COMMISSION IMPLEMENTING REGULATION (EU) 2023/948

of 12 May 2023

authorising the placing on the market of 6′-Sialyllactose sodium salt produced by derivative strains of *Escherichia coli* BL21(DE3) as a novel food and amending Implementing Regulation (EU) 2017/2470

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 ([1]), and in particular Article 12(1) thereof,

Whereas:

(1) Regulation (EU) 2015/2283 provides that only novel foods authorised and included in the Union list of novel foods may be placed on the market within the Union.

(2) Pursuant to Article 8 of Regulation (EU) 2015/2283 Commission Implementing Regulation (EU) 2017/2470 ([2]) has established a Union list of novel foods.

(3) Commission Implementing Regulation (EU) 2021/82 ([3]) authorised the placing on the Union market of 6′-Sialyllactose sodium salt obtained by microbial fermentation using the genetically modified *Escherichia coli* strain K12 DH1 as a novel food under Regulation (EU) 2015/2283.

(4) On 15 May 2020, the company Chr. Hansen A/S ('the applicant') submitted an application for an authorisation to the Commission in accordance with Article 10(1) of Regulation (EU) 2015/2283 to place 6′-Sialyllactose ('6′-SL') sodium salt, obtained by microbial fermentation using two genetically modified strains (a production strain and an optional degradation strain) derived from the host strain *Escherichia coli* BL21(DE3), on the Union market as a novel food. The applicant requested for 6′-SL sodium salt so produced to be used in infant formula and follow-on formula as defined in Regulation (EU) No 609/2013 of the European Parliament and of the Council ([4]), processed cereal-based food for infants and young children and baby food for infants and young children as defined in Regulation

([1]) OJ L 327, 11.12.2015, p. 1.

([2]) 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 (OJ L 351, 30.12.2017, p. 72).

([3]) Commission Implementing Regulation (EU) 2021/82 of 27 January 2021 authorising the placing on the market of 6'-sialyllactose sodium salt as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commission Implementing Regulation (EU) 2017/2470 (OJ L 29, 28.1.2021, p. 16).

([4]) Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009 (OJ L 181, 29.6.2013, p. 35).

(EU) No 609/2013, foods for infants and young children for special medical purposes as defined in Regulation (EU) No 609/2013, foods for special medical purposes as defined in Regulation (EU) No 609/2013 excluding foods for infants and young children, in milk-based drinks and similar products intended for young children, and in food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council ([5]) intended for the general population. Subsequently, on 9 December 2022, the applicant modified the initial request in the application on the use of 6′-SL sodium salt produced with the derivative strains of *Escherichia coli* BL21(DE3) in food supplements to exclude infants and young children. The applicant also proposed that food supplements containing 6′-SL sodium salt produced with the derivative strains of *Escherichia coli* BL21(DE3) should not be consumed if other foods with added 6′-SL sodium salt are consumed the same day.

(5) On 15 May 2020, the applicant also made a request to the Commission for the protection of proprietary scientific studies and data, namely, mass spectrometry ('MS'), nuclear magnetic resonance ('NMR') and a high-performance anion-exchange chromatography with pulsed amperometric detection ('HPAEC-PAD') method validation and the results for the determination of the identity of 6′-SL and of the carbohydrate by-products present in the novel food ([6]); a description ([7]) and certificates of deposition ([8]) of the genetically modified 6′-SL sodium salt production and optional degradation strains; real time quantitative polymerase chain reaction ('qPCR') system and method validation reports for the genetically modified 6′-SL sodium salt production and optional degradation strains ([9]); a bacterial reverse mutation test with 6′-SL sodium salt ([10]); an *in vitro* mammalian cell micronucleus test with 6′-SL sodium salt ([11]); a 7-day dose range finding oral toxicity study in rats with 6′-SL sodium salt ([12]); and, a 90-day oral toxicity study in rats with 6′-SL sodium salt ([13]), submitted in support of the application.

(6) In accordance with Article 10(3) of Regulation (EU) 2015/2283, on 11 December 2020, the Commission requested the European Food Safety Authority ('the Authority') to carry out an assessment of 6′-SL sodium salt obtained by microbial fermentation using two genetically modified strains (a production strain and an optional degradation strain) derived from the host strain *Escherichia coli* BL21(DE3), as a novel food.

(7) On 26 October 2022, the Authority adopted its scientific opinion on the 'Safety of 6′-sialyllactose sodium salt produced by derivative strains of *Escherichia coli* BL21 (DE3) as a novel food pursuant to Regulation (EU) 2015/2283' ([14]) in accordance with the requirements of Article 11 of Regulation (EU) 2015/2283.

(8) In its scientific opinion, the Authority concluded that 6′-SL sodium salt is safe under the proposed conditions of use and for the proposed target populations. Therefore, that scientific opinion gives sufficient grounds to establish that 6′-SL sodium salt produced with the derivative strains of *Escherichia coli* BL21 (DE3), when used in infant formula and follow-on formula as defined in Regulation (EU) No 609/2013, processed cereal-based food for infants and young children and baby food for infants and young children as defined in Regulation (EU) No 609/2013, foods for infants and young children for special medical purposes as defined in Regulation (EU) No 609/2013, foods for special medical purposes as defined in Regulation (EU) No 609/2013 excluding foods for infants and young

([5]) Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements (OJ L 183, 12.7.2002, p. 51).
([6]) Chr. Hansen 2018 and 2021 (unpublished).
([7]) Chr. Hansen 2021 (unpublished).
([8]) Chr. Hansen 2020 and 2021 (unpublished).
([9]) Chr. Hansen 2014 and 2021 (unpublished).
([10]) Chr. Hansen 2018 (unpublished) and Parschat K., Oehme A., Leuschner J., Jennewein S., and Parkot J. 2020. A safety evaluation of mixed human milk oligosaccharides in rats. Food and Chemical Toxicology, 136, 111118.
([11]) Chr. Hansen 2018 (unpublished) and Parschat K., Oehme A., Leuschner J., Jennewein S., and Parkot J. 2020. A safety evaluation of mixed human milk oligosaccharides in rats. Food and Chemical Toxicology, 136, 111118.
([12]) Chr. Hansen 2018 and 2021 (unpublished) and Parschat K., Oehme A., Leuschner J., Jennewein S., and Parkot J. 2020. A safety evaluation of mixed human milk oligosaccharides in rats. Food and Chemical Toxicology, 136, 111118.
([13]) Chr. Hansen 2019 and 2021 (unpublished) and Parschat K., Oehme A., Leuschner J., Jennewein S., and Parkot J. 2020. A safety evaluation of mixed human milk oligosaccharides in rats. Food and Chemical Toxicology, 136, 111118.
([14]) *EFSA Journal* 2022;20(12):7645.

children, in milk-based drinks and similar products intended for young children, and in food supplements as defined in Directive 2002/46/EC, complies with the authorisation requirements of Article 12(1) of Regulation (EU) 2015/2283.

(9) In its scientific opinion, the Authority noted that its conclusion on the safety of the novel food was based on scientific studies and data from the mass spectrometry ('MS'), nuclear magnetic resonance ('NMR') and a high-performance anion-exchange chromatography with pulsed amperometric detection ('HPAEC-PAD') method validation and the results for the determination of the identity of 6′-SL and of the carbohydrate by-products present in the novel food; the description and certificates of deposition of the genetically modified 6′-SL sodium salt production and optional degradation strains; the real time quantitative polymerase chain reaction ('qPCR') system and method validation reports for the genetically modified 6′-SL sodium salt production and optional degradation strains; the bacterial reverse mutation test with 6′-SL sodium salt; the *in vitro* mammalian cell micronucleus test with 6′-SL sodium salt; the 7-day dose range finding oral toxicity study in rats with 6′-SL sodium salt; and, the 90-day oral toxicity study in rats with 6′-SL sodium salt, contained in the applicant's file, without which it could not have assessed the novel food and reached its conclusion.

(10) The Commission requested the applicant to further clarify the justification provided with regard to their proprietary claim over those scientific studies and data, and to clarify their claim to an exclusive right of reference to them in accordance with Article 26(2)(b) of Regulation (EU) 2015/2283.

(11) The applicant declared that they held proprietary and exclusive rights of reference to the scientific studies and data submitted in support of the application, namely, mass spectrometry ('MS'), nuclear magnetic resonance ('NMR') and a high-performance anion-exchange chromatography with pulsed amperometric detection ('HPAEC-PAD') method validation and the results for the determination of the identity of 6′-SL and of the carbohydrate by-products present in the novel food; the description and certificates of deposition of the genetically modified 6′-SL sodium salt production and optional degradation strains; the real time quantitative polymerase chain reaction ('qPCR') system and method validation reports for the genetically modified 6′-SL sodium salt production and optional degradation strains; the bacterial reverse mutation test with 6′-SL sodium salt; the *in vitro* mammalian cell micronucleus test with 6′-SL sodium salt; the 7-day dose range finding oral toxicity study in rats with 6′-SL sodium salt; and, the 90-day oral toxicity study in rats with 6′-SL sodium salt, under national law at the time they submitted the application and that third parties cannot lawfully access, use or refer to those data and studies.

(12) The Commission assessed all the information provided by the applicant and considered that the applicant has sufficiently substantiated the fulfilment of the requirements laid down in Article 26(2) of Regulation (EU) 2015/2283. Therefore, the scientific studies and data submitted in support of the application, namely, mass spectrometry ('MS'), nuclear magnetic resonance ('NMR') and a high-performance anion-exchange chromatography with pulsed amperometric detection ('HPAEC-PAD') method validation and the results for the determination of the identity of 6′-SL and of the carbohydrate by-products present in the novel food; the description and certificates of deposition of the genetically modified 6′-SL sodium salt production and optional degradation strains; the real time quantitative polymerase chain reaction ('qPCR') system and method validation reports for the genetically modified 6′-SL sodium salt production and optional degradation strains; the bacterial reverse mutation test with 6′-SL sodium salt; the *in vitro* mammalian cell micronucleus test with 6′-SL sodium salt; the 7-day dose range finding oral toxicity study in rats with 6′-SL sodium salt; and, the 90-day oral toxicity study in rats with 6′-SL sodium salt, should be protected in accordance with Article 27(1) of Regulation (EU) 2015/2283. Accordingly, only the applicant should be authorised to place 6′-SL sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) on the market within the Union during a period of five years from the entry into force of this Regulation.

(13) However, restricting the authorisation of 6′-SL sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) and the reference to the scientific studies and data contained in the applicant's file for the sole use by them does not prevent subsequent applicants from applying for an authorisation to place on the market the same novel food provided that their application is based on legally obtained information supporting such an authorisation.

(14) In line with the conditions of use of food supplements containing 6′-SL sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3), as proposed by the applicant, it is necessary to inform consumers by appropriate labelling that food supplements containing 6′-SL sodium salt should not be consumed by infants and children under 3 years of age and should not be used if other foods with added 6′-SL sodium salt are consumed the same day.

(15) It is appropriate that the inclusion of 6′-SL sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) as a novel food in the Union list of novel foods contains also the required conditions of use, specifications and other information related to its authorisation, as referred to in Article 9(3) of Regulation (EU) 2015/2283.

(16) 6′-SL sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) should be included in the Union list of novel foods set out in Implementing Regulation (EU) 2017/2470. The Annex to Implementing Regulation (EU) 2017/2470 should therefore be amended accordingly.

(17) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

1. 6′-Sialyllactose sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) is authorised to be placed on the market within the Union.

6′-Sialyllactose sodium salt produced with derivative strains of *Escherichia coli* BL21(DE3) shall be included in the Union list of novel foods set out in Implementing Regulation (EU) 2017/2470.

2. The Annex to Implementing Regulation (EU) 2017/2470 is amended in accordance with the Annex to this Regulation.

Article 2

Only the company Chr. Hansen A/S ([15]) is authorised to place on the market within the Union the novel food referred to in Article 1, for a period of five years from 4 June 2023, unless a subsequent applicant obtains an authorisation for that novel food without reference to the scientific data protected pursuant to Article 3 or with the agreement of Chr. Hansen A/S.

Article 3

The scientific data contained in the application file and fulfilling the conditions laid down in Article 26(2) of Regulation (EU) 2015/2283 shall not be used for the benefit of a subsequent applicant for a period of five years from the date of entry into force of this Regulation without the agreement of Chr. Hansen A/S.

Article 4

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

([15]) Address: Bøge Allé 10-12, 2970 Hørsholm, Denmark.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 12 May 2023.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX

The Annex to Implementing Regulation (EU) 2017/2470 is amended as follows:

(1) in Table 1 (Authorised novel foods), the following entry is inserted in alphabetical order:

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements	Data Protection
'6'-Sialyllactose ('6′-SL') sodium salt (produced by derivative strains of *E. coli* BL21(DE3))	*Specified food category*	*Maximum levels*	The designation of the novel food on the labelling of the foodstuffs containing it shall be '6′-Sialyllactose sodium salt'. The labelling of food supplements containing 6′-Sialyllactose (6′-SL) sodium salt shall bear a statement that (a) they should not be consumed by children under 3 years of age; (b) they should not be consumed if other foods containing added 6′-sialyllactose sodium salt are consumed the same day.		Authorised on 4 June 2023. This inclusion is based on proprietary scientific evidence and scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283. Applicant: "Chr. Hansen A/S", Bøge Allé 10-12, 2970 Hoersholm, Denmark. During the period of data protection, the novel food 6′-Sialyllactose sodium salt is authorised for placing on the market within the Union only by Chr. Hansen A/S unless a subsequent applicant obtains authorisation for the novel food without reference to the proprietary scientific evidence or scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283 or with the agreement of "Chr. Hansen A/S". End date of the data protection: 4 June 2028.'
	Infant formula as defined under Regulation (EU) No 609/2013	0,70 g/L in the final product ready for use, marketed as such or reconstituted as instructed by the manufacturer			
	Follow-on formula as defined under Regulation (EU) No 609/2013	0,70 g/L in the final product ready for use, marketed as such or reconstituted as instructed by the manufacturer			
	Processed cereal-based foods for infants and young children and baby foods for infants and young children as defined under Regulation (EU) No 609/2013	0,70 g/L or 0,70 g/kg in the final product ready for use, marketed as such or reconstituted as instructed by the manufacturer			
	Milk based drinks and similar products intended for young children	0,70 g/L in the final product ready for use, marketed as such or reconstituted as instructed by the manufacturer			
	Foods for special medical purposes for infants and young children as defined under Regulation (EU) No 609/2013	In accordance with the particular nutritional requirements of the infants and young children for whom the products are intended but in any case not higher than 0,70 g/L or 0,70 g/kg in the final product ready for use, marketed as such or reconstituted as instructed by the manufacturer.			

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements	Data Protection
	Foods for special medical purposes as defined under Regulation (EU) No 609/2013 excluding foods for infants and young children	In accordance with the particular nutritional requirements of the persons for whom the products are intended			
	Food Supplements as defined in Directive 2002/46/EC, for the general population, excluding infants and young children	1,8 g/day			

(2) in Table 2 (Specifications), the following entry is inserted in alphabetical order:

Authorised novel food	Specification
'6'-**Sialyllactose ('6'-SL') sodium salt (produced by derivative strains of *E. coli* BL21(DE3))**	**Description:** 6'-Sialyllactose (6′-SL) sodium salt is a purified, white to off-white powder or agglomerate produced by a microbial process and contains limited levels of lactose, 6'-sialyl-lactulose, and sialic acid. **Definition:** Chemical name: N-Acetyl-α-D-neuraminyl-(2→6)-β-D-galactopyranosyl-(1→4)-D-glucose, sodium salt Chemical formula: $C_{23}H_{38}NO_{19}Na$ Molecular mass: 655,53 Da CAS No: 157574-76-0 **Source:** Two genetically modified strains (a production strain and an optional degradation strain) of *Escherichia coli* BL21(DE3) **Characteristics/Composition:** 6′-Sialyllactose sodium salt (% of dry matter): ≥ 90,0 % (w/w) 6′-Sialyl-lactulose (% of dry matter): ≤ 3,0 % (w/w) D-Lactose (% of dry matter): ≤ 5,0 % (w/w) Sialic acid (% of dry matter): ≤ 2,0 % (w/w) N-acetyl-D-glucosamine (% of dry matter): ≤ 3,0 % (w/w) Sum of other carbohydrates (% of dry matter)[a]: ≤ 5,0 % (w/w) Moisture: ≤ 9,0 % (w/w) Ash: ≤ 8,5 % (w/w) Residual protein: ≤ 0,01 % (w/w)

Authorised novel food	Specification
	Sodium: ≤ 4,2 % (w/w) **Contaminants:** Arsenic: ≤ 0,2 (mg/kg) Aflatoxin M1: ≤ 0,025 (µg/kg) **Microbiological criteria:** Standard plate count: ≤ 1 000 CFU/g Enterobacteriaceae: ≤ 10 CFU/g *Salmonella* spp.: Absence in 25 g Yeast and mould: ≤ 100 CFU/g *Cronobacter spp*.: Absence in 10 g Residual endotoxins: ≤ 10 EU/mg [a] Sum of other carbohydrates = 100 (% (w/w) of dry matter) – 6'-Sialyllactose sodium salt (% (w/w) of dry matter) – quantified carbohydrates (% (w/w) of dry matter) – Ash (% (w/w) of dry matter); CFU: Colony Forming Units; EU: Endotoxin Units'