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## SCIENTIFIC OPINION

# Statement in relation to the safety of erythritol (E 968) in light of new data, including a new paediatric study on the gastrointestinal tolerability of erythritol[1]

**EFSA Panel on Food Additives and Nutrient Sources (ANS)**[2, 3]

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## ABSTRACT

Following a request from the European Commission, the Panel on Food Additives and Nutrient Sources added to Food (ANS) provides a scientific opinion on the safety of erythritol (E 968) in light of a paediatric study on the gastrointestinal (GI) tolerability of erythritol. In 1999, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated erythritol and assigned an ADI "not specified". In 2003, the EU Scientific Committee on Food (SCF) concluded that erythritol is safe for use in foods. Erythritol is approved in the EU for the same uses as other polyols, but EU approval does not yet cover its use in beverages because the SCF opinion stated that the laxative threshold may be exceeded, especially by young consumers and through ingestion of erythritol in beverages. A paediatric study on the GI tolerability of erythritol was conducted with the goal to determine the maximum dose level of erythritol that is well-tolerated by young children aged 4-6 years old, in a single drinking occasion. The Panel noted that erythritol intake resulting from an incorporation rate of 2.5% in beverages (i.e. 0.59 g/kg bw) is below the No-Observed-Adverse-Effect Level (NOAEL) for laxative effects (i.e. 0.71 g/kg/bw/day). The Panel noted that the margin of safety (MOS) between this NOAEL and the estimated daily intake of erythritol resulting from an incorporation rate of 2.5% in beverages (0.59 g/kg bw) is 1.24. The Panel concludes that this MOS is too low to ensure that children are adequately protected taking into account the fact that erythritol is also used in other food categories. The Panel concludes that there is a safety concern with respect to GI tolerability for the use of erythritol in beverages at a maximum use level of 2.5% for non-sweetening purposes.

## KEY WORDS

Erythritol, laxation, gastrointestinal tolerability, paediatric study

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**SUMMARY**

Following a request from the European Commission, the Panel on Food Additives and Nutrient Sources (ANS) was asked to deliver an opinion in relation to the safety of erythritol (E 968) in light of new data, including a new paediatric study on the gastrointestinal (GI) tolerability of erythritol.

Erythritol is a four-carbon polyol that is well-tolerated and permitted for use in foods and beverages in many countries around the world including the USA, China, Japan, Russia, Canada, Australia, New Zealand, Brazil, Argentina, Uruguay, Mexico, Korea, Thailand, Singapore, Taiwan, Hong Kong, Philippines, Israel and South Africa.

In 1999, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated erythritol and assigned an Acceptable Daily Intake (ADI) "not specified". In 2003, the EU Scientific Committee on Food (SCF) reviewed the acceptability of erythritol for human consumption and concluded that it is safe for use in foods.

Erythritol is approved in the EU for the same uses as other polyols, but EU approval does not yet cover its use in beverages because the SCF opinion of 2003 stated that the laxative threshold may be exceeded, especially by young consumers and through ingestion of erythritol in beverages. Human studies on GI tolerance of erythritol indicated that the No-Observed-Adverse-Effect Level (NOAEL) for laxation is between 0.5 and 1.0 g/kg bw/day.

A paediatric study on the GI tolerability of erythritol was conducted with the goal to determine the maximum dose level of erythritol that is well-tolerated by young children aged 4-6 years old, in a single drinking occasion. This was a double-blind, randomised, controlled GI tolerance study utilising a cross-over design. Children aged 4 – 6 years were enrolled from multiple sites in France. The cross-over design allowed the incidence of GI-related adverse events following consumption of erythritol to be compared with those following consumption of a placebo (saccharose). Since each child served as its own control, differences in sensitivity between subjects did not affect the evaluation. Three doses of erythritol (5, 15, 25 g) versus an isosweet control (saccharose) were evaluated in 128 children. The primary outcome variable was an estimate of GI tolerability as measured by the incidence of diarrhoea and/or significant GI symptoms following consumption of the study products. Subjects were categorised according to whether or not (yes versus no) they experienced diarrhoea and/or significant GI symptoms during the test periods. The study lasted 27 months. There were no differences between the 3 test groups for gender (42-57% female), age (4.4 to 4.9 years old), weight (21 kg), height (113-114 cm) or BMI (16 kg/$m^2$). For the 5 g and 15 g erythritol test groups, there was no significant difference in the incidence of diarrhoea or significant GI symptoms between the erythritol-sweetened test beverages and the saccharose sweetened (control) product. For the 25 g dose, a greater incidence of diarrhoea and/or significant GI symptoms was observed following consumption of the erythritol-sweetened beverage (32%) versus the control (3.5%) ($p = 0.0002$). This result met the study stopping criteria, thus a higher dose of 35 g erythritol was not tested.

The intake of erythritol from its proposed use in beverages (2.5%), in particular diet concentrated soft drinks (cordials), diet ready-to-drink soft drinks and diet carbonated soft drinks, per drinking occasion, is estimated to range from a mean of 2.4 g/person in 1.5 to 4.5 year old children, to 8.8 g/person in teenagers (15 to 18 years old). Subjects most exposed to erythritol on a g/kg bw basis are 4 to 6-year-old children. At the 97.5$^{th}$ percentile beverage consumption level, the maximum erythritol intake in children 4 to 6 years old is estimated to be 11.6 g/person.

The Panel noted that the results of the paediatric study demonstrate that ingestion of 15 g (0.71 g/kg bw) of erythritol in a beverage consumed by children aged 4-6 years in a single drinking occasion within 15 minutes, indicate a NOAEL for laxation in these young children amounting to 0.71 g/kg bw/day.

The margin of safety between this NOAEL and the estimated daily intake of erythritol resulting from an incorporation rate of 2.5% in beverages (0.59 g/kg bw at the 97.5$^{th}$ percentile) is 1.24.

Given that:

- The NOAEL is based on a study population that consists of a limited number of selected children in the low-dose group and a limited statistical power
- Erythritol is also allowed for use in other food categories,
- There may be synergism with GI effects due to intake of other polyols,

the Panel concludes that this margin of safety is too low to ensure that children are adequately protected taking into account that erythritol is also used in other food categories.

Therefore, the Panel concludes based on the available data that there is a safety concern with respect to the GI tolerability for the use of erythritol in beverages at a maximum use level of 2.5% for non-sweetening purposes.

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## BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Following a request from the Commission, the Scientific Committee on Food (SCF) issued its opinion on erythritol on 5 March 2003. The SCF reached the conclusion that erythritol is safe to use as a food additive. In line with earlier opinions on other polyols, SCF did not consider it appropriate to set a numerical Accepted Daily Intake (ADI) for erythritol.

The Committee also noted that erythritol has a laxative effect, but at higher doses than other polyols and concluded that the NOAEL for the laxative effect of erythritol in humans is around 0.5g/kg bw for a single dose. The SCF expressed concerns that the laxative threshold may be exceeded especially by young consumers and through ingestion of erythritol in beverages. SCF cautioned that their opinion should not be interpreted as meaning the acceptance of unlimited use in all foods at any technological level because the laxative effect should be borne in mind. Thus, Directive 2006/52/EC of the European Parliament and of the Council amending Directives 94/35/EC and 95/2/EC did not include the use of erythritol in beverages.

The Health and Consumers Directorate-General has subsequently received a request for the authorisation of the use of erythritol for purposes other than sweetening at a maximum level of 2.5% in the following beverage categories:

- Water-based flavoured drinks, energy-reduced or with no added sugar
- Milk- and milk-derivative-based or fruit-juice-based drinks, energy-reduced or with no added sugar.

In the application dossier additional information is submitted, including a new paediatric study on the gastrointestinal tolerability of erythritol and exposure estimates of erythritol intake per drinking occasion by children.

## TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to provide on the basis of the new information a scientific opinion on the safety of erythritol, notably on its laxative effect for the proposed use in beverages at a maximum use level of 2.5%.

## 1. Introduction

Erythritol is a four-carbon polyol that is approximately 70% as sweet as saccharose. It is non-cariogenic, non-caloric, non-glycemic and non-insulinemic. It occurs naturally (in fruits, fermented products, mushrooms) and is manufactured by a fermentation process that is in compliance with applicable EU specifications. Several expert committees, including the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1999, and the EU Scientific Committee on Food (SCF) in 2003, have reviewed the acceptability of erythritol for human consumption and respectively assigned an ADI "not specified" (JECFA, 2000), and concluded that it is safe for use in foods (SCF, 2003). Erythritol is permitted for use in foods and beverages in many countries around the world, including the USA, China, Japan, Russia, Canada, Australia, New Zealand, Brazil, Argentina, Uruguay, Mexico, Korea, Thailand, Singapore, Taiwan, Hong Kong, Philippines, Israel and South Africa. EU approval of erythritol for the same uses as other polyols was published in Directive 2006/52/EC[4] amending Directive 95/2/EC on food additives other than colours and sweeteners and Directive 94/35/EC on sweeteners for use in foodstuffs.

Polyols are not permitted for use in beverages in the EU because of their laxation potential.

Although erythritol chemically belongs to the group of polyols, it has a different absorption and metabolic profile resulting in a caloric value of virtually zero and a digestive tolerance that is higher compared to all other polyols (SCF, 2003).

The Panel considers that the terms of reference can be answered by evaluation of the laxation potential of erythritol in humans and children using the following information:

a. Historical background

b. Laxation potential of erythritol in humans

c. Paediatric study on the gastrointestinal (GI) tolerability of erythritol

d. Estimated intake of erythritol.

## 2. Information on existing authorisations and evaluations

On March 5th 2003, the SCF issued its opinion on erythritol following a request by several applicants for the use of erythritol in non-alcoholic beverages up to 3.5%. The conclusion reached by the SCF was that erythritol is safe to use as a food additive. In line with earlier opinions on other polyols, they did not consider it appropriate to set a numerical Accepted Daily Intake (ADI) for erythritol.

The SCF recognised that human clinical study results on the GI tolerance of erythritol indicated a No-Observed-Adverse-Effect Level (NOAEL) of 0.5 to 1.0 g/kg bw/day, with a NOAEL for laxative effects of 0.5 g/kg bw/day when erythritol was administered as a bolus dose in solution on an empty stomach. The SCF expressed concerns that the laxative threshold may be exceeded especially by young consumers and through ingestion of erythritol in beverages. They cautioned that their opinion should not be interpreted as meaning the acceptance of unlimited erythritol use in all foods at any technological level, because the laxative effect should be borne in mind.

[4] Directive 2006/52/EC of the European Parliament and of the Council of 5 July 2006 amending Directive 95/2/EC on food additives other than colours and sweeteners and Directive 94/35/EC on sweeteners for use in foodstuffs. OJ L 204, 26.7.2006, p. 10-22.

In October 2003, the UK Food Standards Agency (FSA) and its Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment[5] (COT) discussed the petitioner's request for a Temporary National Authorisation (TNA) to permit the use of erythritol in foods and also in beverages at a level of 3.5%. The COT considered bolus erythritol intakes to be more important for laxative effects than intakes spread across an entire day. The COT Secretariat's intake calculation revealed that 4 to 6 year-old children had the highest 97.5$^{th}$ percentile intake from soft drink-type beverages consumed in a single drinking occasion, i.e., 0.83 g erythritol per kg body weight at a 3.5% use level. The COT concluded at that time that it was not acceptable for erythritol to be used in beverages at a level of 3.5% because convincing evidence was not available to demonstrate digestive tolerance in young children. In order to resolve this issue, the petitioner convened a digestive tolerance study in young children aged 4 to 6 years old with the purpose to determine the maximum erythritol dose that does not cause laxation or other significant digestive tolerance-related outcomes when consumed in a beverage within a maximum duration of 15 minutes. The results of that study are summarised in section 4.

## 3. Case of need and proposed uses

Erythritol is proposed to be used in foods and/or beverages, for functions including sweetening, binding, bulking, sequestering, thickening, flavour enhancement and as a freezing point depressant (Perko et al., 2006). Erythritol, used in beverages in low levels is claimed to improve the flavour profile and mouthfeel of calorie-reduced and sugar-free beverages such that they taste very similar to full-sugar products (De Cock et al., 2002). However, Erythritol is not permitted for use in beverages in the EU because of its laxation potential.

The taste-enhancement of low and reduced-calorie beverages permits consumers to reduce their energy and sugar intake from beverages without sacrificing taste.

The current application is for approval for use of erythritol for purposes other than sweetening at a maximum use level of 2.5% in the following beverages categories:

- Water-based flavoured drinks, energy-reduced or with no added sugar
- Milk- and milk-derivative-based or fruit-juice-based drinks, energy-reduced or with no added sugar.

## 4. Laxation potential of erythritol in humans

Polyols in general, or sugar alcohols, are widely used to replace sugars in foods, such as confectionery and baked goods; however, they can cause laxative effects, flatulence and abdominal pain when excessive amounts (over 20 g) are consumed acutely or in solution (Munro et al., 1998; Lee et al., 2002; Storey et al., 2007). In general, the behaviour of polyols in the human digestive system varies depending on their molecular size and chemical nature. Undesirable effects occur when a substantial amount (over 20 g) of the malabsorbed carbohydrate enters the large intestine where it acts osmotically to produce a laxative effect (Lifshitz et al., 1992). For erythritol, studies in animals and humans have shown that about 90% of the ingested dose is absorbed from the small intestine and excreted in the urine unchanged or fermented by the gut flora to short-chain fatty acids (Bornet et al., 1996a,b).

[5] COT is an independent scientific committee that provides advice to the UK Food Standards Agency, the Department of Health and other UK Government Departments and Agencies on matters concerning the toxicity of chemicals.

The lowest NOAEL for loose stool formation was determined in a study where erythritol was administered in water as a single bolus dose of 0.5 g/kg bw on an empty stomach (Umeki, 1992). However, according to the petitioner, the results from this study can be criticised because one third of the subjects had previously experienced digestive disorders (Table 1).

**Table 1:** Summary of adult human studies reporting digestive tolerance of erythritol following acute bolus or repeated exposures

| Delivery vehicle | Dose type | No of subjects | NOAEL for laxation (g) | NOAEL for laxation (g/kg bw/day) | Reference |
|---|---|---|---|---|---|
| Beverage | Single, Bolus | n=6 | 30 | 0.51 | Umeki (1992) Unpublished |
| Beverage | Single, Bolus | n=12 | 30 | 0.76 F; 0.55 M | Takahashi (1992a) Unpublished |
| Beverage | Single, Bolus | n=6 | <64 | <1 | Bornet et al. (1996a) |
| Beverage | Single, Bolus | n=5 | 20* | N/A | Ishikawa et al. (1996b) |
| Beverage - Jelly | Single, Bolus | n=38 | 30 | 0.80 F; 0.66 M | Oku and Okazaki (1996a) |
| Beverage | Single, Bolus | n=65 | 50* | 0.78 | Storey et al. (2007) |
| Beverage | Single, Bolus Twice daily, 5days | n=10 | 40* | 0.74 F; 0.64 M | Takahashi (1992b) Unpublished |
| Beverage | Continuous, 14 days | n=11 | 20* | N/A | Ishikawa et al. (1996a) |
| Food (chocolate) | Single, Bolus | n=24 | 52-60* | 0.8 | Bornet et al. (1996b) |
| Food/Beverage | Continuous, 7 days | n=12 | ~79* | 1.0 | Tetzloff et al. (1996) |

*Highest dose tested

In a more recent study, Storey et al., (2007) specifically evaluated the GI tolerance of erythritol when consumed from a beverage as a bolus dose. This study was a randomised, double-blind placebo-controlled study with a control (45 g saccharose) and treatment groups providing 20, 35, or 50 g of erythritol or xylitol to 70 healthy subjects aged 18 to 24 years old. The researchers reported a NOEL for laxation from this study of 50 g erythritol consumed as a bolus. Considering the body weights of the participants in this study, 50 g of test material equates to a mean NOAEL for laxation of 0.78 g/kg bw/day, which is close to the NOAEL determined by Bornet et al., (1996b) and Oku and Okazaki (1996).

Human tolerance to repeated oral doses of erythritol spread over the day has been examined by Tetzloff et al., (1996) in a double-blind, two-way crossover study in 12 healthy male volunteers. The participants consumed erythritol and, for comparison, saccharose for a duration of 7 days each. The daily dose of the test compounds ingested was 0.3 g/kg bw on Day 1, 0.6 g/kg on Day 2, and 1.0 g/kg on subsequent days. The daily dose was consumed under supervision in 5 portions, i.e., with the 3 main meals, a midmorning snack, and during the afternoon. The test compounds were incorporated into yoghurt, cookies, soft drinks, and chocolate. The results demonstrated that the repeated ingestion of erythritol at a daily dose of 1 g/kg bw is well tolerated.

## 5. Paediatric study on the gastrointestinal tolerability of erythritol

The petitioner provides data on a new double-blind, randomised, controlled GI tolerance paediatric study utilising a cross-over design. Children aged 4 – 6 years were enrolled from multiple sites in France. The cross-over design allowed the incidence of GI-related adverse events following consumption of erythritol to be compared with those following consumption of a placebo (saccharose). Since each child served as its own control, differences in sensitivity between subjects did not affect the evaluation.

Three doses of erythritol (5, 15, 25 g) versus an isosweet control (saccharose) were evaluated in 128 children. The primary outcome variable was an estimate of GI tolerability as measured by the incidence of diarrhoea and/or significant GI symptoms following consumption of the study products. Subjects were categorised according to whether or not (yes versus no) they experienced diarrhoea and/or significant GI symptoms during the test periods. Diarrhoea and significant GI symptoms were defined as follows:

1. Diarrhoea was defined as a single watery stool (Bristol Scale Score of 7) and/or >3 defecations (regardless of consistency) in a 24-hour period.

2. Significant GI symptoms were defined as any GI symptoms having a severity recorded (by the parent) as "strong intensity" in the symptom diary.

Secondary outcomes included stool frequency, stool consistency, GI symptoms intensity score, and urinary erythritol excretion. The 5 g dose cohort was conducted first, and the dose was increased by 10 g between each cohort of children only if the preceding dose level was found to be well tolerated. The decision to progress to the next dose level was based on criteria established by the primary outcome variable. When the percentage of subjects with clinically relevant GI symptoms was significantly greater following consumption of the erythritol-sweetened beverage compared to placebo, the study was stopped. The size of the 5 g test group was 14 subjects and increased to 57 subjects for all other groups to improve the power of the study. The inclusion criteria established for the participating children are listed in Table 2, the calculated intake of erythritol by each group are provided in Table 3.

**Table 2:** Subject inclusion criteria for the paediatric trial on erythritol GI tolerability

| Number | Criteria |
|---|---|
| 1 | Healthy, toilet trained children, 4-6 years old |
| 2 | Body mass index ≥ 13kg.m$^{-2}$ |
| 3 | Accustomed to having breakfast |
| 4 | Having a regular stool frequency inferior or equal to two per day |
| 5 | Able to drink 250 ml within 15 minutes |
| 6 | Informed consent of both parents/guardians |
| 7 | Parents/guardians affiliated with French social security |

**Table 3:** Erythritol intake from non-carbonated fruit-flavoured drinks by each test group

| **Test group** | **Number of participants** | **Erythritol concentration per test drink (%w/v)** | **Erythritol dose per drinking occasion** | |
|---|---|---|---|---|
| | | | g/person | g/kg bw (mean) |
| 1 | 14 | 2 | 5 | 0.25 |
| 2 | 57 | 6 | 15 | 0.71 |
| 3 | 57 | 10 | 25 | 1.23 |

The study lasted 27 months. Each subject was seen in the clinic on 2 test dates with at least 5 days having elapsed between the 2 test days. Each test day required one-half day at the clinic. Following observation at the clinic, a parent (or legal guardian) recorded GI symptoms and stooling patterns in a diary during the 48 hours immediately following consumption of the test products. The statistical analyses included descriptive statistics (e.g., number of subjects, percentage, mean, standard deviation, median, minimum-maximum) and comparative analyses using one-tailed tests for paired data; risk of type I error was set to 5%.

The responses of the 128 participants to the three doses of erythritol (5, 15 and 25 g) were evaluated in comparison to the control.

There were no differences between the three test groups for gender (42-57% female), age (4.4 to 4.9 years old), weight (21 kg), height (113-114 cm) or BMI (16 kg/$m^2$). For the 5 g and 15 g erythritol test groups, there was no significant difference in the incidence of diarrhoea or significant GI symptoms between the erythritol-sweetened test beverages and the saccharose sweetened (control) product. At the 25 g dose, a greater incidence of diarrhoea and/or significant GI symptoms was observed following consumption of the erythritol-sweetened beverage (32%) versus the control (3.5%) (p= 0.0002). This result met the study stopping criteria, thus a higher 35 g dose of erythritol was not tested. The average number of stools during the study period was not different between erythritol and control for the 5 g and 15 g groups, while a small but statistically significant increase in daily stool frequency was noted in the 25 g dose group, 2.3 versus 1.9 stools per day for erythritol-sweetened beverage and control, respectively (p =0.0188). A similar observation was made for mean stool consistency measured by the Bristol Scale Score. The incidences of nausea, vomiting, borborygmi, excess flatus, and abdominal pain were not different between erythritol and the control; however, abdominal bloating was higher in the 25 g dose erythritol group compared to the control (7% versus 0%; p =0.046).

The petitioner concluded that the results of this study demonstrate that ingestion of 15 g of erythritol in a beverage without other food, is as well tolerated by 4-6 year old children as an isosweet control beverage sweetened with saccharose. Based on these data, the petitioner concluded that it is possible to support a NOAEL of 15 g, or 0.71 g/kg bw/day for laxation in young children aged 4-6 years old (Table 3). The Panel agrees with this conclusion.

## 6. Estimated intake of erythritol

### 6.1. Estimated acute intake from diet soft drinks

The intake of erythritol in Europe from its use in beverage products at a maximum concentration of 2.5% can be calculated using the National Diet and Nutrition Surveys (NDNS) of the United Kingdom. This database of food intakes by young children, school children (aged 4 to 18 years old), and adults, was previously used to describe the potential intake of erythritol from its proposed use in beverage products at maximum levels of 3.5%. These intake data were presented in a discussion paper prepared for the COT by its Secretariat (COT, 2003). The key concern expressed by the COT was about the intake by young children in one single drinking occasion, while no concern was expressed regarding the intake by older children and adults. Intakes (per drinking occasion) associated with the use of erythritol in beverages at the level proposed by the petitioner (2.5%) can be derived from the COT data simply by applying a 2.5 to 3.5 ratio (0.71) to the tabular results (Table 4).

**Table 4:** Estimated erythritol intakes per drinking occasion if used at 2.5% in diet soft drinks [a]

| Age category | Gram per person per drinking occasion | | Gram per kg body weight per drinking occasion | |
|---|---|---|---|---|
| | Mean | 97.5th percentile | Mean | 97.5th percentile |
| 1.5-4.5[b] years | 2.4 | 7.6 | 0.16 | 0.54 |
| 4-6[c] years | 6.4 | 11.6 | 0.31 | 0.59 |
| 7-10[c] years | 7.2 | 14.0 | 0.24 | 0.48 |
| 11-14[c] years | 8.6 | 17.1 | 0.19 | 0.41 |
| 15-18[c] years | 8.8 | 18.9 | 0.14 | 0.29 |
| 19-64[d] years | 8.2 | 14.8 | 0.11 | 0.21 |

[a] Derived from tabular data presented in COT (2003)
[b] Food consumption data from the UK NDNS: children aged 1.5 to 4.5 years
[c] Food consumption data from the UK NDNS: young people aged 4-18 years
[d] Food consumption data from the new adult NDNS

The intake of erythritol from its proposed use in beverages (2.5%), in particular diet concentrated soft drinks (cordials), diet ready-to-drink soft drinks and diet carbonated soft drinks, per drinking occasion, is estimated by the petitioner to range from a mean of 2.4 g/person in 1.5 to 4.5 year old children, to 8.8 g/person in teenagers (15 to 18 years old). Subjects most exposed to erythritol on a g/kg bw basis are 4 to 6-year-old children. At the 97.5th percentile beverage consumption level, the erythritol intake in children 4 to 6 years old is estimated to be 11.6 g/person. The petitioner concluded that this is well below the NOAEL for laxation in children 4 to 6 years old of 15 g/person per drinking occasion as established in the paediatric study discussed in the previous chapter.

## 6.2. Estimated daily intake from foods and beverages

### 6.2.1. COT estimation of erythritol intake from all foods and beverages

The COT also estimated the erythritol intake from all foods and beverages on a per day basis, based on the proposed use levels of erythritol as outlined in the SCF (2003) opinion (Table 5).

**Table 5:** Maximum level of erythritol in products from different food categories

| Food category | Maximum level of erythritol in product (% by weight) |
|---|---|
| Table top substitutes | 99.9 |
| Low-calorie beverages, including sport drinks | 3.5 |
| Sugar-free chewing gum | 60 |
| Reduced calorie and sugar-free chocolate | 50 |
| Candies, not sugar-free: soft (fudges) | 40 |
| Candies, not sugar-free: hard | 50 |
| Fondants and creams | 60 |
| Lozenges | 99 |
| Bakery (pastry) products (cookies biscuits, cakes pastries with cream filling/topping), not sugar-free | 7-60 |

The COT Secretariat assumed that all bakery products contain 60% erythritol, but actually the maximum use level in all bakery products is 7%, with the exception of fat-based bakery fillings where erythritol can be used up to 60%.

### 6.2.2. Estimated daily intake from all foods and beverages using Dutch food consumption databases

In the application of 14 July 1999 to the European Commission requesting approval for use of erythritol in foods and beverages, estimates of erythritol consumption were determined by the TNO Nutrition and Food Research Institute (TNO) using the Dutch National Food Consumption (DNFC) survey conducted in 1992 (Hulshof, 1997). The DNFC survey represents dietary intake of all individuals (6218 individuals aged 1 to 92 years) in survey households (2475 households) for a 2-day period, including food consumed at home and away from home. Day 1 and Day 2 dietary records were maintained on a household basis by the main housekeeper who provided the meals. Individual daily diaries were also kept to record food consumed away from home.

Prior to completion of the food diaries, a trained dietician instructed members of the household on the use of the food diaries. Following completion of the food diaries, the dietician reviewed the food diaries with the individuals to ensure completeness. Households were surveyed over the entire year of 1992 and on all days of the week. In addition to information on food consumption, the DNFC survey collected physiological and demographic data such as sex, age, self-reported height and body weight. This information allowed assessment of food consumption from different population groups. As described in the TNO report (Hulshof, 1997), erythritol consumption was calculated using a computing system developed by the TNO called Voedings Enquete Verwerkings Systeem (VEVES). All intake calculations were conducted for Day 1 and Day 2 data as well as for the average of the 2 days.

Although erythritol is intended to be used only in low-calorie or dietetic food products, in the DNFC survey database, the number of sugar-free products appropriate for the use of erythritol was small and more importantly, the number of users of these categories was small. In order to ensure that erythritol consumption estimates were not underestimated, regular (i.e., full sugar) products were used as surrogates. Using regular products as surrogates for dietetic products leads to overestimation of erythritol intake from this specific group since the number of dietetic products in this food category will be significantly less than the full calorie products. The data are summarised in Table 6.

**Table 6:** Estimated daily consumption of erythritol by users only using all sugar-free products[1] plus sugar-free surrogate products[2] (DNFC Survey) at their maximum use level (erythritol use level in diet soft drinks 3.5%)

| Population group | Gram per person per day | | | Gram per kg body weight per day | | |
|---|---|---|---|---|---|---|
| | Mean | 90th percentile | 95th percentile | Mean | 90th percentile | 95th percentile |
| Children 1 to 12 years old | 5.9 | 13.2 | 15.8 | 0.29 | 0.64 | 0.82 |
| Teenage boys 13 to 19 years old | 7.6 | 19.3 | ‡ | 0.14 | 0.34 | ‡ |
| Teenage girls 13 to 19 years old | 7.3 | 15.6 | ‡ | 0.13 | 0.28 | ‡ |
| Male adults 19 to 65 years old | 5.5 | 12.8 | 18.9 | 0.07 | 0.16 | 0.24 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Female adults 19 to 65 years old | 5.2 | 12.5 | 16.9 | 0.08 | 0.19 | 0.24 |
| Total population 1-92 years old | 5.6 | 13.0 | 17.8 | 0.12 | 0.32 | 0.48 |

[1] table-top substitutes, sugar-free chewing gum, sugar-free chocolate, dietetic cookies/wafers, low calorie beverages
[2] non sugar-free lozenges, chewy (soft) candy, cookies/biscuits/pastries with cream filling/topping, chocolate, hard candy and biscuits
‡ Value not reported because of small sample size

The highest mean consumption estimate for users only was found in the male teenage population aged 13 to 19 years (7.6 g/day) with a 90$^{th}$ percentile consumption of 19.3 g erythritol/day. On a body weight basis, the highest mean consumption estimate was found in children aged 1 to 12 years (i.e. 0.29 g/kg bw/day) with a 95$^{th}$ percentile consumption of 0.82 g/kg bw/day.

According to the petitioner, the erythritol intake estimates in Table 6 can be considered "worst case" and are likely to be an overestimation because of the following reasons:

- calculations are based on a use level in beverages of 3.5% whereas the petitioner currently is requesting a use level of maximum 2.5%
- intake from all foods and beverages is based on their maximum use levels which is unlikely to occur in reality
- calculations included a number of full sugar surrogate product categories which automatically results in an overestimation.

The Panel agrees with this conclusion of the petitioner.

## 7. Discussion

In its scientific opinion in 2003, the SCF expressed concerns that the laxative threshold for erythritol may be exceeded especially by young consumers and through ingestion of erythritol in beverages (SCF, 2003). The UK COT expressed similar concerns in 2004, concluding that it was not acceptable for erythritol to be used in beverages at a 3.5% use level because convincing evidence was not yet available to demonstrate digestive tolerance for acute bolus (single drinking occasion) exposures in young children, in particular children 4 to 6 years old (COT, 2004).

In order to resolve this issue, the petitioner conducted a double-blind, randomised, controlled GI tolerance study in 128 young children aged 4 to 6 years old, utilising a cross-over design with three doses of erythritol (5, 15, 25 g). The study lasted 27 months. The purpose of this study was to determine the maximum erythritol dose that does not cause laxation when consumed in a beverage within a maximum duration of 15 minutes.

The Panel noted that the results of the paediatric study demonstrate that ingestion of 15 g (i.e. 0.71 g/kg bw) of erythritol in a beverage consumed by children aged 4-6 years in a single drinking occasion within a maximum duration of 15 minutes indicates a NOAEL for laxation in these young children amounting to 0.71 g/kg bw/day.

The intake of erythritol from its proposed use in beverages (2.5%), in particular diet concentrated soft drinks (cordials), diet ready-to-drink soft drinks and diet carbonated soft drinks, per drinking occasion, is estimated to range from a mean of 2.4 g/person for 1.5 to 4.5 year old children, to 8.8 g/person for teenagers (15 to 18 years old). Subjects most exposed to erythritol on a g/kg body weight basis are 4 to 6-year-old children. At the 97.5$^{th}$ percentile beverage consumption level, the maximum erythritol intake in children 4 to 6 years old is estimated to be 11.6 g/person (0.59 g/kg bw/drinking occasion).

The margin of safety between the NOAEL of 0.71 g/kg bw/day and the estimated daily intake of erythritol resulting from an incorporation rate of 2.5% in beverages (i.e. 0.59 g/kg bw at the 97.5$^{th}$ percentile) is 1.24.

Given that:

- the NOAEL is based on a study with a population that consists of only a limited number of selected children in the low-dose group and limited statistical power,
- erythritol is also allowed for use in other food categories,
- there may be synergism with GI effects due to intake of other polyols,

the Panel concludes that this margin of safety is too low to ensure that children are adequately protected, taking into account the fact that erythritol is also used in other food categories.

## CONCLUSION

The Panel concludes based on the available data that there is a safety concern with respect to the GI tolerability, for the use of erythritol in beverages at a maximum use level of 2.5% for non-sweetening purposes.

## DOCUMENTATION PROVIDED TO EFSA

1. Application for use of erythritol in beverages at a level of maximum 2.5%. July 2009. Submitted by Cargill R & D Centre Europe.

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## GLOSSARY/ABBREVIATIONS

| | |
|---|---|
| ADI | Acceptable Daily Intake |
| ANS | Panel on Food Additives and Nutrient Sources added to Food |
| COT | Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment |
| DNFC | Dutch National Food Consumption |
| EC | European Commission |
| EFSA | European Food Safety Authority |
| EU | European Union |
| FSA | UK Food Standard Agency |
| GI | Gastrointestinal |
| JECFA | Joint FAO/WHO Expert Committee on Food Additives |
| MOS | Margin of safety |
| NDNS | National Diet and Nutrition Surveys |
| NOAEL | No-Observed-Adverse-Effect Level |
| SCF | Scientific Committee for Food |
| TNA | Temporary National Authorisation |
| TNO | Nutrition and Food Research Institute |
| VEVES | Voedings Enquete Verwerkings Systeem |