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Sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries: evaluation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006

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Abstract

Following an application from Cargill R&D Centre Europe, submitted for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Belgium, 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 sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of caries. The food proposed by the applicant as the subject of the health claim, sugar-free hard confectionery with at least 90% erythritol, is sufficiently characterised. In the context of this application, the weight of dental plaque, and/or the counts of *Streptococcus mutans* in dental plaque, and/or the concentration of organic acids in plaque (primarily acetic acid and lactic acid) can be considered as risk factor(s) in the development of dental caries, as long as evidence is provided that the consumption of the food that is the subject of the health claim reduces one or more of the proposed risk factors and the incidence of dental caries. One human intervention study did not show an effect of sugar-free hard confectionery with at least 90% erythritol on the incidence of dental caries in children on either mixed or permanent dentition. The Panel concludes that a cause and effect relationship has not been established between the consumption of sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries.

Keywords: erythritol, sugar-free, hard confectionery, dental plaque, dental caries, health claim

Requestor: Competent Authority of Belgium following an application by Cargill R&D Centre Europe

Question number: EFSA-Q-2017-00002

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Summary

Following an application from Cargill R&D Centre Europe, submitted for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Belgium, 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 sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque, which reduces the risk of caries.

The scope of the application was proposed to fall under a health claim referring to disease risk reduction.

The general approach of the NDA Panel for the evaluation of health claims applications is outlined in the EFSA general guidance for stakeholders on health claim applications and the EFSA guidance on the scientific requirements for health claims related to bone, joints, skin and oral health.

The food proposed by the applicant as the subject of the health claim is Zerose® erythritol sugar free hard confectionery. The Panel considers that the food, sugar-free hard confectionery with at least 90% erythritol, which is the subject of the health claim, is sufficiently characterised.

The claimed effect proposed by the applicant is 'reduction of dental plaque which reduces the risk of caries'. The target population proposed by the applicant is the general population aged 5 years and older. In relation to the disease (dental caries) that is the subject of the health claim, the Panel considers that a clinical assessment of dental caries using the ICDAS II classification is an appropriate outcome variable to assess the incidence of the disease in intervention studies conducted in children. The applicant proposes three outcome variables to be used for the assessment of the risk factor(s) in human studies: (a) the weight of freshly collected dental plaque (i.e. collected from all available tooth surfaces during a timed 3-min period); (b) salivary and plaque counts of *Streptococcus mutans* and (c) chemical analysis of dental plaque (i.e. plaque sugars, organic acids and polyols).

The Panel considers that, in the context of this application, the weight of dental plaque, and/or the counts of *S. mutans* in dental plaque, and/or the concentration of organic acids in plaque (primarily acetic acid and lactic acid) can be considered as risk factor(s) in the development of dental caries, as long as evidence is provided that the consumption of the food that is the subject of the health claim reduces one or more of the proposed risk factors and the incidence of dental caries.

The applicant identified two human intervention studies (reported in four publications) as being pertinent to the claim, of which only one study investigated the effect of consuming sugar-free hard confectionery with 90% erythritol on the incidence of dental caries.

The first study was designed as a randomised, three-arm, double-blind parallel trial which investigated the effect of consuming chewable hard candies (four 0.7-g candies three times per day) with 90% erythritol, xylitol or sorbitol on school days for three consecutive years in school children aged 8–9 years at baseline. The intended daily intake of each sugar alcohol was approximately 7.5 g. Children were followed-up for another three years after the end of the intervention.

No significant differences in enamel caries teeth ($Dd_{1-3}Tt$) and surfaces ($Dd_{1-3}Ss$), dentin caries teeth ($Dd_{4-6}Tt$) and surfaces ($Dd_{4-6}Ss$) or caries indices (D_{4-6} MFT + d_{4-6}mft and D_{4-6}MFS + d_{4-6}mfs) were observed in mixed or permanent dentition between the erythritol and the sorbitol (control) groups at any time during the study, or in permanent dentition during the 3-year follow-up.

The second study provided by the applicant was a four-arm parallel study reporting on the effects of consuming either erythritol, xylitol or sorbitol sugar-free hard confectionery for 6 months on dental plaque (i.e. plaque index, plaque fresh weight, counts of 'mutans streptococci' in plaque and saliva) as compared to no treatment in a group of adolescents aged 16–19 years. Incidence of dental caries was not assessed. The applicant also provided one study in animals and five *in vitro* studies in support of the mechanisms by which the food that is the subject of the health claim could exert the claimed effect.

The Panel considers that, in the absence of evidence for an effect on the incidence of dental caries *in vivo* in humans, the results of the human studies investigating the effects of sugar-free hard confectionery with at least 90% erythritol on the proposed risk factors for dental caries and the studies provided on the mechanisms by which the food could exert the claimed effect cannot be used as a source of data for the scientific substantiation of the claim.

In weighing the evidence, the Panel took into account that one human intervention study (reported in three publications) with some methodological limitations (e.g. data analysis in completers only) did not show an effect of sugar-free hard confectionery with at least 90% erythritol on the incidence of dental caries in children on either mixed or permanent dentition.

On the basis of the data provided, the Panel concludes that a cause and effect relationship has not been established between the consumption of sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries.

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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, Articles 14–17 of this Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to of this Regulation, an application for 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 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: sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque.

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of sugar-free hard confectionery with at least 90% erythritol, a positive assessment of its safety, nor a decision on whether sugar-free hard confectionery with at least 90% erythritol 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 17 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 constituent that is the subject of the claim is Zerose® erythritol. Erythritol is a low molecular weight polyol, comprised of four carbon atoms that has zero calories and is non-glycaemic and non-insulinemic. The erythritol is in the form of sugar-free hard confectionery sweetened with at least 90% Zerose® erythritol. Sugar-free hard confectionery are candies with a hard texture with no added sugar as covered in food category 5.2 in Part D of Annex II to Regulation (EU) No 1129/2011. Sugar-free hard confectionery includes hard candies, pastilles, lozenges, tablets and breath-freshening microsweets.

Health relationship as claimed by the applicant

According to the applicant, consumption of erythritol reduces dental plaque which is a risk factor for caries; a reduction in dental plaque relates to reduction of dental caries development and reduces the risk of caries.

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

According to the applicant, the effect of erythritol could be explained by reduction in dental plaque resulting from reduced growth and adherence of common streptococcal oral bacteria to tooth surfaces and reduced acid production by the bacteria.

[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.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: 'Sugar-free hard confectionery sweetened with at least 90% Zerose® erythritol has been shown to reduce dental plaque. High content/level of dental plaque is a risk factor in the development of caries'.

Specific conditions of use as proposed by the applicant

The applicant has proposed an intake of 2–3 g of candies sweetened with at least 90% erythritol at least three times per day; target intake per day is ≥ 7 g. The target population proposed by the applicant is the general population. It is proposed to use erythritol in children in age at least 5 years.

Data provided by the applicant

Health claim application on Zerose® erythritol sugar-free hard confectionery and reduction of dental plaque which reduces the risk of caries pursuant to Article 14 of Regulation 1924/2006, 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.[2]

As outlined in the General guidance for stakeholders on health claim applications,[3] it is the responsibility of the applicant to provide the totality of the available evidence.

This health claim application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006 in relation to manufacturing process and the study by Falony et al. (2016).

The application does not include a request for data confidentiality.

2.2. Methodologies

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

The scientific requirements for health claims related to bone, joints, skin and oral health are outlined in a specific EFSA guidance (EFSA NDA Panel, 2012).

3. Assessment

3.1. Characterisation of the food/constituent

The food proposed by the applicant as the subject of the health claim is Zerose® erythritol sugar-free hard confectionery.

Erythritol ($C_4H_{10}O_4$) is a low molecular weight polyol ((2*R*,3*S*)-butane-1,2,3,4-tetrol) with a molar mass 122.12 g/mol. It occurs naturally in many foods but it is commercially produced from glucose by fermentation with the yeast *Moniliella pollinis*. Erythritol is authorised for use as a sweetener (E 968) (EFSA ANS Panel, 2015).

Zerose® erythritol sugar-free hard confectionery includes hard candies, pastilles, lozenges, tablets and breath-freshening microsweets. Sugar-free hard confectionery is covered in food category 5.2 in Part D of Annex II to Regulation (EU) No 1129/2011 as candies with a hard texture with no added sugar.

Zerose® erythritol sugar-free hard confectionery contains a minimum of 90% erythritol. The remaining 10% is made up of other ingredients, such as other sweeteners or bulking agents, hydrocolloids, flavourings and colours.

An overview of the manufacturing process and batch-to-batch variability data were provided.

Upon a request from EFSA to clarify whether the subject of the claim is (1) erythritol, (2) Zerose® erythritol, (3) Zerose® erythritol sugar-free hard confectionery or (4) erythritol in sugar-free hard confectionery, the applicant explained that all human studies provided to support the claim were performed with Zerose® erythritol sugar-free hard confectionery. However, the applicant did not address in the reply which properties of Zerose® erythritol sugar-free hard confectionery make the product unique in relation to the claimed effect as compared to other sugar-free hard confectionery containing 90% erythritol, which would justify a product-specific claim. The applicant also explained

[2] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1). EFSA Journal 2011;9(5):2170. [36 pp.]. https://doi.org/10.2903/j.efsa.2011.2170

[3] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. General scientific guidance for stakeholders on health claim applications. EFSA Journal 2016;14(1):4367, 38 pp. https://doi.org/10.2903/j.efsa.2016.4367

that hard candies were developed for consumption by sucking in the mouth until complete dissolution of the candy.

The Panel considers that the food, sugar-free hard confectionery with at least 90% erythritol, 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 'reduction of dental plaque which reduces the risk of caries'. The target population proposed by the applicant is the general population aged 5 years and older.

In relation to the disease (dental caries) that is the subject of the health claim, the applicant states that 'the presence of decayed (D), missing (M) and filled (F) teeth (T) or tooth surfaces (S) is the criteria used for diagnosis. The International Caries Detection and Assessment System (ICDAS II) (Ismail et al., 2007) is an internationally recognised standard. Enamel (Dd1, Dd2, Dd3) and dentin caries lesions (Dd4, Dd5, Dd6), filled teeth and surfaces (Ffft and FfSs) and missing teeth and surfaces (MmTt and MmSs) are determined on all surfaces of the teeth (max. 28 teeth, 128 surfaces)'. The Panel considers that a clinical assessment of dental caries using the ICDAS II classification is an appropriate outcome variable to assess the incidence of the disease in intervention studies conducted in children.

As risk factor(s) for the disease, the applicant proposes 'a high amount of dental plaque, and specifically the interactions over time between microorganisms found in dental plaque and dietary fermentable carbohydrate'. In reference to the EFSA guidance (EFSA NDA Panel, 2012), the applicant acknowledges that colonisation by *Streptococcus mutans*, the amount of dental plaque, and a decrease in plaque pH are associated with an increased risk of dental caries. The applicant also acknowledges that these variables may be considered as risk factors for dental caries only if changes in these factors are accompanied by evidence of reduced incidence of dental caries in humans in the context of a particular nutritional intervention.

The applicant proposes three outcome variables to be used for the assessment of the risk factor(s) in human studies: (a) the weight of freshly collected dental plaque (i.e. collected from all available tooth surfaces during a timed 3-min period); (b) salivary and plaque counts of *S. mutans*; and (c) chemical analysis of dental plaque (i.e. plaque sugars, organic acids and polyols).

The Panel considers that, in the context of this application, the weight of dental plaque, and/or the counts of *S. mutans* in dental plaque, and/or the concentration of organic acids in plaque (primarily acetic acid and lactic acid) can be considered as risk factor(s) in the development of dental caries as long as evidence is provided that the consumption of the food that is the subject of the health claim reduces one or more of the proposed risk factors and also the incidence of dental caries.

3.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in Medline, and Cochrane Library with the following key words: dental caries OR (DMF Index[Mesh] OR dental plaque OR ICDAS OR caries increment OR prevented fraction) AND erythritol and human. A secondary search was conducted using the search terms dental caries OR (DMF Index[Mesh] OR dental plaque OR ICDAS OR caries increment OR prevented fraction) AND "sugar alcohols"[Mesh]. Hand searching was also performed.

Human intervention studies

The applicant identified two human intervention studies (reported in four publications) as being pertinent to the claim, of which only one study investigated the effect of consuming sugar-free hard confectionery with 90% erythritol on the incidence of dental caries.

Three publications (Runnel et al., 2013; Honkala et al., 2014; Falony et al., 2016) describe a 3-year intervention trial conducted in Tartu (Estonia), where the fluoride content of drinking water is low. The study was designed as a randomised, three-arm, double-blind, but not placebo-controlled, parallel trial which investigated the effect of consuming polyol-containing candies on dental health in school children aged 8–9 years at baseline.

First- and second-grade primary school children from 10 schools in Tartu were assigned to consume chewable hard candies (four 0.7-g candies three times per day) with 90% erythritol, xylitol, or sorbitol on school days (about 200 days in the calendar year) for three consecutive years. Candies were distributed by the teachers. The intended daily intake of each sugar alcohol was approximately 7.5 g.

All participants received information on dental health, oral hygiene and diet. Every child obtained a toothbrush and fluoride toothpaste (containing sorbitol as sweetener) every 6 months, and was asked to brush the teeth more than once daily.

The participating school classes were randomly divided into erythritol, xylitol and sorbitol (control) intervention groups. Randomisation was done using computer-generated numbers on the list of classes from participating schools. To reduce a potential school bias, first-grade pupils were allocated to different intervention groups than second-graders of the same school.

Double-blind clinical examinations of all participating children were completed once a year, all in the same stomatology centre (baseline and after 12, 24 and 36 months of intervention) by four trained investigators. Each child was assigned to one examiner for the entire duration of the study.

Sample size was calculated based on the estimated difference (1.5 carious surfaces) in the incidence of caries in mixed dentition between the erythritol and xylitol groups (2 carious surfaces) and the control (sorbitol) (3.5 carious surfaces) group (common SD = 4) after 2 years of intervention, with an α error of 0.05, a β error of 0.20 and assuming a 25% of drop-outs. The sample size was calculated as 151 subjects per study group (Honkala et al., 2014).

Among the 522 children who were eligible for the study, 485 were randomised (n = 165, 156 and 164 to the erythritol, xylitol and sorbitol groups, respectively) and 374 completed the study (n = 122, 126 and 126 in the erythritol, xylitol and sorbitol groups, respectively). A total of 43, 30 and 38 children were lost to follow up in the erythritol, xylitol and sorbitol groups, respectively, owing to change of the school or the absence from the school on examination days. Data analysis was carried out in completers only.

Upon a request from EFSA for clarification, the applicant explained that the group consuming sorbitol candies was used as control in this study. The reason for this choice was the lack of significant differences between the sorbitol and the untreated control group in a previous study (Mäkinen et al., 2005 – see description below) with respect to all the outcome variables measured which were considered by the applicant as risk factors for the development of dental caries (e.g. plaque fresh weight, plaque index, levels of 'mutans streptococci' in plaque and saliva). The Panel considers that only the results obtained in the erythritol group as compared to the placebo (sorbitol) are relevant for the scientific assessment of this claim.

Honkala et al. (2014) reported on the incidence of dental caries in mixed dentition, which was assessed using the ICDAS II scoring methodology. Enamel (Dd1, Dd2, Dd3) and dentin caries lesions (Dd4, Dd5, Dd6), filled teeth and surfaces (FfTt and FfSs), and missing teeth and surfaces (MmTt and MmSs) were determined in all examinations on all surfaces of the teeth (max. 28 teeth, 128 surfaces). If a tooth was exfoliated or extracted, all the visible surfaces from the earlier assessment were recorded as missing when calculating caries increments. For data analysis, the ICDAS II caries codes 1–3 were combined to enamel caries teeth ($Dd_{1-3}Tt$) and surfaces ($Dd_{1-3}Ss$). Codes 4–6 were combined to dentin caries teeth ($Dd_{4-6}Tt$) and surfaces ($Dd_{4-6}Ss$). Caries indices (D_{4-6} MFT + d_{4-6}mft and D_{4-6}MFS + d_{4-6}mfs) were calculated as the sum of decayed, missing and filled teeth and surfaces. The number of enamel and dentin caries teeth and surfaces, the number of teeth and surfaces with fillings and the number of caries experience teeth and surfaces at baseline and at 12, 24 and 36 months were compared between the groups using negative binomial regression. Models were adjusted for gender, age ($\leq$ 7 years, 8 years, $\geq$ 9 years) and school. The natural log of the number of teeth or surfaces present was included as an offset when analysing the number of enamel/dentin caries and filled teeth or surfaces. Pearson χ^2 goodness-of-fit statistics were used to assess the fit of the models. Changes in caries indices were analysed with negative binomial regression using generalised estimating equations with exchangeable correlation structure to account for dependency between repeated measures. The significance level was set at $p < 0.05$. Children in the erythritol group (mean $\pm$ SD = 8.6 $\pm$ 0.5 years) were significantly older than children in the sorbitol (8.1 $\pm$ 0.6 years) group ($p < 0.0001$).

No significant differences in enamel caries teeth ($Dd_{1-3}Tt$) and surfaces ($Dd_{1-3}Ss$), dentin caries teeth ($Dd_{4-6}Tt$) and surfaces ($Dd_{4-6}Ss$) or caries indices (D_{4-6} MFT + d_{4-6}mft and D_{4-6}MFS + d_{4-6}mfs) were observed in mixed dentition between the erythritol and the sorbitol (control) groups at any time during the study.

Falony et al. (2016) report on the incidence of dental caries on permanent dentition during the 3-year intervention and after a 3-year observational follow-up. A total of 364 participants we re-examined to identify potential long-term effects of consuming polyol-containing candies (n = 129 in erythritol group, n = 123 in sorbitol group and n = 112 in xylitol group) on caries development.

At baseline, the number of dentin caries surfaces ($Ds_{4-6}Ss$) in the permanent dentition was significantly higher in the sorbitol group than in the erythritol group (relative risk, RR = 3.10, 95%

confidence interval, CI = 1.23–7.80). No other significant differences in enamel caries teeth ($Dd_{1–3}Tt$) and surfaces ($Dd_{1–3}Ss$), dentin caries teeth ($Dd_{4–6}Tt$) and surfaces ($Dd_{4–6}Ss$) or caries indices ($D_{4–6}MFT + d_{4–6}mft$ and $D_{4–6}MFS + d_{4–6}mfs$) were observed in permanent dentition between the erythritol and the sorbitol (control) groups through the 3-year intervention. Three years after cessation of the intervention, no significant differences in decayed, missing, and filled teeth and surfaces were observed among the study groups.

The Panel notes that no significant differences between the erythritol and control (sorbitol) groups were observed in the incidence of dental caries in mixed or permanent dentition in children at any time point during the 3-year intervention study or at the 3-year observational follow-up.

Survival curves (considering the time to caries development for each surface on each subject) were generated during the intervention period (for mixed dentition, Honkala et al., 2014; for permanent dentition, Falony et al., 2016) and 3 years after the intervention (for permanent dentition, Falony et al., 2016). The ICDAS scoring system-based events used for data analysis included enamel/dentin caries development, dentin caries development, increase in caries score, and dentist intervention as outcomes. Upon a request from EFSA to provide the study report, including the study protocol and the original statistical analysis plan, the applicant provided a statistical report (dated 25 November 2014) of the survival analysis, but not the original statistical analysis plan. The Panel notes that no information was provided on whether the statistical analysis on the time course of caries development, a variable which is not the primary outcome of the study, was preplanned or exploratory. The Panel therefore considers that no conclusions can be drawn from this analysis for the scientific substantiation of the claim.

Runnel et al. (2013) reported on a number of outcome variables, including salivary and plaque counts of *S. mutans* (assessed by the Orion Diagnostica (Espoo, Finland) Dentocult® SM procedure), salivary counts of *Lactobacillus* (assessed by the Dentocult® LB Dip Slide procedure), total plaque fresh weight, salivary flow rate and chemical analysis of aqueous plaque extracts (including acetic acid, propionic acid, lactic acid, calcium, glycerol, proteins, sorbitol). The Panel notes that the methods used for the identification of oral bacteria were based on cultural methods and phenotypic features only and do not allow a precise quantification of *S. mutans* at species level.

An additional comparison group (n=162) of children of the same age was created at the end of the intervention. Upon a request from EFSA, the applicant clarified that this group should not be considered as the control group, as the addition was driven 'by scientific interest from the research team on actual caries prevalence in this subpopulation'.

Differences between groups on the above-mentioned variables were analysed using the Kruskal–Wallis test and pair-wise comparisons were made using the Mann–Whitney U-test with Bonferroni correction. The Panel notes that the statistical analysis is not appropriate for a study design with multiple study groups and time points. Therefore, the Panel considers that no conclusions can be drawn from this study with respect to the effects of sugar-free hard confectionery with at least 90% erythritol on the secondary outcomes reported in this publication.

The Panel considers that this study (reported in three publications- Runnel et al., 2013; Honkala et al., 2014; Falony et al., 2016) with some methodological limitations (e.g. data analysis in completers only) does not show an effect of sugar-free hard confectionery with at least 90% erythritol on the incidence of dental caries in children on either mixed or permanent dentition.

The second study provided by the applicant (Mäkinen et al., 2005) was a four-arm parallel study reporting on the effects of consuming either erythritol, xylitol or sorbitol sugar-free hard confectionery for 6 months on dental plaque (i.e. plaque index, plaque fresh weight, counts of 'mutans streptococci' in plaque and saliva) as compared to no treatment in a group of adolescents aged 16–19 years. Incidence of dental caries was not assessed.

The applicant also provided a number of studies in animals (Kawanabe et al., 1992) and *in vitro* (Söderling & Hietala-Lenkkeri, 2010; Ghezelbash et al., 2012; Runnel et al., 2013; Park et al., 2014; Saran et al., 2015) in support of the mechanisms by which the food that is the subject of the health claim could exert the claimed effect.

The Panel considers that, in the absence of evidence for an effect on the incidence of dental caries *in vivo* in humans, the results of the human studies investigating the effects of sugar-free hard confectionery with at least 90% erythritol on the proposed risk factors (Mäkinen et al., 2005) for dental caries and the studies provided on the mechanisms by which the food could exert the claimed effect (Kawanabe et al., 1992; Söderling & Hietala-Lenkkeri, 2010; Ghezelbash et al., 2012; Runnel et al., 2013; Park et al., 2014; Saran et al., 2015) cannot be used as a source of data for the scientific substantiation of the claim.

Weighing of the evidence

In weighing the evidence, the Panel took into account that one human intervention study (reported in three publications: Runnel et al., 2013; Honkala et al., 2014; Falony et al., 2016) with some methodological limitations (e.g. data analysis for completers only) did not show an effect of sugar-free hard confectionery with at least 90% erythritol on the incidence of dental caries in children on either mixed or permanent dentition.

The Panel concludes that a cause and effect relationship has not been established between the consumption of sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries.

4. Conclusions

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

- the food/constituent, sugar-free hard confectionery with at least 90% erythritol, which is the subject of the health claim, is sufficiently characterised.
- the claimed effect proposed by the applicant is 'reduction of dental plaque which reduces the risk of caries'. The target population proposed by the applicant is the general population aged 5 years and older. In the context of this application, a decrease in the weight of dental plaque, and/or in the counts of *S. mutans* in dental plaque, and/or in the concentration of organic acids in plaque (primarily acetic acid and lactic acid) can be considered as risk factor(s) in the development of dental caries, as long as evidence is provided that the consumption of the food that is the subject of the health claim reduces one or more of the proposed risk factors as well as the incidence of dental caries.
- A cause and effect relationship between sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries has not been established.

Steps taken by EFSA

1) Health claim application on sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0452_BE). Submitted by Cargill R&D Centre Europe, Havenstraat 84, B-1800 Vilvoorde, Belgium.
2) This application was received by EFSA on 4/1/2017.
3) The scientific evaluation procedure started on 13/1/2017.
4) On 18/1/2017, 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 19/2/2017 and was restarted on 1/3/2017, in compliance with Article 16(1) of Regulation (EC) No 1924/2006.
5) On 28/2/2017, EFSA received the applicant's reply (which was made available to EFSA in electronic format on 28/2/2017).
6) On 22/3/2017, 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 13/4/2017 and was restarted on 12/5/2017, in compliance with Article 16(1) of Regulation (EC) No 1924/2006.
7) On 12/5/2017, EFSA received the applicant's reply (which was made available to EFSA in electronic format on 12/5/2017).
8) During its meeting on 27/6/2017, the NDA Panel, having evaluated the data, adopted an opinion on the scientific substantiation of a health claim related to sugar-free hard confectionery with at least 90% erythritol and reduction of dental plaque which reduces the risk of dental caries.

References

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources), 2015. Scientific Opinion on the safety of the proposed extension of use of erythritol (E 968) as a food additive. EFSA Journal 2015;13(3):4033, 15 pp. https://doi.org/10.2903/j.efsa.2015.4033

EFSA NDA Panel (EFSA Panel on Dietetic Products Nutrition and Allergies), 2011. Scientific Opinion on the substantiation of health claims related to the sugar replacers xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, D-tagatose, isomaltulose, sucralose and polydextrose and maintenance of tooth mineralisation by decreasing tooth demineralisation (ID 463, 464, 563, 618, 647, 1182, 1591, 2907, 2921, 4300), and reduction of post-prandial glycaemic responses (ID 617, 619, 669, 1590, 1762, 2903, 2908, 2920) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2011;9(4):2076, 2025 pp. https://doi.org/10.2903/j.efsa.2011.2076

EFSA NDA Panel (EFSA Panel on Dietetic Products Nutrition and Allergies), 2012. Guidance on the scientific requirements for health claims related to bone, joints, skin and oral health. EFSA Journal 2012;10(5):2702, 2713 pp. https://doi.org/10.2903/j.efsa.2012.2702

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. General scientific guidance for stakeholders on health claim applications. EFSA Journal 2016;14(1):4367, 38 pp. https://doi.org/10.2903/j.efsa.2016.4367

Falony G, Honkala S, Runnel R, Olak J, Silvia Nömmela R, Russak S, Saag M, Mäkinen P-L, Mäkinen K, Vahlberg T and Honkala E, 2016. Long-term effect of erythritol on dental caries development during childhood: a post treatment survival analysis. Caries Research, 50, 579–588.

Ghezelbash GR, Nahvi I and Rabbani M, 2012. Comparative inhibitory effect of xylitol and erythritol on the growth and biofilm formation of oral Streptococci. African Journal of Microbiology Research, 6, 4404–4408.

Honkala S, Runnel R, Saag M, Olak J, Nömmela R, Russak S, Makinen PL, Vahlberg T, Falony G, Mäkinen K and Honkala E, 2014. Effect of erythritol and xylitol on dental caries prevention in children. Caries Research, 48, 482–490.

Ismail AI, Sohn W, Tellez M, Sen A, Hasson H and Pitts NB, 2007. The International Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. Community Dentistry and Oral Epidemiology, 35, 170–178.

Kawanabe J, Hirasawa M, Takeuchi T, Oda T and Ikeda T, 1992. Noncariogenicity of erythritol as a substrate. Caries Research, 26, 358–362.

Mäkinen KK, Saag M, Isotupa KP, Olak J, Nömmela R, Soderling E and Mäkinen PL, 2005. Similarity of the effects of erythritol and xylitol on some risk factors of dental caries. Caries Research, 39, 207–215.

Park YN, Jeong SS, Zeng J, Kim SH, Hong SJ, Ohk SH and Choi CH, 2014. Anti-cariogenic effects of erythritol on growth and adhesion of Streptococcus mutans. Food Science and Biotechnology, 23, 1587–1591.

Runnel R, Makinen KK, Honkala S, Olak J, Makinen PL, Nommela R, Vahlberg T, Honkala E and Saag M, 2013. Effect of three-year consumption of erythritol, xylitol and sorbitol candies on various plaque and salivary caries-related variables. Journal of Dentistry, 41, 1236–1244.

Saran S, Mukherjee S, Dalal J and Saxena RK, 2015. High production of erythritol from Candida sorbosivorans SSE-24 and its inhibitory effect on biofilm formation of Streptococcus mutans. Bioresource Technology, 198, 31–38.

Söderling EM and Hietala-Lenkkeri AM, 2010. Xylitol and erythritol decrease adherence of polysaccharide-producing oral Streptococci. Current Microbiology, 60, 25–29.

Abbreviations

D	decayed
F	filled
ICDAS	International Caries Detection and Assessment System
M	missing
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
S	surfaces
SD	standard deviation
T	teeth