APPLICATION FOR THE APPROVAL OF THE HUMAN-IDENTICAL MILK OLIGOSACCHARIDE 3-FUCOSYLLACTOSE (3-FL) AS A NOVEL FOOD INGREDIENT FOR USE IN INFANT AND FOLLOW-ON FORMULAE AND IN FOODS

Regulation (EU) No 2015/2283 of the European Parliament and of the Council of 25 November 2015 Concerning Novel Foods and Novel Food Ingredients

Non-Confidential Summary of the Application

SUBMITTED BY:

Glycom A/S
Kogle Allé 4
2970 Hørsholm
Denmark

Glycom A/S is a (sub-) division of DSM Nutritional Products Ltd, a company with registered address at Wurmisweg 576, 4303 Kaiseraugst, Switzerland

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This dossier has been prepared in accordance with the requirements of Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods[1], supported by the European Food Safety Authority (EFSA) NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016 (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 and EFSA's Administrative guidance on the submission of applications for authorisation of a novel food pursuant to Article 10 of Regulation (EU) 2015/2283[2]

[1] Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. C/2017/8874. OJ L 351, 30.12.2017, p. 64–71. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R2469.

[2] Administrative guidance on the submission of applications for authorisation of a novel food pursuant to Article 10 of Regulation (EU) 2015/2283European Food Safety Authority. Available online: http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2018.EN-1381/epdf.

Summary

The novel food 3-fucosyllactose (3-FL) is a trisaccharide human-identical milk oligosaccharide (HiMO) consisting of D-glucose, D-galactose and L-fucose. D-Glucose and D-galactose comprise the milk sugar lactose, and L-fucose is approved as a novel food ingredient for use in a variety of foods including infant and follow-on formula. 3-FL is obtained from microbial fermentation from an *E. coli* K-12 DH1-derived strain and is isolated as a single substance.

As 3-FL has not been previously added as food ingredient to infant or follow-on formula or to foods (*i.e.*, consumed to a significant degree) in the EU before 15 May 1997, it would therefore be considered a novel food under Regulation (EU) No 2015/2283[3] on novel foods pursuant to Art. 3, Point 2(a) and fall under the categories:

i) Food with a new or intentionally modified molecular structure, where that structure was not used as, or in, a food within the Union before 15 May 1997; and

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

Similar to previous HiMOs (*i.e.* 2'-FL, LNnT, 2'-FL/DFL, LNT, 3'-SL, and 6'-SL) approved in the EU, 3-FL is also obtained from microbial fermentation from an *E. coli* K-12 DH1-derived strain and is isolated as a highly purified simple mixture of fully characterised and related compounds. Analytical data demonstrate the absence of the production organism, its DNA, residual protein and any potential endotoxins deriving from the microorganism. The composition and specifications are well defined and fully characterise the ingredient.

3-FL is manufactured in a process that is highly contained, controlled and compliant with Hazards Analysis and Critical Control Points (HACCP) principles. Batch manufacturing data demonstrate that it is produced in a consistent manner and that any potential inherent process and external contaminants are below levels of safety concern. Analytical data also show 3-FL is stable for its intended shelf-life, both alone and within processed food, with no evidence of hazards or harmful degradation products being formed during its storage.

It is proposed for use as ingredient in infant formulas (up to 12 months), follow-on formula, infant and milk-drinks for young children and above at a use levels of up to 2 g/L in ready-to-drink and reconstituted products. The maximum use level for formula milk is proposed on the basis of providing a similar amount of 3-FL to that which occurs naturally in mature human breast milk. 3-FL is also intended for use in foods and beverage targeted towards older population groups (up to 2 g/L or 25 g/kg) and foods for special medical purposes (use level determined on a case-by-case basis). 3-FL is also proposed for use at a maximum level in food supplements up to 4 g/day.

The highest 95th percentile exposure estimates for 3-FL from all proposed foods at its maximum proposed use levels is considerably less than their highest mean consumption per day of from breast milk.

[3] Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001. OJ L 327, 11.12.2015, p. 1–22. Available online: https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32015R2283.

HMOs, including 3-FL, do not undergo any significant digestion in the upper gastrointestinal tract; however, HMOs are orally absorbed intact to a small extent, a small portion of which (approximately 1 to 2% of the total amount of HMO ingested) is excreted unchanged in urine. Therefore, the absorption of 3-FL would be limited and any level of 3-FL product that is absorbed would no different to that exposed to by infants consuming human breast milk. Therefore, the potential absorption of 3-FL from its consumption is not a safety concern for infants. Since infants comprise the most sensitive age group, it may be concluded that the absorption of 3-FL does not pose a safety concern for other age groups.

In the 90-day study in neonatal Sprague Dawley [Crl:CD(SD)] rats, the highest dose tested of 3-FL was 4,000 mg/kg body weight/day (maximum feasible dose).

The results of genotoxicity studies demonstrate that 3-FL is neither mutagenic (as assessed in the bacterial reverse mutation test) nor clastogenic/aneugenic (as assessed in the *in vitro* mammalian cell micronucleus test).

Together, the weight of the available evidence on 3-FL supports the safe use of the ingredient under the proposed conditions of use.