

# Safety of isomaltulose syrup (dried) as a novel food pursuant to Regulation (EU) 2015/2283

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## Abstract

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver an opinion on isomaltulose syrup (dried) as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF consists of a mixture of mono- and disaccharides in powder form, mainly composed of isomaltulose ( $\geq 75\%$ ) and trehalulose ( $< 13\%$ ). The applicant intends to use the NF as a replacement for sucrose already on the market. The information provided on the manufacturing process, composition and specifications of the NF is sufficient and does not raise safety concerns. No absorption, distribution, metabolism and excretion (ADME) or toxicological data were provided for the NF. Instead, the safety of the NF was assessed based on literature data available on isomaltulose and mixtures of isomaltulose and trehalulose. In addition, considering the nature, compositional characterisation and production process of the NF, the Panel considered that such data were sufficient to conclude that the NF is as safe as sucrose.

## KEYWORDS

isomaltulose, isomaltulose syrup, novel foods, trehalulose

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## 1 | INTRODUCTION

### 1.1 | Background and Terms of Reference as provided by the requestor

On 30 April 2018, the company Evonik Creavis GmbH submitted a request to the European Commission in accordance with Article 10 of Regulation (EU) No 2015/2283<sup>1</sup> to place Isomaltulose syrup (dried) on the Union market as a novel food.

The novel food is intended for use in foods for the general population.

In accordance with Article 10(3) of Regulation (EU) 2015/2283, the European Commission asks the European Food Safety Authority to provide a scientific opinion on Isomaltulose syrup (dried).

## 2 | DATA AND METHODOLOGIES

### 2.1 | Data

The safety assessment of this NF is based on data supplied in the application and information submitted by the applicant following several EFSA requests for supplementary information. During the assessment, the Panel identified additional pertinent data which were not included in the application.

Administrative and scientific requirements for NF applications referred to in Article 10 of Regulation (EU) 2015/2283 are listed in Commission Implementing Regulation (EU) 2017/2469.<sup>2</sup>

A common and structured format on the presentation of NF applications is described in the EFSA guidance on the preparation and presentation of a NF application (EFSA NDA Panel, 2016). As indicated in this guidance, it is the duty of the applicant to provide all of the available (proprietary, confidential and published) scientific data (including both data in favour and not in favour) that are pertinent to the safety of the NF.

This NF application does not include a request for the protection of proprietary data.

### 2.2 | Methodologies

The assessment follows the methodology set out in the EFSA guidance on NF applications (EFSA NDA Panel, 2016) and the principles described in the relevant existing guidance documents from the EFSA Scientific Committee. The legal provisions for the assessment are laid down in Article 11 of Regulation (EU) 2015/2283 and in Article 7 of Commission Implementing Regulation (EU) 2017/2469.

Additional information which was not included in the application was retrieved by literature search following a search strategy and standard operating procedure as described by UCT Prague (Dibusz & Vejvodova, 2020).

This assessment concerns only the risks that might be associated with consumption of the NF under the proposed conditions of use and is not an assessment of the efficacy of the NF with regard to any claimed benefit.

## 3 | ASSESSMENT

### 3.1 | Introduction

The NF which is the subject of the application is isomaltulose syrup (dried), a mixture of carbohydrates mainly composed of isomaltulose ( $\geq 75\%$  dry matter). The NF is produced by enzymatic isomerisation of sucrose, and is a white crystalline powder proposed to be used as a replacement of sucrose in products on the market targeted to the general population. According to Article 3.2(a) of NF regulation (EU) 2015/2283, the NF falls under category (i), i.e. 'food with a new or intentionally modified molecular structure, where that structure was not used as, or in, a food within the Union before 15 May 1997'.

### 3.2 | Identity of the NF

The NF which is the subject of the application is a powder with less than 7% water. The dry matter content is a mixture of mono- and disaccharides, mainly composed of isomaltulose ( $\geq 75\%$ ) and trehalulose ( $\leq 13\%$ ) and, to a minor extent, glucose, fructose, sucrose and oligosaccharides (traces), as demonstrated by high-performance liquid chromatography/pulsed amperometric detection (HPLC/PAD) by comparison with authentic specimens.

<sup>1</sup>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>2</sup>Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. OJ L 351, 30.12.2017, pp. 64–71.

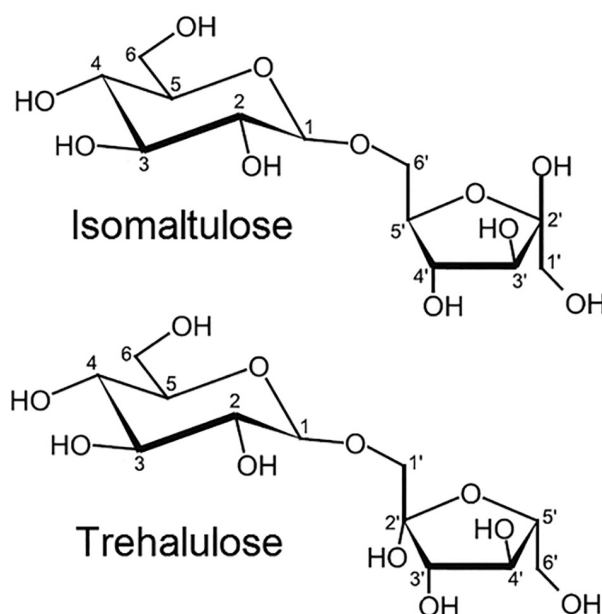
Isomaltulose is a reducing disaccharide and a structural isomer of sucrose. It is composed of a glucose and a fructose moiety linked through an  $\alpha$ -1,6-glycosidic bond. Trehalulose is also a reducing disaccharide and a structural isomer of sucrose, composed of a unit of glucose and a unit of fructose linked through an  $\alpha$ -1,1-glycosidic bond (Tables 1 and 2, Figure 1).

**TABLE 1** Chemical identity of isomaltulose.

Chemical substance	
Chemical (IUPAC) name	$\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 6)-D-fructofuranose
Common name	Isomaltulose
Synonyms, trade names, abbreviations	Palatinose, Lylose
CAS number	13718-94-0
Molecular formula	$C_{12}H_{22}O_{11}$
Molecular weight	342.30 g/mol

**TABLE 2** Chemical identity of trehalulose.

Chemical substance	
Chemical (IUPAC) name	$\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 1)-D-fructofuranose
Common name	Trehalulose
CAS number	51411-23-5
Molecular formula	$C_{12}H_{22}O_{11}$
Molecular weight	342.30 g/mol



**FIGURE 1** Chemical representation of isomaltulose and trehalulose.<sup>3</sup>

### 3.3 | Production process

According to the information provided, the NF is produced in line with Good Manufacturing Practice (GMP) and Hazard Analysis Critical Control Points (HACCP) principles.

The NF is produced by enzymatic isomerisation of sucrose conducted by the intracellular enzyme sucrose isomerase (EC 5.4.99.11). The isomerisation is followed by purification and concentration steps.

#### 3.3.1 | Enzymatic preparation

The biocatalyst sucrose isomerase is present in cells of *Serratia (S.) plymuthica* (G731). This microorganism was obtained from the culture collection 'Centraalbureau voor Schimmelcultures', the Netherlands and originally deposited as *Protaminobacter rubrum* CBS 574.77. The cells are immobilised in a matrix of calcium alginate.

<sup>3</sup>Figure adapted from Xu et al. (2013), <https://doi.org/10.1371/journal.pone.0074788>

The taxonomic identity of the production strain was unambiguously demonstrated at species level by NCBI BLAST analysis, by comparison of the complete genome sequence of the production strain with available sequences in the NCBI database for strains belonging to known species. NCBI BLAST percentages of identity of 97.44% and 99.76% were obtained, respectively, for *S. plymuthica* type strain NCTC 12961 and all three *S. plymuthica* AS12, AS13 and AS9 strains (Neupane, Finlay, Alström, et al., 2012; Neupane, Finlay, Kyrpides, et al., 2012; Neupane, Högberg, Alström, et al., 2012). The absence of acquired antimicrobial resistance genes, toxigenicity and pathogenicity traits in the production strain *S. plymuthica* (G731) was demonstrated according to EFSA FEEDAP Panel (2018) and EFSA (2021) procedures and criteria.

The absence of viable cells from the production strain *S. plymuthica* (G731) in the NF was demonstrated according to EFSA FEEDAP Panel (2018) criteria.

### 3.3.2 | Sucrose isomerisation

An aqueous sucrose solution (30%–45%) is passed through a column packed with beadlets of calcium alginate and *S. plymuthica* (G731). The enzyme sucrose isomerase present in the column catalyses the isomerisation of sucrose to isomaltulose by changing the glycosidic linkage from  $\alpha$ -D-glucopyranosyl-(12)- $\beta$ -D-fructofuranose to  $\alpha$ -D-glucopyranosyl-D-(1,6)-fructofuranose. In addition to the isomerisation to isomaltulose, other mono-, di- and oligosaccharides are formed in smaller amounts and some sucrose remains unmodified. Such a process is known to generally yield about 80%–85% of isomaltulose (Rose, 2002).

### 3.3.3 | Purification and concentration

The eluate of the column is heat-treated for sterilisation and passed through two ion-exchange columns fit for use in food production, charged with cation and anion exchange resins respectively. To obtain the NF, the solution is further concentrated by evaporation and vacuum dried to reduce the water content of the eluate. The final product is a white colourless powder with a water content  $\leq 7\%$ .

The Panel notes that the production process described by the applicant is that of a pilot plant. Current plans to upscale the production process include replacing the batch process to continuous fixed-bed reactor using immobilised cells at room temperature for 12 h. The remaining steps would not change. Any upscale will include an appropriate range of tests that assure that the purity criteria for the authorised product with respect to composition, impurities and microbial contamination (including absence of viable cells of the production strain) will be met. The Panel considers that the upscaling would not lead to any safety concern, provided that the NF complies with the specifications.

## 3.4 | Compositional data

The NF is a mixture of carbohydrates, as demonstrated by HPLC/PAD by comparison with authentic specimens. In order to confirm that the manufacturing process is reproducible and adequate to produce a product with certain characteristics, the applicant initially provided analytical information for five independent batches of the NF. Considering shortcomings identified by the Panel in this first batch-to-batch analysis, the applicant provided a new set of analysis for three newly produced batches of the NF (Table 3).

Information was provided on the accreditation of the laboratories that conducted the analyses presented in the application.

Considering that the NF is exclusively produced from sucrose, the NF is expected to consist of monosaccharides, disaccharides and traces of oligosaccharides, which is confirmed by the batch-to-batch analysis. The isomaltulose content of the NF ranges between 77% and 84% of the dry matter (DM), and trehalulose is identified as a significant secondary compound (around 12% DM of the NF). The other saccharides do not exceed 2.6% DM (fructose), 2.1% DM (glucose) and 1.0% DM (sucrose).

**TABLE 3** Batch-to-batch analysis of the NF.

Parameter (unit)	Batch number			Method of analysis
	#1	#2	#3	
<b>Proximate analysis</b>				
Proteins (g/100 g)	<0.1	<0.1	<0.1	Kjeldahl (N×6.25)
Ash (g/100 g)	<0.05	<0.05	<0.05	Gravimetric
Water content (g/100 g)	5.7	5.7	5.9	Karl Fisher 2014 (rev.0)
<b>Saccharides (g/100 g dry matter)</b>				
Isomaltulose	77.3	82.3	83.8	HPLC-PAD
Trehalulose	12.3	11.9	12.5	HPLC-PAD
Glucose	2.05	2.04	1.95	HPLC-PAD
Fructose	2.57	2.61	2.53	HPLC-PAD
Sucrose	0.916	0.919	0.981	HPLC-PAD
Other minor saccharides	<0.05	<0.05	<0.05	HPLC-PAD
<b>Metals (mg/kg)</b>				
Arsenic	<0.005	<0.005	<0.005	05 (ICP-MS) 2018 rev.3
Cadmium	<0.005	<0.005	<0.005	05 (ICP-MS) 2018 rev.3
Mercury	<0.005	<0.005	<0.005	05 (ICP-MS) 2018 rev.3
Nickel	0.067	0.025	0.034	05 (ICP-MS) 2018 rev.3
Lead	<0.005	<0.005	0.019	05 (ICP-MS) 2018 rev.3
<b>Microbiology<sup>a</sup></b>				
Yeast (CFU/g)	<10	<10	<10	ISO 21527-1 & ISO 21527-2
Mould (CFU/g)	<10	<10	<10	ISO 21527-1 & ISO 21527-2
<i>Listeria monocytogenes</i> (in 25 g)	ND	ND	ND	ISO 11290-1
Presumptive <i>Bacillus cereus</i> (CFU/g)	<10	<10	<10	ISO 7932
<i>Clostridium perfringens</i> (CFU/g)	<10	<10	<10	ISO 7937
<i>Escherichia coli</i> (CFU/g)	<10	<10	<10	ISO 16649-2
<i>Salmonella</i> spp. (in 25 g)	ND	ND	ND	ISO 6579-1
Coagulase-positive staphylococci (CFU/g)	<10	<10	<10	ISO 6888-1

Abbreviations: CFU, colony forming units; HPLC-PAD, high-performance liquid chromatography/pulsed amperometric detection; ICP-MS, inductively coupled plasma mass spectrometry; ISO, International Organization for Standardization; ND, not detected.

<sup>a</sup>Total viable count available in Table 4.

The Panel considers that the information provided on the composition of the NF is sufficient and does not raise safety concerns.

### 3.4.1 | Stability

The applicant carried out stability tests with four trial batches of the NF. The tests were carried out after production and after a period of 12 months upon EFSA request, under normal storage conditions (25°C, 50%–60% relative humidity). Of note is that analyses at both timepoints were carried out in different laboratories. Analyses were carried out for microbiological content and for the respective concentrations of different sugars (isomaltulose, trehalulose, glucose, fructose, sucrose), several oligosaccharides and microbiological parameters. A summary of the results is reported in Table 4.

According to the applicant, the observed variation of the content of isomaltulose and trehalulose is possibly due to the lack of a final mixing step which will be carried out when production is performed on a commercial scale.

The Panel considers that the data provide sufficient information with respect to the stability of the NF for 12 months.

**TABLE 4** Stability tests.

Parameter	Unit	Batch number								Method
		#4		#5		#6		#7		
		0	12	0	12	0	12	0	12	
Water content	g/100 g	6.3	5.28	5.8	5.38	8.2	5.62	9.1	5.52	ISO 760, Karl Fischer
<b>Microbiology</b>										
Total viable count	CFU/g	NA	< 10	NA	40	< 10	< 10	NA	< 10	DIN EN ISO 4833-1
Yeast		NA	< 10	< 10	< 10	< 10	< 10	NA	< 10	ISO-21527-2 and/or 1
Moulds		NA	20	60–70	< 10	< 10	< 10	NA	< 10	ISO-21527-2 and/or 1
Enterobacteriaceae		NA	< 10	NA	< 10	< 10	< 10	NA	< 10	DIN EN ISO 21528-2
<i>E. coli</i>		NA	< 10	< 10	< 10	< 10	< 10	NA	< 10	ISO 14649-2
Coagulase-positive staphylococci		NA	< 10	< 10	< 10	< 10	< 10	NA	< 10	ISO 6888-1 or 2
Presumptive <i>B. cereus</i>		NA	< 10	< 10	< 10	< 10	< 10	NA	< 10	(DIN EN) ISO 7932
Spores of sulfite-reducing bacteria growing under anaerobic conditions (incl. Clostridia)		NA	< 10	NA	< 10	< 10	< 10	NA	< 10	ISO 15213
<i>C. perfringens</i>		NA	< 10	< 10	< 10	< 10	< 10	NA	< 10	(DIN EN) ISO 7937
<i>Salmonella</i> spp.	in 25 g	NA	n.d.	n.d.	n.d.	n.d.	n.d.	NA	n.d.	ISO 6579-1
<i>L. monocytogenes</i>		NA	n.d.	n.d.	n.d.	n.d.	n.d.	NA	n.d.	Bio-Rad AL Short protocol + Rapid L mono or ISO 11290-2
<b>Saccharides</b>										
Isomaltulose	g/100 g DM <sup>a</sup>	77.3	78.9	86.7	82.9	75.6	82.2	76.9	76.0	HPLC-PAD
Trehalulose		10.8	8.4	10.6	9.9	8.95	10.1	9.51	9.5	HPLC-PAD
Glucose		1.64	1.34	1.88	1.84	1.59	1.81	1.62	1.65	HPLC-PAD
Fructose		1.68	1.10	1.97	1.82	1.76	1.54	1.80	1.50	HPLC-PAD
Sucrose		0.62	0.53	1.67	1.96	0.91	1.03	1.46	1.45	HPLC-PAD
Oligosaccharides <sup>b</sup>		< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	< LOQ	HPLC-PAD
<b>Metals</b>										
Arsenic	mg/kg	NA	NA	< LOQ	NA	< LOQ	NA	< LOQ	NA	ICP-MS
Cadmium		NA	NA	< LOQ	NA	< LOQ	NA	< LOQ	NA	ICP-MS
Mercury		NA	NA	< LOQ	NA	< LOQ	NA	< LOQ	NA	ICP-MS
Nickel		NA	NA	< LOQ	NA	< LOQ	NA	0.005	NA	ICP-MS
Lead		NA	NA	< LOQ	NA	< LOQ	NA	< LOQ	NA	ICP-MS

Abbreviations: CFU, colony forming units; DIN, Deutsches Institut für Normung; DM, dry matter; EN, Europäische Norm; ISO, International Organization for Standardization; LOQ, limit of quantification; NA, not analysed; n.d., not detected.

<sup>a</sup>Values at month 12 were converted from g/100 g to g/100 g DM.

<sup>b</sup>Each oligosaccharide below the respective LOQs: 0.005 g/100 g for maltotriose, maltotetraose, maltopentaose, maltohexaose, malto-heptaose, malto-octaose, malto-nonaose, malto-decaose; 0.10 g/100 g for isomaltotriose, raffinose and stachyose (analysed at T12 only).



### 3.5 | Specifications

The specifications of the NF as proposed by the applicant are indicated in [Table 5](#).

**TABLE 5** Specifications of the NF.

<b>Description:</b> Isomaltulose syrup (dried) is a white to yellowish powder produced from sucrose by a microbiological process using <i>Serratia plymuthica</i>	
<b>Parameter</b>	<b>Specification</b>
Isomaltulose (% DM)	≥ 75
Trehalulose (% DM)	≤ 13
Glucose (% DM)	≤ 3
Fructose (% DM)	≤ 4
Sucrose (% DM)	≤ 5
Moisture (%)	≤ 7
Ash (%)	≤ 0.05
Protein (%)	< 0.1
Lead (mg/kg)	< 0.1
<b>Microbial parameters</b>	
TAMC (CFU/g)	< 100
TYMC (CFU/g)	< 100
<i>E. coli</i> (CFU/g)	< 10
Enterobacteriaceae (CFU/g)	< 100
<i>Salmonella</i>	n.d. in 25 g

Abbreviations: CFU, colony forming units; DM, dry matter; TAMC, total aerobic microbial count; TYMC, total yeast and mould count.

The Panel considers that the information provided on the specifications of the NF is sufficient and does not raise safety concerns.

### 3.6 | History of use of the NF and/or of its source

#### 3.6.1 | History of use of the source

The NF is obtained by isomerisation of the common sugar sucrose, which is a disaccharide composed of glucose and fructose naturally produced in plants.

#### 3.6.2 | History of use of the NF

##### 3.6.2.1 | *Isomaltulose*

Isomaltulose is a naturally occurring substance, which is present at low concentrations in cane sugar and honey, also known by the common names palatinose and lylose. Isomaltulose (> 98%) was assessed in 2004 by the United Kingdom Food Standards Agency (UK FSA) and the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR). Based on these initial assessments, isomaltulose was authorised as a novel food ingredient in non-specified amounts in Commission Decisions 2005/457/EC and 2005/581/EC, respectively.

Isomaltulose has a history of use in different areas worldwide, e.g. USA, Argentina, Australia and New Zealand, Korea and has been approved as a food additive in China (std. GB 1886.182–2016).

##### 3.6.2.2 | *Trehalulose*

Trehalulose, the second most abundant carbohydrate in the NF, was identified as a major component of honey from stingless bee species across neotropical and Indo-Australian regions (13–44 g/100 g honey) (Fletcher et al., 2020; Hungerford et al., 2021; Popova et al., 2021; Zawawi et al., 2022).

##### 3.6.2.3 | *Isomaltulose syrup*

The NF was assessed in the United States and was given generally considered as safe (GRAS) status (GRN. 00681) in 2017.

In 2017, the NF was assessed by the Food Safety Authority of Ireland (FSAI) for eligibility to an equivalence opinion with the EU-authorised isomaltulose. Initial discussions with the applicant explored the possibility of achieving a substantial

equivalence opinion with isomaltulose already authorised as novel food by Commission Decisions 2005/457/EC and 2005/581/EC. Although no safety concerns were identified, such an approach was not feasible due to the categorisation as novel food and was recommended for a full evaluation as novel food under (EC) Regulation 258/97.<sup>4</sup>

### 3.7 | Proposed uses and use levels and anticipated intake

#### 3.7.1 | Target population

The target population proposed by the applicant is the general population.

#### 3.7.2 | Proposed uses and use levels

The applicant intends to market the NF as a replacement for sucrose already on the market. No food categories were specified. The applicant does not intend to make use of the NF in infant and follow-on formulae (as per Commission Delegated Regulation (EU) 2016/127<sup>5</sup>), and/or in processed cereal-based foods, and/or baby foods for infants and young children (as per Commission Directive 2006/125/EC<sup>6</sup>).

#### 3.7.3 | Anticipated intake of the NF

The NF is intended to be used as a replacement for sucrose. In a worse-case scenario approach, the Panel assumed that all added sugars would be replaced by the NF. The Panel assimilated the daily intake of the NF to that of added sugars as recently assessed by EFSA as shown in Tables 6 and 7 (EFSA NDA Panel, 2022).

**TABLE 6** Daily intakes of added sugars across EU dietary surveys by population group expressed in g/day – females.<sup>b</sup>

Population group, age range ( <i>n</i> surveys)	Added sugars (g/day)			
	Mean		P95 <sup>a</sup>	
	Min <sup>b</sup>	Max <sup>b</sup>	Min <sup>b</sup>	Max <sup>b</sup>
Infants, ≥ 4 to < 12 months ( <i>n</i> = 13)	1	14	4	35
Toddlers, ≥ 12 months to < 36 months ( <i>n</i> = 16)	8	39	21	89
Other children, ≥ 3 to < 10 years ( <i>n</i> = 19)	22	67	49	120
Adolescents, ≥ 10 to < 14 years ( <i>n</i> = 19)	25	77	59	145
Adolescents (≥ 14 to < 18 years; <i>n</i> = 17)	21	68	58	145
Adults, ≥ 18 to < 65 years ( <i>n</i> = 22)	19	51	50	125
Elderly, ≥ 65 years ( <i>n</i> = 21)	13	43	43	95
Pregnant women ( <i>n</i> = 5)	25	44	66	92
Lactating women ( <i>n</i> = 2)	27	43	60	98

<sup>a</sup>The 95th percentile estimates obtained from dietary surveys and age classes with fewer than 60 subjects may not be statistically robust (Merten et al., 2011) and consequently were not considered in this table.

<sup>b</sup>Minimum (min) and maximum (max) means and 95th percentiles across EU surveys, for each age class.

<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.

<sup>5</sup>Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding.

<sup>6</sup>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.

**TABLE 7** Daily intakes of added sugars across EU dietary surveys by population group expressed in g/day – males.<sup>b</sup>

Population group, age range (n surveys)	Added sugars (g/day)			
	Mean		P95 <sup>a</sup>	
	Min <sup>b</sup>	Max <sup>b</sup>	Min <sup>b</sup>	Max <sup>b</sup>
Infants, ≥ 4 to < 12 months (n = 13)	1	14	8	35
Toddlers, ≥ 12 months to < 36 months (n = 16)	10	45	27	92
Other children, ≥ 3 to < 10 years (n = 19)	23	74	46	139
Adolescents, ≥ 10 to < 14 years (n = 19)	22	92	72	178
Adolescents (≥ 14 to < 18 years; n = 17)	30	96	77	174
Adults, ≥ 18 to < 65 years (n = 22)	24	67	70	163
Elderly, ≥ 65 years (n = 21)	11	51	43	131

<sup>a</sup>The 95th percentile estimates obtained from dietary surveys and age classes with fewer than 60 subjects may not be statistically robust (Merten et al., 2011) and consequently were not considered in this table.

<sup>b</sup>Minimum (min) and maximum (max) means and 95th percentiles across EU surveys, for each age class.

### 3.7.4 | Precautions and restrictions of use

In their assessment, Food Standards Australia New Zealand (FSANZ, 2007) noted that '*individuals with hereditary fructose intolerance (HFI) should completely avoid the intake of any fructose containing foods or foods that yield fructose upon digestion, such as sucrose and isomaltulose*'. The Panel concurs with that judgement.

## 3.8 | Absorption, distribution, metabolism and excretion (ADME)

The Panel notes that no ADME data have been provided for the NF per se. The applicant referred to literature data on the main component of the NF, isomaltulose, and to its previous assessment by the UK FSA (UK FSA, 2004). EFSA completed this information with a literature search update for isomaltulose for years 2017 to 2023, and a literature search on the second principal component of the NF, trehalulose.

### 3.8.1 | Isomaltulose

The hydrolysis of isomaltulose to equal parts of glucose and fructose is catalysed by the sucrase-isomaltase complex present in the intestinal mucosa. Results of studies conducted in both animals and humans indicate that isomaltulose is hydrolysed at a rate 4 to 5 times slower than that of sucrose and is almost completely absorbed in the small intestine. Subsequent to the hydrolysis, glucose is rapidly absorbed by an active process, while fructose is transported through the brush-border membrane. Upon absorption, glucose and fructose are transported to the liver where they enter well-characterised carbohydrate metabolic pathways and are subsequently distributed to all tissues (UK FSA, 2004). Data from 2017 onwards corroborating these previous conclusions are described below.

#### 3.8.1.1 | *In vitro* studies

Hwang et al. (2018) demonstrated that isomaltulose was hydrolysed *in vitro* by small intestinal enzymes only at about one-third the rate of sucrose. The small intestinal enzyme solution contained maltase, sucrase, isomaltase and glucoamylase, with specific activities of 0.70, 0.34, 0.20 and 0.45 U/mL, respectively.

Using a similar enzymatic preparation, a Japanese research group reported an inhibitory action of isomaltulose on the hydrolytic activity of  $\alpha$ -glucosidases in the small intestine *in vitro* (Kashimura et al., 2008). The same group showed an inhibitory effect of isomaltulose on glucose absorption in the everted rat gut model (Kashimura & Nagai, 2007b).

#### 3.8.1.2 | *Rodent studies*

In both rat and mice models, acute intakes of isomaltulose resulted in similar or lower postprandial plasma glucose and insulin concentrations compared to an equivalent amount of sucrose (Keyhani-Nejad et al., 2015; Tonouchi et al., 2011). After prolonged dietary interventions with diets containing isomaltulose or sucrose, plasma glucose and insulin maxima were consistently reached slightly later in isomaltulose than in sucrose-fed rats (Haberer et al., 2009; Hwang et al., 2018; Keyhani-Nejad et al., 2015).

The Panel notes that absorption was not measured per se: the slower absorption rate of isomaltulose compared to sucrose is indirectly concluded from postprandial glucose and insulin concentrations.

### 3.8.1.3 | Human studies

In a study on 10 healthy subjects having undergone colectomy, isomaltulose was found to be absorbed irrespective of the nature of the food (beverage or solid food). Apparent digestibility of 50 g isomaltulose from two different test meals was 95.5% and 98.8%, and apparent absorption was 93.6% and 96.1% (Holub et al., 2010).

Numerous clinical trials investigating the glycaemic and insulinemic response to isomaltulose ingestion confirm absorption in healthy humans. Due to a slower rate of hydrolysis in the small intestine subjects display attenuated increases in serum glucose and insulin concentrations in comparison to similar treatments with sucrose (Achten et al., 2007; Dye et al., 2010; Okuno et al., 2010; Suraphad et al., 2015; van Can et al., 2009), dextrans (Arai et al., 2007), high glycaemic sugar mixtures (Kahlhofer et al., 2016). Similar observations were reported in type-1 (Bracken et al., 2012; West et al., 2011) and type-2 (Ang & Linn, 2014) diabetic patients, as well as overweight subjects (Konig et al., 2012; Suklaew et al., 2015), or subjects with impaired glucose tolerance (Oizumi et al., 2007). Since absorption in the small intestine is almost complete, total exposure to glucose is comparable to that achieved with sucrose.

### 3.8.2 | Trehalulose

As a sucrose isomer, trehalulose is expected to be hydrolysed to glucose and fructose by the isomaltase-sucrase complex in the small intestine. In an ex vivo intestinal homogenates and brush-border membranes model from Wistar rats, trehalulose hydrolysis was observed along the small intestine, with highest activity in the jejunum. Hydrolysis displayed a Michaelis constant ( $K_m$ ) of 3.03 mM and a maximum velocity ( $V_{max}$ ) of 38.8  $\mu\text{M}/\text{mg protein}/\text{h}$ , as opposed to 3.57 mM and 89.2  $\mu\text{M}/\text{mg protein}/\text{h}$  for isomaltulose and 1.59 mM and 349  $\mu\text{M}/\text{mg protein}/\text{h}$  for sucrose (Yamada et al., 1985).

Using the isolated everted intestinal segment model in the rat, Tsuji et al. (1986) demonstrated that trehalulose presented a hydrolysing activity ( $3.03 \pm 0.19$   $\mu\text{mol-glucose-released}/\text{mg protein per hour}$ ) lower than that of sucrose ( $4.15 \pm 0.39$   $\mu\text{mol-glucose-released}/\text{mg protein per hour}$ ). In the same study, the hydrolysing activity of isomaltulose was reported to be  $0.98 \pm 0.05$   $\mu\text{mol-glucose-released}/\text{mg protein per hour}$ .

Ziesenitz (1986) used eight homogenates of jejunal mucosa segments obtained from deceased persons with healthy bowels to study hydrolysis of various disaccharides. In comparison to maltose ( $K_m$  9 mM,  $V_{max}$  900 nmol/min  $\times$  1 mg protein), the hydrolysis velocity for trehalulose was 15% ( $K_m$  21 mM,  $V_{max}$  136 nmol/min  $\times$  1 g protein), and that of isomaltulose was 8% ( $K_m$  9 mM,  $V_{max}$  73 nmol/min  $\times$  1 mg protein).

## 3.9 | Nutritional information

Given the fate of isomaltulose and trehalulose in the gastrointestinal tract and given that the NF is otherwise composed of small amounts of glucose, fructose and sucrose, the NF is calorically-equivalent to isomaltulose as already authorised novel food and to sucrose.

The Panel considers that, taking into account the composition of the NF and the proposed conditions of use, the consumption of the NF is not nutritionally disadvantageous.

## 3.10 | Toxicological information

No toxicological studies were provided on the NF as intended to be put on the market. The Panel notes that the safety of isomaltulose alone has been established when approval was sought for its use as novel food in the European Union and other countries.

Additionally, the applicant carried out a comprehensive literature search on the potential toxicity of isomaltulose, considering available studies in animals and humans published between the initial assessment of the UK FSA until April 8, 2016. EFSA completed the literature search for years 2017 to 2023. Only two studies investigated the effects of isomaltulose syrup, containing both isomaltulose and trehalulose, from other manufacturers (Lim et al., 1997; Yamaguchi et al., 1987). In addition, EFSA carried out a literature search for trehalulose alone, which is a significant component of the NF.

All the information retrieved considered useful to the safety assessment of the NF is described below.

### 3.10.1 | Genotoxicity

The Panel notes that the applicant did not provide genotoxicity tests on the NF as intended to be put on the market.

#### 3.10.1.1 | Isomaltulose

Data included in previous safety assessments demonstrate no mutagenic or clastogenic effect of isomaltulose. Baek et al. (1997) carried out a bacterial reverse mutation test in *Salmonella Typhimurium* (TA1535, TA1537, TA98, TA100) with isomaltulose and isomaltulose syrup from another manufacturer at concentrations up to 10,000  $\mu\text{g}/\text{plate}$ , with or without S9

mix, and did not observe mutagenicity. Additionally, no clastogenicity was observed in an in vitro chromosomal aberration test with isomaltulose and isomaltulose syrup at 0, 1.25, 2.5, 5 mg/mL with or without S9 mix in Chinese Hamster Lung cells.

#### 3.10.1.2 | *Trehalulose*

The applicant did not provide data regarding the genotoxic potential of trehalulose. Furthermore, the outsourced literature search conducted for EFSA did not identify such data.

#### 3.10.1.3 | *Summary on genotoxicity*

Taking into account the available literature data, and considering the nature, source and production process of the NF, the Panel overall considers that there are no concerns regarding the genotoxicity of the NF.

### 3.10.2 | Acute and subacute toxicity

#### 3.10.2.1 | *Isomaltulose*

Adult male rats were fed solid diets containing starch (control), sucrose or 62% isomaltulose for 26 days (trial 1); sucrose and isomaltulose groups were maintained up to 56 days (trial 2). Food intake was somewhat reduced for 2 to 4 days when animals were switched from ground chow to isomaltulose but recovered rapidly to a stable level maintained thereafter ( $23.2 \pm 0.9$  g/day and  $20.6 \pm 0.4$  g/day on average for trials 1 and 2 respectively). In isomaltulose-fed animals, body weight gain, intra-abdominal adipose tissue and liver fat content did not differ from the starch control diet in trial 1, while sucrose-fed animals displayed a statistically significant increase in final body weight (+4.6%). In trial 2, body weight gain was similar in both isomaltulose- and sucrose-fed animals (Haberer et al., 2009).

In contrast, 5-week-old C57BL/6J mice fed diets containing 650 g/kg isomaltulose ad libitum for 5 weeks exhibited a statistically significant increase in food intake and body weight gain ( $5.05 \pm 0.40$  g) compared to a corn-starch control group ( $4.15 \pm 0.67$  g); the increase in body weight gain was not significantly different than that of sucrose-fed animals ( $5.67 \pm 0.28$  g). The food efficiency ratio did not significantly differ between groups. No significant differences in liver weight and histopathological analysis were noted, and AST or ALT concentrations remained comparable between groups (Hwang et al., 2018).

#### 3.10.2.2 | *Trehalulose*

The applicant did not provide data regarding potential acute and subacute toxicity of trehalulose. The literature search conducted for EFSA did not identify such data.

#### 3.10.2.3 | *Mixtures with trehalulose as the main component*

The subacute toxicity of isomaltulose syrup was investigated in Sprague–Dawley rats treated orally with distilled water (control) or 27 g/kg bw per day for 15 days. The syrup used in the study varied significantly from the NF, as it contained 13.4% isomaltulose, 32.5% trehalulose, 10.3% fructose, 8.9% glucose and smaller amounts of other saccharides. Males treated with isomaltulose syrup displayed a decrease in weight gain. There was no significant difference in haematological and biochemical analyses in both male and female rats (Lim et al., 1997).

#### 3.10.2.4 | *Summary on (sub)acute toxicity*

The Panel notes that the above-described (sub)acute toxicity studies did not identify additional safety concerns for the NF in comparison to sucrose.

### 3.10.3 | Repeated dose toxicity

#### 3.10.3.1 | *Isomaltulose*

*Rat studies.* The effects of isomaltulose feeding on tissue mineral content was investigated by Kashimura et al. (1990). Thirty Wistar rats were given 30% sucrose (control), 30% isomaltulose (~15 g/kg bw per day), 10, 20 or 30% isomaltulose condensates for 8 weeks. Final weights were lower in all isomaltulose treated animals, with a dose-dependent decrease in the isomaltulose condensates groups (statistically significant at the high dose; –26%). At necropsy, rats presented with dose-dependent decreases in absolute heart, kidney and liver weights in the isomaltulose condensate groups (statistically significant for all three organs in the middle and high-dose groups, with maximum decreases of 25, 24 and 20% respectively), as well as in the 30% isomaltulose group (statistically significant for the kidney; –22%), compared to the sucrose control. There were no significant differences in mineral concentrations in tissues between the control and treated groups except for a dose-dependent increase in plasma phosphorus (statistically significant in the 30% isomaltulose condensate group; +30%).

In a follow-up study where rats were fed 7.5% or 15% isomaltulose or its condensates for 13 weeks, there were no significant differences in body weight, haematocrit and tissue mineral [calcium (Ca), magnesium (Mg), phosphorus (P) and iron (Fe)] contents between groups, except for a significantly higher plasma P content in the condensates group. Significant changes were observed in trace minerals [zinc (Zn), copper (Cu) and manganese (Mn)] content in the condensate group,

including an increase of Zn concentration in the brain, an increase of Cu concentration in the liver and kidney, an increase of Mn concentration in the brain and tibia, and a decrease of Mn concentration in the liver (Kashimura et al., 1992).<sup>7</sup>

More recently, the safety of isomaltulose was investigated in a GLP-compliant toxicity study conducted in accordance with OECD and FDA guidelines. Briefly, 20 male and 20 female Wistar rats were administered isomaltulose in the diet at levels of 0 (10% sucrose), 2.5, 5 and 10% for 13 consecutive weeks (in the intermediate dose groups, the supplement was made up to 10% with sucrose). The treatment did not affect food or water consumption, and resulted in a mean isomaltulose intake of 1.7, 3.5 and 7 g/kg bw per day in males and 2, 4 and 8.1 g/kg bw per day in females in the low-, middle- and high-dose group respectively. Body and organ weights, gross and histopathological examinations, neurobehavioural observations and motor activity assessment did not reveal any significant abnormality related to exposure to isomaltulose. There were no significant changes in haematological, clinical chemistry, urinary and ophthalmological analyses (Jonker et al., 2002).

Sprague–Dawley rats of both sexes were exposed to 0 (distilled water vehicle), 1500, 3000 or 4500 mg/kg bw per day isomaltulose via oral gavage for 26 weeks. Food intake was reduced in males in the mid- and high-dose groups, while body weight showed a dose-dependent tendency towards an increase, which is likely due to a higher caloric intake. Relative liver weight was dose-dependently increased in males (statistically significant in the high-dose group; +8%), and relative heart weight was reduced at all treatment doses in females (non-dose dependent, statistically significant starting at the low dose, up to –11%). Numerous statistically significant changes were observed in haematological and biochemical blood parameters. Notably, all animals presented with dose-dependently lower blood uric acid (statistically significant starting from the low dose, up to –41%) and reduced creatinine levels (statistically significant starting from the low dose, up to –36%) at the end of the treatment period. Plasma calcium levels displayed a dose-dependent decrease in females (statistically significant at the high dose; –4%) and increase in males (statistically significant from the middle dose up; up to +11%). Plasma inorganic phosphorus levels presented with a tendency towards an increase in both sexes (reaching statistical significance in the high dose; up to +8% in males) (Yamaguchi et al., 1986).<sup>8</sup> Given the fact that there is a high caloric intake difference between the control and treatment groups, the Panel cannot conclude on the specific toxicity of isomaltulose from this study.

*Mice studies.* In 38-weeks-old C57BL/6J mice fed diets containing 0% (control containing 40% sucrose), 18% (containing 22% sucrose) or 40% isomaltulose (no sucrose) for 8 weeks, final body weights were significantly lower in isomaltulose treated animals (control: 36.2±0.8 g; 18%: 32.8±0.9 g; 40%: 33.5±0.8 g;  $p < 0.05$ ). Animals fed isomaltulose presented with a dose-dependent tendency towards a decrease in peri-epididymal and perirenal fat accumulation (significant for the perirenal region in the 40% group). Animals from the high-dose group also presented with a significant increase in triglyceride levels (24±2 mg/dL vs. 18±2 mg/dL in the control group) (Kashimura & Nagai, 2007a).

In adult C57BL/6J male mice, a 22-week dietary intervention with diets containing 440 g/kg isomaltulose or sucrose ad libitum produced comparable body fat and lean mass in exposed animals. Weekly food-consumption and cumulative intake were similar between groups, and energy intake did not differ between groups throughout the study. Liver triacylglycerol and ALT concentrations were lower in isomaltulose-fed vs. sucrose-fed mice (Keyhani-Nejad et al., 2015).

### 3.10.3.2 | Trehalulose

The applicant did not provide data regarding the potential subchronic toxicity of trehalulose. The literature search conducted for EFSA did not identify such data.

### 3.10.3.3 | Mixtures with trehalulose as the main component

Sprague–Dawley rats were administered 0 (distilled water), 1500, 3000 or 4500 mg/kg bw/day isomaltulose syrup by gavage for 26 weeks. The syrup, which is different in composition from the NF, contained 45.7% trehalulose, 18.8% isomaltulose, 14.5% fructose, 11.9% glucose, 3.7% isomaltulose, 3.1% sucrose and 2.3% other sugars. Food consumption was significantly decreased in females from the middle and high-dose groups starting from week 10, while it was only transiently affected in males from the high-dose group. In the high-dose group, male body weights were lower compared to the control group starting from week 15 (statistically significant on week 21 only), while female body weights were not affected. Water consumption was consistently lower in animals from the high-dose group. In females, both the absolute and relative spleen weights were statistically significantly increased starting from the middle dose (+12%), and absolute lung weight was increased (statistically significant at the middle and high doses; +8.8 and +6.4% respectively). As reported after exposure to isomaltulose only (Yamaguchi et al., 1986; cf. section 3.10.4.1.), treated animals presented with decreased uric acid and creatinine levels, with statistical significance starting at the low dose. Females presented with dose-dependently elevated inorganic phosphorus levels (up to +41%, statistically significant starting at the low dose), while males displayed a tendency towards an increase (Yamaguchi et al., 1987).<sup>9</sup>

### 3.10.3.4 | Summary on repeated dose toxicity

The Panel notes that the above-described repeated dose toxicity studies did not identify additional safety concerns for the NF in comparison to sucrose.

<sup>7</sup>Study available in Japanese.

<sup>8</sup>A translation from Japanese was provided by the applicant.

<sup>9</sup>A translation from Japanese was provided by the applicant.

### 3.10.4 | Reproductive and developmental toxicity

The Panel notes that the applicant did not provide any reproductive and/or developmental toxicity study using the NF.

Lina et al. (1997) investigated the embryotoxicity and teratogenicity of isomaltulose in the rat. Briefly, 24 mated female Wistar dams were fed diets containing 0 (control; cereal-based powdered stock diet), 2.5, 5 or 10% isomaltulose from gestational day (GD) 0 to GD21 (10% isomaltulose being equivalent to about 7 g/kg bw per day). There was no difference between groups in dams body weight gain although food intake was transiently increased in the 2.5% and 10% groups. Dams were killed and fetuses examined for abnormalities on GD21. No abnormal clinical signs or severe macroscopic organ abnormalities were observed in the dams. There were no statistically significant differences in fertility and reproductive performance indexes at large, nor on embryonic or foetal development. Skeletal examination did reveal a statistically significant increase in the number of fetuses presenting with more than 20 unossified digits in the phalanges of both the front and hindlimbs in the isomaltulose treated groups. These data are to be put in perspective with the number of fetuses presenting with 10–20 unossified digits, which were statistically significantly reduced in isomaltulose treated animals. The authors deemed the effect non-treatment related because of the absence of dose response relationship. A higher incidence of incomplete ossification of skull bones was also observed in the 2.5% isomaltulose group but was considered artefactual as it was not confirmed at higher doses. Finally, a statistically significant higher incidence of crooked toes in the hindlimbs of the fetuses exposed to 10% isomaltulose was observed but considered artefactual as similar variations had been observed regularly in control rats in foregoing studies.

The Panel concludes that the feeding of isomaltulose from day 0 to 21 of pregnancy at dietary levels up to 7 g/kg bw per day did not provide evidence for adverse effects on maternal performance or on embryonic or foetal development.

The applicant did not provide data regarding potential reproductive and developmental toxicity of trehalulose. The literature search conducted for EFSA did not identify such data.

### 3.10.5 | Human data

The applicant carried out extensive literature searches on the safety of isomaltulose and trehalulose for human consumption, considering that other by-products present in the NF (sucrose, glucose, fructose) were safe. The literature searches were updated by EFSA for years 2017 to November 2023. The Panel notes that there are no human studies conducted with the NF.

#### 3.10.5.1 | Isomaltulose

An exhaustive description of human data following isomaltulose consumption is given in the UK Food Standards Agency opinion (UK FSA, 2004). It was concluded that '[...] there exist clear data to support the tolerability of isomaltulose at doses of up to 1 g/kg bw (~70g isomaltulose) administered under bolus dosing conditions' and that '[...] higher total daily intakes of isomaltulose are expected to be well tolerated, especially when isomaltulose is administered throughout the day'.

A randomised, double-blind, controlled four-week study in infants from 4 to 8 months of age was carried out to assess growth and tolerance of follow-on formula containing 2.1 g/100 mL isomaltulose as opposed to maltodextrin. Both formulae were well accepted and displayed no difference in time of crying, flatulence, stool characteristics and occurrence of adverse events (Fleddermann et al., 2016).

A double-blind, placebo-controlled, randomised trial in 50 healthy Japanese subjects showed that a daily diet containing 40 g of isomaltulose or 40 g of sucrose for 12 weeks produced no diarrhoea or significant side effects. There were no changes from the baseline in body weight, body mass index (BMI), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, triglycerides (TG), diastolic blood pressure and subcutaneous fat area (Okuno et al., 2010).

One hundred and ten type-2 diabetic patients were randomised to receive sweet foods containing 50 g/day isomaltulose for 12 weeks as part of their habitual diet under free-living conditions. The dietary intervention was well tolerated, and no patient dropped out because of side effects (Brunner et al., 2012).

In its 2017 report on the NF (FSAI, 2017), the Food Safety Authority of Ireland concluded that '*Since ingested isomaltulose is rapidly hydrolysed and absorbed as glucose and fructose, several high doses could be consumed in the course of a day without risk of intestinal side effects. Thus, daily doses of 1.0–1.3 g/kg bw per day are expected to be as well tolerated as corresponding doses of sucrose in adults and children*'.

The Panel considers that these studies corroborate the previous assessment of isomaltulose carried out by the UK FSA (2004).

#### 3.10.5.2 | Trehalulose

The applicant did not provide data regarding potential human toxicity of trehalulose. The literature search conducted for EFSA did not identify such data.

### 3.11 | Allergenicity

Analyses of batches of isomaltulose syrup (dried) did not reveal the presence of proteins above the limit of quantification (<0.1%). Consequently, the Panel considers that the NF is unlikely to trigger allergic reactions in the target population under the proposed conditions of use.

## 4 | DISCUSSION

The NF which is the subject of this application is isomaltulose syrup (dried), a mixture of carbohydrates composed of isomaltulose ( $\geq 75\%$  DM), trehalulose ( $\sim 12\%$  DM) and small proportions of other sugars (fructose, glucose, sucrose). The NF is a white powder produced by enzymatic isomerisation of sucrose.

The NF is proposed to be used as a replacement of sucrose in existing products on the market targeted at the general population. The Panel assumes that if all added sugars were replaced by the NF, the daily intake of the NF would be equivalent to that of added sugars as reported by EFSA (EFSA NDA Panel, 2022), in which the highest intake estimate was calculated for young male adolescents at 178 g per day at the 95th percentile.

The Panel notes that, for the NF, no ADME or toxicological data were provided. Instead, the safety of the NF was assessed based on literature data available on isomaltulose and mixtures of isomaltulose and trehalulose. In addition, considering the nature, compositional characterisation and production process of the NF, the Panel considered that such data were sufficient to conclude that the NF is as safe as sucrose.

## 5 | CONCLUSIONS

The Panel concludes that the NF, isomaltulose syrup (dried), is as safe as sucrose.

## 6 | STEPS TAKEN BY EFSA

1. On 21/03/2019, EFSA received a letter from the European Commission with the request for a scientific opinion on the safety of Isomaltulose syrup (dried) [Ref. Ares(2019)1898201].
2. On 21/03/2019, a valid application on Isomaltulose syrup (dried), which was submitted by name of the company, was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2018/0330) and the scientific evaluation procedure was initiated.
3. On 05/07/2019, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
4. On 23/03/2020, additional information was provided by the applicant through the Commission e-submission portal and the scientific evaluation was restarted.
5. On 21/10/2020, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
6. On 22/02/2021, additional information was provided by the applicant through the Commission e-submission portal and the scientific evaluation was restarted.
7. On 19/06/2023, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
8. On 30/09/2023, additional information was provided by the applicant through the Commission e-submission portal and the scientific evaluation was restarted.
9. During its meeting on 29/11/2023, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of Isomaltulose syrup (dried) as a NF pursuant to Regulation (EU) 2015/2283.

### ABBREVIATIONS

ADME	absorption, distribution, metabolism and excretion
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BfR	Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment)
BLAST	basic local alignment search tool
BMI	body mass index
bw	body weight
Ca	calcium
CAS	chemical abstracts service
CBS	Centraalbureau voor Schimmelcultures
CFU	colony forming units
Cu	copper



DIN	Deutsches Institut für Normung
DM	dry matter
EEC	European Economic Community
EN	Europäische Norm
FDA	Food and Drug Administration
Fe	iron
FEEDAP	Additives and Products or Substances used in Animal Feed
FSAI	Food Safety Authority of Ireland
FSANZ	Food Standards Australia New Zealand
GD	gestational day
GLP	good laboratory practices
GMP	Good manufacturing practice
GRAS	generally considered as safe
GRN	GRAS notice
HACCP	hazard analysis critical control points
HDL	high-density lipoprotein
HFI	hereditary fructose intolerance
HPLC/PAD	high-performance liquid chromatography/pulsed amperometric detection
ICP-MS	inductively coupled plasma mass spectrometry
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
kcal	kilocalories
K <sub>m</sub>	Michaelis constant
LDL	low-density lipoprotein
LOQ	limit of quantification
Mg	magnesium
Mn	manganese
Mo	month(s)
NA	not analysed
NCBI	National Center for Biotechnology Information
NCTC	National Collection of Type Cultures
n.d.	not detected
NDA	Nutrition, Novel Foods and Food Allergens
NF	novel food
OECD	Organisation for Economic Cooperation and Development
P	phosphorus
P <sub>95</sub>	95th percentile
S <sub>9</sub>	rat liver mitochondrial fraction
SCF	Scientific Committee on Food
TAMC	total aerobic microbial count
TG	triglycerides
TYMC	total yeast and mould count
UCT Prague	University of Chemistry and Technology, Prague
UK FSA	United Kingdom Food Standards Agency
V <sub>max</sub>	maximum velocity
Zn	zinc

## ACKNOWLEDGEMENTS

The Panel wishes to thank the former member of the EFSA Working Group on Novel Foods Carmen Peláez for the contribution provided to the development of the opinion until November 2023.

## CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact [interestmanagement@efsa.europa.eu](mailto:interestmanagement@efsa.europa.eu).

## REQUESTOR

European Commission

## QUESTION NUMBER

EFSA-Q-2018-00609

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**How to cite this article:** EFSA NDA Panel (EFSA Panel on Nutrition, Novel Foods and Food Allergens), Turck, D., Bohn, T., Castenmiller, J., De Henauw, S., Hirsch-Ernst, K. I., Maciuk, A., Mangelsdorf, I., McArdle, H. J., Naska, A., Pentieva, K., Siani, A., Thies, F., Tsabouri, S., Vinceti, M., Aguilera-Gómez, M., Cubadda, F., Frenzel, T., Heinonen, M. ... Knutsen, H. K. (2024). Safety of isomaltulose syrup (dried) as a novel food pursuant to Regulation (EU) 2015/2283. *EFSA Journal*, *22*(1), e8491. <https://doi.org/10.2903/j.efsa.2024.8491>