Project Officer Application A1253
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Tēnā koe,

Application A1253 – Bovine lactoferrin in infant formula products

New Zealand Food Safety (NZFS) welcomes the opportunity to comment on the Call for Submissions (CFS) for Application A1253 – Bovine lactoferrin in infant formula products.

This Application seeks to amend the Australia New Zealand Food Standards Code (the Code) to permit the voluntary addition of bovine lactoferrin as a nutritive substance to infant formula products (IFP) up to a maximum permitted amount of 40 mg/100 kJ. Synlait Milk Limited has also requested an exclusive use permission for their brand of bovine lactoferrin for a period of 15 months after gazettal.

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.

NZFS provides its preliminary support to permit the voluntary addition of bovine lactoferrin as a nutritive substance to IFP up to a maximum of 40 mg/100 kJ – and has the following comments on the assessment and proposed approach detailed in the CFS:

Regulatory status of bovine lactoferrin

NZFS agrees that the Applicant's intended use of bovine lactoferrin in IFP is as a nutritive substance, and therefore a pre-market assessment and express permission in the Code is required for its use.

While lactoferrin is naturally occurring at low levels in cow's milk, the Applicant intends to add higher levels of bovine lactoferrin that has been concentrated and refined to IFP for the purpose of providing a nutritive benefit to the formula-fed infant. NZFS agrees that it is appropriate to assess bovine lactoferrin as a nutritive substance under the Code.

NZFS notes the proposed draft variation at Attachment A of the CFS. We agree with the proposed approach to limit the permitted form of lactoferrin to bovine lactoferrin only, rather than all sources of lactoferrin. We also support containing the permission for use of lactoferrin as a nutritive substance to IFP only, and not to other foods, as this is consistent with the pre-market safety assessment to date for bovine lactoferrin in foods.

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Risk assessment

Nutrition assessment

FSANZ conducted a literature search to determine whether the addition of bovine lactoferrin (up to 40 mg/100kJ) to IFP has any effect on infant growth and development, compared with human milk or compared with IFP that has no added bovine lactoferrin. Inclusion criteria were based on the requirements in section 3.6.2 A.3.1 (b) of the FSANZ Application Handbook, in addition to the iron content specified for infant formula products in the Code and the applicant's specifications for bovine lactoferrin. NZFS notes that no studies met the pre-specified inclusion criteria – though the findings of selected studies were used to inform FSANZ's conclusion that: *"Despite limitations in the available studies … the consumption of infant formula with added bLf, at up to 1 g/L (equivalent to 40 mg/100 kJ), is unlikely to adversely affect infant growth and development."*

We acknowledge that the inclusion criteria is quite restrictive and note that the Code requires IFP to contain higher amounts of iron than required in many other countries. It would be beneficial for FSANZ to provide a more detailed discussion on the reasons the selected studies (Table 8 of SD1) did not meet the pre-specified inclusion criteria and the likely impact of these limitations on its assessment of whether bovine lactoferrin affects infant growth and development.

Beneficial health effects assessment

NZFS supports FSANZ's conclusion that *in vitro* studies provide evidence for the bacteriostatic, bactericidal and antiviral effects, providing mechanistic evidence for bovine lactoferrin having a role in the reduction in risk of bacterial and viral infection.

FSANZ identified that the evidence from human studies of the ability of bovine lactoferrin to reduce infection in healthy, full-term infants is limited and of low quality, but they do demonstrate a tendency for bovine lactoferrin-supplemented formula to reduce reported gastrointestinal and respiratory illnesses compared to a control formula. The CFS concludes that the findings of the human studies provide "weak but consistent support for the proposed beneficial effect". NZFS's assessment of the evidence agrees that the findings from human studies is limited and not strong, but we consider that 'consistent' may not be a suitable descriptor.

Minimum permitted amount for addition

NZFS notes that no minimum permitted amount of bovine lactoferrin is proposed under A1253 as this was not requested by the applicant and not considered appropriate by FSANZ. Although we note that this is consistent with the permissions in China, the EU and Singapore, the rationale provided by FSANZ stated that 'FSANZ considers that ingredients which are intended to modulate gut microflora may result in variable outcomes in individuals…'. NZFS questions the relevance of this rationale given that evidence to support a potential role for lactoferrin in modulating gut microflora has not formed part of the assessment for A1253. If FSANZ intends to use this rationale, then NZFS considers evidence to support the statement that bovine lactoferrin modulates the gut microflora should be provided.

Specification for bovine lactoferrin

The draft variation at Attachment A includes a specification for bovine lactoferrin to be inserted as S3—46 in the Code. We understand the proposed specification is based on Synlait's manufacturing specification and batch analysis results for its own lactoferrin ingredient product.

NZFS notes the proposed specification appears very detailed compared to other Schedule 3 specifications and is not aligned with overseas specifications for lactoferrin preparations. We suggest that FSANZ reconsiders the level of detail included in the proposed specification for bovine lactoferrin – and to only include criteria that is required for identity and safety purposes, and to consider closer alignment with overseas specifications.

We also note that the maximum for iron in the proposed specification is low compared to overseas specifications – for example, the EU (Regulation EU 2017/2470) and China (GB 1903.17-2016) specifications for bovine lactoferrin state < 350 mg/kg and ≤ 35 mg/100g respectively. We understand the reason for some lactoferrin preparations containing higher levels of iron relates to the manufacturing process, where the lactoferrin may be extracted before or after heat treatment is applied to the raw milk. We question whether the lower iron level proposed by Synlait unnecessarily restricts the choice of manufacturing processes and is not consistent with specifications used internationally. As IFP is a globally traded product and the proposed permission is not for a proprietary product, a review of the iron maximum specification appears appropriate particularly considering the FSANZ Act section 18(2) objectives relating to the promotion of consistency between domestic and international food standards, and the desirability of an efficient and internationally competitive food industry.

In addition, we note a potential error in the draft variation for the specification for bovine lactoferrin to be included in S3—46. The draft specification states: *iron—not more than 15g/100g*, whereas we believe the appropriate unit of measurement in this case is mg/100g.

Labelling requirements

NZFS agrees that the existing generic and specific labelling requirements for IFP as set out by the Code should apply to IFP with added bovine lactoferrin.

These include the requirement for mandatory allergen declarations in accordance with Division 3 of Standard 1.2.3. NZFS considers this an important requirement for IFP with added lactoferrin as bovine lactoferrin is derived from cow's milk and the evidence is insufficient to conclude that bovine lactoferrin does not pose a food allergy risk to consumers with cow's milk allergy.

Exclusivity

NZFS notes the proposed approach to grant Synlait's request for an exclusive use permission for its brand of bovine lactoferrin for a period of 15 months from gazettal. During the proposed period of exclusivity, competitors will be limited to selling IFP that do not contain lactoferrin. Exclusivity of use encourages an innovative food industry, however, should be used with caution as it temporarily creates a monopoly permission.

Unlike for novel foods there is no clear mechanism in the Code to implement exclusive use periods for nutritive substances, nor does the Application Handbook (or elsewhere) provide clear criteria for when exclusivity of use might be granted for a substance. NZFS would welcome clarification from FSANZ in this area – for the benefit of all stakeholders – to clarify the basis for exclusivity provisions in general, the criteria and level of investment required to be met by an applicant, and the associated information required to support such a request.

In relation to A1253, we acknowledge the precedent set under Application A1155 (and subsequent 2'FL applications) to allow exclusivity of use to be granted for nutritive substances in IFP. However, we encourage FSANZ to fully consider the validity and implications of approving exclusivity of use for lactoferrin in IFP, particularly as lactoferrin is not a 'new' substance and the technology to

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incorporate lactoferrin in IFP appears well developed as evidenced by its addition to IFP for sale in overseas markets since 1986.

Summary

Overall, NZFS provides its preliminary support to permit the voluntary addition of bovine lactoferrin as a nutritive substance to IFP up to a maximum of 40 mg/100 kJ.

NZFS notes that lactoferrin is present in human breast milk, that there are no public health and safety concerns with addition of lactoferrin up to a maximum of 40 mg/100 kJ, and that evidence from *in vitro* and human studies generally supports a potential health effect of reduced risk of infection for formula-fed infants. We also note that bovine lactoferrin is permitted for use in many overseas regulations and that lactoferrin-containing IFP has been marketed overseas since 1986.

However, as detailed, NZFS requests that FSANZ clarifies aspects of the risk assessment and the rationale for not specifying a minimum permitted amount. We also encourage FSANZ to reconsider the proposed specification for bovine lactoferrin and the implications of approving exclusivity of use for lactoferrin in IFP.

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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