Lactitol and the maintenance of normal defecation: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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

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Abstract

Following an application from DuPont Nutrition BioSciences ApS, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to lactitol and the maintenance of normal defecation. The food constituent that is the subject of the claim is lactitol. The Panel considers that the food constituent lactitol, which is the subject of the claim, is sufficiently characterised. The Panel considers that the maintenance of normal defecation is a beneficial physiological effect. A total of 15 human intervention studies were identified as pertinent to the health claim. Twelve studies with various methodological limitations consistently showed that consumption of at least 10 g/day lactitol increases stool frequency; five out of six studies found that lactitol softens stool consistency; and two studies showed that lactitol increases stool bulk. The Panel also acknowledges the plausible mechanisms of action by which lactitol could exert the claimed effect. The dose of 10 g/day lactitol does not induce diarrhoea. The Panel concludes that a cause and effect relationship has been established between the consumption of lactitol and the maintenance of normal defecation. The following wording reflects the scientific evidence: "lactitol can contribute to normal defecation". To obtain the claimed effect, 10 g of lactitol should be consumed daily. The target population is the general adult population.

Keywords: lactitol, defecation, bowel function, health claim

Requestor: Competent Authority of the United Kingdom following an application by DuPont Nutrition BioSciences ApS

Question number: EFSA-Q-2015-00375

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Summary

Following an application from DuPont Nutrition BioSciences ApS, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to lactitol and the maintenance of normal defecation.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The general approach of the NDA Panel to the evaluation of health claims applications is outlined in the EFSA general guidance for stakeholders on the evaluation of Article 13(5) and 14 health claims (EFSA NDA Panel, 2011a) and the guidance on the scientific requirements for health claims related to gut and immune function are outlined in a specific EFSA guidance document (EFSA, 2011c).

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

The claimed effect proposed by the applicant is "normal bowel function by increasing stool frequency, increasing stool bulk and moisture, softening stool consistency and reducing transit time". The target population proposed by the applicant is the general population. The Panel notes that the proposed claimed effect refers to the maintenance of normal defecation. The Panel considers that the maintenance of normal defecation is a beneficial physiological effect.

A total of 15 human intervention studies were identified by the applicant as being pertinent to the health claim. The Panel considers that the outcomes measured in one study are not relevant to assess the claimed effect on the maintenance of normal defecation. Out of 14 studies, stool frequency was measured in 12 studies, stool consistency in 12 studies, stool bulk in two studies and transit time in three studies. In some studies, the effect of lactitol was compared with either the baseline value or a control placebo group, and in other studies lactitol was compared with lactulose, assuming that lactulose has an effect on defecation. The Panel notes that these studies were not designed as equivalence studies. Hence, no conclusions can be drawn from them for the scientific substantiation of the claim. The Panel also notes that transit time is not necessarily related to normal defecation. The Panel considers that no conclusions can be drawn from studies assessing transit time for the scientific substantiation of the claim.

In weighing the evidence, the Panel took into account that 12 studies with various methodological limitations consistently showed that consumption of at least 10 g/day lactitol increases stool frequency; that five out of six studies found that lactitol softens stool consistency; and that two studies showed that lactitol increases stool bulk. The Panel also acknowledges the plausible mechanisms of action by which lactitol could exert the claimed effect. The dose of 10 g/day lactitol does not induce diarrhoea.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between the consumption of lactitol and the maintenance of normal defecation.

The following wording reflects the scientific evidence: "lactitol can contribute to normal defecation".

The claimed effect can be obtained by consuming 10 g of lactitol daily. The target population is the general adult population.

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1. Introduction

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

Regulation (EC) No 1924/2006[1] 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 which 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 was 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 lactitol and normal defecation.

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of lactitol, a positive assessment of its safety or a decision on whether lactitol 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

2.1.1. Information provided by the applicant

Food constituent as stated by the applicant

According to the applicant, the food constituent that is the subject of the health claim is lactitol monohydrate, which is disaccharide polyol consisting of galactose and sorbitol. Lactitol is resistant to digestion by the enzymes of the digestive tract but is fermented by the intestinal microbiota mainly to the following short chain fatty acids (SCFAs): acetic, propionic and butyric acids and gaseous products.

Health relationship as claimed by the applicant

According to the applicant, lactitol contributes to normal bowel function by increasing stool frequency, increasing stool bulk and moisture, softening stool consistency and reducing transit time.

Mechanisms by which the food constituent exerts the claimed effect as proposed by the applicant

According to the applicant, there are several mechanisms by which the intake of lactitol contributes to normal defecation. The laxative action of lactitol in the digestive tract is related to the osmotic

[1] 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.

properties of the undigested carbohydrate. The increased biomass resulting from fermentation may also increase stool bulk and decrease transit time, as stool bulk and transit time are inter-related. In addition to a potential osmotic effect, SCFAs produced as a result of fermentation of lactitol in the colon may have a direct effect on gut motility and transit.

Wording of the health claim as proposed by the applicant

The applicant proposed the following wording for the health claim: "lactitol contributes to normal bowel function".

Specific conditions of use as proposed by the applicant

According to the applicant, to obtain the claimed effect, 10 g of lactitol should be consumed daily; the effect should be evident within 3–4 days and the daily intake should be adjusted up or down by 5 g according to individual needs.

The target population proposed by the applicant is the healthy general population.

2.1.2. Data provided by the applicant

The applicant provided a health claim application on lactitol and the maintenance of normal defecation pursuant to Article 13(5) of Regulation (EC) No 1924/2006. The application 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, 2011b).

As outlined in the EFSA general guidance for stakeholders on the evaluation of Article 13(1), 13(5) and 14 health claims (EFSA NDA Panel, 2011a), 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 to the evaluation of health claims applications is outlined in the EFSA general guidance for stakeholders on the evaluation of Article 13(1), 13(5) and 14 health claims (EFSA NDA Panel, 2011a).

The scientific requirements for health claims related to gut and immune function are outlined in a specific EFSA guidance document (EFSA, 2011c).

3. Assessment

3.1. Characterisation of the food constituent

The food constituent that is the subject of the health claim is "lactitol monohydrate".

Lactitol monohydrate is a disaccharide polyol consisting of galactose and sorbitol. It has the chemical formula $C_{12}H_{24}O_{11}$ and the chemical name 4-O-β-D-galactopyranosyl-D-glucitol. Lactitol is made by catalytic hydrogenation of lactose from cow's milk (nickel as catalyst). It is then purified and crystallised to obtain pure lactitol monohydrate (with purity > 95 %).

Lactitol is approved in the European Union as a food additive under the E number E 966 and is used as a synthetic sweetener. Lactitol can be measured in foods using established methods.

Information about stability was provided in the application.

The Panel considers that lactitol, 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 bowel function by increasing stool frequency, increasing stool bulk and moisture, softening stool consistency and reducing transit time". The target population proposed by the applicant is the general population.

The Panel notes that the proposed claimed effect refers to the maintenance of normal defecation.

Constipation is associated with less frequent defecations, with reduced faecal bulk or harder stools, or both. Constipation leads to gastrointestinal discomfort and may contribute to the development of, for example, diverticular disease. More frequent defecations through, for example, a reduction in transit time, increased faecal bulk and softer stools, may contribute to the maintenance of normal defecation, provided that this does not result in diarrhoea.

The Panel considers that the maintenance of normal defecation is a beneficial physiological effect.

3.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in the Medline database using the following key terms: "lactitol" AND [constipation OR bowel function OR stool OR bowel movement OR transit OR frequency OR bowel motility OR ferment*]. A manual search of relevant articles was also performed.

Human studies

A total of 15 human intervention studies were identified by the applicant as pertinent to the health claim.

One study (Ballonque et al., 1997) measured changes in faecal microbiota, faecal moisture and faecal pH after administration of lactitol, but did not address outcomes that are relevant for the claimed effect on the maintenance of normal defecation. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

Of the 14 remaining studies, stool frequency was measured in 12 studies, stool consistency in 12 studies, stool bulk in two studies and transit time in three studies. In some studies, the effect of lactitol was compared with either the baseline value or a control placebo group, while in other studies lactitol was compared with lactulose, assuming that lactulose has an effect on defecation.

The effect of lactitol was compared with the effect of lactulose in relation to stool frequency and stool consistency in six studies, including four studies in adults (Heitland and Mauersberger, 1988; Doffoel et al., 1990; Hammer and Ravelli, 1992; Xu et al., 2012) and two studies in children (Martino et al., 1992; Pitzalis et al., 1995). The doses of lactitol ranged from 10 to 20 g daily and the doses of lactulose varied from 10 to 30 g daily in adults. In children, 150–400 mg/kg body weight lactitol and 150–750 mg/kg body weight lactulose were used. The Panel notes that these studies were not designed as equivalence studies. Hence, no conclusions can be drawn from them for the scientific substantiation of the claim.

In three studies, oro-caecal (Pitzalis et al., 1995) or total intestinal (Minella et al., 1983; Pontes et al., 1995) transit time were assessed. The Panel notes that transit time is not necessarily related to normal defecation. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of the claim.

Twelve human studies, including nine studies conducted in adults (Heitland and Mauersberger, 1988; Walder et al., 1988; Doffoel et al., 1990; Vanderdonckt et al., 1990; Hammer and Ravelli, 1992; Goevaerts and Ravelli, 1993; Vanderdonckt and Ravelli, 1993; Ravelli et al., 1995; Xu et al., 2012) and three studies in children (Martino et al., 1992; Minella et al., 1993; Pitzalis et al., 1995), reported a significant increase in stool frequency with the consumption of lactitol. In these studies, defecation frequency increased from ≤ 3 per week to 5 to 7 per week. The dose of lactitol used ranged from 10 to 40 g/day in adults and from 150 to 800 mg/kg body weight in children.

In a meta-analysis (Miller et al., 2014), which included all of the nine studies conducted in adults mentioned above, lactitol ingestion (median daily intake of 20 g, median treatment period 28 days) increased weekly stool frequency compared with baseline, with a difference between the means of 3.8 stools per weeks (95 % confidence interval (CI) 3.2 to 4.3, $p < 0.001$).

Six studies evaluated stool consistency as a study outcome. In five out six studies in adults (Vanderdonct et al., 1990; Hammer and Ravelli, 1992; Goevaerts and Ravelli, 1993; Ravelli et al., 1995; Xu et al., 2012), stools were softer with supplementation than in the placebo or baseline groups, while in one study (Vanderdonckt and Ravelli, 1993) no significant change in stool consistency was found. A meta-analysis of these six studies (Miller et al., 2014) confirmed that stools were softer with lactitol consumption than in the baseline group. Owing to differences in reporting scales among

studies, the standardised mean difference (SMD) was used to report this outcome, assuming that values of 0.2, 0.5, 0.8 and 1.0 represented small, medium, large and very large effect sizes, respectively. SMD was calculated as 1.04 (95 % CI 0.49 to 1.59, $p < 0.001$), although significant heterogeneity (I^2 = 87 %) was found.

In two studies, stool bulk was measured. Ravelli et al. (1995) found that ingestion of 20 g of lactitol resulted in a 40 % increase in wet stool weight and a 28 % increase in dry stool weight. Van Es et al. (1986) reported that lactitol given in a dose of 50 g/day increased mean faecal mass by 35 % compared with baseline.

The Panel notes that the human intervention studies provided were very different regarding the dose of lactitol used (from 10 to 50 g/day), the duration of the intervention (from 6 days to 12 weeks), the sample size (8 to 141 subjects), the type of subjects recruited (healthy volunteers, subjects with constipation), the age of participants (mean age 6 to 83 years, range of individuals from 8 months to 101 years) and the study settings (free-living individuals, hospitalised subjects, elderly institutionalised subjects). The Panel also notes that stool frequency, stool consistency and stool bulk were only secondary outcomes in a number of studies, and that statistical comparisons between the intervention and control groups were not always reported. However, the Panel considers that, as all studies showed a similar effect, these studies provide evidence for an increase in stool frequency, a beneficial change in the consistency of stools (softer) and higher faecal bulk with the consumption of lactitol.

In several studies, the frequency of diarrhoea related to lactitol consumption was measured. Oku et al. (2005) found that diarrhoea was not present with 10 g/day of lactitol, while 10 % of men and 14 % of women reported diarrhoea with an intake of 20 g daily. The same group of investigators (Oku et al., 2007) reported no occurrence of diarrhoea at an intake of 12 g of lactitol daily and reported the presence of diarrhoea in 2 out of 26 subjects with an intake of 20 g/day. In the study by Delas et al. (1991), 4 out of 114 subjects reported diarrhoea at a dose of lactitol of 20 g/day. The Panel considers that the evidence provided shows that the dose of 10 g lactitol does not cause diarrhoea.

Mechanism by which the food constituent could exert the claimed effect

The applicant indicated that there are several mechanisms by which the intake of lactitol may contribute to normal defecation: "The laxative action of lactitol in the digestive tract is related to the osmotic properties of the undigested carbohydrate. The increased biomass resulting from fermentation may also increase stool bulk and decrease transit time and that stool bulk and transit time are inter-related. In addition to a potential osmotic effect, short-chain fatty acids (SCFAs) produced as a result of fermentation of lactitol in the colon may have a direct action on gut motility and transit."

The studies submitted by the applicant in support of a mechanism by which lactitol could exert the claimed effect showed that lactitol is not hydrolysed by digestive enzymes and is not absorbed to any significant extent during passage through the small intestine (Patil et al., 1987a). They also showed that it is fermented in the right colon to SCFAs, lactic acid and gaseous products (carbon dioxide and a small amount of hydrogen) and contributes to faecal mass (Patil et al., 1987b; Grimble et al., 1988; Ravelli et al., 1995; Ballonque et al., 1997; Clausen et al., 1998; Mäkivuokko et al., 2010).

The Panel considers that lactitol is a non-digestible carbohydrate that could exert an effect on stool frequency and stool consistency by osmotic effect, by stimulating fermentation in the colon and by increasing faecal bulk.

Weighing of the evidence

In weighing the evidence, the Panel took into account that 12 studies with various methodological limitations consistently showed that consumption of at least 10 g/day lactitol increases stool frequency; that five out of six studies found that lactitol softens stool consistency; and that two studies showed that lactitol increases stool bulk. The Panel also acknowledges the plausible mechanisms of action by which lactitol could exert the claimed effect. The dose of 10 g/day lactitol does not induce diarrhoea.

The Panel concludes that a cause and effect relationship has been established between the consumption of lactitol and the maintenance of normal defecation.

3.4. Panel's comments on the proposed wording

The Panel considers that the following wording reflects the scientific evidence: "lactitol can contribute to normal defecation".

3.5. Conditions and restrictions of use

The Panel considers that the claimed effect can be obtained by consuming 10 g of lactitol daily. The target population is the general adult population.

Regulation 1169/2011 (on Food Information to Consumers) contains a provision in Annex III for additional labelling particulars for polyols[2].

4. Conclusions

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

- The food constituent lactitol, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is "normal bowel function by increasing stool frequency, increasing stool bulk and moisture, softening stool consistency and reducing transit time". The target population proposed by the applicant is the general population. The maintenance of normal defecation is a beneficial physiological effect.
- A cause and effect relationship has been established between the consumption of lactitol and the maintenance of normal defecation.
- The following wording reflects the scientific evidence: "lactitol can contribute to normal defecation".
- The claimed effect can be obtained by consuming 10 g of lactitol daily. The target population is the general adult population.

[2] Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004. OJ L 304, 22.11.2011, p. 18–63.

Documentation provided to EFSA

1. Health claim application on lactitol and normal bowel function by increasing stool frequency, increasing stool bulk and moisture, softening stool consistency and reducing transit time pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0435_UK). Submitted by DuPont Nutrition BioSciences ApS, Langebrogade 1, 1001 Copenhagen, Denmark.

2. This application was received by EFSA on 10/06/2015.

3. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

4. On 30/06/2015, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.

5. On 15/07/2015, EFSA received the missing information as submitted by the applicant.

6. The scientific evaluation procedure started on 24/07/2015.

7. During its meeting on 23/09/2015, the NDA Panel, having evaluated the data, adopted an opinion on the scientific substantiation of a health claim related to lactitol and the maintenance of normal defecation.

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Abbreviations

CI	confidence interval
SCFA	short-chain fatty acid
SMD	standardised mean difference