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Tēnā koe,

Application A1251 – 2'-FL combined with galacto-oligosaccharides and/or inulin-type fructans in infant formula products

New Zealand Food Safety (NZFS) welcomes the opportunity to comment on the Call for Submissions (CFS) for Application A1251 – 2'-FL combined with galacto-oligosaccharides and/or inulin-type fructans in infant formula products.

NZFS acknowledges that breastfeeding is the recommended way to feed infants. For infants who are not breastfed, a safe and nutritious substitute for breast milk is needed. Infant formula products are the only safe and suitable alternative to breast milk.

This Application seeks to amend the Australia New Zealand Food Standards Code (the Code) to permit 2'-fucosyllactose (2'-FL) to be added to infant formula products (IFP) in combination with galacto-oligosaccharides (GOS) and/or inulin-type fructans (ITF). The Code currently permits 2′-FL, GOS and ITF to be added alone to IFP, or GOS and ITF combined, but expressly prohibits the addition of 2-FL combined with GOS and/or ITF. It is proposed the current maximum permitted use levels for 2'-FL at up to 2.4 g/L and GOS alone or combined with ITF up to 8 g/L (up to a maximum of 3 g/L ITF) are retained.

NZFS has the following comments on the risk assessment, maximum permitted use levels, labelling requirements and the Applicant's request for an exclusive period of use.

Risk assessment

We note the safety, technological, nutritional impact and beneficial health effects from individual addition of 2'-FL, GOS and ITF to infant formula products has previously been considered under applications A1155, A1190, A1233 and A1055, and proposal P306. The A1251 risk assessment focuses on evidence for use of these ingredients in combination – with a new clinical study (Vandenplas et al., 2020) forming the basis for this assessment.

Toxicology assessment

We have no major concerns with the toxicology assessment. The Vandenplas study shows that the combination is well tolerated, although at a lower concentration. There is some data, although limited, on the additive or synergistic effects. There was no identifiable hazard in toxicological and clinical studies with 2′-FL, GOS and/or ITF, alone or in combination, and the estimated exposures are lower than those of HMOs from human milk.

However, we note in relation to the Vandenplas study that:

- The study focused on tolerance of the product, with some safety criteria included, but not all such as biochemical parameters (urine, blood).
- Water to constitute the infant formula was not tested for contaminations (micro-and environmental contamination). These could be the cause of some of the adverse events, but also could explain regional differences.
- Long-term studies are needed to assess the impact on the infants' developing immune and gastrointestinal systems.

Nutrition assessment

NZFS notes the nutrition assessment conclusion that, based on available evidence, no difference in growth is likely to occur in infants fed IFP that contain 2'-FL, GOS and/or ITF at previously permitted levels.

The CFS report provides a detailed summary of Vandenplas study. However, we consider the findings of the Vandenplas study are not fully discussed in the context of the findings from other literature, which are directly comparable to the current application. We note previous applications have provided more detailed discussions of the studies by Marriage et al. (2015) and Kajzer et al. (2016), which included combinations of two of the relevant oligosaccharides, and request that the forthcoming approval report discusses these studies and their findings alongside the discussion of the Vandenplas study. Since there are so few relevant studies available, evidence from the study by Kajzer et al. (2016) may be useful to discuss, despite the limitation of its short intervention duration.

We also request the forthcoming approval report considers the limitations of the Vandenplas study and the extent to which this may affect the conclusion of the nutrition risk assessment. The Vandenplas study uses an intervention formula that is different from the application formula. Therefore, it is possible that the additional ingredients (e.g. 3'-GL, altered fatty acid profile) exerted an effect on the outcomes, independent of the effect of the 2'FL combined with the scGOS/lcFOS mixture. The possible impact of this limitation should be discussed in more detail to support the conclusions drawn from this key piece of research.

Maximum permitted use levels

It is proposed that the current maximum permitted use levels for 2'-FL, GOS and/or ITF in Standard 2.9.1—7 and Schedule 29 would apply – namely, 2'-FL at up to 2.4 g/L and GOS alone or in combination with ITF up to 8 g/L (up to a maximum of 3 g/L ITF).

Notably, none of the studies mentioned in the risk assessment contained this maximum concentration of 2'-FL – the maximum studied was 1 g/L, less than half the proposed maximum permitted use level. While no safety concerns were identified, there is currently no definitive evidence to confirm the safety of 2'-FL at 2.4 g/L combined with GOS and/or ITF up to 8 g/L. NZFS considers it is important to identify and discuss this limitation in the forthcoming approval report.

We also note that maximum permitted levels for 2'-FL in combination with GOS and/or ITF in the EU and Brazilian regulations are 1.2 g/L and 1 g/L respectively. Again, these levels are significantly lower than the proposed maximum use level of 2.4 g/L for 2'-FL in the Code.

In addition, the dietary intake assessment estimated that mean and P90 intakes of 2'-FL combined with GOS and/or ITF from IFP range between 5 and 17 g/day, and concluded that these intakes are less than intakes of HMOs from human milk. Data suggests that intakes of HMOs from human milk range from 7.3 – 21.7 g/day – so estimated intake of 2'-FL, GOS and/or ITF from IFP is already close to the higher level of intake of HMOs from human milk. Given there are hundreds of HMOs in human milk and evidence may support further innovation in this area, might retaining the maximum use levels when substances are used in combination limit regulatory options in the future?

NZFS requests that FSANZ considers whether the current maximum permitted use levels should be lowered when these substances are used in combination given the matters outlined above.

Labelling requirements

NZFS agrees the existing labelling requirements for ingredient declarations, nutrition information and GM food should apply to infant formula products containing added 2'-FL combined with GOS and/or ITF.

We also agree that existing prohibited representations in Standard 2.9.1—24 of the Code should apply to these products, including the prohibition for the use of the words 'human milk oligosaccharide', 'human milk identical oligosaccharide', and abbreviations 'HMO', 'HiMO', or any word or words or abbreviations having the same or similar effect.

Exclusivity

We note the Applicant's request for a 15-month exclusive period of use for the addition of 2'-FL in combination with GOS and/or ITF in infant formula products and have the following comments.

Exclusivity of use is clearly provided for in the Code for novel foods.

In 2020, exclusivity of use was given to GlyCare for specific microbial sources of 2'-FL and LNnT under application A1155. Similar exclusive use periods have subsequently been granted for applications to FSANZ asking for 2'-FL permissions. We acknowledge that this has created a precedent allowing exclusive use periods to be granted for nutritive substances.

However, we consider approval of the current A1251 request for exclusivity differs from the A1155 precedence in several ways.

Firstly, the requested combination of substances includes GOS and ITF which are *not* considered nutritive substances in the Code. Granting exclusivity relating to non-nutritive substances would appear to be an extension of the A1155 precedence. We are concerned this may create a further precedent that all food businesses no matter the ingredient/substance may apply for exclusive use.

Exclusivity of use is intended to provide an incentive to industry for innovation. It also provides a benefit to an applicant that has expended significant resources into the development of the product. In this instance, 2'-FL, GOS and ITF are not 'new' substances. They are well researched and have previously been assessed as safe for use in IFP. We understand the A1251 applicant is simply requesting to use these substances in combination.

We also consider granting exclusivity of use for A1251 may have unintended implications for standards across the Code, specifically if exclusivity of use is extended beyond novel foods and

nutritive substances, and is applied to combinations of substances rather than a specific substance.

During the period of exclusivity, competitors will be limited to selling products that do not contain the same combination as A1251. Exclusivity of use should thus be used with caution as it temporarily creates a monopoly permission. It is desirable to have a competitive food industry and to avoid unnecessary restrictions on trade.

Recommendations

We encourage FSANZ to fully consider the implications of approving the exclusive period of use requested by the Applicant for 2'-FL combined with GOS and/or ITF.

Furthermore, NZFS considers the precedent (initially set by A1155) requires further discussion at the Food Regulation Standing Committee. Unlike novel foods, there is no clear mechanism in the Code to implement exclusive use periods for nutritive substances.

Thank you for the opportunity to comment on this application and we welcome further discussion on the issues raised.

Nāku noa, nā

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