Summary of the dossier: 3-fucosyllactose

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This is an application for authorisation to place on the market microbiologically produced 3-fucosyllactose (3FL).as a novel food. The 3-FL discussed in this dossier is manufactured through fermentation by a genetically modified microorganism (GMM) and purified to ≥90% purity. 3FL is intended to be used in unflavoured pasteurised and unflavoured sterilised (including UHT) milk (1.2 g:L), unflavoured fermented milk-based products (1.2 g/L), yoghurt (12.0 g/kg), flavoured fermented milk-based products including heat-treated products (1.2 g/l beverages and 12.0 g/kg products other than beverages), dairy analogues, non-dairy yoghurts (1.2 g/l beverages and 12.0 g/kg products other than beverages), breakfast cereals, (40 g/kg), fine bakery wares, cereal bars only (30 g/kg), infant formula, follow-on formula, milk-based drinks and flavoured drinks (1.2 g/l), processed cereal-based food and baby foods (12 g/kg and 1.2 g/l), Foods for Special Medical Purposes (FSMP), total diet replacement (30 g/kg and 2.0 g/l) and food supplements (5.0 g/day for general population and 1.2 g/day for young children).

3FL is a trisaccharide consisting of L-fucose, D-galactose and D-glucose. 3FL is a naturally occurring trisaccharide found in mammalian milk with the highest concentrations occurring in human milk and is therefore typically referred to as one of several human milk oligosaccharides (HMO). More than a hundred different HMOs have been identified so far in human breast milk, but not every woman synthesizes the same set of oligosaccharides. Women with the *Le* locus produce the highest amounts of 3FL (Samuel et al., 2018).

HMO research in general, and studies on fucosylated neutral oligosaccharides, most often 2'-Fucosyllactose (2'-FL), point to the contribution of HMOs to infant health. These studies include observational studies on breastfeeding infants, correlating HMOs in breastmilk with gut microbiota profiles and infection and immune function as well as in vitro cell culture and animal studies. Collectively, these studies indicate that HMOs act as prebiotics, facilitating early colonization of the gut by Bifidobacteria, act as decoy receptors, inhibiting adhesion of potential pathogens to epithelial surfaces in the intestine and have a role in modulating immune responses (Coppa, 2006, German, 2008, Lewis, 2015, Morrow, 2004, Newburg, 2005, Plaza-Diaz, 2018, Triantis, 2018, Yu, 2013). Oligosaccharide concentrations in milk of most farm animals including cows, goats, sheep and pigs are 100–1000-fold lower than that in human milk, with a lower number of different oligosaccharides, a higher abundance of sialylated and a lower abundance of fucosylated oligosaccharides (Sundekilde et al., 2012). Hence, infant formula based on cow's milk provide the human neonate with lower amounts of HMOs as compared to human breast milk.

From the recent systematic review by Thurl et al. (2017), the reported range of levels of 3FL in human breast milk for lactating women is 0.24 – 1.24 g/L for 0 to 100 days lactation. For a 6.85 kg infant consuming 800 mL (average intake) or 1200 mL (high intake) of breast milk per day, the intake of 3FL ranges from 0.19 – 0.99 g/day (average intake) or 1.2 – 1.49 g/day (high intake). On a body weight basis, 3FL intake ranges from 27.7 – 144.5 mg/kg body weight per day (average) or 175.2 – 217.5 mg/kg body weight per day (high). Based on a sample of mothers in France, Germany and Italy, the reported level of 3FL in human milk measured at >31 days lactation was 1.36 g/L (Erney et al.,

2000). Using this value, based on a 6.85 kg infant consuming 800 mL (average intake) or 1200 mL (high intake) of breast milk per day, the intake of 3FL would range from 1.09 g/day (average intake) to 1.63 g/day (high intake). On a body weight basis, 3FL intake would range from 158.8 mg/kg body weight per day (average) to 238.2 mg/kg body weight per day (high).

The 3FL discussed in this dossier is manufactured through fermentation by a genetically modified microorganism (GMM) and purified to ≥90% purity. The remaining ≤10% of the product is mainly mono-, di- and tri-saccharides and are all identified as safe ingredients. Carefully controlled downstream processing yields a highly purified 3FL product with no detectable residual GMM or recombinant DNA. The 3FL molecule in DuPont's 3FL is structurally identical to 3FL molecules isolated from human breast milk. The GMM is considered a processing aid in the production process as the novel ingredient is purified and concentrated from the medium without disruption of the bacterial cells, and the final product Is devoid of the GM production organism and recombinant DNA. Therefore, the authorisation and labelling requirements specific to GM foods do not apply.

A safety assessment was conducted on the 3FL product, and included acute oral toxicity, genetic toxicity, a subchronic (90-day) rodent feeding study and a neonatal piglet study. 3FL was not acutely toxic to rats at 5 000 mg/kg, and there was no evidence of genetic toxicity in a bacterial reverse mutation (AMES) test, in vitro micronucleus and chromosomal aberration assays, and an in vivo micronucleus study. Dietary subchronic exposure of rats to 3FL at 5% and 10% was not associated with any statistical or biologically-relevant differences in growth, food intake or efficiency, clinical observations, or clinical or anatomic pathology changes at average daily intakes of 5.98 and 7.27 g/kg/day for males and females, respectively. The weight of evidence from the studies included in this assessment support the safe use of 3FL produced using biotechnology as a nutritional ingredient in foods. Results from a 6 months stability study of the 3FL product, under ambient (25°C and 65% RH) and accelerated conditions (40°C and 75% RH) conditions in various food matrixes showed that the 3FL product is stable.

Based on the data presented in this dossier, we conclude that the 3FL of DuPont Nutrition & Biosciences ApS discussed in this dossier, is safe for consumption in the applications described in this dossier.

The application has been compiled in line with the administrative and scientific requirements of Commission Implementing Regulation (EU) 2017/2469 laying down for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. It is also in line with the European Food Safety Authority (EFSA) guidance on the preparation and presentation of an application for authorisation of a Novel Food in the Context of Regulation (EU) 2015/2283

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