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Safety of a change in the conditions of use of galacto-oligosaccharides as a novel food ingredient in food supplements 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 change in the conditions of use of galacto-oligosaccharides (GOS) as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF is mainly composed of GOS, consisting of different galactosyl residues (two to nine) linked to a terminal glucose by a β-glycosidic bond but also contains lactose and its monomers (galactose and glucose). The NF is a syrup containing ≥ 55% GOS (w/w dry matter) and is produced enzymatically by two β-galactosidases. GOS produced by β-galactosidases according to the same production process is already authorised and included in the EU Union list of novel foods. This application is limited to an assessment of the proposed increase of the use level as food supplement. The proposed change in the conditions of use increases the maximum level in food supplements from 0.333 kg GOS/kg food supplement (33.3%) to 0.450 kg GOS/kg food supplement (45.0%). Since it is recommended that individuals consume no more than 3 servings of 12 g/day, the maximum recommended daily intake would be no more than 16.2 g GOS. No new food uses or other increases to the already approved use levels are being proposed. The information provided on the proposed use levels and anticipated intake do not raise safety concerns. The Panel concludes that the proposed increase in the maximum level of galacto-oligosaccharides as a NF in food supplements is safe under the proposed changes in conditions of use.

Keywords: galacto-oligosaccharides, GOS, dietary fibre, novel foods, food supplement

Requestor: European Commission

Question number: EFSA-Q-2020-00211

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1. Introduction

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

On 3 March 2020, the company Yakult Pharmaceutical Industry Co., Ltd. submitted a request to the European Commission to change the conditions of use of the novel food galacto-oligosaccharide within the meaning of Article 10(1) of Regulation (EU) 2015/2283.

The application requests to increase the use level of galacto-oligosaccharide in food supplements.

In accordance with Article 29(l)(a) of Regulation (EC) No 178/2002, the European Commission asks EFSA to provide a scientific opinion by carrying out the assessment of the change of the conditions of use of galacto-oligosaccharide as a novel food in accordance with Article 10(3) of Regulation (EU) 2015/2283.

1.2. Interpretation of the Terms of Reference

The application is referring exclusively to a request for a change in the maximum use levels for galacto-oligosaccharides (GOS) when used as a food supplement. GOS produced by the same production process using lactose and microbiologically produced β-galactosidases are already authorised to be added to several food categories and as a food supplement and included in the EU Union list of novel foods (Commission Implementing Regulation (EU) 2017/2470[1]).

Therefore, the current assessment is exclusively focussed on the proposed changes with respect to the possible impact on the safety and nutritional aspects of the novel food (NF).

1.3. Additional information

Information on existing evaluations and authorisations.

The original GOS were considered to be not novel due to their use in foods in the EU prior to 15 May 1997.

GOS are already permitted for use in the European Union and their inclusion in the Union List was based on a substantial equivalence evaluation conducted in 2013 by the Food Safety Authority of Ireland (FSAI, 2013). This application seeks to increase the maximum use level of GOS, the main components of the NF, from 0.333 kg GOS/kg food (current) to 0.450 kg GOS/kg food (proposed) when used as an ingredient in food supplements. No changes in the production process, composition or final product specifications have been proposed with respect to the 2013 evaluation.

No formal evaluation has been conducted by EFSA due to the exemption of GOS from the recently established Novel Food process.[2]

2. Data and methodologies

2.1. Data

The safety assessment of the change in the conditions of use of the NF is based on data supplied in the application.

During the assessment, the NDA Panel identified additional data which were not included in the application (Villaluenga-Martinez et al., 2008; Ruiz-Matute et al., 2012; Kunz et al., 2014).

Administrative and scientific requirements for NF applications referred to in Article 10 of Regulation (EU) 2015/2283 are listed in the Commission Implementing Regulation (EU) 2017/2469[3].

A common and structured format on the presentation of NF applications is described in the EFSA guidance on the preparation and presentation of an 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.

[1] Commission Implementing regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods OJ L 351, 30.12.2017, pp. 72–201.

[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; OJ L 327, 11.12.2015, pp. 1–22.

[3] 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.

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 (called Oligomate®55N) which is the subject of the application, is mainly composed of galacto-oligosaccharides (GOS), which consist of different galactosyl residues (two to nine) linked to a terminal glucose by a β-glycosidic bond. The NF is produced enzymatically by two β-galactosidases and also contains lactose, glucose and limited amounts of other monosaccharides.

The NF is proposed to be used as a food supplement with use levels higher than the already authorised maximum levels. The target population is the general population.

GOS are an established form of dietary fibre (EFSA NDA Panel, 2010).

According to Regulation (EU) 2015/2283, this NF falls under the following categories:

i) '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'; and
ii) 'food consisting of, isolated from or produced from microorganisms, fungi or algae'.

3.2. Identity of the NF

The NF which is subject of this application is in the form of a syrup containing ≥ 55% w/w GOS on a dry matter basis and is produced from refined lactose using two β-galactosidases. One enzyme, derived from *Sporobolomyces singularis,* promotes ß-O-glycosylation of lactose and the other one, derived from *Kluyveromyces lactis,* hydrolyses residual lactose. GOS are oligosaccharides containing 2–9 galactosyl units linked to a terminal glucose via β-glycosidic bonds such as β (1→2), β (1→3), β (1→4), or β (1→6).

3.3. Production process

The Panel notes that an assessment of the production process for GOS when produced by microbial β-galactosidases was conducted by FSAI in 2013 (FSAI, 2013). This opinion supported the substantial equivalence with Vivinal®, GOS already permitted for use in foods. The production process has not changed since then.

3.4. Compositional data

The Panel notes that the composition of the NF meets the specifications of 'galacto-oligosaccharides' in term of GOS content as reported in the Union List of Authorised Novel Foods (Commission Implementing Regulation (EU) 2017/2470) and previously reviewed by FSAI (2013).

The NF is a syrup containing ≥ 55% β-linked GOS (w/w dry matter, in addition to other saccharides). Since the NF contains approximately 75% dry matter, the GOS fraction comprises ≥ 41.25% GOS on a wet weight basis. The major saccharide in the GOS fraction of the NF is the trisaccharide 4'-galactosyllactose (*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-D-glucose) (Sar et al., 2004; Mwenya et al., 2005). Impurities in the NF include lactose and the monomers of lactose (galactose and glucose).

3.5. History of use of the NF and/or of its source

3.5.1. History of use of the source

GOS are naturally occurring in bovine colostrum and milk-related products such as fermented milk. Bovine colostrum has been reported to contain up to 8.5 mg/L GOS, while mature bovine milk contained only traces of total oligosaccharides and no GOS at all (Saito et al., 1987; Kunz et al., 2000). However, fermented milk products (e.g. yoghurt) can contain a significant amount of GOS due to the enzymatic activity of microbial β-galactosidases on the lactose. It is reported that commercial yoghurts may contain from 0.03% up to 0.58% of GOS, with the content being dependent on the microbial culture used to manufacture the product (Toba et al., 1982; Villaluenga-Martinez et al., 2008). Lactose-free milks can also contain GOS as a result of lactose hydrolysis and subsequent GOS formation with concentrations up to 0.43% (Ruiz-Matute et al., 2012).

GOS are not present in human breast milk (Kunz et al., 2014) or present only as a minimal fraction up to 14.8 mg/L (Yamashita and Kobala, 1974; Sumiyoshi et al., 2004).

3.5.2. History of use of the NF

According to the applicant GOS have a history of use in the food industry and industrial scale GOS production began in the 1980s. Currently, GOS are permitted for use in foods in several countries including Australia, Canada, the United States and Japan. In the European Union, GOS-containing products were marketed prior to 1997. GOS are added to many products, including infant formulae, baby foods and functional foods.

The original GOS (Vivinal®) were considered to be not novel due to their use in foods in the EU prior to 15 May 1997. Other GOS-containing products which were subject to the Novel food regulation (including Oligomate®55N) were deemed substantially equivalent to Vivinal® GOS in 2013 and have been marketed in the EU since the publication of that opinion (FSAI, 2013). Since then several GOS products have been determined as substantially equivalent (FSAI, 2016, 2017a,b).

3.6. Proposed uses and use levels and anticipated intake

3.6.1. Target population

GOS are currently permitted in the European Union for use in foods for the general population, in food supplements and in infant and follow-on formulae. There is no age restriction for the use of GOS-containing food supplements established in the Union List (Commission Implementing Regulation (EU) 2017/2470).

3.6.2. Proposed uses and use levels

The proposed expanded use increases the maximum level in food supplements (as defined in Directive 2002/46/EC)[4] from 0.333 kg GOS/kg food supplement (33.3%) to 0.450 kg GOS/kg food supplement (45.0%). No new food uses or other increases to the already approved use levels are being proposed.

3.6.3. Anticipated intake of the NF

GOS are consumed in the European Union as a source of dietary fibre in a variety of food products and food supplements, in accordance with Commission Implementing Regulation (EU) 2017/2470.

With the current maximum level of 33.3%, the daily intake of GOS results in an overall intake of 12 g (4 g per serving and 3 servings/day).

The applicant proposes to market food supplements containing the NF in a single or multi-serving bottle that does not contain any additional ingredients. The proposed serving size for the food supplement is 12 g of the NF corresponding to up to 5.4 g GOS (when GOS are present at 45% on a wet basis). It will be recommended that individuals consume no more than three servings/day. Therefore, at the proposed maximum use level of 45% GOS in the NF, the maximum recommended daily intake would be 16.2 g GOS.

[4] 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.

3.6.4. Precautions and restrictions of use

The applicant indicates that the NF is intended for consumption by the general population.

The use of the NF-containing supplements should not exceed 3 servings/day of 12 g of syrup per serving.

3.7. Nutritional information

Dietary fibre is, by definition, resistant to hydrolysis and absorption in the small intestine and enters the colon substantially unmodified. Dietary fibre components may be subject to anaerobic fermentation by the colonic microbiota. The extent of fermentation is also dependent on host factors (EFSA NDA Panel, 2010). It is known that fermentable dietary fibre components (e.g. oligosaccharides) may play a role in modulating the intestinal microbiota (Tanaka et al., 1983; Gopala et al., 2003; Matsumoto et al., 2004). The Panel does not expect that the proposed increased intake of this undigestible carbohydrate is of nutritional concern.

The Panel considers that taking into account the characteristics of the NF and the proposed changes in the conditions of use, its consumption is considered not nutritionally disadvantageous.

3.8. Allergenicity

According to data provided by the applicant (Kjeldahl analysis performed on representative batches of NF), the NF contains $\leq$ 0.1% of protein. The only potential source of protein would be β-galactosidases, the production enzymes that are expected to be removed during the purification steps.

The Panel considers that the likelihood of allergenic reactions to the NF is low.

4. Discussion

The NF which is the subject of the application is a syrup containing $\geq$ 55% β-linked GOS (w/w dry matter) and other substances such as lactose and related monomers (galactose and glucose). GOS are an established form of dietary fibre or non-digestible carbohydrate and are already authorised and included in the EU Union list of novel foods. GOS are used as food ingredients in several food categories, in infant formulae, baby foods and as food supplements.

The Panel noted that the current application is limited to a change in the use levels when GOS are used as food supplements while no changes are expected in the manufacturing process and characteristics of the already authorised NF.

The NF is a syrup containing $\geq$ 55% GOS (w/w dry matter or $\geq$ 41.25% on a wet basis). The proposed new use level increases the maximum level in food supplements from 0.333 kg GOS/kg food (33.3%) to 0.450 kg GOS/kg food (45.0%). Thus, the GOS intake would increase from 4 g (when GOS are present at 33.3%) to up to 5.4 g (when GOS are present at 45.0%) per serving. In addition, since it is recommended that individuals consume no more than 3 servings/day, the maximum recommended daily intake would be no more than 16.2 g GOS, with an estimated maximum increase of approximately 4.2 g/day from the current authorised use at 33.3%, corresponding to 12 g GOS/day.

Available evidence with regard to its effect on bowel function was the most suitable criterion for establishing an adequate intake of dietary fibre. EFSA considers dietary fibre intakes of 25 g per day to be adequate for a normal gastro-intestinal function in adults (EFSA NDA Panel, 2010). However, the evidence available to set adequate intakes for children is limited, but it can be extrapolated using the values set for adults, with appropriate adjustment for energy intake (a fibre intake of 2 g per megajoule is considered adequate for normal laxation in children from the age of one year). In addition, data on dietary fibre intake collected across European countries reported population intakes (5th to 95th percentiles) ranging from 6 to 46 g/day for children and from 6 to 51 g/day for adults (EFSA NDA Panel, 2010).

On this basis, the proposed increased use level of the NF in supplements would result in an increased total daily intake from 48% to 65% of the adequate daily intake of dietary fibre in adults.

The impurities present in the NF (lactose, galactose, glucose) are the same as those evaluated in the previous assessment (FSAI, 2013) and are normal components of the standard diet.

The Panel considers that the proposed increase in the maximum use level of GOS in food supplements does not raise safety concerns.

5. Conclusions

The Panel concludes that the NF, that is composed of ≥ 55% galacto-oligosaccharides (GOS) dry matter, lactose and related saccharides, is safe under the proposed changes in conditions of use.

6. Steps taken by EFSA

1) On 18/06/2020 EFSA received a letter from the European Commission with the request for a scientific opinion on the safety of the change in condition of use of GOS Ref. Ares(2020) 3176607.
2) On 18/06/2020, a valid application on GOS, which was submitted by Yakult Pharmaceutical Industry Co., Ltd., was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2020/1607) and the scientific evaluation procedure was initiated.
3) During its meeting on 17/12/2020, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of GOS as a NF pursuant to Regulation (EU) 2015/2283.

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Abbreviations

bw	body weight
FSAI	Food Safety Authority of Ireland
GOS	galacto-oligosaccharides
NDA	Scientific Panel on Nutrition, Novel Foods and Food Allergens
NF	novel food