Submitted to

Food Standards Australia New Zealand (FSANZ)

Application to Amend the Australia New Zealand Food Standards Code:

2'-Fucosyllactose (2'-FL), 3-Fucosyllactose (3-FL), Lacto-*N*-tetraose (LNT), 3'-Sialyllactose (3'-SL) sodium salt, and 6'-Sialyllactose (6'-SL) sodium salt for Use as Nutritive Substances in infant formula products

Executive Summary

Prepared by Chr. Hansen A/S (Part of Novonesis Group)

V2 (Amended 15 August 2025)

Executive Summary

Chr. Hansen A/S (hereafter referred to as (Chr. Hansen"), part of Novonesis group, is seeking to amend Schedule 25 of the Australia New Zealand Food Standards Code to include 2'-Fucosyllactose (2'-FL), 3-Fucosyllactose (3-FL), Lacto-*N*-tetraose (LNT), 3'-Sialyllactose sodium salt (hereafter referred to as 3'-SL), and 6'-Sialyllactose sodium salt (hereafter referred to as 6'-SL) for use as nutritive substances in infant formula products. These five HMOs may be used in combination (trademarked as MyOli™, hereafter referred to as "5HMO-Mix") or as single HMOs.

Humans are exposed to oligosaccharides such as 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL during the early years of life, especially while nursing as infants. Human milk oligosaccharides (HMOs) represent the third largest component of human milk after lactose and total lipids. These HMOs are structurally diverse compounds consisting of monosaccharide building blocks, specifically glucose, galactose, *N*-acetylglucosamine, fucose, and *N*-acetylneuraminic acid. These building blocks are typically connected by various glycosidic linkages. Although diverse, HMOs can be assigned to three main classes; neutral fucosylated HMOs containing fucose (such as 2'-FL and 3-FL), neutral core HMOs containing *N*-acetylglucosamine (such as LNT), and acidic HMOs containing sialic acid (such as 3'-SL and 6'-SL).

Several studies have shown that consumption of HMOs from breastmilk is associated with changes in microbiota composition in infants, and that consumption of infant formula containing HMOs shifted the microbiome composition of formula-fed infants to that of breastfed infants. Additional studies have also suggested that HMOs are able to support intestinal barrier function, show anti-infective activity, and modulate effects on the immune system, and affect neurodevelopment.

The manufacture of these five HMOs includes upstream processing (including the fermentation process of the individual HMOs), downstream processing (including the recovery and purification of the individual HMOs), drying (spray-drying of the final product powder), and for use as a 5HMO-Mix, blending (dry blending or wet-blending) before a final drying process. A purification process is used to remove the production organism, resulting in a highly purified product. The production processes of Chr. Hansen's HMOs are compliant to European Regulation (EC) No. 178/2002, and production is controlled by the Food Hygiene Regulation (EC) No. 852/2005. The manufacturing process for Chr. Hansen's HMOs are in accordance with current Good Manufacturing Practice for Food (GMP) and the principles of Hazard Analysis of Critical Control Points (HACCP). It is to note that these HMO ingredients (i.e., Chr. Hansen's 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL) will not be manufactured in Australia or New Zealand, rather only the finished ingredient or product containing these finished ingredients will be imported into Australia and New Zealand.

The 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL ingredients as manufactured by Chr. Hansen (using *E. coli* BL21(DE3)) have gained approval and notification in the European Union as novel food ingredients for use in a variety of food products including infant formula, follow-on formula, processed cereal-based food and baby food for infants and young children, and in milk-based drinks and similar products intended for young children. These ingredients have also achieved Generally Recognized as Safe (GRAS) status for use in the United States.

This application includes comprehensive data from both clinical and pre-clinical toxicological studies, including assessments by EFSA's NDA Panel. In general, the EFSA NDA Panel recognised that HMOs are non-digestible carbohydrates as they do not undergo any significant digestion in the upper gastrointestinal tract. The 5HMO-Mix has been evaluated in a 21-day tolerance study in neonatal

piglets, as well as a 13-week dietary toxicity study. Additionally, the 5HMO-Mix has been evaluated in a bacterial reverse mutation assay and an *in vitro* micronucleus assay, and the 5HMO-Mix was concluded to be not genotoxic.

The maximum proposed use levels, either alone or in combination, for Chr. Hansen's **2'-FL** is 3.0 g/L in infant formula, and 3.64 g/L in follow-on formula. The maximum proposed use levels, either alone or in combination, for Chr. Hansen's **3-FL** is 0.9 g/L in infant formula, and 1.2 g/L in follow-on formula. The maximum proposed use levels, either alone or in combination, for Chr. Hansen's **LNT** is 1.82 g/L in infant formula and follow-on formula. The maximum proposed use levels, either alone or in combination, for Chr. Hansen's **3'-SL** is 0.28 g/L in infant formula and follow-on formula. The maximum proposed use levels, either alone or in combination, for Chr. Hansen's 6'-SL is 0.7 g/L in infant formula and follow-on formula. The proposed use levels of 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL either alone or in combination in infant formula and follow-on formula are considered safe when compared to intake levels of these HMOs from human breastmilk.

Overall, with the available scientific evidence and history of safe consumption of 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL from human milk, there is evidence to support the safe use of 2'-FL, 3-FL, LNT, 3'-SL, and 6'-SL for application in infant formula products. It is also anticipated that the approval of these HMOs for use either alone or in combination will benefit Australian consumers by increasing the available product options.