APPLICATION FOR THE EXTENSION OF USE OF ISOMALTO-OLIGOSACCHARIDES (EC 103) IN THE EUROPEAN UNION

Pursuant to

Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on Novel Foods

NON-CONFIDENTIAL SUMMARY

SUBMITTED BY:
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Summary

The subject matter of this application is isomalto-oligosaccharides (IMO), a novel food that is currently authorised for use in the European Union (EU). BioNeutra North America Inc. (BioNeutra) gained approval to market isomalto-oligosaccharide (IMO; EC 103) as both a syrup and powder in the EU in 2013[1]. The initial application was filed with the United Kingdom (UK) Food Standards Agency (FSA), and the safety of the material was subsequently endorsed by all of the Member States. These products with a sweet, light taste have been incorporated into various food products and consumed throughout the EU for the past 8 years, without any reported adverse effects. BioNeutra wishes now to extend the use of IMO to additional food categories in the EU.

BioNeutra's IMO syrup and powdered products are marketed under the trade name VitaFiber® (previously Vitasugar™). BioNeutra does not seek to change the production process from that which has originally been considered and approved. Briefly, starch is treated with enzymes for liquefaction and saccharification of starch, followed by fermentation for the removal of monosaccharides. Following a series of filtration and purification steps, the final IMO ingredient is produced by concentration and drying (powdered IMO only) of the final product. BioNeutra does not seek to amend specifications for syrup and powder IMO preparations indicated on the Union list of novel foods [Commission Implementing Regulation (EU) 2017/2470[2]]. The composition of BioNeutra's IMO products remains identical to those filed within the original application for IMO in 2008. The majority of oligosaccharides found in BioNeutra's IMO products consist of 3 to 6 monosaccharide units linked together; however, disaccharides, as well as longer polysaccharides (up to 9 units), also are present.

In addition to the current status within the EU, IMOs are approved and consumed within many other countries of the world including Australia/New Zealand, Canada, China, Israel, India, Japan, Korea, and the United States. Approvals and sales within many of these jurisdictions predate those of the EU with no adverse effects reported.

IMO is currently authorised for use in certain beverages, cereal products, sugar confectionery, nutritionally complete and fortified foods, as specified on the Union list of novel foods [Commission Implementing Regulation (EU) 2017/2470]. BioNeutra requests the extension of use of IMO in the EU to 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, at use levels ranging from 2.5 to 100% of the final food as consumed. IMO 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, which are intended to be consumed alternatively to foods permitted or proposed to contain IMO. As a result, IMO intake from food supplements is not intended to add to the daily intake of IMO from food sources. The labelling of IMO food supplements will, therefore, bear a statement that they should not be used if other foods containing added IMO are consumed the same day. The proposed extensions of use are **bolded** in Table 1. Anticipated intakes of IMO under permitted and proposed conditions of use in the EU were assessed using chronic food consumption statistics from the European Food Safety Authority (EFSA) Comprehensive European Food Consumption Database. As consumption data from this database

[1] https://acnfp.food.gov.uk/sites/default/files/mnt/drupal_data/sources/files/multimedia/pdfs/isomalto.pdf.

[2] Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. C/2017/8878. OJ L 351, 30.12.2017, p. 72–201. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1533914206967&uri=CELEX:32017R2470 (Latest Consolidated Version: 23/02/2021).

have not previously been used to evaluate the anticipated intake of IMO, for which summary statistics of food consumption for pre-determined food categories only are publicly available, IMO intakes were first estimated from permitted food uses only to determine current anticipated daily intakes of IMO in the EU, followed by the evaluation of IMO intakes from permitted and proposed food uses to determine the impact of the additional proposed food uses. IMO syrup and powder ingredients have been marketed throughout the EU over the past 8 years under the permitted conditions of use with no associated adverse health effects reported. The addition of the proposed food uses resulted in a 19 g/person/day (21% increase) to the highest high-level intake estimate. Dietary intake estimates of IMO from the assessment are considered conservative based on the assumption that all foods in permitted and/or proposed food categories contain IMO at the maximum specified level of use, and that summary statistics of food consumption from the EFSA Comprehensive European Food Consumption Database are intended to be used as a screening tool.

Table 1 Permitted and Proposed[a] Food Uses and Use Levels of IMO

Specified Food Category	Maximum Levels	Additional Specific Labelling Requirements
Energy-Reduced Soft Drinks	6.5%	1. The designation of the novel food on the labelling of the foodstuffs containing it shall be "isomalto-oligosaccharide". 2. Foods containing the novel ingredient must be labelled as "a source of glucose". 3. **Food supplements containing isomalto-oligosaccharide shall bear a statement that the food supplement should not be used if other foods with added isomalto-oligosaccharide are consumed the same day.**
Energy Drinks	5.0%	
Foods intended to meet the expenditure of intense muscular efforts, especially for sportsmen (including isotonic drinks)	6.5%	
Fruit Juices	5.0%	
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%	
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%**	
Food Supplements as defined in Directive 2002/46/EC[b]	**30 g/day for the general population older than 10 years**	

IMO = isomalto-oligosaccharide.

[a] Food uses proposed for the extension of use are **bolded**.

[b] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51–57. Available online: http://eur-

Table 1 Permitted and Proposed[a] Food Uses and Use Levels of IMO

Specified Food Category	Maximum Levels	Additional Specific Labelling Requirements
lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32002L0046&qid=1442597959590 (Latest Consolidated Version: 26/07/2017).		

The safety of IMO mixtures has been confirmed through a detailed knowledge of the metabolic profile of the individual IMO components, as well as the results from a series of published animal toxicity studies and several human tolerance studies, including a recent triple-blind tolerability study, reporting no adverse toxicological effects relevant to the conditions of intended use in foods within the EU.

In vivo animal and human studies evaluating IMO metabolism demonstrate that the larger IMOs are resistant to enzymatic hydrolysis in the upper gastrointestinal (GI) tract and remain unabsorbed following oral consumption. Findings from recent *in vitro* assays and an *in vivo* study in ileal-cannulated pigs evaluating the digestibility of VitaFiber® (IMO) support the lack of absorption of isomalto-oligomers with alpha-1,6-linkages from IMO. In the large intestine, the unabsorbed IMOs are subject to fermentation by the microflora, resulting in the generation of short-chain fatty acids with the fermentation products subsequently absorbed and utilised in well-characterised biochemical pathways. The smaller saccharides are subject to enzymatic hydrolysis in the upper GI tract. Glucose, produced as a result of the hydrolysis of the digestible saccharides, is absorbed in the upper GI tract and used by the body as a source of energy.

IMO products were found to be non-mutagenic/genotoxic when examined *in vitro*, in bacterial and mammalian cells, with or without metabolic activation.

Short-term animal feeding studies conducted at dose levels up to 20% IMO in the diet (equivalent to approximately 20 g/kg body weight/day) for periods up to 35 days showed no significant treatment-related effects other than an increase in caecal weight or caecal content when compared to untreated controls, which are considered common physiological effects in rodent studies when the animals are fed large concentrations of a non-absorbable material.

Human studies ranging in duration from 7 to 30 days have also been conducted to assess various indices related to the putative prebiotic properties of IMO preparations, the glycaemic and insulinemic response to IMO, and also to evaluate their tolerability. While some increases in minor GI symptoms (*e.g.* flatulence, abdominal pain and distension, borborygmi) were reported following consumption of 10 to 30 g of IMO preparations, none of these study subjects experienced increased incidences or severity of diarrhoea. A threshold value of 1.5 g/kg body weight or greater (approximately 90 g and 105 g for a 60-kg and 70-kg person, respectively) has been determined for the induction of transient diarrhoea resulting from the consumption of single bolus doses of IMOs. In 2 trials that included evaluations of biochemistry, no significant variations were observed in several clinical chemistry parameters when elderly subjects or haemodialysis patients were provided 24 or 30 g of an IMO preparation for 30 and 28 days, respectively. In comparison to pre-treatment values, the haemodialysis patients did, however, exhibit elevated haemoglobin and haematocrit values following ingestion of the IMO mixture, which, as suggested by the study authors, may have been at least in part due to enhanced iron absorption.

BioNeutra has conducted 2 human studies on their IMO product to evaluate its safety and tolerability in healthy adults over a period of 4 weeks. Safety and tolerability endpoints evaluated included adverse effects, bowel habits, GI symptoms, and clinical chemistry and haematology measurements. In both studies, IMO was found to be safe and well-tolerated at the doses evaluated.

The weight of the available evidence on the safety of IMO demonstrates that there are no systemic safety concerns from the use of IMO in foods and that anticipated intakes of IMO from permitted and proposed conditions of use are supported by human tolerability studies of IMO.