Queensland Government

Queensland Health

Enquiries to: Food Safety Standards and Regulation
Health Protection Branch
Department of Health
Telephone: (07) 3328 9310
Facsimile: (07) 3328 9354
File Ref: QCHO/011194

02 September 2019

Standards Management Officer
Food Standards Australia New Zealand
PO Box 5423
Kingston ACT 2604

Dear Sir / Madam

Submission – Application A1155 - 2′-FL and LNnT in infant formula and other products: 2nd Call for submissions (2nd CFS)

Thank you for the opportunity to provide a submission on the 2nd Call for Submissions paper for Proposal A1155.

This submission provides comment on the proposed changes to the *Australia New Zealand Food Standards Code* (the Code). The submission does not represent a Queensland Government position, which will be a matter for the Queensland Government should notification be made by the FSANZ Board to the Australia and New Zealand Ministerial Forum on Food Regulation.

Application A1155 has been prepared to consider permission to voluntarily add 2′-FL (2-O-fucosyllactose) and LNnT (lacto-N-neotetraose) in infant formula and formulated supplementary food for young children (FSFYC) as a nutritive substance and a food produced using gene technology.

Summary

Queensland does not support the Application to permit the voluntary addition 2′-FL and LNnT in infant formula and FSFYC, as the Applicant has not provided sufficient evidence to support a beneficial health outcome for the purposes of compliance with the *Ministerial Policy Guideline for infant formula products* (Policy Guideline.) Additionally, Queensland considers the evidence provided by the Applicant to support their beneficial health outcome claims is insufficient to substantiate general level health-, and nutrient content-claims permissible for FSFYC under Standard 1.2.7 of the Code. This is irrespective of the permissions pertaining to *health claims* or *compositional permissions*.

Please find below additional information and evidence below in relation to this summary.

Queensland requests FSANZ respond to the issues and concerns raised in this submission, after which Queensland may reconsider its position with respect to permission for the voluntary addition 2′-FL and LNnT in infant formula and FSFYC.

In response to the 1st call for submission regarding A1155:

Queensland expressed concerns regarding the insufficiency of evidence provided by the Applicant to support (a) immune modulation, intestinal barrier function and moderation of allergic response, (b) bifidogenic effect and (c) anti-campylobacteriosis claims as *physiological, biochemical or functional effects* related to addition of 2′-FL and LNnT to infant formula and other foods. This was particularly the case with respect to compliance with the Policy Guideline's requirements for clearly substantiated evidence of specific health outcomes for use in infant-, and follow-on formulas. The anti-campylobacteriosis health claim appears to constitute a high-level health claim of prevention of (an infectious) disease, which is not permitted under Code 1.2.7-8(a).

Queensland also sought clarification from FSANZ regarding its policy with respect to a bifidogenic effect *per se* as a *substantiated beneficial health effect*, including whether prebiotics whose physiological impact is indirect, and which are specifically not directly absorbed or metabolized by humans can be considered nutritive substances for the purposes of section 1.2.7 and Schedule 4 of the Code.

Queensland recognised FSANZ did not support listing of "gut health" in Proposal 293 as an approved substantiated beneficial health effect from probiotics and prebiotics. Queensland recognised the weight-of-evidence approach used by FSANZ, but recommended FSANZ convene an independent scientific expert group to determine the status of the bifidogenic effect (and the criteria for determination of same) as beneficial health effects for classification in the Code, and criteria for verification of the bifidogenic effect and associated health outcomes.

Queensland supported, and continues to support, FSANZ' proposed labelling prohibition on use of terms implying human breast milk equivalence such as "human milk oligosaccharide", "HMO" on infant formula and FSFYC.

Queensland supported the restriction to use of 2′-O-fucosyllactose (2′-FL) and Lacto-N-neotetraose (LNnT) on the ingredients or nutrition information panel, where these ingredients are added.

Response to 2nd call for submission regarding A1155:

<u>FSFYC</u>

FSFYC are designed to supplement children's diets that are inadequate with respect to energy and nutrients. Adding 2'-FL and LNnT to FSFYC is also not consistent with supplementing an inadequate food intake. The composition does not rely on breastmilk as a primary reference. FSFYC are not considered breastmilk substitutes in Australia and NZ (which FSANZ notes on pg. 31). FSANZ also notes (pg. 26) that the addition of 2'-FL and LNnT may not have strong alignment with the definition of FSFYC. Therefore, Queensland questions why 2'-FL and LNnT are being considered for FSFYC. Reasoning based solely on a lower "plausible" substantiation standard for "compositional permissions" is insufficient for this vulnerable group. This could create difficulties regarding provision of adequate information to enable consumers to make informed choices.

<u>Permitted levels</u>

Where voluntary addition of 2'-FL and LNnT in infant formula or FSFYC is supported, Queensland do not support the higher maximum 2'-FL level. The applicant sought permission for a maximum level equivalent to that allowed by the EU. However, FSANZ is proposing permitting a maximum

Office
Queensland Health
15 Butterfield Street
Herston QLD 4006

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PO Box 2368
Fortitude Valley QLD 4006

Phone
07 3328 9323

Fax
07 3328 9354

limit double this amount, on what seems to be primarily a trade basis, given the US allows a higher 2'-FL level. This higher level has not been tested in the target group.

Health benefit claims for compositional permission

Queensland supports FSANZ determination that the beneficial immune modulation, intestinal barrier and allergic mediation health effects are not supported by the evidence supplied by the Applicant.

FSANZ indicates the Applicant's health effects assessment of 2′-FL and LNnT indicates the *plausibility* of (a) an anti-infective effect against campylobacteriosis, and (b) bifidogenic effect (FSANZ-defined as the proliferation and increase in the relative abundance of bifidobacteria in intestinal microflora). And that the evidence provided appropriately substantiates the *plausibility* of a link between the presence of the substances at the levels proposed for addition to infant formula and/or FSFYC; physiological, biochemical and/or functional effects, and specific associated health outcomes for infants or young children. This suggests a lower "plausibility" threshold linking physiological, biochemical and/or functional effects of substances and specific health outcomes for compositional *permissions* as opposed to *health claims*.

Queensland questions whether FSANZ had adequately considered consistency with the existing Ministerial Council Policy Guidelines *Specific Policy Principle – Overarching Principles (c)* which emphasises regulation of infant formula products should take into account the vulnerability of the population for whom they are intended; and *Specific Policy Principle – Overarching Principles (j)* which indicates particular caution should be applied by the Authority where links between physiological, biochemical and/or functional effects of substances to specific health outcomes are less clear. This suggests a *clear*, rather than *plausible*, link is required for substantiation. The Policy Guidelines indicate evidence supporting a potential beneficial effect must be rigorous, given infants and young children are a vulnerable population group, and should be afforded a higher level of protection. Queensland is also concerned that FSANZ' approval of such a low level of evidence substantiating a link between the physiological, biochemical and/or functional effects of these substances and specific health outcomes via a "biological and mechanistic plausibility" standard sets a concerning precedent regarding criteria for permitting the addition of substances to infant formula in the future. The Policy Guideline refers to a 'substantiated beneficial role in the normal growth and development of infants or children' – a *plausible* benefit is not synonymous with a *substantiated* benefit.

Queensland does not believe FSANZ and the Applicant have presented appropriate evidence clearly linking addition of 2′-FL and/or LNnT to a *substantiated beneficial role in the normal growth and development of infants or children* via evidence of *physiological, biochemical and/or functional effects* in compliance with the above Policy Guidelines.

Queensland also considers it would experience practical and resource difficulties enforcing potential industry complaints regarding comparative beneficial nutrient content claims on FSFYC during the proposed exclusivity period. Such complaints would require Queensland to allocate limited resources to undertake compliance and potential enforcement actions in the absence of a definitive established Code Schedule 4 food-health relationship.

Anti-infective (campylobacteriosis) effect

The Policy Guideline specifically prohibits any health claims associated with infant formula. In addition, Code 1.2.7-8 *Claims not to be therapeutic in nature* prohibits claims in all foods that "refer to the prevention, diagnosis, cure or alleviation of a disease, disorder or condition;". Queensland considers the Applicant's anti-infective claim with respect to prevention of campylobacteriosis a high-level health claim due to a claim of a therapeutic and/or prophylactic effect against an infectious disease.

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In the absence of a *health claim*, *compositional permission* as an ingredient must still provide appropriate evidence linking the physiological, biochemical and/or functional effects of the substance *to specific health outcomes*. The evidence provided to substantiate an anti-campylobacteriosis health outcome is limited to: *in vitro* cell culture competitive binding studies; animal studies using 2'FL-only in far higher doses than proposed in the Application for compositional permission, and breastfed infants in which breastmilk comprised only 49% of overall diet, and causation of an anti-campylobacteriosis effect was assigned to relative percentages of 2'-FL-only (relative to total oligosaccharides) in the breastmilk. *In vitro* competitive binding studies do not definitively demonstrate *in vivo* anti-infective efficacy, nor do animal studies in which artificially high doses are applied. Given infants varied diets, and the large number of potentially infection-protective components of breast milk, definitively assigning the effect to 2'FL-specifically is not scientifically valid, and FSANZ' conclusion that such a beneficial role is substantiated via the plausibility of such an effect and beneficial role is not supported.

Although the Policy Guideline prohibition refers to infant formula, the nature of the anti-campylobacteriosis claim as per Code 1.2.7-8(a) should also preclude such claims in all foods, including FSFYC. Queensland therefore also recommends the general prohibition on health claims for infant formula also apply to FSFYC. Given the nature of the proposed health benefit, there is a risk a consumer may erroneously rely on products containing these substances as, in-effect, substitutes/supplements to antimicrobials, i.e. antibiotics.

If further information can be provided by the Applicant which supports a clear link substantiating the presence of the substances and an anti-campylobacteriosis health effect, Queensland may reconsider its position.

Bifidogenic effect

Although FSANZ applied a weight-of-evidence approach with respect to evaluation of the bifidogenic health claim of 2′-FL and LNnT at the levels specified by the applicant, we feel the scientific evidence presented is currently insufficient to warrant such a beneficial health claim. This is due to: (a) the low number of applicable peer-reviewed studies cited, (b) low numbers of study participants, (c) variable end-point determinants of health benefit between studies, (d) uncertainty regarding the precise definition of a bifidogenic effect. That is, is the bifidogenic effect characterised by an increase in intestinal microflora total number of *Bifidobacterium* spp., or an increase in the population-relative proportion of this genus or specific *Bifidobacterium* species, or both?

While 2'-FL and LNnT are key oligosaccharides in breastmilk, they do not work in isolation – there are approximately 200 oligosaccharides in breastmilk which work together to impact microbiota. Addition of 2'-FL and LNnT to formula in isolation may not have the same effect in formula-fed-, as in breastfed-infants. FSANZ considered an additional study provided by the Applicant. However, the study looked at obese children aged 5 to 12 years. Infant formula and FSFYC are not aimed at this age group.

In addition, although "FSANZ has previously recognized (under Proposal P306 and Application A1055) the dominance of *Bifidobacterium* in the intestinal microflora is generally considered to be beneficial to the host", the scientific evidence supporting this "general recognition" is frequently qualified in the indicated respective Proposal and Application, for similar reasons to those cited in a-d above. The only health effect found in A1055 was stool softening, and neither P306 nor A1055 conclusively determined health outcomes related *specifically* to a bifidogenic effect. Therefore, Queensland does not support the bifidogenic health claim in the current Application at this time and recommend FSANZ seek additional evidence from the Applicant to substantiate this claim.

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Queensland recognises FSANZ did not support listing of “gut health” in Proposal 293 as an approved substantiated health effect from probiotics and prebiotics. Queensland seeks clarification as to FSANZ’ current position regarding this issue. Considering the likelihood of future Proposals and/or Applications associated with health claims based on pre-, or pro-biotic effects assessed using metagenomic intestinal microbiome profiling, such review is additionally warranted.

Queensland recommends FSANZ convene the Independent Scientific Expert Group for Infant Formula Products (Expert Group) proposed in the Policy Guidelines to review the Applicant’s evident for substantiation of a bifidogenic effect. This could include broader delineation of the status of prebiotics as nutritive substances for classification in the Code. This includes general criteria related to human normal flora indicative of an impact on same, i.e. increase/decrease in total population of an organism/class of organisms, their relative proportion of the total microbial population, or both. As part of the review, the Expert Group should consider reviewing other countries assessment criteria in this regard (e.g., EU, US, Canada).

Queensland would reconsider An Expert Group finding that the Applicant’s bifidogenic effect claim is substantiated, and/or that a bifidogenic effect constitutes a specific heath outcome in terms of a beneficial role in the normal growth and development of infants and children (and potentially adults) and satisfy compliance with Policy Guidelines *Specific Policy Principle – Overarching Principles (j.)* However, such a finding should commensurately define criteria for substantiating a bifidogenic effect in terms of microbial and human physiological criteria.

Labelling

Queensland supports the 1st-CFS labelling restriction to use of 2′-O-fucosyllactose (2′-FL) and Lacto-N-neotetraose (LNnT) on the ingredients or nutrition information panel, where these ingredients are added, and prohibition of health claims and indications of human breast milk equivalency of these substances. Queensland does not support FSANZ proposed change to allow generic names, and that the proscribed names still allow consumers to identify these substances in products. Once beneficial health outcomes (substantiated beneficial role in the normal growth and development of infants and young children) associated with 2’FL and LNnT has been demonstrated, this will allow informed consumer choice through label associated identification of these substances. Therefore, Queensland prefers FSANZ’ original (1st-CFS) position restricting labelling to use of 2′-O-fucosyllactose (2′-FL) and Lacto-N-neotetraose (LNnT) on the ingredients or nutrition information panel.

Queensland believes the potential for labelling using generic names risks general assumptions of a health benefit by consumers in the absence of approval of the establishment of evidence proving such benefit. Queensland also feels that these restrictions and prohibitions *should extend to both infant formula and FSFYC/follow-on formula*, as current health claims labelling restrictions apply only to infant formula. This presents the risk of cross-promotion, particularly considering the Applicant’s proposed trade name “Glycare”. This may imply a health claim, making it difficult for consumers to make informed choices between a FSFYC in which a health claim may be made, and an infant formula under the same trade name for which health claims are prohibited.

Should you require further information in relation to this matter, please contact Food Safety Standards and Regulation, Health Protection Branch, Department of Health on (07) 3328 9310 or at foodsafety@health.qld.gov.au

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