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SCIENTIFIC OPINION

Extension of use of isomalto-oligosaccharide 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 the extension of use of isomalto-oligosaccharide (IMO) as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF consists of glucose oligomers with degrees of polymerisation of 3–9, along with various amounts of mono- and disaccharides. The NF comes in both syrup and powder form. The applicant intends to extend the current uses of the NF as an ingredient in several foods, and use the NF in food supplements aimed at the general population older than 10 years of age. The information provided on the manufacturing process, composition and specifications of the NF is sufficient and does not raise safety concerns. Along with literature data, the applicant carried out a tolerability study in adult volunteers with the NF at doses up to 120 g/day. The Panel concludes that this study provides reassurance that the NF is tolerable at doses of 120 g/day. Conservative intake estimates resulting from the use of the NF as an ingredient according to the currently authorised uses and new proposed uses result in a highest intake estimate in adolescents of 112 g/day at the 95th percentile, and reach 142 g/day in adolescents when the use as a food supplement is included. The Panel notes this amount is higher than the dose of 120 g/day for which tolerability has been demonstrated. However, considering the source, compositional characterisation, production process and nature of the NF, as well as the available nutritional and toxicological data on the NF, the Panel considers that the NF does not present safety concerns under the proposed conditions of use.

KEYWORDS

extension of use, food supplement, IMO, isomalto-oligosaccharide, novel foods

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1 | INTRODUCTION

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

Isomalto-oligosaccharide (IMO) was authorised under certain conditions of use pursuant to Article 4 of the former Regulation (EC) No 258/97[1] by the United Kingdom (UK) Food Safety in February 2016 (https://ec.europa.eu/food/system/files/2016-11/novel-food_authorisation_2016_auth-letter_isomalto-oligosaccharide_en.pdf).

On 26 March 2021, the company BioNeutra North America Inc. submitted a request to the European Commission (EC) in accordance with Article 10 of Regulation (EU) 2015/2283[2] for an extension of use of IMO as a novel food.

The application requests to extend the use of IMO to include ice cream and dairy desserts, instant coffee and tea, table-top sweeteners, cakes, muffins, pies, pastries, breakfast cereals, condiments/relishes, gravies and sauces, gelatines, puddings, fillings, jams and jellies, yoghurts, milk-based drinks, snack foods, and sweet sauces, toppings and syrups. It is also proposed for use in food supplements as defined in Directive 2002/46/EC[3] for the general population older than 10 years.

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

In addition, the EFSA is requested to include in its scientific opinion a statement as to if, and if so to what extent, the proprietary data for which the applicant is requesting data protection was used in elaborating the opinion in line with the requirements of Article 26(2)(c) of Regulation (EU) 2015/2283.

1.2 | Additional information

In February 2009, an application from Bioneutra was accepted by the United Kingdom Food Standards Agency (UK FSA) to place IMO on the European Union (EU) market as a novel food ingredient.

On 7 December 2012, the UK FSA concluded that IMO meets the criteria for acceptance as a novel food, as defined in Article 3(1) of Regulation (EC) No 258/97.

The Commission forwarded the initial assessment report to all Member States on 31 January 2013. No reasoned safety objections were presented by the Commission or the Member States, and the applicant's IMO powder and syrup were considered to have complied with the criteria laid down in Article 3(1) of Regulation No 258/97.

In June 2014, the applicant requested labelling requirement amendment, so that foods containing the novel food (NF) can be labelled as 'a source of glucose'. The Advisory Committee on Novel Foods and Processes (ACNFP) concluded that the new proposed labelling did not pose any safety concerns for diabetics and was consistent with the way that other glycaemic carbohydrates are labelled in the EU.

On 23 October 2015, Member States and the European Commission were consulted on the proposed change and no reasoned safety objections were presented. The authorisation was amended to replace the requirement to label products containing IMO as unsuitable for diabetics with a requirement to label the products as 'a source of glucose'. The NF was authorised under certain conditions of use pursuant to Article 4 of the former Regulation (EC) No 258/97 by the UK FSA in February 2016 (https://ec.europa.eu/food/system/files/2016-11/novel-food_authorisation_2016_auth-letter_isomalto-oligosaccharide_en.pdf).

2 | DATA AND METHODOLOGIES

2.1 | Data

The safety assessment of this NF is based on data supplied in this application and the previous assessment of the NF (UK FSA, 2012) and information submitted by the applicant following EFSA's requests for supplementary information.

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.[4]

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 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.

[1]Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients.

[2]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.

[3]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.

[4]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.

This NF application includes a request for protection of proprietary data in accordance with Article 26 of Regulation (EU) 2015/2283. The data requested by the applicant to be protected comprise: two safety and tolerability studies of IMO in healthy adults (2012, 2020), their summaries and supplemental data, the compositional data and related expert opinion, the original NF application to the UK FSA, product batch data, certificates of analysis, description of analytical methods, laboratory accreditation certificates, intake reports and stability 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.

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 this application for extension of use is isomalto-oligosaccharide (IMO). The NF is produced via enzyme-catalysed hydrolysis of food grade starch from different plant-based crops and consists of glucose oligomers with degrees of polymerisation (DP) of 3–9, along with various amounts of mono- and disaccharides. 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'.

In addition to its current authorised uses, the NF is herein proposed to be used as a food ingredient in ice cream and dairy desserts, instant coffee and tea, tabletop sweeteners, cakes, muffins, pies, pastries, breakfast cereals, condiments/relishes, gravies and sauces, gelatines, puddings, fillings, jams and jellies, yoghurts, milk-based drinks, snack foods, and sweet sauces, toppings and syrups. The target population is the general population. The NF is also proposed for use in food supplements at a maximum use level of 30 g/day for the general population older than 10 years of age.

3.2 | Identity of the NF

The NF is isomalto-oligosaccharide. Other names include IMO (soluble fibre from pea/tapioca/corn), IMO (fibre sources from vegetable) and oligo-isomaltose. Its current trade name is VitaFiber® (IMO syrup and IMO-powder) [previously VitaSugar™ (IMO syrup and IMO-powder)].

IMOs are defined as any oligosaccharide possessing an isomaltose moiety [i.e. two D-glucopyranoside units joined by an α-(1–6) glucosidic linkage]. The NF is a mixture of glucose oligomers linked through α-(1–4) or α-(1–6) glucosidic bonds, including mono- and disaccharides (about 30%), as well as oligomers with DP of 3–9 (about 70%). The NF comes in both syrup and powder form.

Size exclusion chromatography was used to separate and quantify oligosaccharides up to DP 6 using authentic standards, whereas the characterisation of higher DP oligosaccharides was prevented by technical constraints and the lack of representative standards. Further analysis was conducted using hydrophilic interaction high-performance liquid chromatography with fluorescence and mass selective detection (HILIC-HPLC-FLD-MS), which allowed separation and identification of DP groups based on their oligomeric mass, confirming the presence of DP 7, DP 8 and DP 9 oligosaccharides. The presence of the isomaltose moiety was verified by 1H NMR, which allowed to determine the α-1,6 linkage proportion in the individual fractions of separated DP 3 to DP 9 oligosaccharides. 1H NMR analysis of six different production lots without DP fractionation showed that the product as a whole is composed of 55%–59% oligosaccharides with α-1,6 linkages.

The applicant notes that the exact distribution of the individual di-, tri- and larger oligosaccharides in the NF will vary depending on the manufacturing conditions used to produce the mixture.

3.3 | Production process

The Panel notes that an assessment of the production process for the NF when produced via enzyme-catalysed hydrolysis of starch from different sources of plant-based crops was conducted by the UK FSA (2012) and did not raise any concern. The applicant does not seek to amend the production process from what was assessed at that time, but indicated a change in enzyme in the saccharification phase of the process because of the discontinuation of the original product. Considering the important increase in anticipated intake of the NF based on the new proposed uses and use levels, EFSA carried out a thorough re-assessment of the production process.

Briefly, IMO is produced in accordance with current Good Manufacturing Practice (GMP) via enzyme-catalysed hydrolysis of starch from different sources of plant-based crops (e.g. cereals, legumes, and roots). The safety of all enzymes used in the production process was assessed by the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids with a positive outcome. The manufacturing process is briefly summarised in Figure 1.

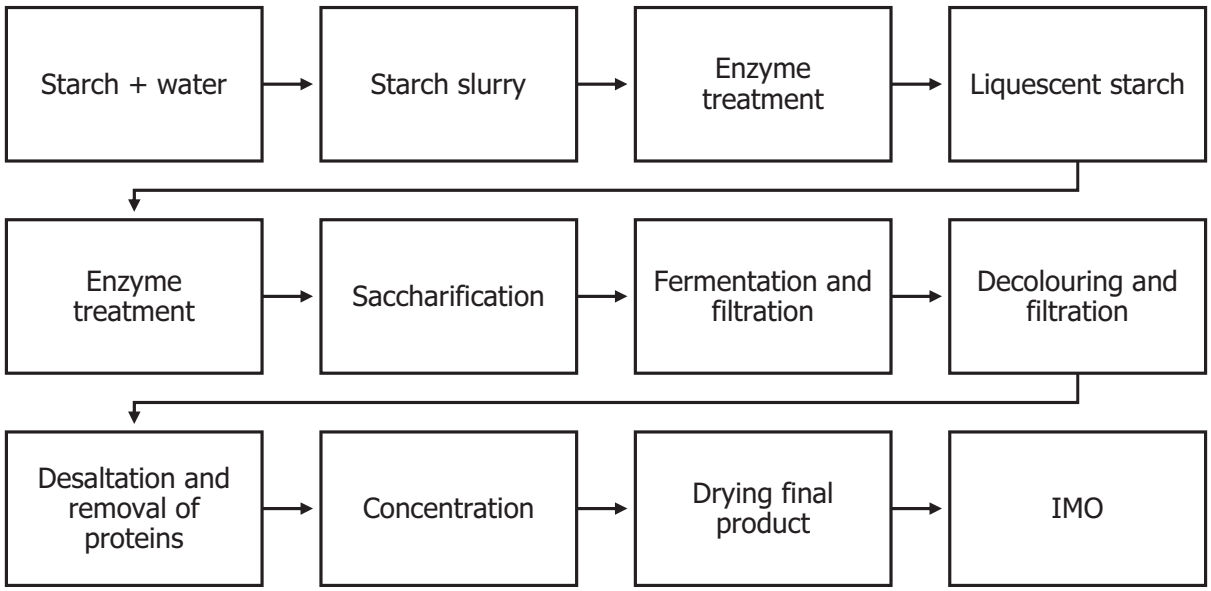

FIGURE 1 Summary of the manufacturing process of IMO.

Certificates of analysis were provided for all raw materials.

The Panel considers that the production process is sufficiently described and does not raise safety concerns.

3.4 | Compositional data

The NF consists of a mixture of glucose oligomers linked through α-(1–4) or α-(1–6) glucosidic bonds, with DP of 3–9, along with various amounts of mono- and disaccharides, in syrup or powder form. In order to confirm that the manufacturing process is reproducible and adequate to produce the NF with the required characteristics on a commercial scale, the applicant provided updated analytical information for five independent batches of the NF in each form (Table 1), demonstrating that the NF is compliant with specifications laid out in the Union List of novel foods for syrup and powder preparations of IMO.

The Panel notes that there are no standardised nationally or internationally recognised methods available for the identification and quantification of individual types of saccharides. The applicant developed and validated two in-house methods using size exclusion and normal phase high-performance liquid chromatography with a refractive index detector (SE-HPLC-RI and NP-HPLC-RI).

The applicant investigated the solubility of the NF in powder form at different temperatures. Solubility at 25°C was characterised by 79.2% Brix and 78.41% dissolved solids.

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

The Panel considers that the information provided on the composition is sufficient to characterise the NF.

TABLE 1 Batch to batch analysis of the NF.

Parameter (unit)	Syrup					Powder					
Batch number	**#1**	**#2**	**#3**	**#4**	**#5**	**#1**	**#2**	**#3**	**#4**	**#5**	**Method of analysis**
Physicochemical properties											
Viscosity (mPas/cP)	4025	4025	4300	4375	4775	N/A	N/A	N/A	N/A	N/A	USP <912>
Total fat (g/100 g)	0.0874	0.141	0.104	0.104	0.114	0.136	0.165	0.130	0.134	0.150	SOP6_217
Protein (g/100 g)	0.0388	0.0371	0.0502	0.0452	0.0661	0.131	0.175	0.0851	0.0913	0.0644	SOP6_558
Total dietary fibre (g/100 g)	19.6	21.4	19.9	18.5	15.7	31.6	30.1	32.8	26.8	22.3	AOAC_2009.01
Total solids (g/100 g)	76.5	75.9	76.5	76.5	76.2	N/A	N/A	N/A	N/A	N/A	AOAC 932.14C
Water content (%)[a]	23.5	24.1	23.5	23.5	23.8	N/A	N/A	N/A	N/A	N/A	Calculation
Moisture (g/100 g)	N/A	N/A	N/A	N/A	N/A	3.66	3.16	3.34	3.00	4.03	Oven drying at 105°C
Water activity (a_w)	0.8	0.8	0.8	0.8	0.8	N/A	N/A	N/A	N/A	N/A	USP <1112>
Ash (g/100 g)	0.00	0.00	0.006	0.00	0.00	0.00	0.00	0.239	0.00	0.00	AOAC 923.03
Total carbohydrates (g/100 g)[b]	56.95	54.32	56.43	57.85	60.32	64.47	66.4	63.4	69.97	73.45	Calculation
pH	4.8	4.4	4.6	4.5	5.2	4.8	4.7	5.8	4.7	5.8	USP <791>
Mono- and oligosaccharides (%)											
Glucose	0.86	0.78	0.81	1.41	0.57	0.25	0.47	1.26	0.92	0.68	HPLC-RI
Maltose	9.04	9.02	8.91	7.96	8.69	8.59	6.97	8.38	8.92	8.48	HPLC-RI
Isomaltose + DP3 to DP9	90.10	90.20	90.22	90.55	90.74	90.96	92.34	89.88	90.08	90.73	HPLC-RI
Heavy metals (mg/kg)											
Lead	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02	< 0.004	< 0.02	< 0.02	< 0.003	< 0.010	USP <233>, ICP-MS
Arsenic	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	0.015	< 0.03	< 0.03	< 0.005	< 0.05	USP <233>, ICP-MS
Cadmium	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02	< 0.004	< 0.02	< 0.02	< 0.003	< 0.005	USP <233>, ICP-MS
Mercury	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02	< 0.004	< 0.02	< 0.02	< 0.003	< 0.002	USP <233>, ICP-MS
Microbiological analysis											
Total aerobic count (CFU/g)	10	< 10	< 10	< 10	< 10	10	130	10	< 10	10	USP <2021/2022>
Yeast and mould (CFU/g)	< 10	< 10	< 10	< 10	< 10	< 10	40	< 10	< 10	< 10	USP <2021/2022>
Escherichia coli (/10 g)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	USP <2021/2022>
Salmonella (/25 g)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	USP 40-NF35 S1 2022
Staphylococcus aureus (/25 g)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	USP <2021/2022>
Coliforms (CFU/g)	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	MFHPB-34
Enterobacteriaceae (CFU/g)	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	USP <2021/2022>

Abbreviations: AOAC, Association of Official Analytical Chemists; CFU, colony forming units; DP, degrees of polymerisation; HPLC-RI, high-performance liquid chromatography-refractive index; ICP-MS, inductively coupled plasma mass spectrometry; MFHPB, Microbiology Food Health Protection Branch (Canadian Food Inspection Agency); N/A, non applicable; nd, not detected; NF, novel food; USP, United States Pharmacopeia.

[a]Moisture/100 g = 100 – total solids.

[b]Total carbohydrates/100 g = 100 – (total fat + total protein + ash + moisture).

3.4.1 | Stability

The applicant referred to the stability data provided in its original submission dossier to the UK FSA and did not provide additional data.

3.5 | Specifications

The specifications of the NF are indicated in Tables 2 and 3 for syrup and powder forms, respectively. The specifications will be kept as indicated in the Union List, with the addition of microbiological parameters, which the Panel considers will reinforce the safety of the NF.

TABLE 2 Specifications of the NF in syrup form.

Description: Isomalto-oligosaccharide is a light-yellow transparent syrup produced via enzyme-catalysed hydrolysis of food grade starch from different plant-based crops	
Parameter	**Specification**
Dried solids (g/100 g)	> 75
Glucose (% dry basis)	≤ 5
Isomaltose + DP3 to DP9 (% dry basis)	≥ 90
pH	4 to 6
Sulfated ash (g/100 g)	≤ 0.3
Heavy metals	
Lead	≤ 0.5 mg/kg
Arsenic	≤ 0.5 mg/kg
Microbiological	
TAMC	< 1000 CFU/g
TYMC	< 100 CFU/g
Escherichia coli	Not detected in 10 g
Salmonella	Not detected in 25 g

Abbreviations: CFU, colony forming units; DP, degree of polymerisation; TAMC, total aerobic microbial count; TYMC, total yeast and mould count.

TABLE 3 Specifications of the NF in powder form.

Description: Isomalto-oligosaccharide is a white powder produced via enzyme-catalysed hydrolysis of food grade starch from different plant-based crops	
Parameter	**Specification**
Solubility (water) %	≥ 99
Glucose (% dry basis)	≤ 5
Isomaltose + DP3 to DP9 (% dry basis)	≥ 90
Moisture (%)	≤ 4
Sulfated ash (g/100 g)	≤ 0.3
Heavy metals	
Lead	≤ 0.5 mg/kg
Arsenic	≤ 0.5 mg/kg
Microbiological	
TAMC	< 1000 CFU/g
TYMC	< 100 CFU/g
Escherichia coli	Not detected in 10 g
Salmonella	Not detected in 25 g

Abbreviations: CFU, colony forming units; DP, degree of polymerisation; 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 produced from unmodified food-grade starch derived from different plant-based crops, i.e. wheat, barley, corn, pulses (peas, beans, lentils), oats, cassava, rice, potato and other starch sources meeting Food Chemical Codex (FCC) specifications. There are no changes to the source materials from that outlined in the original application for IMO.

According to the UK FSA (2012), IMO has been classified as a complex novel food from non-genetically modified source, the source of the novel food has a history of food use in the EU (class 2.2) according to the scheme in Commission Recommendation 97/618 (EC).[5]

3.6.2 | History of use of the NF

Pursuant to Article 4 of the former Regulation (EC) No 258/97, and in accordance with the authorisation released by the UK FSA in February 2016, the NF is currently authorised to be marketed as a food ingredient in beverages (energy-reduced soft drinks, energy drinks, sports and isotonic drinks, fruit juices, processed vegetables and vegetable juices, and other soft drinks), cereal products (cereal bars, cookies, biscuits, breakfast cereal bars), sugar confectionery (hard candies, soft candies/chocolate bars), and nutritionally complete and fortified foods (meal replacement bars, milk based meal replacement). In addition to the current status within the EU, IMOs are approved and consumed in other countries including Australia, New Zealand, Canada, China, India, Israel, Japan, Korea and the US.

3.7 | Proposed uses and use levels and anticipated intake

3.7.1 | Target population

For use as a food ingredient, the target population proposed by the applicant is the general population. For use in food supplements, the target population proposed by the applicant is the general population older than 10 years of age.

3.7.2 | Proposed uses and use levels

In addition to the currently authorised uses (cf. Section 3.6.2), the NF is proposed to be used as an ingredient in several food products. These food products, defined using the FoodEx2 hierarchy, and the proposed maximum use levels, are reported in Table 4.

The applicant also intends to market the NF for use in food supplements, at a maximum dose of 30 g/day.

TABLE 4 Food categories and maximum use levels intended by the applicant.

FoodEx2 level	FoodEx2 code	Food category	Max use level (mg NF/100 g)
L2	A02PT	Dairy desserts and similar	8000
L2	A0C68	Spoonable desserts and ice creams (generic)	8000
L3	A03KE	Instant coffee (beverage)	10,000
L2	A0F7R	Table-top sweeteners formulations	100,000
L3	A00AN	Cakes	20,000
L3	A00BV	Shortcrust (pies-tarts)	20,000
L3	A00AG	Choux pastry	15,000
L3	A00CJ	Various pastry	15,000
L3	A00CV	Breakfast cereals	10,000

[5]Commission Recommendation of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council.

TABLE 4 (Continued)

FoodEx2 level	FoodEx2 code	Food category	Max use level (mg NF/100 g)
L3	A00EJ	Muesli and similar mixed breakfast cereals	10,000
L3	A04LH	Breakfast cereals, plain	10,000
L3	A04LK	Processed and mixed breakfast cereals	10,000
L3	A043V	Savoury sauces	10,000
L3	A044L	Vinegar	10,000
L3	A036F	Water-based desserts spoonable	15,000
L5	A041E	Rice pudding	15,000
L4	A01MM	Jam of fruit/vegetables	50,000
L3	A0C69	Fermented milk products	2500
L4	A02MP	Flavoured milks	5000
L2	A0EZX	Fried or extruded cereal, seed or root-based products	5000
L2	A046F	Dessert sauces/toppings	50,000

Abbreviation: NF, novel food.

3.7.3 | Anticipated intake of the NF

EFSA carried out an intake assessment of the anticipated daily intake of the NF based on the currently authorised uses and the applicant's proposed extended uses and maximum use levels of the NF, using individual data from the EFSA Comprehensive European Food Consumption Database (EFSA, 2011).[6] The lowest and highest mean and 95th percentile anticipated daily intake of the NF (on a mg/kg body weight (bw) basis), among the EU dietary surveys, are presented in Tables 5–7.

The estimated daily intake of the NF for each population group from each EU dietary survey is available in the excel files annexed to this scientific opinion (under supporting information).

3.7.3.1 | *Intake estimate from already authorised food uses in the union list*

The NF is currently authorised to be marketed as a food ingredient in beverages (energy-reduced soft drinks, energy drinks, sports and isotonic drinks, fruit juices, processed vegetables and vegetable juices, and other soft drinks), cereal products (cereal bars, cookies, biscuits, breakfast cereal bars), sugar confectionery (hard candies, soft candies/chocolate bars), and nutritionally complete and fortified foods (meal replacement bars, milk based meal replacement). Table 5 presents the intake estimate resulting from the use of the NF as an ingredient in the currently authorised uses.

TABLE 5 Intake estimate resulting from the use of the NF as an ingredient in the authorised uses as per the Union List.

		Mean intake (g/day)		P95 intake (g/day)	
Population group	Age (years)	Lowest[a]	Highest[a]	Lowest[b]	Highest[b]
Infants	< 1	0.2	2.7	1.2	11.9
Young children[c]	1 to < 3	1.8	9.0	6.9	26.9
Other children	3 to < 10	6.8	18.3	19.9	46.0
Adolescents	10 to < 18	7.2	33.4	24.7	94.1
Adults[d]	≥ 18	5.1	23.6	19.0	73.3

Abbreviations: NF, novel food; P95, 95th percentile.

[a]Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 11/10/2023. The lowest and the highest averages observed among all EU surveys are reported in these columns.

[b]Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 11/10/2023. The lowest and the highest P95 observed among all EU surveys are reported in these columns (P95 based on less than 60 individuals are not considered).

[c]Referred as 'toddlers' in the EFSA food consumption comprehensive database (EFSA, 2011).

[d]Intakes are assessed separately for adults [18–64 years], elderly [65–74 years] and very elderly (≥ 75 years); the maximum intake among these three sub-populations is reported here.

3.7.3.2 | *Intake estimates from already authorised food uses and extended proposed uses as a food ingredient*

Table 6 presents the intake estimate resulting from the use of the NF as an ingredient in the currently authorised uses according to the Union List and proposed extended uses (as per Table 4).

[6]https://www.efsa.europa.eu/en/data-report/food-consumption-data#the-efsa-comprehensive-european-food-consumption-database.

TABLE 6 Intake estimate resulting from the use of the NF as an ingredient in the authorised uses as per the Union List and proposed extended uses.

Population group	Age (years)	Mean intake (g/day)		P95 intake (g/day)	
		Lowest[a]	Highest[a]	Lowest[b]	Highest[b]
Infants	< 1	0.6	7.1	3.5	24.8
Young children[c]	1 to < 3	6.4	19.2	17.1	45.2
Other children	3 to < 10	14.6	31.4	29.5	62.5
Adolescents	10 to < 18	14.6	46.3	37.4	111.7
Adults[d]	≥ 18	11.4	41.6	32.7	99.9

Abbreviations: NF, novel food; P95, 95th percentile.

[a]Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 11/10/2023. The lowest and the highest averages observed among all EU surveys are reported in these columns.

[b]Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 11/10/2023. The lowest and the highest P95 observed among all EU surveys are reported in these columns (P95 based on less than 60 individuals are not considered).

[c]Referred as 'toddlers' in the EFSA food consumption comprehensive database (EFSA, 2011).

[d]Intakes are assessed separately for adults [18–64 years], elderly [65–74 years] and very elderly (≥ 75 years); the maximum intake among these three sub-populations is reported here.

3.7.3.3 | *Intake estimates from proposed use as a food supplement*

The proposed extended use from the applicant includes the use as a food supplement at a maximum dose of 30 g/day for the general population older than 10 years of age.

3.7.3.4 | *Total intake estimates*

Table 7 presents the total intake estimates resulting from the currently authorised uses of the NF as a food ingredient, the proposed extended uses as a food ingredient, and the proposed extended uses as food supplements.

TABLE 7 Total intake resulting from the uses of the NF as an ingredient and as a food supplement.

Population group	Age (years)	Highest[a] P95 intake from the NF used as an ingredient (g/day)	Intake from the NF used as a food supplement (g/day)	Total intake[b] (g/day)
Infants	< 1	24.8	N/A	24.8
Toddlers	1 to < 3	45.2	N/A	45.2
Other children	3 to < 10	62.5	N/A	62.5
Adolescents	10 to < 18	111.7	30	141.7
Adults	≥ 18	99.9[c]	30	129.9

Abbreviations: N/A, non applicable; NF, novel food; P95, 95th percentile.

[a]Intakes are assessed for all EU dietary surveys available in the food comprehensive database. The highest P95 observed among all surveys is reported in this column (P95 calculated based on less than 60 individuals are not considered).

[b]Total intake is the sum of the intake from NF ingredient use (highest P95) and from the NF used as a food supplement, for each population group.

[c]Intakes are assessed separately for adults [18–64 years], elderly [65–74 years] and very elderly (≥ 75 years); the maximum intake among these three sub-populations is reported here.

According to EFSA's current intake assessment approach using the DietEx tool, the highest P95 daily intake of the NF from the already authorised conditions of use as an ingredient is higher than previously estimated (UK FSA, 2012). The highest P95 total intake of authorised and suggested extension of use (Table 6) and as a food supplement ranges up to 142 g/day in adolescents (Table 7).

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

The NF consists of about 60% of glycaemic (i.e. digestible, available) carbohydrates – including monosaccharides, disaccharides and oligosaccharides – and 20% of 'dietary fibre' by weight (c.f. Sections 3.4 and 3.9).

While monosaccharides are directly absorbed in the small intestine, glycaemic carbohydrates with higher DP are enzymatically degraded, first through the action of salivary amylase and then in the small intestine by pancreatic amylase. Their degradation products are further hydrolysed to glucose by enterocyte brush border membrane enzymes. Isomaltase (i.e. oligo-1,6-glucosidase) hydrolyses the α-1,6 linkage in isomaltose and oligosaccharides. Absorbed monosaccharides are transported to the liver and then to the systemic circulation (EFSA NDA Panel, 2010).

Dietary fibres are passing to the large intestine undigested and form a substrate for the colonic microflora (EFSA NDA Panel, 2010).

Within the framework of this request for extension of use, further corroborating information on the fate of the NF has been provided by the applicant and is summarised below.

3.8.1 | *In vitro* models

The digestibility of the NF was investigated using two *in vitro* models: (i) an enzymatic mixture of pancreatin, invertase and amyloglucosidase, a technique validated to quantify starch digestibility in swine, and (ii) a rat intestinal mucosa acetic extract (Hu et al., 2017). In both experiments, maltose and resistant maltodextrin were used as digestible and non-digestible controls, respectively. With the rat intestinal mucosa extract, the NF was found to lead to a release of available glucose of about 20%, compared to about 5% for resistant maltodextrins and up to about 40% for maltose.

In a follow-up study (Hu et al., 2020), the digestibility of the NF was investigated *in vitro* using brush border enzymes from the rat intestinal mucosa and was found to reach about 50%.

3.8.2 | Animal studies

Hu et al. (2020) also determined the nutrient digestibility of the NF in vivo using ileal-cannulated swine for a period of 11 days, whereby digestibility of macronutrients was quantified by determination of the apparent ileal digestibility (AID) and apparent total tract digestibility (ATTD) of dry matter, crude protein, and gross energy. Animals were allocated to four different treatment groups, where they were fed with corn starch-casein based diets formulated to include 3% of either the NF, an IMO formulation with oligosaccharides with a greater DP and more α-(1 → 4) linkages than the NF, maltodextrin (positive control) or non-digestible resistant maltodextrin (negative control). Values for AID, ATTD and hindgut fermentation (ATTD-AID) of the NF for gross energy, dry matter and crude protein did not significantly differ from positive and negative controls. Values for AID and ATTD-AID consistently fell in between the positive and negative control values, indicating partial digestibility. Values for ATTD were comparable between the NF and both the positive and negative controls.

Additionally, oligosaccharide profiles were analysed in ileal samples. All ileal samples from pigs fed resistant maltodextrins showed a characteristic pattern, indicating that resistant maltodextrins partially resisted hydrolysis in the small intestine. Digesta samples from pigs fed the NF showed peaks corresponding to isomaltose and isomaltotriose standards, suggesting that the NF partially resisted hydrolysis in the small intestine.

The content of free glucose, as well as α-glucans following hydrolysis with H_2SO_4, were determined in ileal digesta and expressed relatively to dry matter. Total glucose levels following exposure to the NF were about 50% that of resistant maltodextrin, but not statistically significantly different from the latter. Contrary to both positive and negative control groups, high levels of free glucose were detected in the IMO group. The Panel notes that the IMO group data displayed very high variability for both total and free glucose levels.

Lactate and short chain fatty acid concentrations in ileal digesta did not significantly differ between IMO- and (resistant or not) maltodextrin-fed groups. The NF had little to no effect on the composition of faecal microbiota as compared to maltodextrin (as assessed by high throughput sequencing of 16S rRNA sequence tags).

3.9 | Nutritional information

From a nutritional point of view, the NF consists of about 60% of glycaemic (i.e. digestible, available) carbohydrates, including monosaccharides, disaccharides and oligosaccharides, and 20% of dietary fibre (i.e. non-digestible carbohydrates, assessed by the AOAC 2009.01 method) by weight (c.f. Section 3.4).

Dietary Reference Values (DRVs) have been established by EFSA for glycaemic carbohydrates (Reference Intake range between 45 and 60 E%) and dietary fibre (Adequate Intake of 25 g/day for adults) from mixed diets (EFSA NDA Panel, 2010). EFSA's definition of dietary fibre in that context (i.e. non-digestible carbohydrates plus lignin) does not reflect the additional requirement of having a beneficial physiological effect demonstrated by generally accepted scientific evidence laid down in Annex I of Regulation (EC) 1169/2011 for:

a. edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic, or chemical means and,
b. edible synthetic carbohydrate polymers.

It is out of the scope of this opinion to establish whether the fraction of non-digestible carbohydrates present in the NF meets the legal definition of dietary fibre in the EU or not.

The Panel assumes that the NF, under the proposed conditions of use and use levels, will replace other sources of digestible and non-digestible carbohydrates in the diet.

The Panel considers that the NF per se is not nutritionally disadvantageous.

3.10 | Toxicological information

In its application to the UK FSA, the applicant summarised a series of data relating to genotoxicity, toxicity and human tolerance of IMO from other manufacturers, and presented a human tolerability study of its own (Unpublished Study, 2012).

At the time, the UK FSA Committee did not identify any concerns relating to the toxicity or tolerability of IMO at the proposed intake levels.

Within the framework of this extension of use, the applicant carried out a new tolerability study in humans with the NF (Unpublished Study, 2020), and updated the information available in the literature regarding human exposure to IMO. No new original studies investigating the genotoxicity, (sub)acute or (sub)chronic exposure to the NF were provided.

In the light of the available data, the Panel considered that no new toxicological studies on the NF were required.

3.10.1 | Human data

In their previous application, the applicant had summarised a series of studies (Bouhnik et al., 2004; Chen et al., 2001; Kaneko et al., 1993; Kohmoto et al., 1988, 1992; Oku & Nakamura, 2002, 2003; Oku & Okazaki, 1999; Wang et al., 2001) relating to toxicological tests and human tolerance of IMO from other manufacturers, which did not raise safety concerns for the NF. The applicant also provided an unpublished human tolerance study of their own (Unpublished Study, 2012), indicating that consumption of the NF was safe and well-tolerated at a dose of 36 g/day. The UK FSA Committee considered that the latter provided reassurance that there were no concerns relating to tolerance at the intake levels proposed then, i.e. up to 15.6 g per serving or 31.2 g/day.

Studies involving human subjects and using the NF as a test substance that were not included in the previous risk assessment are summarised below.

3.10.1.1 | *New tolerability study carried out by the applicant*

In a new triple-blind, randomised, placebo-controlled, five-arm parallel study, the applicant investigated the safety and tolerability of the NF at doses of 60, 80, 100 and 120 g/day, compared to a control consisting of 60 g of maltodextrin (Unpublished Study, 2020). Participants (100 healthy, normal weight and overweight adults; 18–65 years) were instructed to take three servings of the investigational product per day (one after each meal) for 28 days (20 participants per group).

The sample size was determined to detect differences in several tolerance and safety parameters at a 5% significance level with 80% power, assuming a drop-out rate of 20%. Product compliance was assessed by counting the returned unused product at each visit; compliance was > 99% in all groups.

The tolerability of the NF was examined using a modified Gastrointestinal Symptoms Rating Scale (GSRS), a bowel habits diary (BHD), and a product perception questionnaire. The total GSRS score is a composite of individual gastrointestinal (GI) symptoms, with a higher sum indicative of greater discomfort. The mean total GSRS scores were 2.37, 4.42, 1.78 and 2.88 for the 60, 80, 100 and 120 g/day groups, respectively. The scores in the current study are consistent with low GSRS norm values, between 1.5 and 1.6 out of 7, in a healthy reference group of over 4600 participants (Dimenas et al., 1996). There was no difference in flatulence, bloating, soft stools or diarrhoea between the placebo and treatment groups.

No clinically relevant changes in glucose and insulin levels, electrolytes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, or creatinine levels were observed. There were statistically significant decreases in estimated glomerular filtration rate (eGFR) observed between the placebo and 80 and 100 g/day groups (−8% and −7% respectively), but the levels remained within the laboratory ranges expected in this age group. No clinically relevant changes were observed between groups in haematological parameters.

No significant changes across groups were observed in fasting glucose or insulin concentrations. There was a statistically significant increase in fasting glucose levels at Day 29 compared to Day 0 for participants supplemented with 60 g/day of the NF. Participants supplemented with 60 or 80 g/day displayed statistically significant increases in fasting insulin after 29 days. However, all insulin levels for these groups remained within reference intervals for fasting glucose, except for one participant in each group with a value outside the range at day 29.

No significant changes across groups were noted in fasting triglyceride concentrations or the total/high-density lipoprotein (HDL)-cholesterol ratio. However, a significant increase from baseline in both parameters was observed in all groups, except for fasting triglyceride concentrations in the control group. The Panel notes that increasing carbohydrate intakes (in the range of about 30–70 E%) replacing fat on an energy basis induces a decrease in plasma concentrations of HDL-cholesterol and an increase in the total/HDL-cholesterol ratio and triglyceride concentrations. The adverse effects of increasing total carbohydrate intakes on the blood lipid profile provided a basis for the NDA Panel to set the upper bound of the Reference Intake range for total (glycaemic) carbohydrates (EFSA NDA Panel, 2010) at 60%E (c.f. Section 3.9).

The Panel concludes that the study provides reassurance that the NF is tolerable at doses up to 120 g/day.

3.10.1.2 | *Literature data not considered in the previous assessment of the NF*

Subhan et al. (2020) investigated the glycaemic, insulin and incretin responses to the consumption of water, dextran (control), 20 g of dextrose or 20 g of the NF in two single blind crossover trials. Blood samples were collected from participants ($n = 12$ in trial 1; $n = 10$ in trial 2; 28.5 ± 4.4 years) at intervals up to 2 h after consumption. The NF and dextrose elevated blood glucose levels in a similar manner up to 1 h following intake. These results were substantiated by calculation of the 2-h incremental area under the curve (iAUC) for plasma glucose, which showed that the NF iAUC displayed no statistically significant difference from that of dextrose, while being significantly higher than that of the controls. Similar findings were obtained for plasma insulin. The responses to the NF of incretins active glucagon like peptide-1 (GLP-1) and glucose-dependent

insulinotropic polypeptide (GIP) were comparable to that of dextrose. No gastrointestinal adverse effects were reported by the participants (Subhan et al., 2020).

The Panel notes that no adverse events related to the consumption of the NF were reported. The Panel notes, however, that human studies designed to investigate tolerability rather than safety are of limited value to the safety assessment.

3.11 | Allergenicity

In its 2012 assessment, the UK FSA Committee did not raise any concerns relating to allergenicity, other than stating that the NF will need to be labelled in accordance with requirements for food allergens if it is derived from one of the allergenic crops identified in EU labelling legislation (Directive 2000/13/EC and Regulation (EU) 1169/2011), unless a specific exemption is obtained following an evaluation by EFSA.

The Panel considers that, owing to the low amount of protein present, 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 for extension of use is IMO. The NF is produced via enzyme-catalysed hydrolysis of food grade starch from different plant-based crops and consists of glucose oligomers with DP of 3–9, along with various amounts of mono- and disaccharides.

Pursuant to Article 4 of the former Regulation (EC) No 258/97 by the UK FSA in February 2016, the NF is currently authorised to be marketed as a food ingredient in certain beverages, cereal products, sugar confectionery, and nutritionally complete and fortified foods. The applicant herewith intends to extend these uses as a food ingredient to several food products for the general population, as well as food supplements at a maximum dose of 30 g/day for the general population older than 10 years of age.

Within the framework of this extension of use, the applicant carried out a new tolerability study in adult volunteers with the NF at doses up to 120 g/day. The Panel concludes that this study provides reassurance that the NF is tolerable at doses of 120 g/day.

Conservative intake estimates resulting from the use of the NF as an ingredient in the authorised uses as per the Union List and new proposed uses were carried out for the general population, based on the EFSA Comprehensive European Food Consumption Database. The highest intake estimate was calculated for adolescents at 112 g/day at the 95th percentile, and reaches 142 g/day in adolescents when the use as a food supplement is included. The Panel notes this amount is higher than the dose of 120 g/day for which tolerability has been demonstrated.

However, considering the source, compositional characterisation, production process and nature of the NF, as well as the available nutritional and toxicological data on the NF, the Panel considers that the NF does not present safety concerns under the proposed conditions of use.

5 | CONCLUSIONS

The Panel concludes that the NF, IMO, is safe under the proposed conditions of use.

5.1 | Protection of proprietary data in accordance with Article 26 of Regulation (EU) 2015/2283

The Panel could not have reached the conclusion on the safety of the NF under the proposed conditions of use without the data claimed as proprietary by the applicant [two safety and tolerability studies of IMO in healthy adults (2012, 2020), their summaries and supplemental data, the compositional data and related expert opinion, the original NF application to UK FSA, product batch data, certificates of analysis, description of analytical methods, laboratory accreditation certificates, intake reports and stability data].

6 | STEPS TAKEN BY EFSA

1. On 15/10/2021, EFSA received a letter from the European Commission with the request for a scientific opinion on an extension of use of Isomalto-oligosaccharide as a novel food [Ref. Ares(2021)6276757].
2. On 15/10/2021, a valid application on isomalto-oligosaccharide, which was submitted by BioNeutra North America Inc., was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2021/2469) and the scientific evaluation procedure was initiated.

3. On 18/02/2022, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
4. On 24/06/2022, additional information was provided by the applicant through the Commission e-submission portal and the scientific evaluation was restarted.
5. During its meeting on 14/12/2023, the NDA Panel, having evaluated the data, adopted a scientific opinion on the extension of use of Isomalto-oligosaccharide as a novel food pursuant to Regulation (EU) 2015/2283.

ABBREVIATIONS

1H NMR	proton nuclear magnetic resonance
ACNFP	Advisory Committee on Novel Foods and Processes
ADME	absorption, distribution, metabolism and excretion
AID	apparent ileal digestibility
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AOAC	Association of Official Analytical Chemists
AST	aspartate aminotransferase
ATTD	apparent total tract digestibility
BHD	bowel habits diary
bw	body weight
CFU	colony forming units
DP	degrees of polymerisation
DRV	dietary reference value
eGFR	estimated glomerular filtration rate
FCC	Food Chemical Codex
FLD	fluorescence detection
GI	gastrointestinal
GIP	glucose-dependent insulinotropic polypeptide
GLP	good laboratory practice
GLP-1	glucagon-like peptide-1
GMP	good manufacturing practice
GSRS	gastrointestinal symptoms rating scale
HDL	high-density lipoprotein
HILIC	hydrophilic interaction chromatography
HPLC	high-performance liquid chromatography
iAUC	incremental area under the curve
ICP	inductively coupled plasma
IMO	isomalto-oligosaccharide
MFHPB	Microbiology Food Health Protection Branch (of the Canadian Food Inspection Agency)
MS	mass spectrometry
n.d.	not detected
N/A	non applicable
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NF	novel food
NOAEL	no observed adverse effect level
NP	normal phase
P95	95th percentile
RI	refractive index
rRNA	ribosomal ribonucleic acid
SE	size exclusion
TAMC	total aerobic microbial count
TYMC	total yeast and mould count
UK FSA	United Kingdom Food Standards Agency
USP	United States Pharmacopeia

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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.

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SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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ANNEX

Annex A Dietary exposure estimates to the Novel Food for each population group from each EU dietary survey: already authorised uses

Information provided in this Annex is shown in an Excel file (downloadable at https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2024.8543#support-information-section).

Annex B Dietary exposure estimates to the Novel Food for each population group from each EU dietary survey: already authorised uses and extended proposed uses as a food ingredient

Information provided in this Annex is shown in an Excel file (downloadable at https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2024.8543#support-information-section).