Summary of the dossier: 3’-Sialyllactose sodium salt

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The novel food that is the subject of this application is 3'-Sialyllatose (3'-SL) sodium salt, which is a sialylated oligosaccharide composed of 3 monosaccharides, namely N acetylneuraminic acid (NeuAc), D galactose, and D glucose. NeuAc is conjugated to the galactose unit of lactose (comprised of glucose and galactose) at the 3 position.

Kyowa Hakko Bio Co., Ltd. (Kyowa) submits the present application in order to gain the approval of 3'-SL sodium salt as a novel food ingredient in the European Union (EU) in a variety of conventional food uses, including infant and follow-on formula, and food supplements.

Kyowa’s 3'-SL sodium salt ingredient is manufactured by fermentation with a genetically modified strain of Escherichia coli W using food-grade raw materials and processing aids in accordance with a detailed hazard analysis and critical control points (HACCP) plan. The production microorganism is cultured in chemically defined nutrient media under sterile, tightly controlled (e.g., time, temperature, pH) conditions. The 3'-SL ingredient is secreted into the media, isolated, and purified in the sodium salt form. The final 3'-SL sodium salt ingredient contains ≥82% 3' SL and minor levels of other carbohydrates, such as NeuAc, D glucose, D lactose, 3'-sialyllactulose, and 6' sialyllactose (6'-SL) sodium salt. Kyowa’s 3'-SL is chemically and structurally equivalent to 3'-SL from human milk.

Analytical results of Kyowa’s 3'-SL sodium salt ingredient demonstrate that the manufacturing process consistently produces a product that conforms to the established product specifications and which is free of microbial or chemical hazards that would pose a safety concern. Results from an accelerated stability study demonstrate that Kyowa’s 3'-SL sodium salt ingredient is stable for up to 6 months when stored at 40 ± 2°C and 75 ± 5% RH, which supports a shelf-life of 3 years. A stability study under normal storage conditions (25 ± 2°C; 60 ± 5% RH) is ongoing. Stability in proposed food matrices has previously been demonstrated for a 3'-SL sodium salt ingredient that is structurally and chemically identical to 3'-SL in bovine milk or colostrum, and these results support the stability of Kyowa’s 3'-SL sodium salt ingredient in the proposed food matrices.

Kyowa proposes the same uses and maximum use levels of 3'-SL sodium salt in foods as those recently evaluated by EFSA . Kyowa also proposes to market 3'-SL sodium salt as a food supplement for infants, young children, and individuals above 3 years of age. Food supplements with 3'-SL sodium salt are intended to be used as alternatives to other sources of 3'-SL.

Dietary intakes resulting from the proposed uses were previously concluded to be safe by EFSA . The anticipated intake of 3'-SL sodium salt from food supplements in target populations does not exceed the estimated high daily intake of 3'-SL from human milk in breastfed infants. Notably, intakes will not be additive as food supplements with 3'-SL sodium salt are not intended to be used if natural sources of 3'-SL or foods containing added 3'-SL are consumed on the same day.

Kyowa’s 3'-SL is structurally and chemically identical to 3'-SL that is naturally present in human milk. Therefore, the ADME of Kyowa’s 3'-SL would be identical to 3'-SL consumed from human breast milk, with a limited amount of 3'-SL absorbed and the majority fermented by the intestinal microbiota or excreted in the faeces. As the amount absorbed from Kyowa’s 3'-SL sodium salt would be no different

than from human breast milk, there is no concern for safety from the potential limited absorption of 3'-SL.

The safety of Kyowa's 3'-SL sodium salt ingredient was assessed using a modified Tier 1 approach. Kyowa's 3'-SL sodium salt was non-mutagenic at concentrations up to 5,000 µg/plate in the bacterial reverse mutation assay and did not demonstrate any potential for induction of chromosomal aberrations in male ICR mice at doses up to 2,000 mg/kg body weight. In a 90-day oral repeat dose toxicity study, there were no statistically significant, toxicologically relevant, test item-related adverse effects, and the no-observed-adverse-effect level (NOAEL) was concluded by the study authors to be 2,007 mg/kg body weight/day (the highest dose tested). The results of these studies support the safety of Kyowa's 3'-SL sodium salt ingredient.

As noted by the EFSA NDA Panel "as with other oligosaccharides, which are natural components of human milk, the safety assessment is mainly based on the comparison between the natural intake in breastfed infants and the estimated intake as NF. The same considerations apply for lactose and other mono- and oligosaccharides (i.e. sialic acid) that are only present as a very small fraction in the NF and considered of no safety concern". Kyowa's 3'-SL sodium salt ingredient is of comparable purity to the 3'-SL sodium salt ingredient evaluated by the EFSA NDA Panel with similar low levels of other carbohydrates. As Kyowa proposes the same uses and maximum use levels of 3'-SL sodium salt in foods as those previously requested, the intakes of Kyowa's 3'-SL sodium salt novel food ingredient will be the same as those previously evaluated and concluded by EFSA to not pose safety concerns as they either do not exceed or are unlikely to exceed the highest level of 3'-SL intake in breast fed infants . Therefore, it is concluded that Kyowa's 3'-SL sodium salt does not pose safety concerns under the intended conditions of use in food as intakes either do not exceed or are unlikely to exceed those resulting from the natural intake of human breast milk. Furthermore, it is concluded that the use of Kyowa's 3'-SL sodium salt in food supplements is not of concern to safety, as intakes do not exceed those resulting from the natural intake of human breast milk.