

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to lactase enzyme and breaking down lactose (ID 1697, 1818) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)²

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to lactase enzyme and breaking down lactose. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claim is lactase enzyme. The Panel considers that lactase enzyme is sufficiently characterised.

The claimed effect is “digestion”. In the context of the proposed wording, the Panel assumes that the claimed effect relates to breaking down lactose (i.e. hydrolyse lactose). The Panel considers that breaking down lactose may be beneficial to the health of individuals with symptomatic lactose maldigestion.

Although the results presented are derived from studies with small sample sizes and some also had a weak design, the Panel notes the known mechanism of action and the biological plausibility of the effect.

The Panel concludes that a cause and effect relationship has been established between the consumption of lactase enzyme and breaking down lactose in individuals with symptomatic lactose maldigestion. The following wording reflects the scientific evidence: “Lactase enzyme contributes to breaking down lactose”.

The Panel considers that consumers should be made aware that lactase enzyme is intended for individuals with lactose (milk sugar) maldigestion and with associated clinical symptoms, i.e. individuals with symptomatic lactose intolerance. The recommended dose is 4500 FCC (Food

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Chemicals Codex) units with each lactose containing meal. The dose may have to be adjusted to individual needs for lactase supplementation and consumption of lactose containing products.

KEY WORDS

Lactase enzyme, breaking down lactose, maldigestion, health claims.

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EFSA DISCLAIMER

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The members of the Claims/Sub-Working Group Gut/Immune: Miguel Gueimonde, Martinus Løvik, Bevan Moseley, Seppo Salminen, Stephan Strobel, Hania Szajewska and Hendrik van Loveren.

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation 1924/2006³ submitted by Member States contains main entry claims with corresponding conditions of use and literature from similar health claims. The information provided in the consolidated list for the health claims subject to this opinion is given in Table 1.

Table 1. Main entry health claims related to lactase enzyme, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food component	Health Relationship	Proposed wording
1697	Lattasi (beta-galattosidasi)	Digestion	It helps lactose digestion by reducing fermentation and gas production.
	Conditions of use - 300/600 LacU/day		
1818	Food or Food component	Health Relationship	Proposed wording
	Lactase enzyme	Digestion	Breaks down lactose. Useful for people whose own lactase enzyme production is insufficient for breaking down lactose.
	Conditions of use - Food supplement with 4500 FCC units of lactase in the daily dose. - Product with 125-250mg/dose of lactase enzyme.		

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is “lactase enzyme”.

The intestinal enzyme lactase hydrolyses the mammalian milk sugar lactose into galactose and glucose. Externally administered enzymes with lactose-splitting activity are bacterial or yeast derived beta-glucosidases. These enzymes have different lactose splitting activities and optimal conditions for use. For greater lactose splitting efficacy, milk can be incubated with lactase before milk consumption. The amount of active enzyme needed for the alleviation of symptoms in lactose intolerant individuals depends on the mode of administration, the amount of intended milk intake and the lactose sensitivity of the individual.

The references provided identified lactase enzyme (beta-galactosidase) preparations from fungal sources, e.g. *Aspergillus oryzae* and *Kluyveromyces lactis*. This opinion applies also to other sources presenting standardised lactase (Food Chemicals Codex, (FCC)).

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

³ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

2. Relevance of the claimed effect to human health

The claimed effect is “digestion”. The target population is individuals whose own lactase enzyme production is insufficient for breaking down lactose.

“Digestion” is not sufficiently defined. In the context of the proposed wording, the Panel assumes that the claimed effect relates to breaking down lactose (i.e. hydrolyse lactose).

Lactose maldigestion is a common condition characterised by intestinal lactase deficiency. In Europe, around 5% - 22% of the population have primary lactose maldigestion but are usually able to tolerate small amounts of lactose. Lactose maldigestion is an inherited deficiency present in the majority of the world’s population, and is most prevalent in Asian, African, Hispanic and Indian populations. Recently discovered genetic polymorphisms may be used as first stage screening tests for adult type hypolactasia. Individuals who show an abnormal breath hydrogen excretion test, the standard test for diagnosis of lactose maldigestion, can often tolerate up to 12g of lactose (around 240 mL of cows milk). However, some individuals may react to lower amounts with intestinal symptoms. These include bloating, abdominal pain, nausea, diarrhoea, cramps and distension. Improvement of lactose digestion may be of interest in lactose intolerant subjects. The alleviation of lactose intolerance symptoms may be a health benefit conferred by externally administered lactase enzymes which hydrolyse lactose.

The Panel considers that breaking down lactose may be beneficial to the health of individuals with symptomatic lactose maldigestion.

3. Scientific substantiation of the claimed effect

The references provided consist of small scale clinical studies with different enzyme preparations and activities in different lactase-deficient populations.

Of the submitted references, one was a review, three references related to management of lactose intolerance/treatment approaches of lactose maldigestion (Savaiano and Kotz, 1989; Montalto et al., 2006; Swagerty et al., 2002) and another evaluated the impact of lactose intolerance on quantitative bone parameters (Segal et al., 2003). The Panel notes that these references do not address the relationship between the consumption of lactase enzyme and the claimed effect and therefore considers that no scientific conclusions can be drawn from these references for the substantiation of the claimed effect.

The references evaluating the effect of lactase preparations which are pertinent to the claimed effect are given below:

Reference	Study design	Study Population	Hydrogen excretion	Clinical symptoms	Enzyme activity / amount	Source of enzyme
Biller et al., 1987	Open challenged	16; 3-16 years USA	reduced	reduced	125 – 375 mg	Asp. oryzae
DiPalma & Collins, 1989	Open challenged	10; adults mean 43.5 years, USA	reduced	reduced	250 – 500 mg ~4000 FCC	Asp. oryzae
Barillas & Solomons, 1987	Open challenged	27 school children, 2.5-6 years, Guatemala	reduced	Not assessed	~6500 FCC	Asp oryzae; Kluyveromyces lactis
Lami et al., 1988	Open challenged	52; 20-65 years, Italy	reduced	38 – 75% symptom free	325 FCC / drop (+pre incubation) ~2600 FCC	Kluyveromyces lactis

Reference	Study design	Study Population	Hydrogen excretion	Clinical symptoms	Enzyme activity / amount	Source of enzyme
Montalto et al., 2005	Crossover double-blind placebo controlled study	30; 18-65 years, Italy	reduced	75 - 90% symptom free	~6500 – 7800 FCC	Kluyveromyces lactis
Rask Pedersen et al., 1982	Double blind, crossover	11; 20-67 years, Denmark	reduced	Non-significant	~4200 FCC (3205 U)	Kluyveromyces lactis
Moskovitz et al., 1987	Open challenged	16 lactose intolerant adults, USA	reduced	5/9 reduced	~ 4000 FCC (250/500 mg Lactase)	Asp. oryzae
Ramirez et al., 1994	Randomised placebo-controlled	10 lactose intolerant volunteers, USA	reduced	reduced	6600 – 9900 FCC; 500 mg Lactase (~ 6600 FCC)	Asp. oryzae; Kluyveromyces lactis

NB: the definition of enzyme activity units has differed in publications. To provide comparative activity information, units have been converted to FCC using a conversion factor 1.3 from neutral units. Effects are listed after administration of the active enzyme preparation.

Assuming a fully active enzyme preparation, the intended dose of 4500 FCC (Food Chemicals Codex) units has been shown to reduce H₂ exhalation and clinical symptoms in small scale clinical studies. Enzyme activity is defined by the amount of substrate that a unit of specific enzyme will break down per unit of time according to the United States Pharmacopoeia (USP) and the Food Chemicals Codex (FCC). Doses used in the studies range from: 2600-9900 FCC.

The results presented are derived from studies with small sample sizes and some also had a weak design. However, the Panel notes the known mechanism of action and the biological plausibility of the effect.

The Panel concludes that a cause and effect relationship has been established between the consumption of lactase enzyme and breaking down lactose in individuals with symptomatic lactose maldigestion.

4. Panel's comments on the proposed wordings

The Panel considers that the following wording reflects the scientific evidence: "Lactase enzyme contributes to breaking down lactose".

5. Conditions and possible restrictions of use

The Panel considers that consumers should be made aware that lactase enzyme, which is the subject of health claim, is intended for individuals with lactose (milk sugar) maldigestion and with associated clinical symptoms, i.e. individuals with symptomatic lactose intolerance.

The recommended dose is 4500 FCC (Food Chemicals Codex) units with each lactose containing meal. The Panel considers that the dose may have to be adjusted to individual needs for lactase supplementation and consumption lactose containing products.

CONCLUSIONS

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

- The food constituent, lactase enzyme, which is the subject of the health claim is sufficiently characterised.
- The claimed effect is “digestion”. The target population is individuals whose own lactase enzyme production is insufficient for breaking down lactose. Breaking down lactose may be beneficial to the health of individuals with symptomatic lactose maldigestion.
- A cause and effect relationship has been established between the consumption of lactase enzyme and breaking down lactose in individuals with symptomatic lactose maldigestion.
- The following wordings reflect the scientific evidence: “Lactase enzyme contributes to breaking down lactose”.
- Lactase enzyme is intended for individuals with lactose (milk sugar) maldigestion and with associated clinical symptoms, i.e. individuals with symptomatic lactose intolerance. The recommended dose is 4500 FCC (Food Chemicals Codex) units with each lactose containing meal. The dose may have to be adjusted to individual needs for lactase supplementation and consumption of lactose containing products.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-2433, EFSA-Q-2008-2551). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: <http://www.efsa.europa.eu/panels/nda/claims/article13.htm>.

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APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁴ (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

- a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- b) psychological and behavioural functions; or
- c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

- (i) based on generally accepted scientific evidence; and
- (ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13(1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD⁵

Foods are commonly involved in many different functions⁶ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

⁴ OJ L12, 18/01/2007

⁵ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁶ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

- (a) the claimed effect of the food is beneficial for human health,
- (b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),
- (c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,
- (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. 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 wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.