Summary of the dossier: 2’-Fucosyllactose

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The novel food that is the subject of this application is 2'-Fucosyllactose (2’-FL), which is a fucosylated oligosaccharide composed of 3 monosaccharides, namely L-fucose, D-galactose, and D glucose. 2’-FL is currently authorised as a novel food ingredient under 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 for use in a variety of food products , including infant formula and follow-on formula and food supplements, excluding food supplements for infants. Currently authorised sources of 2’-FL include chemical synthesis, or fermentation with a genetically modified strain of Escherichia coli K-12 or a genetically modified strain of E. coli BL21.

Kyowa is seeking to amend the specifications for 2'-FL in Table 2 of the Union list to include another microbial source for 2' FL, namely a genetically modified strain of E. coli W. The host organism, E. coli W, is well characterised and is 1 of 4 E. coli strains designated as Risk Group 1 organisms in biological safety guidelines (Archer et al., 2011), as it does not cause disease in healthy adult humans (NIH, 2019), and does not colonise the human gut (Bauer et al., 2008). Evaluation of the production strain according to EFSA’s Guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use (EFSA GMO Panel, 2011) for category 1 genetically modified microorganisms indicates no safety concerns resulting from the genetic modifications.

Kyowa’s 2'-FL produced by microbial fermentation using a genetically modified strain of E. coli W is manufactured using food-grade raw materials and processing aids and is conducted in accordance with a detailed HACCP plan. The production microorganism is cultured in chemically defined nutrient media under sterile conditions in tightly controlled (e.g., time, temperature, pH) conditions. In the main fermentation process, the production microorganism synthesises 2'-FL, which is excreted into the media. 2’-FL is isolated and purified from the fermentation medium using a series of filtration and cationic and anionic exchange steps, followed by concentration and spray-drying to obtain the final 2’-FL product.

Kyowa’s 2'-FL has been demonstrated by high-performance liquid chromatography with pulsed amperometric detection (HPLC-PAD), proton nuclear magnetic resonance spectroscopy (1H NMR), and carbon-13 nuclear magnetic resonance spectroscopy (13C NMR) to be structurally and chemically identical to 2'-FL that is naturally present in human breast milk. Kyowa’s purity limit for 2’-FL (≥82%) is similar to 2’-FL ingredients authorised on the Union list (≥ 83 to ≥ 95%). Minor differences in the carbohydrate profile of Kyowa’s 2’-FL ingredient in comparison to those authorised on the Union list do not pose a safety concern, as the carbohydrates are all naturally occurring in human breast milk or are human breakdown products of naturally occurring components of human milk, and exposures to these carbohydrates from the intended uses of Kyowa’s 2'-FL are expected to be insignificant compared to background exposures.

Analytical data on Kyowa’s 2-FL ingredient demonstrate that the modifications to the source of 2’-FL proposed by Kyowa (i.e., to include a genetically modified strain of E. coli W), do not adversely affect the composition or the level of undesirable substances in the novel food ingredient.

Kyowa is also seeking to extend the conditions of use to include use in dietary supplements intended for infants at a maximum intake of 1.2 g/day. 2'-FL food supplements for infants are intended to be used as alternatives to other sources of 2'-FL for this population group and are not intended to be consumed if other sources of 2'-FL are consumed on the same day. The maximum daily intake of 2'-FL from the proposed extension of use in food supplements for infants does not exceed levels that were previously concluded to be safe. Therefore, consumption of Kyowa's 2'-FL ingredient from use in dietary supplements intended for infants does not pose a concern for safety. The proposed extension of use to food supplements for infants does not alter the dietary exposure assessment of currently authorised uses of 2'-FL in the EU. Furthermore, Kyowa's 2-FL ingredient is intended as an alternative source of 2'-FL in the EU marketplace, and the requested amendments to the specifications on the Union list to include 2'-FL from a genetically modified strain of E. coli W will not alter the current dietary intakes of 2'-FL from the authorised conditions of use.

Toxicology studies on Kyowa's 2'-FL ingredient were conducted in accordance with the tiered approach to the safety assessment of food additives as described in the EFSA Guidance for submission for food additive evaluations (EFSA ANS Panel, 2012). Kyowa's 2'-FL ingredient was not mutagenic in a bacterial reverse mutation assay or in an in vivo micronucleus study. In a 90-day toxicity study, there were no toxicologically relevant compound-related adverse effects reported, and the study authors determined the no-observed-adverse-effect level to be 2,000 mg/kg body weight/day, the highest dose tested. The results of these studies support the safety of Kyowa's 2'-FL ingredient. Considering that Kyowa's 2'-FL ingredient is chemically and compositionally similar to other 2'-FL ingredients currently authorised on the Union list, the existing safety conclusions by EFSA on these other 2'-FL ingredients may be extended to support the safety of Kyowa's 2'-FL produced by microbial fermentation of a genetically modified strain of E. coli W.

The results of recently published studies of other 2'-FL ingredients further support the safety of Kyowa's 2'-FL under the intended conditions of use and are in agreement with the pre-clinical and human studies of 2'-FL previously evaluated by EFSA. The amendments proposed by Kyowa to the specifications and microbial source of 2'-FL do not affect the nutritional value, metabolism, or level of undesirable substances in the ingredient, and therefore do not affect the results of the existing risk assessment for 2'-FL as currently included in the Union list.

The totality of the available data on 2'-FL produced by microbial fermentation of a genetically modified strain of E. coli W supports the safe use of the ingredient under the proposed conditions of use in dietary supplements intended for infants as well as the conditions of use previously authorised in the Union list for 2'-FL.