
# Glycom Submission

## 2nd Consultation Paper for Application 1155 (A1155) − 2′-FL and LNnT in infant formula and other products

29 August, 2019

## Glycom Submission

## A1155: 2′-FL and LNnT in infant formula and other products

### Opening remarks

This submission is made on behalf of Glycom A/S, Denmark. Glycom A/S is the manufacturer of the oligosaccharide ingredients 2'-fucosyllactose (2'-FL) and lacto-*N*-neotetraose (LNnT) being the subject of application A1155.

These ingredients are highly purified and structure-identical to the same 2'-FL and LNnT molecules of human breastmilk, which are known since the 1950s by their collective term „human milk oligosaccharides" (HMOs).

Glycom A/S manufactures a range of structure-identical human milk oligosaccharides by modern biotechnology and uses the term „human-identical milk oligosaccharides (HiMOs)" to distinguish these manufactured forms from the isolated molecules from the natural source (i.e. human breastmilk). Isolation from natural sources is commercially not feasible due to human breastmilk being the only relevant natural source of HMOs.

Glycom A/S has gained regulatory approvals for its structure-identical HiMOs in a growing number of global markets (e.g. EU, US, Singapore, Malaysia, Israel) and wishes to make these innovative ingredients available to the consumers of the common market that is regulated by FSANZ (e.g. Australia and New Zealand).

Glycom A/S thanks FSANZ for the 2nd consultation paper for Application 1155 (A1155), and appreciates the opportunity to take part in continued discussion on the modulated views proposed, and to provide comment to Food Standards Australia New Zealand (FSANZ) relating to the regulation of the voluntary use of 2'-fucosyllactose (2'-FL) alone or in combination with lacto-*N*-neotetraose (LNnT).

We thank FSANZ for their consideration of the comments, issues and views raised in this submission.

## Comments on the 2nd Consultation Paper

Glycom wishes to comment on selected aspects of the 2nd Call for Submissions for Application A1155, namely by addressing selected topics in the order of the Risk management section (2.3) of the assessment (page 24 onwards of 2nd CFS).

| Section of Consultation Document | Glycom's comment |
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| **2.3.2** (page 26)<br><br>In permitting 2′-FL and LNnT as proposed above, express permission would be provided for both 2′-FL and LNnT to be used as a nutritive substance (i.e. in Schedule 29) and as food produced using gene technology (i.e. in Schedule 26) (as discussed in section 1.3.1). | Whilst we understand and support this approach, we do not see any reference to "nutritive" within the proposed entry to Schedule 26 and would request that it is included for clarity. We would also like to recommend that the conditions of use should refer to the food categories using only their food standard numbers instead of the explicit names.<br><br>For example:<br>"1. May only be added as a nutritive substance to foods specified under Standard 1.5.2."<br><br>The addition to Schedule 26 itself does set a new precedent. Because of this and its nature we ask that the first entries are clear in distinguishing products purpose and avoid the potential risk for scientifically unjustified controversy when possible. |
| **2.3.2** (page 26/27)<br><br>At 1st CFS, FSANZ had proposed linking approval of 2′-FL and LNnT to the applicant's specific GM production strains *E. coli* SCR6 and *E. coli* MP572, respectively. However, after considering industry submissions, FSANZ now proposes to link permission to the following gene-gene donor information specific to the production of the oligosaccharides.<br><br>• 2′-FL derived from *E. coli* K-12 containing the gene for alpha-1,2-fucosyltransferase from *Helicobacter pylori*<br>• LNnT derived from *E. coli* K-12 containing the gene for *beta-1,3-N-acetyl-glucosaminyltransferase* from *Neisseria meningitides* and the gene for *beta-1,4-galactosyltransferase* from *Helicobacter pylori.* | Having discussed the proposed measures further internally, Glycom's position is that the approvals should be granted for the exact production strains as have been specifically safety assessed in the application (i.e. *E. coli* K-12 DH1 MDO SCR6 for 2'-FL and *E. coli* K-12 DH1 MDO MP572 for LNnT), as also originally proposed by FSANZ in the 1st CFS.<br><br>Alternatively, not agreeing with FSANZ current proposal (of 2nd CFS), Glycom could also consider a compromise as explained below to be more consistent with the safety assessment data provided:<br><br>**Strain:** in practice, *E. coli* K-12 is a large group designation for diverse strain variants of the initial historical isolate. Glycom suggests linking the approval to the derivative of the actual host strain that was used: *E. coli* K-12 DH1, and which is indeed characterised as a safety strain. |

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| This approach is consistent with how production microorganisms are typically listed in the Code (e.g. in the case of enzyme processing aid approvals in Schedule 18). There are no public health and safety concerns associated with this approach. | **Gene and gene donor:** Glycom performed allergen and toxin homology searches on the *distinct* amino acid sequences used. Within the family of donor strains (falling under the species name) there are many functional homologs of the same genes with different amino acid sequences (carrying the same protein name). Glycom therefore suggests linking the approval to specific amino acid sequence(s).<br><br>We could only fully agree that there are no public health and safety concerns associated with an approach that is safety strain-specific and specific to actual amino acid sequences used. |
| **2.3.2** (page 27)<br><br>FSANZ also proposes amending Schedule 26 to add a new, separate table for food produced using gene technology of microbial origin, which lists 2′-FL and LNnT from the permitted source as listed above. Consequently, an amendment to the existing table in Schedule 26 would be made to clarify the existing list of approvals are of plant origin (i.e. food produced using gene technology of plant origin). This approach clearly delineates the different sources of permitted GM foods (i.e. plant origin and microbial origin), similar to the existing approach used in S18—4 of the Code which lists permitted enzymes in separate tables for plant, animal and microbial origin. | It could be more clearly mentioned or referred to next to the proposed entry in Schedule 26 that the approval is specific to 2'-FL and LNnT that "no source organism should be present" and/or they "should not contain any measurable production microorganism or its novel DNA".<br><br>In case of isolated and highly purified ingredients from microbial sources such as the risk assessed 2'-FL and LNnT (that are to be added as a second separate table into Schedule 26) there would be no reasonable justification to allow for such ingredients to contain the production microorganism or its novel DNA and which therefore would need to be labelled as GM. It would therefore be misleading to allow for both cases for these ingredients in the Code on basis of the currently performed scientific risk assessment. |
| **2.3.4** (page 30)<br><br>FSANZ's approach is to prohibit the addition of 2′-FL alone, or with LNnT, in combination with existing permissions for GOS and ITF for infant formula products and FSFYC (i.e. permissions for 2′-FL and LNnT would be used as alternatives to GOS and ITF). | Glycom supports this approach. |
| **2.3.5.2** (page 2)<br><br>FSANZ's approach is to specifically prohibit the following terms on the label of infant formula products/FSFYC:<br>• the words 'human milk oligosaccharide', 'human milk identical oligosaccharide' or any word or words having the same or similar effect | Our view is that there is no reason for these specific clauses to be added and there is no precedent for doing so. It is apparent that the suggested approach would differ from the overall structure and presentation of the Food Standards Code, which typically avoids redundancies. |

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| • the abbreviations 'HMO' or 'HiMO' or any abbreviation having the same or similar effect. | |
| **2.3.6** (page 34)<br><br>FSANZ's approach is to set specifications for 2′-FL and LNnT in the Code using those provided by the applicant (without specifying the methods of analysis). | Glycom supports this approach because this specifically approves the ingredient as risk assessed.<br><br>As previously expressed (in our submission to the 1st CFS), Glycom wishes additionally to propose for the strain to be located together with the specification in Schedule 3.<br><br>Glycom also would like to comment that in case that FSANZ would provide the approval on wider strain families (as proposed under 2.3.2 (page 26/27); see our comment above) the maintenance of the current set of specifications would constitute a crucial remaining element of the scientific risk assessment.<br><br>Furthermore, we would like to comment that harmonisation of specifications in mere anticipation of additional applications does not appear to be justified. In our view, harmonisation of specifications should only be made on basis of independently scientifically risk assessed ingredients and technical processes. This was the case for the EU Union list of authorised novel foods, where the harmonised specifications were based retrospectively on independently authorised food ingredients. |
| **2.3.7** (page 34)<br><br>FSANZ's approach is to provide 15 months exclusivity from the date of gazettal for the applicant's brand of 2′-FL and LNnT. | Glycom supports this approach since it is particularly justified considering the substantial investments that Glycom had to do in order to generate all the different data elements underlying the scientific risk assessment. |