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Dominique Turck, Torsten Bohn, Jacqueline Castenmiller, Stefaan de Henauw, Karen I. Hirsch-Ernst, Helle K. Knutsen, Alexandre Maciuk, Inge Mangelsdorf, Harry J. Mcardle, Androniki Naska, et al.

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## Isomaltulose and normal energy-yielding metabolism: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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Sophia Tsabouri, Marco Vinceti, Jean-Louis Bresson and Alfonso Siani

### Abstract

Following an application from BENEIO GmbH submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to isomaltulose and normal energy-yielding metabolism. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The food proposed by the applicant as the subject of the health claim is isomaltulose. The Panel considers that isomaltulose is sufficiently characterised. The claimed effect proposed by the applicant is 'normal energy-yielding metabolism'. The Panel considers that contribution to normal energy-yielding metabolism is a beneficial physiological effect. A number of human studies applying indirect calorimetry measurements or stable isotope methodologies have shown the postprandial metabolic utilisation of isomaltulose as energy source. However, all energy-containing macronutrients (i.e. carbohydrates, proteins, and lipids) supply the body with energy and this property is not specific to isomaltulose. The Panel concludes that a cause and effect relationship has been established between the intake of isomaltulose and contribution to energy-yielding metabolism. The following wording reflects the scientific evidence: 'isomaltulose contributes to normal energy-yielding metabolism'. Since the contribution to energy-yielding metabolism is not specific to isomaltulose but applies to all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids) that supply the body with metabolisable energy and any amount would contribute to the claimed effect, the Panel cannot set conditions of use for this claim. The applicant proposes that isomaltulose should replace other sugars in foods and/or beverages. The target population is the general population.

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**Keywords:** isomaltulose, energy-yielding metabolism, health claim

**Requestor:** Competent Authority of Germany following an application by BENEIO GmbH

**Question number:** EFSA-Q-2021-00073

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## 1. Introduction

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

Regulation (EC) No 1924/2006 harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health), which are based on newly developed scientific evidence or include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3). According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

### 1.2. Interpretation of the Terms of Reference

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: isomaltulose and normal energy-yielding metabolism.

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of isomaltulose, a positive assessment of its safety, nor a decision on whether isomaltulose is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

## 2. Data and methodologies

### 2.1. Data

#### Information provided by the applicant

##### Food/constituent as stated by the applicant

According to the applicant, the food for which the health claim is made is *isomaltulose (Palatinose)*. *Isomaltulose is a reducing disaccharide that consists of one glucose and one fructose moiety linked by an alpha-1,6-glycosidic bond*.

##### Health relationship as claimed by the applicant

According to the applicant, the health effect is related to Consumption of foods/drinks containing Isomaltulose (Palatinose™) replacing other sugars contributes to normal energy-yielding metabolism yet via a slower hydrolysis'. Upon a request from EFSA stating that the contribution of glycaemic carbohydrates (including isomaltulose) to energy-yielding metabolism does not depend on the rate of hydrolysis to glucose, the applicant agreed to restrict the claim to the contribution of isomaltulose as a source of glucose to normal energy-yielding metabolism.

##### Mechanism by which the food/constituent could exert the claimed effect as proposed by the applicant

The applicant claims that *isomaltulose is a fully digestible disaccharide consisting of a glucose and a fructose moiety and thus "isomaltulose is a source of glucose and fructose" as also specified in the Authorisation of isomaltulose as Novel Food (Commission Implementing Regulation (EU) 2017/2470). As outlined by the EFSA NDA Panel (2012) "it is well established that glucose is used within cells as a source of energy. The oxidation of glucose leading to CO<sub>2</sub> and water releases energy in the form of ATP, which is required by the body for all metabolic processes, as well as for the performance of any function or activity. Glucose contributes to energy-yielding metabolism as a source of energy, which is*

a property inherent to the food constituent". Accordingly, EFSA concluded in its Scientific Opinion that a cause and effect relationship has been established "between the intake of glucose and contribution to energy-yielding metabolism" (EFSA NDA Panel, 2012).

### Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: 'Consumption of foods/drinks containing isomaltulose (Palatinose™) replacing other sugars contributes to normal energy-yielding metabolism yet via a slower hydrolysis'. As described above, the applicant agreed to restrict the scientific evaluation on the contribution of isomaltulose as a source of glucose to normal energy-yielding metabolism.

### Specific conditions of use as proposed by the applicant

According to the applicant, the target population for the intended health claim is 'the general population'. The applicant states that 'the claimed effect refers to isomaltulose replacing other sugars in foods/drinks which is beneficial due to its slower hydrolysis. The European Commission has established the conditions of use that equivalent amounts of other sugars should be replaced in foods or drinks by isomaltulose so that foods or drinks contain reduced amounts of other sugars by at least the amount referred to in the claim REDUCED [NAME OF NUTRIENT] as listed in the Annex to Regulation (EC) No 1924/2006 (Commission Regulation (EU) No 432/2012). Foods or drinks should be a significant source of glucose from all dietary sources, this means at least 55% of the energy content of the foods or drinks is provided by glycaemic carbohydrates and other sugars should be replaced in those foods or drinks by isomaltulose (Palatinose™) so that foods or drinks contain reduced amounts of other sugars by at least the amount referred to in the claim REDUCED [NAME OF NUTRIENT] as listed in the Annex to Regulation (EC) No 1924/2006. Isomaltulose is offered to the food industry as an ingredient to e.g. replace other sugars in final food products. The claimed effect refers to a single intake of an isomaltulose-containing food'.

### Data provided by the applicant

The health claim application on isomaltulose and normal energy-yielding metabolism pursuant to Article 13.5 of Regulation 1924/2006, was presented in a common and structured format as outlined in the Scientific and technical guidance for the preparation and presentation of applications for authorisation of health claims (EFSA NDA Panel, 2017).

As outlined in the General guidance for stakeholders on health claim applications (EFSA NDA Panel, 2016), it is the responsibility of the applicant to provide the totality of the available evidence.

## 2.2. Methodologies

The general approach of the NDA Panel for the evaluation of health claim applications is outlined in EFSA's General guidance for stakeholders on health claim applications (EFSA NDA Panel, 2016).

The application does not contain data claimed as proprietary and confidential.

## 3. Assessment

In assessing each specific food/health relationship, which forms the basis of a health claim the NDA Panel considers the following key criteria:

- i) the food/constituent is defined and characterised;
- ii) the claimed effect is based on the essentiality of a nutrient; OR the claimed effect is defined and is a beneficial physiological effect for the target population and can be measured *in vivo* in humans;
- iii) a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use).

Each of these three criteria needs to be assessed by the NDA Panel with a favourable outcome for a claim to be substantiated. In addition, an unfavourable outcome of the assessment of criterion (i) and/or (ii) precludes the scientific assessment of criterion (iii).

### 3.1. Characterisation of the food/constituent

The food/constituent proposed by the applicant as the subject of the health claim is isomaltulose.



Isomaltulose, 6-*O*- $\alpha$ -D-glucopyranosyl-D-fructofuranose (CAS number 58166-27-1), is a disaccharide that consists of one glucose and one fructose molecule linked by an alpha-1,6-glycosidic bond. It is obtained from sucrose by enzymatic isomerisation in which the d-glucopyranosyl group is transferred from the O2 position to the O6 position of the  $\alpha$ -d-fructofuranosyl unit. Isomaltulose is authorised as Novel Food (Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017<sup>1</sup>). It is used as a sucrose substitute in various food categories including solid, semi-solid and liquid foods. According to the applicant, its sweetening power is about 50% that of sucrose when tested as 10% solutions.

Information related to the manufacturing process, stability and batch to batch variability (purity 99.4%) was provided.

The Panel considers that the food/constituent, isomaltulose, which is the subject of the health claim, is sufficiently characterised.

### 3.2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is 'normal energy-yielding metabolism'. The proposed target population is the general population.

The Panel notes that the claimed effect relates to the conversion of energy from foods into energy in the form of ATP which may be readily used by the body.

The Panel considers that contribution to normal energy-yielding metabolism is a beneficial physiological effect.

### 3.3. Scientific substantiation of the claimed effect

A total of 11 human intervention studies (MacDonald and Daniel 1983; Achten et al., 2007; Arai et al., 2007; van Can et al. 2009; Holub et al., 2010; König et al., 2012; van Can et al. 2012; Ang and Linn, 2014; Kahlhöfer et al., 2016; König et al., 2016; Henry et al., 2017) and three review publications (Lina et al., 2002; Maresch et al., 2017; Pfeiffer and Keyhani-Nejad, 2018) were submitted for the scientific substantiation of the claim. The search strategy used to retrieve these publications was not described in the application.

The studies submitted have investigated the digestion, absorption, utilisation and energy-yield of isomaltulose when consumed in mixed diets.

Isomaltulose is a disaccharide consisting of glucose and fructose. It is well established that glucose is used within cells as a source of energy. The oxidation of glucose generating CO<sub>2</sub> and water releases energy in the form of ATP that provides the energy for many cellular processes and body functions. Glucose contributes to normal energy-yielding metabolism as a source of energy, which is a property inherent to the food constituent (EFSA NDA Panel, 2012). Fructose is metabolised in the gut, liver and kidney that process fructose carbons into ubiquitous energy substrates such as lactate, glucose, and fatty acids (EFSA NDA Panel, 2010; Tappy, 2018).

The digestion and absorption of isomaltulose were investigated in 10 patients with ileostomy without ileal resection (mean age 47 years, range 33–67 years, 8 women) (Holub et al., 2010). The participants consumed 50 g of isomaltulose as part of a liquid or solid breakfast (not containing fructose or glucose) on two different occasions. Ileostomy fluid homogenate samples were analysed for isomaltulose, glucose and fructose content. The digestibility of isomaltulose was calculated as the proportion of the total isomaltulose intake that was not excreted unchanged within 8 h after intake. The absorption was calculated as a percentage of intake of isomaltulose minus its excretion over 8 h. For the liquid meal, the mean digestibility and absorption were 95.5% and 93.6%, respectively, while for the solid meal these were 98.8% and 96.1%, respectively.

A number of human studies applying indirect calorimetry measurements or stable isotope methodologies have shown the postprandial metabolic utilisation of isomaltulose as source of energy (Achten et al., 2007; Van Can et al., 2009; Holub et al., 2010; Van Can et al., 2012; Ang and Linn, 2014; Kahlhöfer et al., 2016; König et al., 2016; Henry et al., 2017). The Panel notes that isomaltulose provides a similar energy yield than other sugars (e.g. glucose and sucrose).

The Panel also notes that the contribution to energy-yielding metabolism is not specific to isomaltulose, glucose or fructose. It applies to all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids) that supply the body with metabolisable energy.

<sup>1</sup> 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 (Text with EEA relevance). <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R2470>

The Panel concludes that a cause and effect relationship has been established between the intake of isomaltulose and contribution to normal energy-yielding metabolism. The Panel notes, however, that contribution to energy-yielding metabolism is a property of all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids).

#### 4. Panel comments on the proposed wording

The Panel considers that the following wording reflect the scientific evidence: 'isomaltulose contributes to normal energy-yielding metabolism'.

#### 5. Conditions and possible restrictions of use

Since the contribution to energy-yielding metabolism is not specific to isomaltulose but applies to all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids) that supply the body with metabolisable energy and any amount would contribute to the claimed effect, the Panel cannot set conditions of use for this claim. The applicant proposes that isomaltulose should replace other sugars in foods and/or beverages. The target population is the general population.

#### 6. Conclusions

On the basis of the data presented, the Panel concludes that:

- the food/constituent, isomaltulose, which is the subject of the health claim, is sufficiently characterised.
- the claimed effect proposed by the applicant is 'normal energy yielding metabolism'. The target population proposed by the applicant is the general population. Contribution to normal energy-yielding metabolism is a beneficial physiological effect.
- a cause and effect relationship between the consumption of isomaltulose and contribution to normal energy-yielding metabolism has been established. However, contribution to energy-yielding metabolism is a property of all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids).
- the following wordings reflect the scientific evidence: 'isomaltulose contributes to normal energy-yielding metabolism'.
- since the contribution to energy-yielding metabolism is not specific to isomaltulose but applies to all energy containing macronutrients (i.e. carbohydrates, proteins, and lipids) that supply the body with metabolisable energy and any amount would contribute to the claimed effect, the Panel cannot set conditions of use for this claim. The applicant proposes that isomaltulose should replace other sugars in foods and/or beverages. The target population is the general population.

#### 7. Documentation as provided to EFSA

Health claim application on isomaltulose and contribution to normal energy-yielding metabolism pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0503\_DE). Submitted by BENE GmbH; Maximilianstrasse 10, 68165 Mannheim, Germany.

#### Steps taken by EFSA

- 1) This application was received by EFSA on 4/2/2021.
- 2) The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
- 3) The scientific evaluation procedure started on 21/5/2021.
- 4) On 18/5/2021, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The scientific evaluation was suspended on 31/5/2021 and was restarted on 14/6/2021, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- 5) During its meeting on 15/9/2021, the NDA Panel, having evaluated the data, adopted an opinion on the scientific substantiation of a health claim related to the consumption of isomaltulose and contribution to normal energy-yielding metabolism.



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## Abbreviations

- ATP adenosine triphosphate  
 CAS Chemical Abstracts Service  
 NDA Nutrition, Novel Foods and Food allergens