Position papers

Committee Advice Document: Change of conditions of use for the novel food, isomalto-oligosaccharides

Reference Number RP1033

Assessment finalised: 15th of November 2023

Summary

An application was submitted to the Food Standards Agency (FSA) and Food Standards Scotland (FSS) in April 2021 from Bioneutra Incorporated, North America (“the applicant”) for the authorisation of the proposed extension of use of isomalto-oligosaccharides (IMOs) as a novel food.

The novel food are IMOs which are intended to be used as a food ingredient and as an ingredient in food supplements. IMOs are manufactured by the enzyme hydrolysis of starch which is sourced from different plant crops (e.g., cereals, legumes, and roots).

IMOs are currently authorised as a novel food in the UK (assimilated Commission Implementing Regulation (EU) 2017/2470). This new application is an extension of the intended uses of IMOs, seeking to use the novel food within the food categories: 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, and as an ingredient in food supplements.

To support the FSA and FSS in their evaluation of the application, the Advisory Committee on Novel Foods and Processes (ACNFP) were asked to review the safety dossier and supplementary information provided by the applicant. Please

note the Committee did not consider any potential health benefits or claims arising from consuming the food, as the focus of the novel food assessment is to ensure the extension of use of the food is safe, and not putting consumers at a nutritional disadvantage.

The Committee concluded that the applicant had provided sufficient information to assure the proposed extension of use for IMOs, was safe under the proposed conditions of use. The anticipated intake levels and the proposed use in foods was not considered to be nutritionally disadvantageous.

1. Introduction

1. The ACNFP assessed the food safety risks of IMOs and its production under the proposed uses, in line with Article 7 of assimilated Commission Implementing Regulation (EU) 2017/2469. The basis and structure of the assessment was conducted using the assimilated regulatory framework and the technical guidance put in place by the European Food Safety Agency (EFSA) for full novel food applications (EFSA NDA Panel, 2021).

2. In April 2021, Bioneutra Incorporated, North America (“the applicant”) submitted an application to change the conditions of use of isomalto-oligosaccharides (IMOs). The novel food is a powder containing ≥ 99% w/w IMOs or a syrup containing ≥ 75% w/w IMOs on a dry matter basis IMOs are manufactured by the enzyme hydrolysis of starch sourced from different plant crops (e.g., cereals, legumes, and roots) and are intended to be used as a food ingredient and as an ingredient in food supplements.

3. Following the review by the ACNFP in February 2023, further information was requested from the applicant concerning the proposed uses of IMOs, in order to address information gaps in the initial dossier. The final advice from the Committee was agreed at the 163rd meeting, allowing the FSA and FSS to complete the risk assessment.

4. The Committee advice document (CAD) outlines the conclusions of the ACNFP on the safety of the extension of use of IMOs as a novel food.

2. Assessment

2.1 Identity of the novel food

5. The novel food is produced in the form of a powder containing ≥ 99% w/w IMOs or a syrup containing ≥ 75% w/w IMOs on a dry matter basis. Enzyme catalysed hydrolysis of plant derived starch yields IMOs consisting of approximately 30% mono- and disaccharides, and 70% oligosaccharides characterised by three or more degrees of polymerisation. The oligosaccharides are linked together by α-(1,6)-bonds.

6. There is no change to the specification of the novel food as currently defined in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

2.2 Production Process

7. The novel food is manufactured via the enzyme catalysed hydrolysis of potato- or wheat-derived starch slurry to yield IMOs. The assessment of the production process was conducted by the FSA (2012) and did not raise any concerns.

8. The production process has not changed; however, additional sources of starch, derived from corn, pea, or tapioca, are now utilised in the novel food manufacturing process. Certificates of analysis for each additional starch source have been provided.

2.3 Compositional information

9. Analytical results from five new independent batches of IMOs as a syrup (Table 1) demonstrate that the novel food consistently meets the specification levels published in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

Table 1. Compositional analysis of the novel food as a syrup.

Test Parameter	Batch 1S	Batch 2S	Batch 3S	Batch 4S	Batch 5S
Viscosity (mPa-s/cP)	4,025	4,025	4,300	4,375	4,775
Solid content (g/100g)	75.8	76.2	76.1	76	75.7

Test Parameter	Batch 1S	Batch 2S	Batch 3S	Batch 4S	Batch 5S
Water activity	0.8	0.8	0.8	0.8	0.8
pH	4.8	4.4	4.6	4.5	5.2
Sulphated ash (g/100g)	0.219	0	0.044	0.058	0
Glucose (% dry basis)	0.86	0.78	0.81	1.41	0.57
Isomaltose + DP3 to DP9 * (% dry basis)	89.81	90.20	90.22	90.56	90.74
Lead (mg/kg)	0.02	0.02	0.02	0.02	0.02
Arsenic (mg/kg)	0.03	0.03	0.03	0.03	0.03
Cadmium (mg/kg)	0.02	0.02	0.02	0.02	0.02
Mercury (mg/kg)	0.02	0.02	0.02	0.02	0.02
Total aerobic count (CFU/g)	10	10	10	10	10
Yeast and mould (CFU/g)	10	10	10	10	10
Escherichia coli (Absent in 10g)	Absent	Absent	Absent	Absent	Absent

Test Parameter	Batch 1S	Batch 2S	Batch 3S	Batch 4S	Batch 5S
Salmonella (Absent in 375g)	Absent	Absent	Absent	Absent	Absent
Staphylococcus aureus (Absent in 25g)	Absent	Absent	Absent	Absent	Absent
Coliform (CFU/g)	10	10	10	10	10
Enterobacteriaceae (CFU/g)	10	10	10	10	10
Viscosity (mPa-s/cP)	4,025	4,025	4,300	4,375	4,775
Solid content (g/100g)	75.8	76.2	76.1	76	75.7
Water activity	0.8	0.8	0.8	0.8	0.8

mPa-s = millipascal seconds; cP = centipoises; DP = degrees of polymerisation; CFU = colony forming units

* isomaltose + DP3 to DP9 saccharides have α-(1,6)-bonds

10. Analytical results from five new independent batches of IMOs as a powder (Table 2) demonstrated that the novel food consistently meets the specification levels published in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

Table 2. Compositional analysis of the novel food as a powder

Test Parameter	Batch 1P	Batch 2P	Batch 3P	Batch 4P	Batch 5P

Moisture (%)	3.17	2.92	2.63	2.48	3.34
pH	4.8	4.7	5.8	4.7	5.8
Sulphated ash (g/100g)	0.195	0.215	0.045	0.081	0.117
Glucose (% dry basis)	0.25	0.47	1.26	0.92	0.68
Isomaltose + DP3 to DP9 * (% dry basis)	90.97	92.33	90.32	90.08	90.73
Lead (mg/kg)	0.004	0.02	0.02	0.003	0.010
Arsenic (mg/kg)	0.015	0.03	0.03	0.005	0.05
Cadmium (mg/kg)	0.004	0.02	0.02	0.003	0.005
Mercury (mg/kg)	0.004	0.02	0.02	0.003	0.002
Total aerobic count (CFU/g)	10	130	10	10	10
Yeast and mould (CFU/g)	10	40	10	10	10
Escherichia coli (Absent in 10g)	Absent	Absent	Absent	Absent	Absent
Salmonella (Absent in 375g)	Absent	Absent	Absent	Absent	Absent
Staphylococcus aureus (Absent in 25g)	Absent	Absent	Absent	Absent	Absent

Coliform (CFU/g)	10	10	10	10	10
Enterobacteriaceae (CFU/g)	10	10	10	10	10

DP = degrees of polymerisation; CFU = colony forming units

* isomaltose + DP3 to DP9 saccharides have α-(1,6)-bonds

Heavy metal analysis conducted at different analytical laboratories – Batches 1 and 4 (Lab 1); Batches 2 and 3 (Lab 2); Batch 5 (Lab 3).

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

12. The new analytical data demonstrate that the novel food can be consistently produced to meet the specification published in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470). The specification is reproduced in Table 3.

2.4 Stability

13. Information concerning the stability of the novel food was assessed in the original authorisation (FSA, 2013) and did not raise concerns.

2.5 Specification

14. The specification for the novel food (Table 3) is currently defined in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

Table 3: Specification for the novel food reproduced from the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

Specification Parameter	Syrup	Powder	Method
Solubility (% in water)	NA	≥ 99	

Specification Parameter	Syrup	Powder	Method
Dried solids (g/100g)	> 75	NA	USP 831>
Glucose (% dry basis)	≤ 5	≤ 5	HPLC-RI
Isomaltose + DP3 to DP9 * (% dry basis)	≥ 90	≥ 90	HPLC-RI
Moisture	NA	≤ 4 %	AOAC 972.20
pH	4 to 6	NA	USP 791>
Sulphated ash (g/100g)	≤ 0.3	≤ 0.3	USP 281>
Lead (mg/kg)	≤ 0.5	≤ 0.5	USP 233>
Arsenic (mg/kg)	≤ 0.5	≤ 0.5	USP 233>
Total Aerobic Plate Count (CFU/g)	1,000	1,000	USP 2021/2022>
Yeast and mould (CFU/g)	100	100	USP 2021/2022>
Escherichia coli (Absent in 10g)	Absent	Absent	USP 2021/2022>
Salmonella (Absent in 375g)	Absent	Absent	USP 2021/2022>
Staphylococcus aureus (Absent in 25g)	Absent	Absent	USP 2021/2022>

Specification Parameter	Syrup	Powder	Method
Coliform (CFU/g)	10	10	MFHPB-34
Enterobacteriaceae (CFU/g)	10	10	USP 2021/2022>

USP = United States Pharmacopeia; HPLC-RI – High Performance Liquid Chromatography – Refractive Index; DP = degrees of polymerisation; NA = not applicable; AOAC = Association of Official Analytical Chemists; CFU = colony forming units; MFHPB = Microbial Analysis of Food Health Protection.

* Isomaltose and DP3 to DP9 saccharides have α-(1,6)-bonds.

2.6 History of Use

15. IMOs are currently authorised as a novel food in the UK (assimilated Commission Implementing Regulation (EU) 2017/2470). The current authorised uses for IMOs are listed in Table 4.

Table 4: Current authorised uses and maximum use levels of the novel food reproduced from the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

Specified Food Category	Maximum Use Levels (%) *
Energy-Reduced Soft Drinks	6.5
Energy Drinks	5.0
Foods intended to meet the expenditure of intense muscular efforts, especially for athletes (including isotonic drinks)	6.5
Fruit Juices	5.0

Specified Food Category	Maximum Use Levels (%) *
Processed Vegetables and Vegetable Juices	5.0
Other Soft Drinks	5.0
Cereals Bars	10
Cookies, Biscuits	20
Breakfast Cereal Bars	25
Hard Candies	97
Soft Candies/Chocolate Bars	25
Meal replacement for weight control (as bars or milk based)	20

* Maximum use levels of IMOs reported as % in table derived from g/100g or g/100ml of final food or beverage, on a consumed basis.

16. IMOs are also approved for use as a food in Australia/New Zealand, Canada, China, India, Israel, Japan, Korea, and the USA.

2.7 Proposed Use and Anticipated Intake

17. The general population are identified as the target population for the novel food.

18. The extension of use for the novel food will increase the number of permitted food categories for IMOs by fourteen, from twelve to twenty-six. The further intended food use categories and their respective maximum use levels are listed in Table 5.

Table 5: Further intended food use categories for the novel food and their maximum use levels

Specified Food Category	Maximum Use Level (g/100g or g/100ml)
Ice Cream and Dairy Desserts	8
Instant Coffee and Tea	10
Table-Top Sweeteners	100
Cakes, Muffins, Pies	20
Pastries	15
Breakfast Cereals	10
Condiments/Relishes; Gravies and Sauces	10
Gelatines, Puddings, Fillings	15
Jams and Jellies	50
Yoghurts	2.5
Milk Based Drinks	5
Snack Foods	5
Sweet Sauces, Toppings and Syrups	50

- Ingredient in Food Supplements *
- Chewable supplements 25
- Tablet format 97

* Food Supplements as defined in the Food Supplements (England) Regulations 2003, the Food Supplements (Wales) Regulations 2003 and the Food Supplements (Scotland) Regulations 2003 – IMOs to be used as a sweetener only, and not the active ingredient(s) in food supplements.

19. An intake assessment using the summary statistics of consumption from the UK National Diet and Nutrition Survey (NDNS data, Years 9 to 11) was conducted by matching the proposed conditions of use with the appropriate food categories. The estimated mean and high-level intakes of IMOs from the current authorised food uses and the intended food use categories are presented in Tables 6 and 7.

Table 6: Estimated daily intake of the novel food from current food uses of IMOs using NDNS data (Years 9 – 11).

Population Group	Mean intake (g/day)	P95 intake (g/day)	Mean intake (g/kg BW/day)	P95 intake (g/kg BW/day)
Young children	9	24	0.7	1.8
Other children	15	37	0.6	1.5
Adolescents	23	53	0.5	1.1
Adults	20	57	0.3	0.7
Elderly	11	28	0.1	0.4

P95 = 95^{th} percentile; young children ≤ 2 years; other children 3 – 9 years; adolescents 10 – 17 years; adults 18 – 64 years; elderly ≥ 65 years.

Table 7: Estimated daily intake of the novel food from intended food uses of IMOs using NDNS data (Years 9 – 11).

Population Group	Mean intake (g/day)	P95 intake (g/day)	Mean intake (g/kg BW/day)	P95 intake (g/kg BW/day)
Young children	6	13	0.5	1.0
Other children	12	26	0.5	1.1
Adolescents	12	27	0.2	0.6
Adults	11	26	0.1	0.4
Elderly	12	29	0.2	0.4

P95 = 95th percentile; young children ≤ 2 years; other children 3 – 9 years; adolescents 10 – 17 years; adults 18 – 64 years; elderly ≥ 65 years.

20. The combined estimated intake assessment for IMOs (Table 8) reports that adolescents are expected to have the highest estimated mean intake for IMOs at 35 g/day; adults are expected to have the highest estimated 95th percentile intake of IMOs at 70 g/day. Young children and other children report the highest estimated mean intakes of IMOs on a body weight basis. The highest estimated 95th percentile intakes of IMOs on a body weight basis are reported for young children.

21. The percentage of consumers of the novel food was 100% among all population groups, except for young children at 98.8% and other children at 99.4%.

Table 8: Estimated daily intake of the novel food from intended and current food uses of IMOs using NDNS data (Years 9 – 11).

Population Group	Mean intake (g/day)	P95 intake (g/day)	Mean intake (g/kg BW/day)	P95 intake (g/kg BW/day)
Young children	15	30	1.2	2.5
Other children	27	52	1.2	2.1
Adolescents	35	69	0.7	1.5
Adults	30	70	0.4	0.9
Elderly	23	47	0.3	0.6

P95 = 95th percentile; young children ≤ 2 years; other children 3 – 9 years; adolescents 10 – 17 years; adults 18 – 64 years; elderly ≥ 65 years.

22. In terms of contribution to total mean intake of IMOs, diet soft drinks, carbohydrate-electrolyte, isotonic and sport drinks, and regular soft drinks, were the main sources of intake across all population groups on an absolute basis and on a body weight basis.

2.8 Absorption, Distribution, Metabolism and Excretion (ADME)

23. Information concerning the ADME of the novel food was assessed in the original authorisation (FSA, 2013) and did not raise concerns.

2.9 Nutritional information

24. The novel food is expected to replace sugar as an ingredient in the intended food categories because IMOs have a lower glycaemic index. The Committee looked in detail at the food supplement use and whether the dose proposed would represent a nutritional disadvantage. It was clarified that in food supplements, IMOs are present as a sweetener rather than the active ingredient(s). In the context of high sugar consumption in the diet, replacing sugar or starches with the novel food was not considered nutritionally disadvantageous at the dose

proposed.

25. Based on this information, the consumption of the novel food is not expected to be nutritionally disadvantageous for consumers at the maximum use levels specified in this application.

2.10 Toxicological information

2.10.1 *In vitro* and *in vivo* toxicology studies

26. Peer reviewed *in vitro* and *in vivo* studies concerning the safety of IMOs were assessed in the original authorisation (FSA, 2013) and did not raise concerns.

27. No new *in vitro* or *in vivo* safety studies conducted under Good Laboratory Practice (GLP) standards and following OECD guidelines were identified.

2.10.2 Human studies

28. Prior to the original authorisation of the novel food, the FSA requested a human trial should be conducted to provide reassurance on the tolerance of the IMOs at the proposed levels of use (FSA, 2012). The 4-week study established that the novel food was safe and tolerable at doses of up to 54 g/day (Bioneutra, 2012 [unpublished]).

29. Evidence was provided to support the extension of use of the novel food. Copies of peer reviewed human trials on the tolerability of IMOs, published after the original authorisation, were provided (Yen *et al.*, 2011; Gourineni *et al*., 2018; Grubic *et al.*, 2018). However, as these IMO products are manufactured by other companies, a new human trial was conducted to investigate the tolerability of the novel food at higher doses in a four-week, triple-blind, randomised, parallel study (Bioneutra, 2020 [unpublished]).

30. No clinically relevant differences in the clinical chemistry, haematology, lipid profile, or glucose and insulin parameters between the placebo and IMO dose groups were reported. In addition, there were no differences in the adverse effects (flatulence, bloating, soft stools, or diarrhoea) between the placebo and the IMO dose groups. Based on these observations, doses of up to 120 g/day of the novel food are expected to be well-tolerated.

2.11 Allergenicity

31. Post-fermentation, the IMOs are filtered and passed through a series of anionic and cationic exchange resins to remove yeast cells, residual enzymes, and protein contaminants. Information concerning the potential allergenicity of the novel food from these contaminants was assessed in the original authorisation (FSA, 2013). No concerns were raised on the extension of use.

3. Discussion

32. The novel food are isomalto-oligosaccharides (IMOs), a mixture of approximately 30% mono- and disaccharides, and 70% oligosaccharides characterised by three or more degrees of polymerisation.

33. IMOs are derived from food grade starch and manufactured *via* enzyme-catalysed hydrolysis, followed by filtration and purification steps to generate either a powder or liquid (syrup) form of the novel food. In the original authorisation, the starch was sourced from potato and wheat. With this extension of use application, the production process can also utilise additional sources of starch derived from corn, pea, or tapioca.

34. Analytical data from new independent batches of the novel food, in syrup and powder formats, confirmed that IMOs can be manufactured in accordance with the specification currently defined in the List of Novel Foods (assimilated Commission Implementing Regulation (EU) 2017/2470).

35. The food applications of IMOs will be extended from the current authorised uses 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, and as an ingredient in food supplements.

36. The estimated highest 95^{th} percentile intakes from existing and new uses of IMOs, calculated from the UK National Diet and Nutrition Survey, were reported as 69 and 70 g/day in the adolescent and adult sub-populations, respectively. In comparison, a human trial conducted to assess the safety and tolerability of the novel food (Bioneutra, 2020 [unpublished]) reported that IMOs were well-tolerated in doses of up to 120 g/day. This suggests a margin of safety of 1.7 which is considered appropriate given this is based on human data and the nature of the effects seen.

4. Conclusion

37. The ACNFP have undertaken the assessment of the extension of use of isomalto-oligosaccharides (IMOs) and concluded that the composition of the novel food is safe under the proposed conditions of use and does not pose a safety risk to human health. The anticipated intake levels and the proposed uses in food and food supplements was not considered to be nutritionally disadvantageous.

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

- Human studies on the tolerance of the novel food at the proposed conditions of use (Bioneutra unpublished report, 2020).

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