such as in the first months of an infants life[2].

- SA Health believes FSANZ has not provided sufficient substantiated evidence to link the physiological, biochemical and/or functional effects of 2'-FL and LNnT to specific health outcomes nor benefits to meet the Ministerial Policy Guideline: Regulation of Infant Formula Products.

- It is questioned what FSANZ guidelines were used by FSANZ when considering the quality and sufficiency of evidence for benefit? The European Food Safety Authority (EFSA) uses a guidance document on the use of the weight of evidence approach in scientific assessments for use in all areas under EFSA's remit. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4971 Similarly, the Therapeutic Drugs Administration uses evidence guidelines for evaluation of complimentary medicines. https://www.tga.gov.au/publication/evidence-guidelines

[1] Australia and New Zealand Food Regulation Ministerial Council: Food Regulation Standing Committee (2011), 'Regulation of Infant Formula Products'. Accessed: https://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-Infant-Formula-Products Date Accessed: 26/08/2019

[2] Koletzko, B et al.(2005) Global Standard for the Composition of Infant Formula: Recommendations of an ESPGHAN Coordinated International Expert Group', Journal of Paediatric Gastroenterology and Nutrition. 41 (5): 584-599.

- Given the absence of clarity on how FSANZ has assessed the weight of evidence for this application, SA Health does not agree that appropriate evidence of sufficient quantity or quality has been provided by the applicant. SA Health supports the **formation of an Independent Scientific Expert Group** as stated in the Ministerial Policy Guideline for Infant Formula Products to assess the evidence of a substantiated beneficial role of 2'-FL and LNnT.[1]

- SA Health suggests that FSANZ do not approve the voluntary addition of 2'FL and LNnT to infant formula on the basis that **insufficient substantiation of evidence exists to support the claimed health benefit to infants.**

- **SA Health does not support the addition to FSFYC** as it is not consistent with the Ministerial Policy Guideline on the Intent of Part 2.9 – Special Purpose Foods regarding the 'intended purpose' of this food category.

- SA Health welcomes and **supports FSANZ's proposed amended regulatory measure to "prohibit terms such as 'human milk identical oligosaccharide' or 'HiMO'** (or similar words or abbreviations) on infant formula products and FSFYC" .

At the 1st CFS SA Health's position was:

- SA Health does not support development of a food regulatory measure to permit voluntary addition of 2'-FL and LNnT to infant formula and formulated supplementary food for young children (FSFYC) on the basis that the evidence provided does not constitute 'appropriate evidence' for the proposed health benefits of a bifidogenic or anti-infective effect of 2'-FL and LNnT.

- SA Health does not agree with the increased levels proposed by FSANZ of a maximum of 2.4 g/L for 2'-FL and LNnT. While these higher levels of 2'-FL and LNnT may be present in breast milk this application is regarding the addition of microbially produced 2'-FL and LNnT to infant formula, and these levels are not the levels used in the clinical trial presented by the applicant. Given there is no history of use of 2'-FL and LNnT in Australia and New Zealand in infant formula, safe levels should be based on this use not on the levels found in breast milk which is a more complex biofluid.

- SA Health strongly supports FSANZ's proposal not to permit the use of 'human milk-identical' or similar terms on infant formula or FSFYC labels. SA Health would additionally like to see the restriction of associated acronyms such as human milk oligosaccharide (HMO), HMO or HM-O on labels of infant formula or FSFYC. It has been noted that these terms are used overseas on infant formula and FSFYC labelling, these terms directly or indirectly infer that the use of 2'-FL or LNnT make the formula equivalent to breast milk, which is potentially misleading to the public.

FSANZ's response in the second Call for Submissions has not adequately responded to SA concerns.

Rationale

Addition of 2'-FL and LNnT to infant formula

The safety of 2'-FL and LNnT at 2.4g/L has not been demonstrated in the target population. FSANZ assert that the proposed addition of 2'-FL alone or combined with LNnT is supported by appropriate evidence regarding safe levels of consumption. However, levels should not

be determined through studies based around breast milk and breast fed infants, which is a more complex biofluid. The amount and composition of HiMOs varies over the course of lactation, therefore, in the absence of additional trials, it is unknown if the maximum levels proposed are comparable to the range present in mature human milk, at any one time nor across tan infant's feeding lifespan.[3] Other studies are based around lower intake levels and few address safety as an outcome.[4] [5]
FSANZ has not demonstrated the safety of this maximum permissible amount in the target population as provided in infant formula. Given the availability of products containing 2'-Fl and LNnT overseas, there is opportunity to demonstrate the safety of these products, through future high quality research.

Benefit to Infants

The Applicant proposed three health effects of 2'-FL and LNnT, a bifidogenic effect, a health benefit on immune modulation, intestinal barrier function and allergic response and an anti-infective effect.

- **Bifidogenic effect** – There is insufficient evidence of positive or negative effects on formula fed infants. FSANZ has reiterated that the available evidence supports the plausibility of the products having a bifidogenic effect. Whilst Steenhout et al (2016) suggest infants fed formula containing 2'-FL and LNnT had the composition and function of stool microbiota and metabolic signature closer to that of breastfed infants, the researchers also state that further studies are warranted to evaluate if a shift in gut ecology towards the breastfed standard produces any health benefit.[4] Adequate research to demonstrate short term beneficial health outcomes to infants being fed formula containing 2'-FL and LNnT are warranted.

- **Health benefit on immune modulation, intestinal barrier function and allergic response**. FSANZ's assessment is that these health effects are not supported by the evidence presented. SA Health agree with this response. To date, no studies demonstrate health benefit to infants fed these isolated oligosaccharides in the few high quality trials that are available.[3]

- **Anti-infective effect.** SA Health determines the evidence of a direct anti-infective effect of the combination of 2'-FL & LNnT added to infant formula is weak. Evidence was summarised from breastmilk studies and in vitro studies for the substances. The one study using infant feeding trials, was suggestive that there was no anti-infective benefit and we are agreeable that this provides only limited evidence.[5] This suggests further research to babies fed infant formula is desirable.

[3] Plaza-Díaz J, Fontana L, & Gil A (2018). Human Milk Oligosaccharides and Immune System Development. Nutrients, 10(8), 1038.
[4] Steenhout P, Sperisen P, Martin F-P, Sprenger N, Wernimont S, Pecquet S, Berger B (2016). Term infant formula supplemented with human milk oligosaccharides (2'fucoyllactose and lacto-n-neotetraose) shifts stool microbiota and metabolic signatures closer to that of breastfed infants. FASEB J 30:275.
[5] Puccio G, Alliet P, Cajozzo C, Janssens E, Corsello G, Sprenger N, Wernimont S, Egli D, Gosoniu L, Steenhout P (2017) Effects of Infant Formula with Human Milk Oligosaccharides on growth and morbidity: A randomised Multicenter trial. Journal Pediatric Gastroenterology Nutrition 64:624-631.

Addition to Formulated supplementary foods for young children (FSFYC)

The proposed addition of 2'-FL and LNnT to FSFYC is not consistent with the Ministerial Policy Guideline on the intent of Part 2.9 of the Food Standards Code – Special Purpose Foods. FSFYC is a supplement to a normal diet for children aged 1 - <4 to address situations where intakes of energy and nutrients may not be adequate to meet an individual's requirements. SA Health believes there is not sufficient evidence to demonstrate that the addition of 2'-FL and LNnT is '*essential for normal growth and development of infants'*. In FSANZ response in Table 1: Summary of Issues of the 2nd CFS, FSANZ continues to acknowledge that the *proposed addition to FSFYC may not strongly align with the policy guideline regarding the 'intended purpose' of this food category.* SA Health does not support FSANZ's argument that because *the addition is safe and **may** provide beneficial health outcomes for toddlers* it warrants the addition as proposed.

Labelling of FSFYC

Advertising of FSFYC does not fall under the strict guidelines that exist for infant formula under the Marketing in Australia of Infant Formula: Manufacturers' and Importers' Agreement (MAIF) Although SA Health is in support of FSANZ's proposal to prohibit terms such as 'human milk identical oligosaccharide' or 'HiMO' (or similar words or abbreviations) on infant formula products and FSFYC" there remains concern that industry may be able to market the FSFYC products more freely and as there is evidence of consumer confusion as to the distinction between infant formula and toddler milk advertising, it could be misleading for the public and result in cross-marketing to infant formula[6].

Conclusion

SA Health is concerned that our concerns raised in the first submission regarding benefit to, and lack of evidence to confirm that no harm will be done to, infants at the proposed quantity have not been adequately addressed by the FSANZ response. If FSANZ is able to demonstrate a substantiated health benefit, and safety to infants fed with formula, at proposed levels, the Department could support the voluntary addition of 2'-FL and LNnT to infant and toddler formula.

[6] Berry, N., S. Jones, and D. Iverson, Toddler milk advertising in Australia: the infant formula ads we have when we don't have infant formula ads., in ANZMAC Annual Conference 2010: Australian and New Zealand Marketing Academy Conference 2010. 2010, P. Ballantine & J. Finsterwalder (Eds.): Christchurch, New Zealand.