

**COMMISSION IMPLEMENTING REGULATION (EU) 2023/1583****of 1 August 2023****amending Implementing Regulation (EU) 2017/2470 as regards the specifications of the novel food  
Lacto-N-neotetraose (microbial source)****(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 <sup>(1)</sup>, and in particular Article 12 thereof,

Whereas:

- (1) Regulation (EU) 2015/2283 provides that only novel foods authorised and included in the Union list 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 <sup>(2)</sup> has established a Union list of authorised novel foods.
- (3) Commission Implementing Decision (EU) 2016/375 <sup>(3)</sup> authorised, in accordance with Regulation (EC) No 258/97 of the European Parliament and of the Council <sup>(4)</sup>, the placing on the market of chemically synthesized Lacto-N-neotetraose as a novel food ingredient.
- (4) Pursuant to Article 5 of Regulation (EC) No 258/97, on 1 September 2016, the company Glycom A/S informed the Commission of its intention to place on the market Lacto-N-neotetraose of microbial source produced with genetically modified *Escherichia coli* strain K-12 as a novel food ingredient. Lacto-N-neotetraose of microbial origin produced with genetically modified *Escherichia coli* strain K-12 was included in the Union list of novel foods on the basis of that notification when the Union list was established.
- (5) Commission Implementing Regulation (EU) 2019/1314 <sup>(5)</sup> amended the specifications of the novel food Lacto-N-neotetraose (microbial source) produced with genetically modified *Escherichia coli* strain K-12.
- (6) Commission Implementing Regulation (EU) 2021/912 <sup>(6)</sup> amended the specifications of the novel food Lacto-N-neotetraose (microbial source) to allow Lacto-N-neotetraose produced by the combined activity of the genetically modified strains PS-LNnT-JBT and DS-LNnT-JBT derived from *Escherichia coli* strain BL21(DE3) to be placed on the market under the same conditions of use as the ones previously authorised for Lacto-N-neotetraose.

<sup>(1)</sup> OJ L 327, 11.12.2015, p. 1.

<sup>(2)</sup> 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).

<sup>(3)</sup> Commission Implementing Decision (EU) 2016/375 of 11 March 2016 authorising the placing on the market of Lacto-N-neotetraose as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council (OJ L 70, 16.3.2016, p. 22).

<sup>(4)</sup> Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients (OJ L 43, 14.2.1997, p. 1).

<sup>(5)</sup> Commission Implementing Regulation (EU) 2019/1314 of 2 August 2019 authorising the change of the specifications of the novel food Lacto-N-neotetraose produced with *Escherichia coli* K-12 under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commission Implementing Regulation (EU) 2017/2470 (OJ L 205, 5.8.2019, p. 4).

<sup>(6)</sup> Commission Implementing Regulation (EU) 2021/912 of 4 June 2021 authorising changes in the specifications of the novel food Lacto-N-neotetraose (microbial source) and amending Implementing Regulation (EU) 2017/2470 (OJ L 199, 7.6.2021, p. 10).

- (7) On 15 November 2022, the company Chr. Hansen A/S ('the applicant') submitted an application to the Commission in accordance with Article 10(1) of Regulation (EU) 2015/2283 for a change of the specifications of Lacto-N-neotetraose (microbial source) produced by the combined activity of the derivative strains PS-LNnT-JBT and DS-LNnT-JBT of *Escherichia coli* strain BL21(DE3). The applicant requested for the reference to the specific genetically modified derivative strains PS-LNnT-JBT and DS-LNnT-JBT of *Escherichia coli* BL21(DE3) used to produce Lacto-N-neotetraose (microbial source) to be replaced by the generic mention of both strains. In addition the applicant requested a change in the specifications of Lacto-N-neotetraose (microbial source) so that it can be produced using authorised derivative strains of *Escherichia coli* K-12 and/or of *Escherichia coli* BL21(DE3) rather than the current limitation of using either the authorised derivative strain of *Escherichia coli* K-12 or the authorised derivative strains of *Escherichia coli* BL21(DE3).
- (8) The applicant justified the request for the proposed changes in the specifications of Lacto-N-neotetraose (microbial source) to replace the specific mention of PS-LNnT-JBT and DS-LNnT-JBT of *Escherichia coli* strain BL21(DE3) by a more generic mention of production and optional degradation strains as being a more accurate way to describe the respective functions of the two strains in the production process as assessed <sup>(7)</sup> by the European Food Safety Authority ('the Authority'), and as a means to allow for more flexibility to the applicant and other food business operators to use authorised derivatives of *Escherichia coli* strain BL21(DE3) in line with their respective functions rather than limiting their production to the specific derivative strains PS-LNnT-JBT and DS-LNnT-JBT. In addition, in the applicant's view this modification would also align the authorised specifications of Lacto-N-neotetraose produced with derivative strains of *Escherichia coli* strain BL21(DE3) to the authorised specifications of other novel foods produced with production and optional degradation derivative strains of *Escherichia coli* BL21(D3) in which specific derivative strains are not mentioned. The applicant also justified the request to allow use of combinations of authorised derivative strains of the *Escherichia coli* strains, namely *Escherichia coli* K-12 and/or *Escherichia coli* BL21(DE3) as an additional means to allow for flexibility to the applicant and other food business operators to use authorised derivative strains of *Escherichia coli* in the production of Lacto-N-neotetraose.
- (9) The Commission considers that the requested update of the Union list concerning the change of the specifications of Lacto-N-neotetraose proposed by the applicant, is not liable to have an effect on human health and that a safety evaluation by the Authority in accordance with Article 10(3) of Regulation (EU) 2015/2283 is not necessary. The parent *Escherichia coli* strains BL21(DE3) and K-12 and their genetically modified derivative strains used in the production of Lacto-N-neotetraose have been positively assessed by the Authority <sup>(8)</sup> and in the context of a notification pursuant to Article 5 of Regulation (EC) No 258/97, respectively. Their use in the production of Lacto-N-neotetraose with or without the additional use of the optional degradation derivative strain of *Escherichia coli* strain BL21(DE3) will produce Lacto-N-neotetraose in line with the authorised specifications, and consequently will not affect the safety profile of the authorised novel food.
- (10) The information provided in the application and the above Opinion of the Authority give sufficient grounds to establish that the changes to the specifications of Lacto-N-neotetraose (microbial source), are in accordance with the conditions of Article 12 of Regulation (EU) 2015/2283 and should be approved.
- (11) The Annex to Implementing Regulation (EU) 2017/2470 should therefore be amended accordingly.
- (12) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

<sup>(7)</sup> EFSA Journal 2020;18(11):6305.

<sup>(8)</sup> EFSA Journal 2020;18(11):6305.

HAS ADOPTED THIS REGULATION:

*Article 1*

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

*Article 2*

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

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

Done at Brussels, 1 August 2023.

*For the Commission*  
*The President*  
Ursula VON DER LEYEN

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In the Annex to Implementing Regulation (EU) 2017/2470, in Table 2 (Specifications), the entry for Lacto-*N*-neotetraose (microbial source) is replaced by the following:

<b>Lacto-<i>N</i>-neotetraose (microbial source)</b>	<p><b>Definition</b>            Chemical name: <math>\beta</math>-D-Galactopyranosyl-(1 <math>\rightarrow</math> 4)-2-acetamido-2-deoxy-<math>\beta</math>-D-glucopyranosyl-(1 <math>\rightarrow</math> 3)-<math>\beta</math>-D-galactopyranosyl-(1 <math>\rightarrow</math> 4)-D-glucopyranose            Chemical formula: C<sub>26</sub>H<sub>45</sub>NO<sub>21</sub>            CAS No: 13007-32-4            Molecular weight: 707,63 g/mol</p> <p><b>Description/Source</b>            Lacto-<i>N</i>-neotetraose is a white to off-white powder that is produced by a microbiological process using genetically modified strain of <i>Escherichia coli</i> K-12, and/or of <i>Escherichia coli</i> BL21(DE3). An additional optional genetically modified degradation strain of <i>Escherichia coli</i> BL21(DE3) may be used in the production process to degrade intermediate carbohydrate by-products and remaining starting carbohydrate substrates.</p> <p><b>Purity</b>            Assay (water free): <math>\geq</math> 80 %            D-Lactose: <math>\leq</math> 10,0 %            Lacto-<i>N</i>-triose II: <math>\leq</math> 3,0 %  <i>para</i>-Lacto-<i>N</i>-neohexaose: <math>\leq</math> 5,0 %            Lacto-<i>N</i>-neotetraose fructose isomer: <math>\leq</math> 1,0 %            Sum of saccharides (Lacto-<i>N</i>-neotetraose, D-Lactose, Lacto-<i>N</i>-triose II, <i>para</i>-Lacto-<i>N</i>-neohexaose, Lacto-<i>N</i>-neotetraose fructose isomer): <math>\geq</math> 92 % (% w/w dry matter)            pH (20 °C, 5 % solution): 4,0-7,0            Water: <math>\leq</math> 9,0 %            Ash, sulphated: <math>\leq</math> 1,0 %            Residual solvents (methanol): <math>\leq</math> 100 mg/kg            Residual proteins: <math>\leq</math> 0,01 %</p> <p><b>Microbiological criteria</b>            Aerobic mesophilic bacteria total count: <math>\leq</math> 500 CFU/g            Yeasts and moulds: <math>\leq</math> 50 CFU/g            Residual endotoxins: <math>\leq</math> 10 EU/mg            CFU: Colony Forming Units; EU: Endotoxin Units'</p>
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