

Safety Assessment of 3'-Sialyllactose (3'-SL) Sodium Salt Used as a Novel Food in Food and Food Supplements (RP2121)

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FSA Research and Evidence

The Food Standards Agency (FSA) and Food Standards Scotland (FSS) received an application from Chr. Hansen A/S, Denmark ("the applicant") for the authorisation of 3'-sialyllactose (3'-SL) sodium salt as a novel food, in September 2023.

The novel food 3'-SL sodium salt is a human identical milk oligosaccharide produced by fermentation using a new production strain of genetically modified *E. coli* BL21 (DE3). The applicant is seeking authorisation of this novel food for use in a range of foods including infant formula and follow-on formula, foods for infants and young children, foods for special medical purposes and food supplements.

The FSA and FSS in their evaluation of the application reviewed the safety dossier and supplementary information provided by the applicant. Please note the FSA did not consider any potential health benefits or claims arising from consuming the food, as the focus of the novel food assessment is to ensure the food is safe, and not putting consumers at a nutritional disadvantage.

The FSA and FSS concluded that the applicant had provided sufficient information to assure the novel food, 3'-SL sodium salt, was safe under the proposed conditions of use. The anticipated intake levels and the proposed use in food and food supplements was not considered to be nutritionally disadvantageous.

The safety assessment represents the opinion of the FSA and FSS.

This is a joint FSA and FSS publication.



1. Introduction

FSA and FSS have undertaken a safety assessment for 3'-SL sodium salt under the novel foods legislation, in line with Article 11 of assimilated Regulation (EU) 2015/2283.

The evaluation by the FSA and FSS assessed the food safety risks of the novel food and its production, in line with Article 11 of assimilated Regulation (EU) 2015/2283 and Article 7 of assimilated Commission Implementing Regulation (EU) 2017/2469. The basis and structure of the assessment was conducted in accordance with the relevant technical guidance put in place by the European Food Safety Agency (EFSA) for full novel food applications (EFSA NDA Panel, 2016) which the FSA and FSS consider is relevant and should be applied to this novel food application owing to similarities in the regulatory regimes.

This assessment outlines the conclusions of the FSA and FSS on the safety of 3'-SL sodium salt as a novel food.

2. Assessment

2.1. Identity of the novel food

The novel food is a white to ivory-coloured spray-dried powder containing $\geq 88.0\%$ 3'-SL sodium salt by dry weight. Other saccharides are present in smaller quantities: D-lactose ($\leq 5.0\%$ w/w dry weight), 3'-sialyllactulose ($\leq 5.0\%$ w/w dry weight), sialic acid ($\leq 1.5\%$ w/w dry weight), N-acetyl-D-glucosamine ($\leq 1.0\%$ w/w dry weight) and a small fraction of other related saccharides (sum of other carbohydrates $\leq 5.0\%$ w/w dry weight).

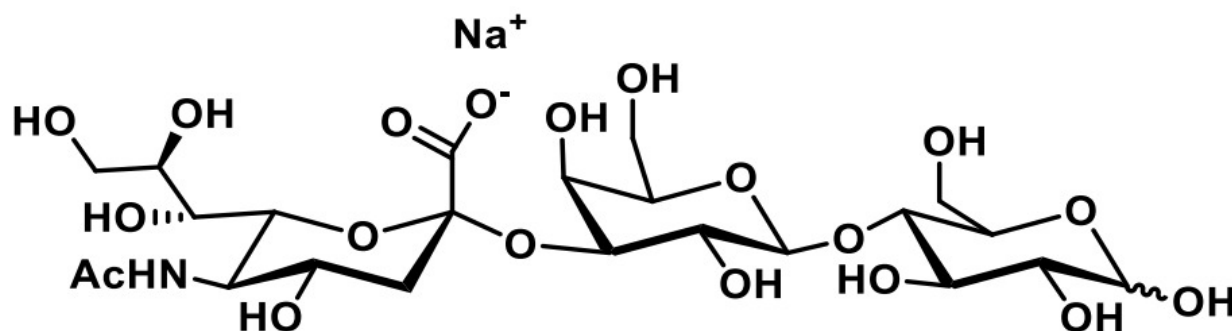


Figure 1. The structural formula of 3'-sialyllactose (3'-SL) sodium salt

3'-SL sodium salt is a trisaccharide composed of D-glucose, D-galactose and N-acetyl-D-neuraminic acid (see [Figure 1](#)), where the N-acetyl-D-neuraminate is linked through a α -(2-3) bond to D-galactose, and D-galactose is linked through a β -(1-4) bond to D-glucose, in its α - and β -anomeric forms.

3'-SL is a regioisomer of 6'-SL, which contains the same monosaccharide moieties as those present in 3'-SL but with the linkage between N-acetyl-D-neuraminic acid and D-galactose being α -(2-6) rather than α -(2-3).

3'-SL sodium salt is characterised by the following information:

- IUPAC name: N-acetyl- α -D-neuraminy-(2 $\rightarrow$ 3)- β -D-galactopyranosyl-(1 $\rightarrow$ 4)-D-glucopyranose, sodium salt
- CAS number: 128596-80-5
- Molecular formula: $C_{23}H_{38}NNaO_{19}$
- Molecular mass: 655.53 g/mol

The molecular structure of 3'-SL sodium salt was determined by high-performance liquid chromatography – electrospray ionisation – tandem mass spectrometry (HPLC-ESI-MS/MS). The collision induced decay (CID) fragmentation patterns and multiple reaction monitoring (MRM) analysis of 3'-SL sodium salt in the novel food were compared with a high purity in-house standard and a commercially available substance standard.

The identity of the novel food was also confirmed by high-performance anion-exchange chromatography – pulsed amperometric detection (HPAEC-PAD) with a high purity in-house standard.

Confirmation that 3'-SL sodium salt in the novel food is equivalent to 3'-SL sodium salt found in human breast milk was provided by comparative mono-dimensional nuclear magnetic resonance (NMR) spectroscopy, including 1H , ^{13}C and ^{13}C -DEPT-90 (distortionless enhancement by

polarisation transfer) spectra, and two-dimensional NMR spectroscopy, including double-quantum filtered $^1\text{H}^1\text{H}$ -correlated spectroscopy (COSY) NMR, phase-sensitive $^1\text{H}^{13}\text{C}$ -heteronuclear single quantum correlation (HSQC) NMR, phase-sensitive $^1\text{H}^{13}\text{C}$ -heteronuclear multiple bond correlation (HMBC) NMR and phase-sensitive $^1\text{H}^{13}\text{C}$ -heteronuclear single quantum correlation total correlation (HSQC-TOCSY) NMR spectra.

2.2. Production process

The novel food is manufactured using a two-step batch fermentation process. In step 1, the raw material lactose is converted into 3'-SL sodium salt using a genetically modified microorganism (GMM) derived from *E. coli* BL21 (DE3) ('production strain'). A second GMM, derived from the same *E. coli* strain, can also be used to break down saccharide by-products and any remaining substrates ('degradation strain'). Glycerol, glucose and/or sucrose can be used as carbon sources for the cultivation of both strains. In step 2, a series of purification and isolation steps are used to concentrate and purify the novel food. The novel food is then spray dried to a powder containing $\geq 88\%$ 3'-SL sodium salt by dry weight.

A novel food produced by a GMO does not fall under the remit of the GMO legislation, assimilated Regulation (EC) No 1829/2003 or assimilated Regulation (EC) No 1830/2003, when the production microorganism is removed during the manufacturing process and therefore no recombinant DNA remains. This has been confirmed in the compositional analysis as detailed below.

The novel food is classified as category 1 under the EFSA GMO guidance (EFSA GMO Panel, 2011): chemically defined purified compounds and their mixtures in which both genetically modified microorganisms (GMMs) and newly introduced genes have been removed. This guidance categorises GMMs and their products for risk assessment purposes and has been retained by the FSA for the purposes of technical review.

Information on the hazard identification, hazard characterisation, and exposure assessment for the genetically modified derivatives of *E. coli* BL21 (DE3) was provided in line with EFSA guidance (EFSA GMO Panel, 2011). Although *E. coli* is not considered to be suitable for qualified presumption of safety (QPS) status (EFSA BIOHAZ Panel, 2023), *E. coli* BL21 (DE3) is widely used for biotechnological applications. *E. coli* BL21 (DE3) is regarded as non-pathogenic and unlikely to survive in host tissues or to cause disease (Chart et al., 2000). Genomic analysis confirms the absence of genes encoding invasion factors, adhesion molecules and enterotoxins associated with virulence (Jeong et al., 2009). Furthermore, production and degradation strains do not contain (1) any episomal DNA that can be transferred to other bacteria, (2) a fertility plasmid, thus they are unable to transfer DNA via conjugation, and (3) any plasmids or other episomal

vectors that can be transferred to other bacteria. On the basis of this information, the new production strain organism does not introduce any new risks that need to be evaluated and managed.

The absence of bacteria from the *Enterobacteriaceae* family (ISO 21528-2: 2019-05) and residual bacterial DNA in the production strain (four antimicrobial resistance genes) and degradation strain (a specific DNA sequence) confirmed that the genetically modified *E. coli* BL21 (DE3) strains were not present in the novel food.

Batch-to-batch analysis of the novel food confirmed the presence of very low levels of microbial endotoxins and residual proteins which were not considered to be a safety concern.

Information on the production process of the novel food does not raise safety concerns.

2.3. Compositional information

Batch-to-batch analysis of 10 non-consecutive batches (see [Tables 1–3](#)) confirmed that the novel food primarily consists of 3'-SL sodium salt (88.1 – 96.8% w/w DM). Other saccharides are present: D-lactose and N-acetyl-D-glucosamine are recognised constituents of human breast milk (Garrido et al., 2012); sialic acid is an endogenous human and ubiquitous nutritional monosaccharide (EFSA NDA Panel, 2017; Röhrig et al., 2017); and 3'-sialyllactulose is derived from 3'-SL by isomerisation of the terminal D-glucose moiety into D-fructose mainly under alkaline conditions during the production process (Zeng et al., 2018).

Data from ten non-consecutive batches of 3'-SL sodium salt demonstrates that the manufacturing process consistently produces a finished novel food that complies with the outlined specifications.

The maximum levels of aflatoxin M1 permitted in infant formula, follow-on formula and young-child formula are 0.025 µg/kg as per assimilated Commission Regulation (EU) 2023/915. Analyses performed on a routinely basis for contaminants such as heavy metals and aflatoxin M1 show that the finished novel food consistently complies with the outlined specifications.

Lipopolysaccharides are contaminants originating from the outer membrane of gram-negative bacteria such as *E. coli*, *Salmonella* spp. and other *Enterobacteriaceae*. They act as endotoxins and can induce immune responses in animals. Endotoxins were either not detected or were found only in extremely low concentrations. Microbiological analyses performed on three batches show that the finished novel food consistently complies with the outlined specifications and with the requirements set in Regulation (EC) 2073/2005 for *Listeria* and *B. cereus*.

Table 1. Batch-to-batch analysis of the novel food (composition)

Composition	Method of analysis	Specification	Batch #1	Batch #2	Batch #3	Batch #4	Batch #5	Batch #6	Batch #7	Batch #8	Batch #9	Batch #10
3'-SL sodium salt (% w/w DM)	HPAEC-PAD	≥ 88.0% w/w DM	93.9	94.1	93.8	91.4	92.1	91.3	88.1	96.8	92.1	90.1
D-Lactose (% w/w DM) *	HPAEC-PAD	≤ 5.0% w/w DM	0.3	0.3	0.4	0.4	0.3	< LOQ	0.5	< LOQ	< LOQ	< LOQ
Sialic acid (% w/w DM) *	HPAEC-PAD	≤ 1.5% w/w DM	0.2	0.3	0.3	0.4	0.2	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
N-acetyl-D-glucosamine (% w/w DM) *	HPAEC-PAD	≤ 1.0% w/w DM	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
3'-Sialyllactulose (% w/w DM) *	HPAEC-PAD	≤ 5.0% w/w DM	-	-	-	-	-	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ
Sum of other carbohydrates (%w/w DM)	Calculation **	≤ 5.0% w/w DM	1.76	1.06	1.96	4.76	1.16	0.05	3.09	0.0	0.25	0.0
Protein (%) *	Nanoquant (modified Bradford)	≤ 100 µg/g	14.2	16.3	13.7	18.6	20.2	11.4	15.7	19.4	20.2	18.8
Ash (%) *	ASU L 06.00-4	≤ 8.5 %	3.7	4.1	3.4	2.9	6.1	7.1	6.9	3.3	6.1	8.4
Moisture (%)	Karl-Fischer titration	≤ 9.0 %	8.3	8.8	8.5	8.7	6.0	6.3	6.9	6.3	6.0	6.4
Sodium (%)	PV-347-ICP-MS: 2016-06 (ASU L 00.00-13)	≤ 4.2 %	3.0	3.1	3.0	3.2	2.8	3.1	3.08	3.4	2.8	3.0

ASU = Official collection of analysis methods according to § 64 of the German Food and Feed Code (LFGB); DM = Dry matter; HPAEC-PAD: High-performance anion-exchange chromatography – pulsed amperometric detection; ICP-MS = Inductively coupled plasma – mass spectrometry.

* LOQ: 3'-Sialyllactulose = 1.13% w/w DM; D-Lactose = 0.14% w/w DM; Sialic acid = 0.14% w/w DM; N-acetyl-D-glucosamine = 0.14% w/w DM; Ash = 0.01%; Protein = 10 µg/g.

** Sum of other carbohydrates (% w/w DM) = 100 (% w/w DM) – 3'-SL sodium salt (% w/w DM) – Quantified carbohydrates (% w/w DM) – Ash (% w/w DM).

Table 2. Batch-to-batch analysis of the novel food (contaminants)

Contaminants	Method of analysis	Specification	Batch #1	Batch #2	Batch #3	Batch #4	Batch #5	Batch #6	Batch #7	Batch #8	Batch #9	Batch #10
Arsenic (mg/kg) *	ASU L 00.00-135: 2011-01 ICP-MS	≤ 0.2 mg/kg	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Cadmium (mg/kg) *	ASU L 00.00-135 – ICP-MS	≤ 0.1 mg/kg **	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Lead (mg/kg) *	ASU L 00.00-135 – ICP-MS	≤ 0.02 mg/kg **	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	0.011
Mercury (mg/kg) *	ASU L 00.00-135 – ICP-MS	≤ 0.1 mg/kg **	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Aflatoxin M1 *** (µg/kg)	DIN EN ISO 14501: 2008-01 IAC-HPLC-FD	≤ 0.025 µg/kg	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025

ASU = Official collection of analysis methods according to § 64 of the German Food and Feed Code (LFGB); DIN = German Institute for Standardisation; IAC-HPLC-FD = Immunoaffinity chromatography – high-performance liquid chromatography – fluorescence detection; ICP-MS = Inductively coupled plasma – mass spectrometry; ISO = International Organisation for Standardisation

* LOD: Arsenic = 0.05 mg/kg; ; Cadmium = 0.01 mg/kg; Mercury = 0.005 mg/kg; Lead = 0.01 ppm.

** Internal specification.

*** LOQ: Aflatoxin M1 = 0.025 µg/kg.

Table 3. Batch-to-batch analysis of the novel food (microbial parameters)

Microbial parameters	Method of analysis	Specification	Batch #1	Batch #2	Batch #3	Batch #4	Batch #5	Batch #6	Batch #7	Batch #8	Batch #9	Batch #10
Standard plate count (CFU/g)	ISO 4833-2	≤ 1,000 CFU/g	<10	<10	<10	<10	<10	<10	<10	<10	<10	<10
Yeast and mould (CFU/g)	ISO 21527-2: 2008-07	≤ 50 CFU/g for yeast ≤ 50 CFU/g for mould	<10	<10	<10	<10	<10	<10	<10	<10	<10	<10
<i>Enterobacteriaceae</i> (CFU/g)	ISO 21528-2: 2019-05	≤ 10 CFU/g	<10	<10	<10	<10	<10	<10	<10	<10	<10	<10
<i>Salmonella</i> (in 25 g)	DIN EN ISO 6579-1: 2017-07	Absent in 25 g	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
<i>Cronobacter</i> spp. (in 10 g)	ISO/TS 22964: 2017-04	Absent in 10 g	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
<i>Listeria monocytogenes</i> (in 25 g)	DIN EN ISO 11290-1	Absent in 25 g *	ND	-	-	ND	ND	-	-	-	-	-
<i>Bacillus cereus</i> (in 5 g)	ASU L 00.00-108: 2007-04 (a)	ND in 5 g *	ND	-	-	ND	ND	-	-	-	-	-
Endotoxins ** (EU/mg)	Ph. Eur. 2.6.14	≤ 10 EU/mg	0.018	0.010	0.011	0.026	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	0.289

ASU = Official collection of analysis methods according to § 64 of the German Food and Feed Code (LFGB); CFU = Colony forming unit; DIN = German Institute for Standardisation; EN = European norm; EU/mg = Endotoxin unit per milligram; ISO = International Organisation for Standardisation; Ph. Eur. = European Pharmacopeia; TS = Technical specification.

* Internal specification.

** LOQ: Endotoxins = 0.005 EU/mg.

Information on the composition of the novel food does not raise safety concerns.

2.4. Stability

The applicant performed stability tests on one batch of a human-identical milk oligosaccharides (HiMOs) mixture containing 2'-FL (47.7% w/w DM), 3-FL (15.1% w/w DM), LNT (24.7% w/w DM), 3'-SL sodium salt (4.3% w/w DM), 6'-SL sodium salt (5.6% w/w DM) and other carbohydrates (5.7% w/w DM). The tests were carried out at normal (25°C and 60% relative humidity (RH)) and accelerated (40°C and 75% RH) storage conditions for a period of 156 and 26 weeks, respectively. The samples were analysed for 3'-SL sodium salt and moisture content using the same methods applied for batch qualification.

Under normal storage conditions, the 3'-SL sodium salt content remained stable (average content of 5.4% w/w DM). Moisture content increased from 5.7 to 10.9% after 156 weeks, which exceeds the specification for moisture content ($\leq 9.0\%$). Under accelerated storage conditions, the 3'-SL sodium salt content remained stable (average content of 5.5% w/w DM). Moisture content increased from 5.7 to 9.9% after 26 weeks testing period, which also exceeds the specification for moisture content ($\leq 9.0\%$).

In light of the increase in the moisture content throughout the storage period, the applicant provided a microbiological analysis (total viable counts, yeast and mould) of three batches of the novel food and three batches of the above-mentioned HiMO mixture, stored under warehouse conditions for 25 months. Microbial levels were below the respective limits of detection and the moisture content was within the specification (average content of $8.7 \pm 1.2\%$ in the novel food and $6.6 \pm 1.2\%$ in the HiMO mixture).

The applicant provided sufficient stability data to confirm a shelf-life for the novel food of 1 year from the date of production when stored under ambient conditions.

Information on the stability of the novel food does not raise safety concerns.

2.5. Specification

The novel food (see [Table 4](#) for specification) is produced by microbial fermentation using two new genetically modified microorganisms as production strains derived from *E. coli* BL21 (DE3). Further isolation, purification and concentration steps yield a white- to ivory-coloured spray-dried powder.

Table 4. Specification of the novel food

Parameter	Specification	Method of Analysis
3'-Sialyllactose	≥ 88.0% w/w DM	HPAEC-PAD (internal validated method)
3'-Sialyllactulose	≤ 5.0% w/w DM	HPAEC-PAD (internal validated method) *
D-Lactose	≤ 5.0% w/w DM	HPAEC-PAD (internal validated method) *
Sialic acid	≤ 1.5% w/w DM	HPAEC-PAD (internal validated method) *
N-acetyl-D-glucosamine	≤ 1.0% w/w DM	HPAEC-PAD (internal validated method) *
Sum of other carbohydrates	≤ 5.0% w/w DM	Calculation **
Moisture	≤ 9.0 %	Karl-Fischer titration
Protein content	≤ 100 µg/g	Nanoquant (modified Bradford)
Ash	≤ 8.5 %	ASU L 06.00-4
Sodium	≤ 4.2 %	PV-347-ICP-MS: 2016-06 (ASU L 00.00-13)
Arsenic	≤ 0.2 mg/kg	ASU L 00.00-135: 2011-01 ICP-MS ***
Aflatoxin M1	≤ 0.025 µg/kg	DIN EN ISO 14501: 2008-01 IAC-HPLC-FD
Standard plate count	≤ 1,000 CFU/g	ISO 4833-2
Yeast	≤ 50 CFU/g	ISO 21527-2: 2008-07
Mould	≤ 50 CFU/g	ISO 21527-2: 2008-07
<i>Enterobacteriaceae</i>	≤ 10 CFU/g	ISO 21528-2: 2019-05
<i>Salmonella</i>	Absent in 25 g	DIN EN ISO 6579-1: 2017-07
<i>Cronobacter spp.</i>	Absent in 10 g	ISO/TS 22964: 2017-04
Endotoxins	≤ 10 EU/mg	Ph. Eur. 2.6.14

ASU = Official collection of analysis methods according to § 64 of the German Food and Feed Code (LFGB); DM = Dry matter; CFU = Colony forming unit; DIN = German Institute for Standardisation; EN = European norm; EU/mg = Endotoxin unit per milligram; HPAEC-PAD: High-performance anion-exchange chromatography – pulsed amperometric detection; IAC-HPLC-FD = Immunoaffinity chromatography – high-performance liquid chromatography – fluorescence detection; ICP-MS = Inductively coupled plasma – mass spectrometry; ISO = International Organisation for Standardisation; Ph. Eur. = European Pharmacopeia; TS = Technical specification. * LOQ: 3'-Sialyllactulose = 1.13% w/w DM; D-Lactose = 0.14% w/w DM; Sialic acid = 0.14% w/w DM; N-acetyl-D-glucosamine = 0.14% w/w DM; Ash = 0.01%; Aflatoxin M1 = 0.025 µg/kg; Endotoxins = 0.005 EU/mg; Protein = 10 µg/g.

** Sum of other carbohydrates (% w/w DM) = 100 (% w/w DM) – 3'-SL sodium salt (% w/w DM) – Quantified carbohydrates (% w/w DM) – Ash (% w/w DM).

*** LOD: Arsenic = 0.05 mg/kg.

Certification was provided to demonstrate that the contract laboratories were accredited to perform these analytical studies. Where in-house analysis was utilised, full methodology and supporting validation documentation was provided.

Information on the specification of the novel food does not raise safety concerns.

2.6. History of Use

Human milk contains a family of structurally related oligosaccharides known as human milk oligosaccharides (HMOs). 3'-SL sodium salt belongs to the sub-fraction of acidic HMOs. Unlike other HMOs, 3'-SL sodium salt concentration stays relatively constant over the course of lactation and is relatively consistent across different geographical regions. A review of published studies reporting levels of 3'-SL sodium salt in mothers' milk (Soyyilmaz et al., 2021) identified the mean of means and maximum mean for 3'-SL sodium salt as 0.19 g/L and 0.70 g/L, respectively.

Using these values and considering the average and high daily intake of breast milk (800 mL and 1,200 mL, respectively) for infants from 0 to 6 months (EFSA NDA Panel, 2013), the daily intake levels of 3'-SL sodium salt from human milk for a 6.7 kg body weight (bw) infant are 84 mg/kg bw/day (800 mL) and 125 mg/kg bw/day (1,200 mL).

The applicant has included in their submission to FSA/FSS a more recent review on HMO concentrations in human breast milk, which identified the mean of means and 90th percentile mean for 3'-SL sodium salt as 0.28 g/L and 0.49 g/L, respectively (Conze et al., 2022). In this case, the daily intake levels of 3'-SL sodium salt from human milk for a 6.7 kg bw infant are 59 mg/kg bw/day (800 mL) and 88 mg/kg bw/day (1,200 mL).

It is worth noting that EFSA has recently published a scientific and technical report on the evaluation of HiMOs as novel foods due to the increase in the number of authorisations (EFSA, 2024). A scoping literature review was outsourced to update the database of mean concentrations of single and total HMOs (including 3'-SL sodium salt) in human milk. The results of this report are discussed in section 2.7.

3'-SL sodium salt produced by fermentation using genetically modified *E. coli* K-12 DH1 (Glycom A/S, Denmark) is already authorised as a novel food in GB for use in infant formula (0.2 g/L) and follow-on formula, foods for infants and young children, foods for special medical purposes and food supplements (0.5 g/day for general population¹) (FSA, 2022).

3'-SL sodium salt produced by fermentation using genetically modified *E. coli* BL21 (DE3) has no history of use as a novel food in GB. A full authorisation is requested by the applicant since the production organism is different to the one currently authorised (*E. coli* K-12 DH1) and the recent assessment for *E. coli* NE03 (FSA and FSS, 2024).

¹ The use of 3'-SL sodium salt in food supplements for infants and young children is not authorised in the EU but has been assessed as safe by EFSA (EFSA NDA Panel, 2022).

In 2022, EFSA assessed the novel food produced by fermentation using genetically modified *E. coli* BL21 (DE3) for lower proposed use levels in the same categories and concluded in a positive opinion (EFSA NDA Panel, 2022). This novel food is currently authorised in the EU (Commission Implementing Regulation (EU) 2023/1582)² for the same intended food categories and intended use levels requested by the applicant without further assessment.

3'-SL sodium salt produced by fermentation using genetically modified *E. coli* BL21 (DE3) is Generally Regarded as Safe (GRAS) as a food ingredient for infant formula, follow-on formula and various food categories (GRN 921 – FDA, 2020; GRN 1015 – FDA, 2022). In addition, 3'-SL sodium salt produced by enzymatic synthesis (GRN 766 – FDA, 2019) or fermentation using genetically modified *E. coli* K-12 DH1 (GRN 880 – FDA, 2020) is GRAS as a food ingredient for infant formula, follow-on formula and various food categories.

2.7. Proposed Use and Anticipated Intake

In 2022, Conze *et al.* published a new review on the concentration of human milk oligosaccharides. The review by Conze *et al.* states a higher mean concentration of 3'-SL sodium salt in human milk than the previously reported one by e.g. Soyylmaz *et al.* (2021), used by EFSA for their assessment (EFSA NDA Panel, 2022).

A new application was submitted to the European Commission in February 2023 for this form of 3'-SL sodium salt produced by fermentation using genetically modified *E. coli* BL21 (DE3) with the aim to increase the use level of the novel food in infant formula from 0.23 g/L to 0.28 g/L and in food supplements for infants and young children from 0.23 g/day to 0.28 g/day. This was done to allow higher use levels in light of new data on the natural levels of 3'-SL sodium salt in human breast milk, as described by Conze *et al.* (2022).

This new application was not forwarded to EFSA by the European Commission for a safety assessment; the Commission acknowledged that the safety considerations of the proposed modifications of the use of 3'-SL sodium salt produced by fermentation using genetically modified *E. coli* BL21 (DE3) had already been addressed by the previously published EFSA opinion. Therefore, the higher use level of this novel food for infant formula (0.28 g/L) was approved in August 2023 (Commission Implementing Regulation (EU) 2023/1582) and it is the proposed use level by the applicant for authorisation in GB.

² The use of 3'-SL sodium salt in food supplements for infants and young children is not authorised in the EU but has been assessed as safe by EFSA (EFSA NDA Panel, 2022).

This safety assessment took account of EFSA's positive opinion on the novel food (including different proposed use levels and anticipated intake) as part of the evidence to support the conclusions of the FSA and FSS. The proposed use levels as sought by the applicant and evaluated in this assessment are those currently authorised in the EU (0.28 g 3'-SL sodium salt/L in infant formula).

The target population of the novel food is the general population. The intended food categories and proposed maximum use levels are listed in [Table 5](#), which are the same as those listed in assimilated Commission Implementing Regulation (EU) 2023/1582.

Table 5. Food Categories and proposed maximum use levels for 3'-SL sodium salt from the novel food

Food Category Name	Maximum Use Level
Infant formula, powder	224 mg/100g *
Infant formula, liquid	28 mg/100g
Follow-on formula, powder	224 mg/100g *
Follow-on formula, liquid	28 mg/100g
Cereals with an added high protein food which are reconstituted with water or other protein-free liquid	112 mg/100g *
Simple cereals which are reconstituted with milk or other appropriate nutritious liquids	196 mg/100g *
Cereals with an added high protein food reconstituted	28 mg/100g
Simple cereals for infants and children, reconstituted	28 mg/100g
Biscuits, rusks and cookies for children	28 mg/100g
Pasta for children (dry, to be cooked)	28 mg/100g
Ready-to-eat dairy-based meal for children	28 mg/100g
Special food for children's growth	28 mg/100g
Fruit and vegetable juices and nectars specific for infants and young children	28 mg/100g
Foods for special medical purposes	In accordance with the particular nutritional requirements of the persons for whom the products are intended
Food supplements ** for infants and young children	0.28 g/day
Food supplements ** for other children, adolescents and adults	0.7 g/day

* Relevant dilution factors (EFSA, 2018) have been used to calculate intake estimates.

** Food Supplements as defined in the Food Supplements (England) Regulations 2003, the Food Supplements (Wales) Regulations 2003 and the Food Supplements (Scotland) Regulations 2003.

The anticipated high intake for 3'-SL sodium salt in infants up to the age of 16 weeks is estimated to be 73 mg/kg bw/day, equivalent to 489 mg/day for a 6.7 kg infant. This value was calculated from the proposed use of 3'-SL sodium salt in infant formula (0.28 g/L) at a high consumption level of 260 mL/kg bw/day, as established by the EFSA Scientific Committee (EFSA SC, 2017). This value does not exceed the estimated high-level daily

intake for 3'-SL sodium salt of 125 mg/kg bw/day and 88 mg/kg bw/day in breastfed infants identified by Soyylmaz *et al.* (2021) and Conze *et al.* (2022), respectively.

An intake assessment using the summary statistics of consumption from the dietary surveys in the EFSA comprehensive database was conducted by matching the proposed conditions of use with the FoodEx2 categories. The estimated mean and 95th percentile intakes of 3'-SL sodium salt from the proposed conditions of use for each sub-population are presented in [Table 6](#).

Table 6. Estimated daily intake of 3'-SL sodium salt on a body weight basis from the proposed food uses

Population Group	Mean Intakes of 3'-SL Sodium Salt (mg/kg bw/day) *	95 th Percentile Intakes of 3'-SL Sodium Salt (mg/kg bw/day) *
Infants	6.5 – 28.4	24.2 – 61.9
Young children	0.4 – 9.4	3.8 – 23.5
Other children	0.0 – 0.4	0.0 – 3.1
Adolescents	0.0 – 0.1	0.0 – 0.8
Adults	0.0 – 0.0	0.0 – 0.2

Infants (≤ 11 months); young children (1 to < 3 years); other children (3 to < 10 years); adolescents (10 to < 18 years); adults (≥ 18 years) which includes pregnant and lactating women, elderly, and very elderly.

* The content of 3'-SL sodium salt in the novel food accounts for about 92.4%. Figures have been calculated considering a 100% purity, therefore resulting in a slightly overestimate of the actual intake.

The estimated daily intake of 3'-SL sodium salt from the intended uses and use levels does not exceed the estimated high-level daily intake for 3'-SL sodium salt of 125 mg/kg bw/day and 88 mg/kg bw/day in breastfed infants identified by Soyylmaz *et al.* (2021) and Conze *et al.* (2022), respectively.

The estimated intake for 3'-SL sodium salt in food supplements on a body weight basis for all population groups at the proposed use levels is presented in [Table 7](#).

Table 7. Estimated daily intake of 3'-SL sodium salt from food supplements on a body weight basis

Population Group	Proposed Use Level (g/day)	Mean Body Weight (kg) *	Estimated Intake (mg/kg bw/day) **
Infants	0.28	5.0	56
Young children	0.28	12.0	23
Other children	0.7	23.1	30
Young Adolescents	0.7	43.4	16
Older adolescents	0.7	61.3	11

Population Group	Proposed Use Level (g/day)	Mean Body Weight (kg) *	Estimated Intake (mg/kg bw/day) **
Adults	0.7	70.0	10

Infants (≤ 11 months); young children (1 to < 3 years); other children (3 to < 10 years); adolescents (10 to < 18 years); adults (≥ 18 years) which includes pregnant and lactating women, elderly, and very elderly.

* EFSA SC, 2012.

** Calculation: [Proposed Use Level (g/day) / Mean Body Weights] $\times$ 1,000.

The use level for 3'-SL sodium salt in food supplements is 0.28 g/day for infants and young children, and 0.7 g/day for all other population sub-groups. These estimated daily intake levels do not exceed the estimated high-level daily intake for 3'-SL sodium salt of 125 mg/kg bw/day and 88 mg/kg bw/day in breastfed infants identified by Soyylmaz *et al.* (2021) and Conze *et al.* (2022), respectively.

Food supplements are not intended to be used if other foods with the novel food are consumed on the same day. For infants and young children, food supplements are not intended to be used if breast milk or other foods with added 3'-SL sodium salt are consumed on the same day.

3'-SL sodium salt produced by another source, a genetically modified strain of *E. coli* K-12 DH1, is already authorised in GB. The combined daily intake of 3'-SL sodium salt from the authorised and proposed uses, for each population group from each EU dietary survey is shown in [Table 8](#).

Table 8. Estimated daily intake of 3'-SL sodium salt on a body weight basis from the authorised and proposed food at the maximum use levels

Population Group	Mean Intakes of 3'-SL Sodium Salt (mg/kg bw/day)	95 th Percentile Intakes of 3'-SL Sodium Salt (mg/kg bw/day)
Infants	10.4 – 51.9	26.5 – 105.3
Young children	7.0 – 23.1	16.8 – 78.2
Other children	2.7 – 8.2	5.6 – 14.8
Adolescents	0.5 – 3.2	2.0 – 7.5
Adults	0.4 – 1.7	1.4 – 4.1

Infants (≤ 11 months); young children (1 to < 3 years); other children (3 to < 10 years); adolescents (10 to < 18 years); adults (≥ 18 years) which includes pregnant and lactating women, elderly, and very elderly.

The estimated daily intake from authorised and intended uses for all population sub-groups does not exceed the estimated high-level daily intake for 3'-SL sodium salt of 125 mg/kg bw/day in breastfed infants identified by Soyylmaz *et al.* (2021). Only the estimated highest 95th percentile daily intake from authorised and intended uses for infants (105.3 mg/kg bw/day) is 1.2 times greater than the estimated high-level daily intake for 3'-SL sodium salt of 88 mg/kg bw/day in breastfed infants identified by Conze *et al.* (2022).

The estimated natural intakes are based on maximum mean concentrations noted across several studies and populations, and not on the highest individual values analytically determined. Therefore, infants may be naturally exposed to even higher HMO intakes. Gastrointestinal disorders are the most common adverse effect of high consumption of the novel food (Parschat et al., 2021). Given the natural exposure may be higher, and the calculation of exposure from the novel food is likely to be an over estimation, it was considered unlikely that there would be adverse effects of consuming the novel food at the proposed use levels.

It is also relevant that the highest mean daily intake of HMOs is considered as an upper end of an average natural intake rather than a health-based guidance value (HBGV). Therefore, a higher intake does not necessarily imply a safety concern (EFSA, 2024). Moreover, a scoping literature review recently outsourced by EFSA showed a revised highest mean daily 3'-SL sodium salt intake from human milk of 219 mg/kg bw/day (Malih et al., 2024). This is considerably higher than the estimated highest 95th percentile daily intake from authorised and intended uses of the novel food for infants.

Additional sources for the 3'-SL sodium salt contained in the novel food will be cow milk and milk-derived products. However, in comparison to the natural intake of 3'-SL sodium salt from human milk and the intake from the suggested uses and use levels of the novel food, the contribution from consumption of cow milk and milk-derived products is small.

It is worth noting that EFSA has recently published a scientific and technical report on the evaluation of HiMOs as novel foods due to the increase in the number of authorisations (EFSA, 2024). A scoping literature review was outsourced to update the database of mean concentrations of single and total HMOs (including 3'-SL) in human milk. Relevant HMO intakes were updated and compared with the estimated intakes for the most exposed population groups (i.e., infants and young children), considering the highest maximum use levels authorised in those food categories with the highest contribution to the overall HiMO intake (i.e., infant and follow-on formula, ready-to-eat meals, yoghurt and cow milk). The resulting highest 95th percentile daily HiMO intakes were unlikely to be higher than the highest mean daily HMO intakes. EFSA therefore concluded that currently there are no safety concerns resulting from the authorised HiMO intakes from their concurrent combined uses.

There is no concern with respect to the exposure to undesirable substances from the consumption of novel food at the proposed uses.

2.8. Absorption, Distribution, Metabolism and Excretion (ADME)

Most human milk oligosaccharides are reported to undergo limited oral absorption intact. Human milk oligosaccharides do not undergo significant digestion in the upper gastrointestinal tract but can undergo fermentation in the colon. Human milk oligosaccharides are predominantly excreted unchanged in the faeces, with a small proportion excreted unchanged in the urine.

The absorption of 3'-SL sodium salt from consumption of the novel food is not expected to differ from the intake of human milk oligosaccharides following infant consumption of breast milk. Therefore, this was not expected to pose a safety concern for infants or other age groups.

The ADME of human milk oligosaccharides are well understood and the information does not indicate any further areas of concern.

2.9. Nutritional information

The novel food is primarily composed of the oligosaccharide, 3'-SL sodium salt, which is structurally identical to the naturally occurring counterpart in human breast milk.

The novel food, being a sodium salt, may contribute to the daily sodium intake (maximum sodium content of 4.2% as per specification). EFSA has provided advice on levels of sodium intake that are considered safe and adequate for infants up to the age of 6 months consuming infant formula, older infants aged 7–11 months (EFSA NDA Panel, 2019b) and population groups aged 1 year and older (EFSA NDA Panel, 2019a).

For infants up to the age of 6 months consuming infant formula, the maximum sodium intake from the novel food would be approximately 21 mg/day considering a daily intake of infant formula of 260 mL/kg bw. This corresponds to about 18% of the daily sodium intake of breastfed infants (120 mg sodium/day).

For older infants aged 7–11 months, the maximum sodium intake from the novel food is estimated to be approximately 27 mg/day, which corresponds to about 14% of the established adequate intake (AI) of 200 mg/day.

For young children (1 to < 3 years), the intake of sodium is expected to represent up to 1.1% (up to 12 mg sodium/day) of the sodium intake of 1.1 g/day considered as safe and adequate.

For other children and adults, the intake of sodium from the novel food can represent up to 0.3% of the sodium intake levels and is considered safe and adequate for these age groups.

Overall, consumption of the novel food represents a minor contribution to the sodium levels in the diet.

The novel food contains up to 5.0% w/w DM of D-lactose. Therefore, there is a potential risk of adverse effects (e.g. abdominal pain, bloating, diarrhoea) for those consumers with lactose intolerance.

Consumption of the novel food at the proposed use levels is not expected to be nutritionally disadvantageous for consumers.

2.10. Toxicological information

The applicant provided a set of toxicological studies conducted on the novel food as supporting evidence to inform the interpretation of the natural exposure to 3'-SL sodium salt through breastmilk as an upper intake level. It is worth noting that Parschat *et al.* (2020) have summarised all the individual studies described in sections 2.10.1–2.10.3. No new toxicological concerns were raised.

2.10.1. Genotoxicity

In vitro genotoxicity testing of an HMO mix was conducted under Good Laboratory Practice (GLP) conditions and according to the following OECD guidelines: *in vitro* bacterial reverse mutation test (OECD TG 471) and *in vitro* mammalian cell micronucleus test (OECD TG 487). The HMO mix consisted of 2'-FL (47.1%), 3-FL (16.0%), LNT (23.7%), 3'-SL sodium salt (4.1%), 6'-SL sodium salt (4.0%) and other carbohydrates (5.1%).

The *in vitro* bacterial reverse mutation test (Spruth, 2018b [unpublished]) demonstrated that the HMO mix is non-mutagenic (up to 25 mg 3'-SL sodium salt/plate), in the absence or presence of metabolic activation. The *in vitro* mammalian cell micronucleus test (Spruth, 2018a [unpublished]) demonstrated that the HMO mix is non-clastogenic and non-aneugenic (up to 2.5 mg 3'-SL sodium salt/mL) in the absence or presence of metabolic activation. The results from these *in vitro* studies support the conclusion that the novel food is not genotoxic.

2.10.2. Sub-acute toxicity

A seven-day pilot feeding study (Leuschner, 2018 [unpublished]) was conducted under GLP conditions in two groups of five female rats fed either a standard diet or a standard diet plus 10% HMO mix *ad libitum* (the calculated intake of 3'-SL sodium salt ranged from 0.27 to 0.56 g/kg bw/day). No deaths or differences in clinical signs, food consumption or body weight were reported. The 10% HMO mix dose was chosen for the Repeated Dose 90-Day Oral Toxicity Study.

2.10.3. Sub-chronic toxicity

A Repeated Dose 90-Day Oral Toxicity Study in Rodents (Hansen, 2019 [unpublished]) was conducted under GLP conditions according to OECD TG 408 guidelines. Each group consisted of 10 female and 10 male rats which were fed a standard diet or a standard plus 10% HMO mix *ad libitum*.

There were no deaths, test item-related clinical abnormalities, or ocular changes. Episodes of decreased or increased food consumption were reported (male only). Statistically significant changes were observed in functional observation tests (male only) and a slight increase in body temperature was noted (female only). Variations in haematology (female only), clinical chemistry, urinalysis (female only), organ weights, and histopathology (male only) were observed. These changes were of low magnitude and/or limited to one sex and were not considered to be biologically relevant.

Therefore, the no observable adverse effect level (NOAEL) for the HMO mix was 6,320 mg/kg bw/day, which is equivalent to 260 mg/kg bw/day for 3'-SL sodium salt.

Additionally, the applicant provided two publications where the toxicological evaluation of enzymatically synthesised 3'-SL sodium salt has been described (Kim et al., 2018; Phipps et al., 2019). Both sets of data provide supplementary data to support the safety of the novel food in the context of the consumption of the substance in the diet of breastfed infants.

2.10.4. Human studies

The applicant provided a clinical study report (Parschat et al., 2021) corresponding to a double-blind, controlled, randomised interventional study conducted in infants with infant formula containing 5.75 g/L of an HMO mix (2.99 g/L 2'-FL, 0.75 g/L 3-FL, 1.5 g/L LNT, 0.23 g/L 3'-SL, 0.28 g/L 6'-SL) produced by the applicant. The main goal of the study was to investigate the suitability of the HMO mix in comparison with standard infant formula and breastfed infants.

No statistically significant differences in body weight, length or head circumference gain were observed between the two formula groups. The formula supplemented with the HMO mix was considered non-inferior to the control formula with respect to mean daily body weight gain. Total incidence of adverse effects and serious adverse effects were comparable across all three groups. Therefore, addition of the HMO mix to infant formula was considered safe and well-tolerated for healthy term infants at the concentration tested.

2.11. Allergenicity

The protein content in the novel food is low ($\leq 0.01\%$). The applicant provided evidence for the absence of viable cells of production and optional degradation strains in the novel food.

The potential allergenicity of the introduced proteins expressed in *E. coli* BL21 (DE3) (Allergen Online tool, version 19 – University of Nebraska) was assessed using the 'higher than 35% identity in a sliding window of 80 amino acids' as the criterion (EFSA GMO Panel, 2010). None of the proteins were predicted to be an allergen.

The likelihood that the novel food will trigger allergic reactions in the target population under the proposed conditions of use was considered to be low.

3. Discussion

The novel food is a purified white- to ivory-coloured spray-dried powder primarily composed of 3'-SL sodium salt. D-lactose, 3'-sialyllactulose, sialic acid, N-acetyl-D-glucosamine and a small fraction of other related saccharides are also present. The novel food is manufactured by microbial fermentation using two new strains of genetically modified *E. coli* BL21 (DE3), a production strain and an optional degradation strain.

The target population is the general population. The novel food is intended to be added in a variety of foods, including infant formula and follow-on formula, foods for infants and young children, foods for special medical purposes and food supplements.

3'-SL sodium salt is a naturally occurring oligosaccharide present in human milk. The history of human exposure to 3'-SL sodium salt concerns breastfed infants; however, consumption of 3'-SL sodium salt is expected to be safe for other population groups.

3'-SL sodium salt produced by genetically modified *E. coli* BL21 (DE3) has previously been assessed by EFSA and received a positive opinion (EFSA NDA Panel, 2022). On the basis of the information provided by the applicant and assessed by FSA and FSS, the new production and degradation strains derived from *E. coli* BL21 (DE3) did not raise any safety concerns.

The toxicology studies did not raise any safety concerns. No adverse effects were observed in the Repeated Dose 90-Day Oral Toxicity Study in Rodents and the NOAEL for 3'-SL sodium salt was reported as 260 mg/kg bw/day. This along with the known safe human exposure to the novel food in breastmilk were considered in evaluating the novel foods safety for the UK population.

The estimated high-level intakes of 3'-SL sodium salt by children up to 16 weeks of age consuming infant formula only, and from the intended food uses at their respective maximum use levels in all population groups, do not exceed the highest daily intake level of 3'-SL sodium salt in breastfed infants on a body weight basis.

The combined high-level intake of 3'-SL sodium salt from authorised and intended food uses does not exceed the highest daily intake level of 3'-SL sodium salt in breastfed infants on a body weight basis identified by Soyylmaz *et al.* (2021). Only the estimated highest 95th percentile daily intake from authorised and intended uses for infants is 1.2 times greater than the highest daily intake level of 3'-SL sodium salt in breastfed infants on a body weight basis identified by Conze *et al.* (2022). This could lead to the potential for mild gastrointestinal disorders in infants. However, these estimated natural intakes are based on maximum mean concentrations noted across several studies and populations, and not on the highest individual values analytically determined. Therefore, infants may be naturally exposed to even higher HMO intakes.

The maximum daily intake of 3'-SL sodium salt in food supplements is 0.28 g/day for infants and young children, and 0.7 g/day for the general population. These levels do not exceed the highest intake level of 3'-SL sodium salt in breastfed infants on a body weight basis. Food supplements are not intended to be used if other foods with added 3'-SL sodium salt (as well as human milk for infants and young children) are consumed on the same day.

The novel food, being a sodium salt, may contribute to the daily sodium intake. However, the maximum sodium intake from 3'-SL sodium salt does not exceed the daily sodium intake considered safe and adequate by EFSA for all population sub-groups.

Consumption of the novel food under the proposed conditions of use is not expected to be a safety concern because of the limited absorption of human milk oligosaccharides, the absence of adverse effects reported in the toxicology studies, and the fact that breastfed infants are naturally exposed to these substances at levels consistent with those found in the novel food.

4. Conclusions

The FSA and FSS have undertaken the assessment of 3'-SL sodium salt and concluded that the novel food is safe under the proposed conditions of use and does not pose a safety risk to human health. The anticipated intake levels and the proposed use was not considered to be nutritionally disadvantageous.

These conclusions were based on the information in the novel food dossier submitted by the applicant plus the supplementary information and could not have been reached without the following data claimed as proprietary by the applicant.

The annexes and section of the dossier considering:

- GMM Description JBT-3'-SL
- Deposition Number
- PCR Validation JBT-3SL
- PCR Validation JBT-DS-SL
- Validation report 3'-SL HPAEC-PAD
- Valid report by prod HPAEC-PAD
- Clinical Study Report
- 90 Day Oral Tox Study HMOMi
- Bacterial Reverse Mutation Test
- in vitro Micronucleus test
- 7-day pilot toxicological study
- Validation Repots qPCR GeneCon

Abbreviations

Abbreviation	Definition
2'-FL	2'-fucosyllactose
3'-FL	3'-fucosyllactose
3'-SL	3'-Sialyllactose
6'-SL	6'-Sialyllactose
ADME	Absorption, Distribution, Metabolism and Excretion
AI	Adequate Intake
ASU	Official collection of analysis methods according to § 64 of the German Food and Feed Code
BW	Body Weight
CAS	Chemical Abstracts Service
CFU	Colony Forming Unit
CID	Collision Induced Decay
COSY	Correlated Spectroscopy
DEPT	Distortionless Enhancement by Polarisation Transfer
DIN	German Institute for Standardisation e. V
DM	Dry Matter
EC	European Commission
EFSA	European Food Safety Authority

Abbreviation	Definition
EN	European Norm
ESI	Electrospray Ionisation
EU	European Union
EU/mg	Endotoxin Unit per Milligram
FD	Fluorescence Detection
FDA	Food and Drug Administration
FSA	Food Standards Agency
FSS	Food Standards Scotland
GB	Great Britain
GLP	Good Laboratory Practice
GMM	Genetically Modified Microorganism
GRAS	Generally Regarded as Safe
GRN	GRAS Notification
HBGV	Health-Based Guidance Value
HiMO	Human-Identical Milk Oligosaccharide
HMBC	Heteronuclear Multiple Bond Correlation
HMO	Human Milk Oligosaccharide
HPAEC	High-Performance Anion-Exchange Chromatography
HPLC	High-Performance Liquid Chromatography
HSE	Health and Safety Executive
HSQC	Heteronuclear Single Quantum Correlation
IAC	Immunoaffinity Chromatography
ICP	Inductively Coupled Plasma
ISO	International Organisation for Standardisation
LFGB	German Food and Feed Code
LNT	Lacto-N-tetraose
LOD	Limit of Detection
LOQ	Limit of Quantification
MRM	Multiple Reaction Monitoring
MS	Mass Spectrometry
NDA	Nutrition, Novel Foods and Food Allergens
NMR	Nuclear Magnetic Resonance
NOAEL	No Observable Adverse Effect Level
OECD	Organisation for Economic Co-operation and Development
PAD	Pulsed Amperometric Detection
Ph. Eur.	European Pharmacopeia
TOCSY	Total Correlated Spectroscopy
TS	Technical Specification
RP	Regulated Product
SC	Scientific Committee
UK	United Kingdom

Article updated on April 04, 2025 to include additional information after the conclusion.

Updated 19/06/26 to correct value of Molecular Mass within Section 2.1

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