Consultation request to determine the status of L-fucose (produced by microbial fermentation), pursuant to Article 4(2) of Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods

Request by: Setenta e Três Mil e Cem Lda, Lisboa, Portugal

Recipient Member State: the Netherlands

Assessment by the Novel Food Unit of the Medicines Evaluation Board Agency , 24 May 2019

Name of the food: L-fucose (produced by microbial fermentation).

Description of the food: The food in question is a preparation that mainly consists of the monosaccharide L-fucose. It is the result of an elaborate production process, starting with the formation of a biopolymer that is excreted by the microorganism *Enterobacter* A47, during a fermentation process. This biopolymer is then isolated and further processed by hydrolysis, followed by several purification steps, aimed at isolating the free L-fucose. The resulting preparation would be a powder with a purity of at least 95% L-fucose, according to the dossier. The applicant proposes to use this L-fucose preparation "as part of food supplements formulations to be ingested in Infant Formulas (IFs) or Young Children Formulas (YCFs) by infants and toddlers respectively". In the dossier, the applicant argues that L-fucose has been consumed by humans in the EU before 15 May 1997 in quantities of one gram or more per day.

Status: This product has to be regarded as a novel food, since no evidence was presented, related to previous consumption to a significant degree of the applicant's L-fucose preparation, nor of the monosaccharide L-fucose itself, for that matter.

Novel food category: The applicant has suggested that the appropriate category from the Novel Food Regulation for this food would be:

(ii) food consisting of, isolated from or produced from microorganisms, fungi or algae.

We agree with this suggestion, but would also like to mention that EFSA proposed in paragraph 2.2 of the relevant guidance document that for certain products, relevant information for multiple classes of novel foods may need to be provided for the purpose of the scientific assessment, in case of a future authorization dossier (EFSA, 2016). As an example, it was mentioned that both the classes "chemical substances" and "food produced by a microorganism" could be relevant for some products. We feel that this may be the case for the L-fucose preparation of this request.

Reasons statement: The applicant has not demonstrated a history of consumption for this specific L-fucose preparation, which is produced by a combination of fermentation, hydrolysis, and purification steps, nor for any other L-fucose preparation of similar origin and composition. Information regarding previous consumption in the dossier does not concern the actual L-fucose preparation, but rather concerns compounds containing L-fucose as a sugar moiety within their molecular structure, and - to a very limited degree - concerns the free monosaccharide L-fucose itself.

There is no doubt that the chemical structure corresponding to L-fucose is part of many macromolecules, as a sugar moiety. The dossier refers to human milk oligosaccharides, fucoidan polysaccharides, and plant cell wall polysaccharides. As an integral part of such compounds, the L-fucose structure is ubiquitous in nature, but this fact does not constitute a history of consumption before 1997 for L-fucose as a compound. Put in more general terms, information on previous consumption of macromolecular compounds containing the main constituent of a new product as an integral part of their molecular structure, would not demonstrate a valid history of consumption of that constituent itself. Instead, it could possibly be used as supportive information in a full safety dossier, to be considered in connection with other types of information, as described in detail by EFSA (EFSA, 2016).

Although information referring to possible previous consumption of L-fucose containing macromolecules is not clearly distinguished from information regarding free L-fucose in the dossier, the applicant also claims free L-fucose is present in food. Generally speaking, we would not consider previous consumption data for only the main constituent of a new product of this type as a valid history of consumption for the actual new product, since even in the case of a highly purified preparation, a chemical characterization in itself will not be sufficient to rule out the presence of unknown minor compounds that could constitute a potential risk for food safety. Instead, such composition data would be an important element of a full safety dossier, to be considered in connection with other types of information, as described in detail by EFSA (EFSA, 2016). Nevertheless, we would like to point out that a history of consumption to a significant degree for the monosaccharide L-fucose itself has not been demonstrated by the applicant, either. The only evidence presented, that may indicate direct consumption of free L-fucose, concerns the presence of a limited amount of this monosaccharide in human milk. A low and variable presence of L-fucose in human milk is indeed documented in scientific literature, which is likely due to the presence of L-fucose containing oligosaccharides in the milk of some mothers, in combination with the activity of sugar cleaving enzymes (as reviewed by Choi *et al*., 2015 in a safety evaluation for a different L-fucose preparation). In our opinion, this represents only a very special type of consumption, and does not equal “consumption to a significant degree” as described in Regulation (EU) 2015/2283. It should be noted that, similarly, preparations of some oligosaccharides naturally present in human milk, such as 2’-FL and LNnT, were previously subject of a full safety assessment as novel foods in the EU.

Finally, the applicant has also pointed out that 2’-FL authorized as a novel food in the EU can contain free L-fucose, according to the product specification described in the European Union List for novel foods. (EC, 2017). By definition, however, the possible presence of L-fucose as a minor compound of this authorized novel food, does not constitute a history of consumption before 1997.

References:

Choi SS, Lynch BS, Baldwin N, Dakoulas EW, Roy S, Moore C, Thorsrud BA, Röhrig CH. Safety evaluation of the human-identical milk monosaccharide, l-fucose. Regul Toxicol Pharmacol. 2015 Jun;72(1):39-48. (https://doi.org/10.1016/j.yrtph.2015.02.016)

EFSA NDA Panel, 2016. Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4594. (https://www.efsa.europa.eu/en/efsajournal/pub/4594)

EC, 2017. Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods (as amended). (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R2470&qid=1558602179707&from=EN)