**TOX/2019/36**

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Discussion paper on potential risks from various sweeteners in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

### Introduction

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that will inform the Government's dietary recommendations for infants and young children. The SACN is examining the nutritional basis of the advice. The Committee on Toxicity in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the diet of infants, most of which has been completed, and young children. The reviews will identify new evidence that has emerged since the Government's recommendations were formulated and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years.

2. As part of the work, the safety of the most commonly used sweeteners in the United Kingdom will be assessed. These are: acesulfame K, aspartame, saccharin, sorbitol, sucralose, stevia and xylitol (NHS, 2018).

3. In the EU (EC 2008, EU 2011) sweeteners are referred to as food additive substances used to 'impart a sweet taste to foods or in table-top sweeteners'. Table-top sweeteners 'shall mean preparations of permitted sweeteners, which may contain other food additives and/or food ingredients, and which are intended for sale to the final consumer as a substitute for sugars'.

4. In order to be included in the list of EU approved food additives, and in addition to the general requirements of food additives, sweeteners must serve one or more of these purposes: i) 'replacing sugars for the production of energy-reduced food, non-cariogenic food or food with no added sugars' or ii) 'replacing sugars where this permits an increase in the shelf life of the food'.

5. Sweeteners can be of two categories: high-intensity sweeteners, which are substances with an intense sweet taste and with no energy value that are used to replace sugars in foods (EFSA,2011) and polyols, defined as 'alcohols containing more than two hydroxyl groups', which are low calorie sugar replacers, but which can also exert other technological functions in food and can be used for purposes other than sweetening.

6. Artificial sweeteners are considered safe to consume up to the Acceptable Daily Intake (ADI) in the general population with the exception of foods for infants and young children. In line with EU regulation, the use of sweeteners is prohibited in all foods for infants (under 12 months old) and young children (1- 3 years old). This includes foods specifically prepared for infants and young children (i.e., 'baby food') (The British Dietetic Association, 2016).

## References


- BDA(2016): Policy Statement- The Use of Artificial Sweeteners. Available online at: https://www.bda.uk.com/improvinghealth/healthprofessionals/policy_statements/sweetners
- NHS (2018): The truth about sweeteners. Available online at: https://www.nhs.uk/live-well/eat-well/are-sweeteners-safe/ Accessed Jan.2019
- BHF (2019): Are artificial sweeteners better than sugar?, Heart Matters Magazine, Available online at: https://www.bhf.org.uk/informationsupport/heart-matters-magazine/nutrition/ask-the-expert/artificial-sweeteners
- EC (2008): Regulation (EC) No 1333/2008 on food additives. Official Journal of the European Union L:345/16
- EU (2011): Regulation (EU) No 1129/2011 amending Annex II to Regulation (EC) No 1333/2008. Official Journal of the European Union L295/1

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Aspartame

### Background

1. Aspartame (E 951) is a dipeptide of L-phenylalanine methyl ester and L-aspartic acid bearing an amino group at the α-position from the carbon of the peptide bond (α-aspartame). Aspartame is a sweetener authorised as a food additive in the EU. In previous evaluations by the Joint FAO/WHO Expert Committee on Food Additives [JECFA] (1980) and the Scientific Committee on Food [SCF] (1985) an ADI of 40 mg/kg bw/day was set. This has been reconfirmed in a number of occasions (JECFA 1981; SCF 1989,2002). More recently, in 2013 the European Food Safety Authority (EFSA) have re-evaluated the safety of aspartame as a food additive and concluded that the ADI of 40 mg/kg bw/d was still appropriate, following the review of new available data. The COT commented on the EFSA evaluation during its public consultation and agreed with its analysis and conclusions.

2. In 1974, the US Food and Drug Administration (FDA) approved aspartame for restricted use in dry foods in the United States. This was followed by its full approval for use as an artificial sweetener in 1981. The FDA has set the ADI for aspartame at 50 mg/kg bw.

### Toxicity

3. Following oral ingestion, aspartame is hydrolysed in the gastrointestinal tract to yield aspartic acid, phenylalanine and methanol. These metabolites are then absorbed and enter normal endogenous metabolic pathways. In humans, only subjects heterozygous for phenylketonuria (PKU) showed a somewhat reduced capacity to metabolise the phenylalanine moiety of the aspartame molecule. (EFSA, 2013).

4. In its re-evaluation of aspartame, the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) also considered the safety of its gut derived metabolites, methanol, phenylalanine and aspartic acid and its degradation products 5-benzyl-3,6-dioxo-2-piperazine acetic acid (DKP) and β-aspartame, which also may be present in the sweetener as an impurity.

5. The Panel reviewed the extensive literature addressing all aspects of safety of aspartame, including addressing the results reported in the studies from Soffritti *et al.* (2006, 2007 and 2010) as well as from Chiozzotto *et al.* (2011). These studies reported a number of carcinomas in the test animals (both male and female rats and mice). However, on a number of occasions as well as in the 2013 the validity of the studies has been questioned by a

number of EFSA scientific panels including the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (ACF) and ANS Panels and the Committee on Carcinogenicity (COC). In particular, the high background incidence observed in a number of vital organs and tissues of the animals was highlighted. Additionally, the interpretation of some of the results was brought to question. For instance, the ANS Panel noted that "the increase in incidence of mammary carcinomas was not considered indicative of a carcinogenic potential of aspartame since the incidence of mammary tumours in female rats is rather high and varies considerably between carcinogenicity studies". Moreover, there has been evidence of high rates of infection in the European Ramazzini Foundation (ERF), where the studies were performed. The US National Toxicology Programme (NTP-EPA,2011) reviewed the original histopathological slides and reported a lack of formal quality assessment process and the reviewers did not confirm the malignant observations reported by ERF. In agreement with the EFSA concerns on the methodology, the Committee on Carcinogenicity in 2006 and in light of the study design limitations and the use of animals with high infection rates, they concluded that no valid conclusions could be derived by the 2006 Soffritti study. The ANS Panel considered that these would also apply to the subsequent studies by Soffritti *et al.* that were also carried out at the ERF.

6. Regarding the 2010 Soffritti *et al.* study in mice, a dose related increase in hepatocellular carcinomas for the two highest dose groups (2000 and 4000 mg/kg bw/d) and an increase in the incidence of alveolar/bronchiolar carcinomas in males of the high dose group. The ANS Panel in 2011 concluded that these tumours fell within their historical control ranges for spontaneous tumours and also noted that Swiss mice are known to known have high background incidents of these two particular tumour types. It was thus concluded that the results of this study do not provide evidence for carcinogenic effects of aspartame.

7. Overall, the Panel considered the previous No Adverse Effect Level (NOAEL) of 4000 mg/kg bw/d from a carcinogenicity study in rats was still applicable, however noted that developmental effects seen in rabbits at lower doses should not be ignored. Following a mode of action analysis, it was considered that the adverse effects were attributable to the metabolite phenylalanine. The Panel noted that adverse developmental effects were seen in children born to PKU mothers and seemed to be related to maternal phenylalanine levels. The current clinical guidelines recommending that plasma levels of phenylalanine should be maintained below an average value of 360 µM were also taken into consideration for the risk assessment.

8. The Panel modelled the plasma phenylalanine levels in humans following aspartame administration. The Panel made a number of decisions that resulted in an overestimation of the potential phenylalanine exposure from the diet, as a worst-case approach. Data following single bolus doses (4 to 200 mg/kg bw) were used to represent the total daily intake of aspartame, thus overestimating peak plasma concentration resulting from daily dietary intake. Moreover, the peak plasma levels following single bonus

administration were used as surrogate for the response at the administered dose, which would be higher than those resulting from intake of aspartame in a normal dietary pattern. This was due to the fact that phenylalanine has a short half-life (approximately 1.7 hours) therefore phenylalanine peaks in the blood are likely to be transient between meals and of lower magnitude. Lastly, comparisons were based on the mean plasma levels, which were assumed clinically safe for the critical endpoint (effects during pregnancy) in PKU patients as this was the most susceptible population identified. The Panel considered that the threshold utilised for comparisons to the modelling should be lowered to allow for simultaneous intake of the food additive with meals. In toddlers it was assumed that the mean daily exposure to phenylalanine from diet is taken up in five meals and in children in four meals, rendering the phenylalanine intake per kg bw and meal into 18.6-33.4 mg/kg bw/meal (toddlers), 18.1-34.2 mg/kg bw/meal (children). The highest concentration reported in children, which corresponds to 120 µM as calculated by the dose-response output, was subtracted from the clinical guideline of 360 µM resulting in a maximum safe plasma concentration of 240 µM of aspartame.

9. Based on the model, a plasma phenylalanine concentration of 240 µM would result from the administration of a bolus dose of 103 mg aspartame/kg bw (lower bound distributions: 88 mg aspartame/kg bw (CI 59-125) using a confidence level of 0.95) to a normal subject. For an individual heterozygous for PKU, the concentration would be reached by the administration of a bolus dose of 59 mg aspartame/kg bw (lower bound distributions: 50 mg aspartame/kg bw (CI 28-69) using a confidence level of 0.95. The Panel considered that given the conservative assumptions, realistic dietary intake of aspartame and the confidence intervals provided by the modelling, the peak plasma phenylalanine levels would not exceed the clinical target threshold when a normal individual consumed aspartame at levels below the current ADI of 40 mg/kg bw/day. It was concluded based on the above that the current ADI is protective of the general population and that there would not be a risk of adverse effects on pregnancy. As the modelling was based on a sensitive sub-population (PKU patients) no further uncertainty factors were applied for inter-individual variability (EFSA, 2013).

**Exposure**

10. No information on breastmilk data in the UK could be located. As sweeteners are prohibited for use in baby food, an exposure assessment of the intakes from baby formula(s) was not carried out.

11. Based on the data submitted to EFSA, information on toddler (from 12 up to and including 35 months of age) intakes were submitted by: Belgium, Bulgaria, Finland, Germany, Italy, Netherland and. Spain. No data were submitted by UK. For children (36 months up to and including 9 years of age) data was made available from: Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Spain and Sweden. Based on the available information, the estimated exposures based on Maximum Permitted Levels are presented in Table 1 and the estimated

exposures based on reported use levels or analytical data are presented in Table 2.

Table 1: Estimated exposures based on Maximum Permitted Levels in Toddlers and Children

| **Age group** | **Mean exposure (mg/kg bw/d)** | **95th percentile (mg/kg bw/d)** |
|---|---|---|
| Toddlers (12-≤35 months) | 3.2-16.0 | 11.8-37.0 |
| Children (3-≤9 years) | 2.3-13.0 | 7.1-33.0 |

*Exposures rounded to 2 SF

Table 2: Estimated exposures based on reported use levels or analytical data in Toddlers and Children

| **Age group** | **Mean exposure (mg/kg bw/d)** | **95th percentile (mg/kg bw/d)** |
|---|---|---|
| Toddlers (12-≤35 months) | 1.6-16.0 | 7.5-36.0 |
| Children (3-≤9 years) | 1.8-13.0 | 6.3-32.0 |

*Exposures rounded to 2 SF

12. Additionally, the dietary intake of four artificial sweeteners in Irish children (n=500) aged 1-4 has been assessed (Martyn *et al.,* 2016), using information from the National Pre-School Nutrition Survey (NPNS) (2010-11) in which food intakes were recorded using a 4-day weighted food diary along with anthropometric, health and lifestyle and demographic information. Food categories included cereals, desserts carbonated and non-carbonated flavoured drinks, confectionery.

13. Four exposure scenarios were presented:

- Scenario 1: Exposure using NPNS data and Maximum Permitted Levels (MPL) for sweeteners assuming that where legally permitted the sweetener is always present in food.

- Scenario 2: Exposure using NPNS data and the MPL and taking into account occurrence data from the Irish National Food Ingredient Database v4 (INFID v4).

- Scenario 3: Exposure using NPNS intake data and concentrations for sweetener in foods based on the information from the National Chemical Food Sampling program, conducted by official agencies in Ireland.

- Scenario 4: Exposure using NPNS intake data and concentrations for sweeteners in food from the INFID v4.

14. Exposures were also refined by the authors for sub-population groups based on consumption of only the foods that were identified as containing the sweetener of interest (sweeteners only).

15. The results are presented in the table below:

Table 3: Estimated exposures to aspartame in Irish Pre School Children:

| | **Total Population** | | **Sweetener only** | |
|---|---|---|---|---|
| | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) |
| Scenario 1 | 4.2 | 16.0 | 4.6 | 18.0 |
| Scenario 2 | 3.5 | 16.0 | 5.1 | 18.0 |
| Scenario 3 | 0.93 | 3.1 | 1.0 | 3.3 |
| Scenario 4 | 0.66 | 2.7 | 0.76 | 2.3 |

*Exposures rounded to 2 SF

**Conclusion**

16. Despite the lack of UK- specific data, the reported intakes in European populations are below the ADI of 40 mg/kg bw/d reconfirmed by EFSA in 2013. Based on the data presented in the review, EFSA determined that there was no safety concern at the current levels of exposure.

17. Information on exposure to children aged less than one year old is not available, however considering that sweeteners are not permitted in baby foods and the smaller intake of solid foods in that age group, it is unlikely that the ADI will be exceeded.

**Questions on which the views of the Committee are sought**

i) Do Members agree with the conclusions of the EFSA evaluation?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

**References:**


- Chiozzotto D, Soffritti M, Falcioni L, Tibaldi E, Manservisi F, Manservigi M, Bua L and Belpoggi F (2011): Results of life span carcinogenicity bioassay on Sprague-Dawley rats exposed to aspartame since foetal life, *European Journal of Oncology*, 16, 81-97.

- COC (2006): Statement on a Carcinogenicity Study of Aspartame by the European Ramazzini Foundation. Statement COC/06/S2 – December 2006.

- EFSA (2013): Scientific Opinion on the re-evaluation of aspartame (E 951) as a food additive, *EFSA Journal,* 11(12), 3496.

- JECFA (1980): Toxicological evaluation of certain food additives: aspartame, *WHO Food Additives Series No 15*, World Health Organization, Geneva.

- JECFA (1981): Toxicological evaluation of certain food additives: aspartame*, WHO Food Additives Series No 16*, World Health Organization, Geneva

- Martyn DM, Nugent AP, McNulty BA, O'Reily E, Tlustos C, Walton J, Flynn A, Gibney MJ (2016): Dietary intake of four artificial sweeteners by Irish Pre-School Children, *Food Additives & Contaminants: Part A*,333(4), 592-602.

- NTP-EPA (2011): Summary Report of the National Toxicology Program and Environmental Protection Agency-Sponsored Review of Pathology Materials from Selected Ramazzini Institute Rodent Cancer Bioassays, Available online: https://ntp.niehs.nih.gov/ntp/about_ntp/partnerships/international/summarypwg_report_ri_bioassays.pdf

- SCF (1985): Sweeteners, Reports of the Scientific Committee for Food (Sixteenth Series), EUR 10210 EN, Commission of the European Communities, Luxembourg.

- SCF (1989): Sweeteners, Reports of the Scientific Committee for Food (Twenty-first Series), EUR 11617 EN, Commission of the European Communities, Luxembourg.

- SCF (2002): Opinion of the Scientific Committee on Food: Update on the Safety of Aspartame (expressed on 4 December 2002). Available online: http://ec.europa.eu/food/fs/sc/scf/out155_en.pdf

- Soffritti M, Belpoggi F, Cevolani D, Guarino M, Padovani M and Maltoni C (2002): Results of long-term experimental studies on the carcinogenicity of methyl alcohol and ethyl alcohol in rats, *Annals of the New York Academy of Sciences*, 982, 46-69.

- Soffritti M, Belpoggi F, Degli Esposti D, Lambertini L, Tibaldi E and Rigano A (2006): First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats, *Environmental Health Perspectives*, 114, 379-385.

- Soffritti M, Belpoggi F, Esposti DD and Lambertini L (2005): Aspartame induces lymphomas and leukaemias in rats, *European Journal of Oncology*, 10,107–116.

- Soffritti M, Belpoggi F, Manservigi M, Tibaldi E, Lauriola M, Falcioni L and Bua L (2010): Aspartame administered in feed, beginning pre-natally through life span, induces cancers of the liver and lung in male Swiss mice, *American Journal of Industrial Medicine*, 53, 1197-1206.

- Soffritti M, Belpoggi F, Tibaldi E, Degli Esposti D and Lauriola M (2007): Life-span exposure to low doses of aspartame beginning during pre-natal life increases cancer effects in rats, *Environmental Health Perspectives*, 115, 1293-1297.

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Saccharin

### Background

1. Saccharin is the oldest sugar substitute. The substance and its sodium, potassium and calcium salts (E954) are authorized through the Directive 94/35/EC as a sweetener for use in a wide variety of foodstuffs such as non-alcoholic drinks, desserts and similar products, confectionery and food supplements, at the maximum usable dose from 80 to 3000 mg/kg food depending on the types of food.

2. The Acceptable Daily Intake of Saccharin was set at 5 mg/kg bw/d by 1993 by JECFA (WHO, 1993) and in 1995 by the SCF (SCF1995). The Scientific Committee for food maintained the temporary ADI of 0-2.5 mg/kg bw/d established in 1977 until 1995, where the safety of saccharin was re-in light of new data. The Committee established an ADI of 0-5 mg/kg bw/d, expressed as 0-3.8 mg.kg bw/d free acid.

3. Saccharin and its salts are currently on EFSA's call for data list and due to be re-evaluated.

### Toxicity

4. In experimental animals' saccharin is absorbed on a pH dependent rate. In more acidic pH conditions saccharin exists as the non- ionised form which is rapidly absorbed in comparison to the low form absorption rate. In humans it is likely that the rate of absorption will also depend on food intake, which affects the acidity of the stomach.

5. In humans and rat, saccharin is slowly absorbed in the intestines and rapidly excreted in the urine. Urinary excretion is considered a measure of gastrointestinal absorption, whereas faecal excretion is an indicator of unabsorbed saccharin (WHO, 1993).

6. Following a single oral dose to adult rats, saccharin was found to be distributed to most organs with the highest concentrations in the kidney and bladder, the organs responsible for elimination followed by the plasma. There is no evidence of bioaccumulation of saccharin in any tissue (WHO, 1993). Accumulation of saccharin in plasma and tissues when dietary administration to rats exceeded 5% of the diet was due to decreased renal clearance.

7. Based on information in a number of species including humans, rats, guinea-pigs, rabbits and monkeys, saccharin does not get metabolised.

Studies in humans and rats indicate that the majority of saccharin administered in the diet (80–85%) is slowly absorbed and rapidly excreted unchanged in the urine.

8. Acutely, saccharin is of low toxicity. Saccharin seems to be well tolerated in humans based on single and repeated exposure studies.

*9.* Saccharin was not found to be genotoxic *in vitro* or *in vivo.*

10. The ADI was based on a two-generation carcinogenicity study in male Charles River CD rats fed with sodium saccharin at 1%, 3%, 4%, 5%, 6.25% and 7.5% in the diet (Schoenig *et al*., 1985). Starting at 3%, the animals showed a marked disturbance in homeostasis, with a dose-related decrease in body weight gain despite increased food consumption. This was related to inhibitory effects of saccharin on carbohydrate and protein digestion. Bladder tumours induced by saccharin to be specific for the male rat and not equally relevant for female rats and mice, hamsters and monkeys, and not relevant for humans (WHO, 1993; SCF, 1995). The lowest dose level (1%- equivalent to 500 mg/kg bw/d) was set as the NOAEL based on the lack of relevant treatment related findings at this level. An Uncertainty Factor of 100 was applied to derive the ADI of 5 mg/kg bw/d.

11. In the International Agency for Research in Cancer (IARC) evaluation(1999) it was concluded that “sodium saccharin produces urothelial bladder tumours in rats by a non-DNA-reactive mechanism that involves the formation of a urinary calcium phosphate-containing precipitate, cytotoxicity and enhanced cell proliferation. This mechanism is not relevant to humans because of critical interspecies differences in urine composition.”

12. Saccharin and its salt were classed as Group 3 by the IARC (not classifiable as to their carcinogenicity to humans) and considered that there was inadequate evidence in humans for the carcinogenicity of saccharin salts used as sweeteners, sufficient evidence in experimental animals for the carcinogenicity of sodium saccharin and inadequate evidence in experimental animals for the carcinogenicity of saccharin (acid form) and calcium saccharin.

**Exposure**

13. No information for concentrations of saccharin in breastmilk were located for the UK. It is legally prohibited for baby foods to contain saccharin and therefore an exposure assessment for that food group was not carried out.

14. The exposure information from the dietary intake of four artificial sweeteners in Irish children (n=500) aged 1-4 has been assessed (Martyn *et al.,* 2016), using information from the National Pre-School Nutrition Survey (2010-11) in which food intakes were recorded using a 4-day weighted food

diary along with anthropometric, health and lifestyle and demographic information. Food categories included cereals, desserts carbonated and non-carbonated flavoured drinks, confectionery.

15. Four exposure scenarios were presented:

- Scenario 1: Exposure using NPNS data and MPL for sweeteners assuming that where legally permitted the sweetener is always present in food.
- Scenario 2: Exposure using NPNS data and the MPL and taking into account occurrence data from the INFID v4.
- Scenario 3: Exposure using NPNS intake data and concentrations for sweetener in foods based on the information from the National Chemical Food Sampling program.
- Scenario 4: Exposure using NPNS intake data and concentrations for sweeteners in food from the INFID v4.

16. Exposures were also refined by the authors for sub-population groups based on consumption of only the foods that were identified as containing the sweetener of interest (sweeteners only).

17. The results are presented in the table below:

Table 4: Estimated exposures to saccharin in Irish Pre School Children:

| | **Total Population** | | **Sweetener only** | |
|---|---|---|---|---|
| | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) |
| Scenario 1 | 0.65 | 2.4 | 0.71 | 2.5 |
| Scenario 2 | 0.33 | 1.8 | 0.51 | 2.0 |
| Scenario 3 | 0.28 | 1.0 | 0.31 | 1.0 |
| Scenario 4 | 0.18 | 0.71 | 0.20 | 0.76 |

*Exposures rounded to 2 SF

## Conclusion

18. Based on the available data on intake for children aged 1-4, the exposures are below the ADI. Due to the fact that it is legally prohibited to include sweeteners in baby food, combined with the generally lower consumptions of solid foods in younger infants, it is unlikely that the ADI would be exceeded in these populations.

**Questions on which the views of the Committee are sought**

i) Do Members agree with the conclusions presented in this document?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

**References:**


- IARC (1999): Some Chemicals that Cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances, Saccharin and its salts, *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans,*73. Available online at: https://monographs.iarc.fr/wp-content/uploads/2018/06/mono73-24.pdf

- Martyn DM, Nugent AP, McNulty BA, O'Reily E, Tlustos C, Walton J, Flynn A, Gibney MJ (2016): Dietary intake of four artificial sweeteners by Irish Pre-School Children, *Food Additives & Contaminants: Part A*,333(4), 592-602.

- SCF (1995): Saccharin and its sodium, potassium and calcium salts, Opinion expressed on 2 June 1995. Published by Commission of the European Communities. Brussels.

- WHO (1993): Evaluation of certain food additives and contaminants, Forty-first report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva, 9-18 February 1993. *WHO Technical Report Series*, no. 837, Geneva.

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Acesulfame K

### Background

1. Acesulfame K (AceK) is an EU approved sweetener that is approximately 200 times sweeter than sucrose. Due to its water solubility and heat resistance it is approved for use in a wide range of products such as baked good, candies and puddings.

2. The safety of AceK has been addressed multiple times by both JECFA (1983, 1991) and the SCF (1985, 1991). The most recent evaluation was carried out by the SCF in 2000, where the previously established ADI of 0-9 mg/kg bw/d was reaffirmed (SCF,2000).

3. AceK is currently on EFSA's call for data list and due to be re-evaluated.

### Toxicity

4. AceK was rapidly absorbed and excreted unchanged in urine in both animals and humans, indicating that it does not undergo metabolism.

5. Initially, the JECFA evaluated the safety of AceK in 1983. An ADI of 0-9mg/kg bw/d was allocated based on a two-year study in dogs. The SCF established the same ADI based on the same study in 1985. In the JECFA re-evaluation in 1991, the ADI was raised to 0-15 mg/kg bw/d. The basis of this was a two-year carcinogenicity study in rats that was considered more representative of lifetime exposure given the lifespan of rats versus that of dogs and the fact that ADME data showed that AceK does not get metabolised.

6. Following a submission for an extension of the ADI (SCF, 2000), the SCF re-evaluated the safety of AceK taking into account new scientific data. The Panel reaffirmed its conclusion that AceK is not mutagenic or genotoxic and endorsed previous specifications regarding impurities (specifically 5-chloro-acesulfame) for which toxicological data are limited.

7. Regarding the ADI the Panel considered the 2-year study in dogs and the 2-year study in rats, where for both the NOAEL was set at the highest dose tested (900 mg/kg bw/d and 1500 mg/kg bw/d respectively). Taking into account toxicokinetic data, where systemic exposure has been shown to be higher in dogs than in rats, it could be assumed that systemic exposure was higher in dogs than in rats. Furthermore, they noted that there was limited

evidence on the toxicokinetic differences between humans and dogs and concluded that the dog remained the most appropriate species for establishing the Health Based Guidance Value, thus reaffirming the ADI of 0-5 mg/kg bw/d.

8. In 2016 EFSA received a proposal for the extension of use of AceK in foods for special medical purposes in young children (1-3 years). The Panel "considered that the available toxicological assessments of acesulfame K by the SCF establishing an ADI would remain valid".

**Exposure**

9. In their 2016 evaluation, EFSA noted that although currently acesulfame K is not permitted in products intended solely for the age group of interest, the consumption of products intended for older consumers may occur, but exposures to acesulfame K from these sources could not be assessed. Furthermore, although some proposed exposure scenarios were presented these would not be applicable to the general population and are therefore not considered in this assessment. Data on occurrence of AceK in breastmilk could not be located.

10. The exposure information from the dietary intake of four artificial sweeteners in Irish children aged 1-4 has been assessed (Martyn *et al.,* 2016), using information from the National Pre-School Nutrition Survey (2010-11) in which food intakes were recorded using a 4-day weighted food diary along with anthropometric, health and lifestyle and demographic information. Food categories included cereals, desserts carbonated and non-carbonated flavoured drinks, confectionery.

11. Four exposure scenarios were presented:

- Scenario 1: Exposure using NPNS data and MPL for sweeteners assuming that where legally permitted the sweetener is always present in food.
- Scenario 2: Exposure using NPNS data and the MPL and taking into account occurrence data from the INFID v4.
- Scenario 3: Exposure using NPNS intake data and concentrations for sweetener in foods based on the information from the National Chemical Food Sampling program.
- Scenario 4: Exposure using NPNS intake data and concentrations for sweeteners in food from the INFID v4.

12. Exposures were also refined by the authors for sub-population groups based on consumption of only the foods that were identified as containing the sweetener of interest (sweeteners only).

13. The results are presented in Table 5:

Table 5: Estimated exposures to AceK in Irish Pre School Children:

| | **Total Population** | | **Sweetener only** | |
|---|---|---|---|---|
| | Mean Exposure (mg/kg bw/d) | 95th percentile (mg/kg bw/d) | Mean Exposure (mg/kg bw/d) | 95th percentile (mg/kg bw/d) |
| Scenario 1 | 2.6 | 9.7 | 2.8 | 11.0 |
| Scenario 2 | 1.4 | 7.5 | 2.2 | 8.6 |
| Scenario 3 | 0.74 | 2.6 | 0.81 | 2.7 |
| Scenario 4 | 0.51 | 2.0 | 0.58 | 2.1 |

*Exposures rounded to 2 SF

**Conclusion**

There is limited amount of information regarding the exposure to AceK in these age groups. However, in the exposure scenarios available AceK intakes remain below the ADI even when assuming the presence of the sweetener at the Maximum Permitted Level, apart in Scenario 1 which, however assumes presence of AceK in foods at the MPL. When exposures were refined based on analytical data, the intakes were over 3 times below the ADI for children aged between 1-4 years old. Although no information could be located for infant intakes, consumption of solid foods at those ages would be lower and therefore the ADI unlikely to be exceeded.

**Questions on which the views of the Committee are sought**

i) Do Members agree with the conclusions presented in this document?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

## References


- EFSA (“016): Safety of the proposed extension of acesulfame K (E 950) in foods for special medical purposes in young children, *EFSA Journal,* 14(4),4337.

- Martyn DM, Nugent AP, McNulty BA, O’Reily E, Tlustos C, Walton J, Flynn A, Gibney MJ (2016): Dietary intake of four artificial sweeteners by Irish Pre-School Children, *Food Additives & Contaminants: Part A*,333(4), 592-602.

- SCF (1985): Sweeteners, Reports of the Scientific Committee for Food (Sixteenth Series), EUR 10210 EN, Commission of the European Communities, Luxembourg.

- SCF (1989): Sweeteners, Reports of the Scientific Committee for Food (Twenty-first Series), EUR 11617 EN, Commission of the European Communities, Luxembourg.

- SCF (2000): Re-evaluation of acesulfame K with reference to the previous SCF opinion of 1991, Opinion expressed on 9 March 2000. Published by Commission of the European Communities. Brussels.

- WHO (1983): Evaluation of certain food additives,*WHO Technical Report Series*,18, 12-14, Geneva.

- WHO (1991): Evaluation of certain food additives, *WHO Technical Report Series*, 28, 183-218, Geneva.

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Sucralose

### Background

1. Sucralose is an artificial sweetener, about 600 times sweeter than sugar. It is approved for use in the EU (E955) and due to its heat stability can be found in a wide range of products including baked goods, pre-sweetened breakfast cereals, beverages, chewing gums and desserts.

2. Both the JECFA and the SCF have evaluated the safety of sucralose, and an ADI of 0-15 mg/kg bw/d was allocated in both instances.

3. Sucralose is currently on EFSA's call for data list and due to be re-evaluated.

### Toxicity

4. In humans orally, administered sucralose is absorbed at levels ranging from 8-22%. It is rapidly excreted unchanged in urine. Following administration of single oral doses, the terminal elimination half-life was around 5, 25, 39 and 79 hours for rat, man, rabbit and dog respectively.

5. Following their first evaluation of sucralose, JECFA (1989) established a temporary ADI of 0-3.5 mg/kg bw/d based on a NOAEL of 750 mg/kg bw/d from a 1-year dog study and an uncertainty factor of 200. Further data on human metabolism, chronic toxicity and information on developmental effects as well as considerations of safety for diabetic populations were requested at the time. In 1991 and following the evaluation of newly submitted data an ADI of 0-15 mg/kg bw/d was set, based on a No Effect Level (NOEL) (1500 mg/kg bw/d) from a 2-year study in rats that included exposure *in utero* and the application of an uncertainty factor of 100. The reduction in body weight gain in all treated groups was considered secondary to the reduced food consumption due to the impalpability of high sucralose concentrations in the diet. The Committee also recommended additional studies on immunotoxicity to assess the significance of weight changes seen in the spleen and thymus and investigate changes in lymphocyte counts to address potential causality to exposure to sucralose. These were based on observations in a study by Cummins *et al. (1983)* where rats were exposed to sucralose in the diet for either 4 or 8 weeks. These recommendations were in line with the conclusions of the SCF evaluation of 1989. Additionally, the SCF highlighted the weak mutagenic activity of 1,6-dichloro-1,6-dideoxyfructose (1,6-DCF), a

hydrolysis product of sucralose. This was considered of potential relevance as 1,6-DCF could be formed in the acidic pH of soft drinks. They were however satisfied that the sweetener as such did not possess genotoxic or carcinogenic potential and had not shown serious target-directed organ toxicity.

6. In 2000, the SCF re-evaluated the safety of sucralose. Addressing the concerns for immunotoxicity, the Committee established a NOEL of 3000 mg/kg bw/d for any effects on lymphoid organs and the immune system that might occur, whether caused directly by sucralose, or indirectly via stress and/or dietary factors. New studies on the mutagenicity of 1,6-DCF *in vitro* and *in vivo* indicated no cause of concern. Addressing the NOAEL of 350 mg/kg bw/d for maternal gastrointestinal effects in rabbits, the Committee concluded that these were attributable to the sensitivity of the species to high concentrations of poorly absorbed substances (sucralose absorption in rabbit was shown to be about 20%) and they were unlikely to occur in other species, including humans.

7. The Committee considered the body weight reduction seen even at low doses in rats to be the main effect for establishing an ADI. They determined that in feeding studies the reduction in body weight gain was not dose related and was attributable to the impalatability of sucralose containing diets. Based on a NOAEL of 1500 mg/kg bw/d from dietary and gavage studies for this endpoint and the application of an uncertainty factor of 100, an ADI of 0-15 mg/kg bw/d was set.

**Exposure**

8. No UK information on exposure to sucralose for ages 0-1 years, including occurrence in breastmilk, could be located.

9. The exposure information from the dietary intake of four artificial sweeteners in Irish children aged 1-4 has been assessed (Martyn *et al.,* 2016), using information from the National Pre-School Nutrition Survey (2010-11) in which food intakes were recorded using a 4-day weighted food diary along with anthropometric, health and lifestyle and demographic information. Food categories included cereals, desserts carbonated and non-carbonated flavoured drinks, confectionery.

10. Four exposure scenarios were presented:

- Scenario 1: Exposure using NPNS data and MPL for sweeteners assuming that where legally permitted the sweetener is always present in food.

- Scenario 2: Exposure using NPNS data and the MPL and taking into account occurrence data from the INFID v4.

- Scenario 3: Exposure using NPNS intake data and concentrations for sweetener in foods based on the information from the National Chemical Food Sampling program.

- Scenario 4: Exposure using NPNS intake data and concentrations for sweeteners in food from the INFID v4.

11. Exposures were also refined by the authors for sub-population groups based on consumption of only the foods that were identified as containing the sweetener of interest (sweeteners only).

12. The results are presented below:

Table 6: Estimated exposures to sucralose in Irish Pre School Children:

| | **Total Population** | | **Sweetener only** | |
|---|---|---|---|---|
| | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) |
| Scenario 1 | 2.3 | 8.9 | 2.5 | 9.1 |
| Scenario 2 | 0.6 | 3.1 | 1.0 | 4.6 |
| Scenario 3 | 0.8 | 2.9 | 0.91 | 2.9 |
| Scenario 4 | 0.6 | 1.9 | 0.65 | 2.0 |

**Conclusion**

13. There is limited amount of information on exposure to sucralose for children aged 0-5 years. However, in the exposure scenarios available sucralose intakes remain below the ADI both when assuming the presence of the sweetener at the Maximum Permitted Level and following refinement based on analytical data. Although no information could be located for infant intakes, consumption of solid foods at those ages would be lower and therefore the ADI unlikely to be exceeded.

***Questions on which the views of the Committee are sought***

i) Do Members agree with the conclusions presented in this document?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

## References


- Cummins HA, Yallup V, Lee P, Rhenius ST and Whitney J (1983): 1,6-dichloro-1,6- dideoxy-ß-D-fructofuranosyl-4-chloro-4-deoxy-α-D-galactopyranoside (TGS): Eight-week dietary toxicity study in rats. Life Science Research Limited, UK. Report No 11 82/MSPO21/392. Unpublished report submitted by Tate & Lyle Speciality Sweeteners, UK

- JECFA (1989): Toxicological evaluation of certain food additives and contaminants, *WHO Food Additive Series*, No 24, Cambridge University Press, Cambridge, UK.

- JECFA (1991): Toxicological evaluation of certain food additives and contaminants, *WHO Food Additive Series*, No 28. WHO, Geneva.

- SCF (1989): Report of the Scientific Committee on Food on Sweeteners, Reports of the Scientific Committee for Food (Twenty-first Series),19-37, CEC, Luxembourg.

- SCF (2000): Opinion on the Scientific Committee on Food on Sucralose, SCF/CS/ADDS/EDUL/190 Final.

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Steviol glycosides (stevia)

### Background

1. Stevia is a relatively new sugar alternative that comprises of mixtures of steviol glycosides extracted from the leaves of the stevia plant and is about 300 times sweeter than sugar. It has been assessed both by the JECFA and EFSA's ANS Panel and has been allocated an ADI of 4mg/kg bw/d. The initial risk assessments for steviol glycosides were for mixtures of specific compositions based on the information provided by applicants, however in later opinions this has been expanded to some other compositions which are reflected in specifications on the identity and purity of steviol glycosides for use in food.

2. In Europe, steviol glycosides are permitted for use as a sweetener in food (E 960).

### Toxicology

3. Steviol glycosides are poorly absorbed following oral exposure, but hydrolysis occurs by the gut microflora to steviol, which is readily absorbed. The rest is excreted in the faeces. The absorbed fraction undergoes conjugation with glucuronic acid in the liver, resulting to the formation of steviol glucuronide.in humans steviol glucuronide is excreted in urine (EFSA, 2010).

4. In humans, following single exposure to steviol glycosides, blood pressure and glucose homeostasis were not affected. This was also reported for repeated exposures (Maki *et al*., 2008) to doses up to 1000 mg rebaudioside A/day (approximately 5.5 mg steviol equivalent/kg bw/d for a 60 kg individual).

5. JECFA have evaluated the safety of steviol glycosides multiple times, most lately in 2016. Initially a temporary ADI of 0-2 mg/kg bw/d was established based on a NOEL of 2.5% in the diet, equal to 383mg/kg bw/d expressed as steviol in a 2-year study in rats and an application of an uncertainty factor of 200. This was due to the need for more information on the pharmacological effects of steviol glycosides in humans. In 2008 the ADI of 0-4 mg/kg bw/d expressed as steviol was established and it was confirmed in 2016. New studies considered during the 2008 evaluation showed no adverse effects of steviol glycosides when taken at doses of about 4 mg/kg bw per day, expressed as steviol, for up to 16 weeks by individuals with type 2

diabetes mellitus and individuals with normal or low-normal blood pressure for 4 weeks. The additional uncertainty factor of 2 was therefore removed.

6. In their evaluation in 2010, the EFSA considered steviol glycosides from 3 petitioners comprising not less than 95% stevioside and/or rebaudioside A. As in rats and humans these two components exhibit similar toxicokinetic profiles, the Panel considered the toxicological information on either chemical to be suitable for the evaluation of steviol glycosides in general.

7. The Panel concluded that overall, stevioside and rebaudioside A did not show genotoxic potential *in vitro* or *in vivo.* A Comet assay by Nunes *et al*. (2007) reported DNA damage following exposure to stevioside in drinking water. The Panel highlighted the methodological limitations of this study such as the use of only one small dose group (n=5), the lack of measurement of the quantities of water consumed and the lack of image analysis when reporting the results. The Panel considered this study of little biological relevance and concluded it did not provide substantive evidence to support a genotoxic potential for stevioside, especially considering the methodological limitations and the fact that similar findings were not observed in other studies. Regarding carcinogenicity, based on the available data there was no indication for carcinogenic potential for steviol glycosides. the NOAEL was based on the only 2-year study in F344 rats in which the test material complied with JECFA specifications (Toyoda *et al*., 1997).The NOAEL for this study was 2.5% (967 and 1120 mg stevioside/kg bw/day in males and females respectively, equivalent to 388mg/kg bw/d of steviol glycosides) based on a lower survival rate at the highest dose (5%) compared to controls, reduced absolute kidney weights, absolute statistically significantly decreased left ovary weights, and relative brain weights were statistically significantly increased in the 5% group females compared to controls. No statistically significant neoplastic changes were reported, and the Panel noted that the tumours reported were typical of the species.

8. Developmental and teratogenicity studies were also evaluated, with no effects being reported on these endpoints.

**Exposure**

9. No information for exposure via breastmilk was located.

10. Dietary exposures for children were calculated in two tiers:

- Scenario 1: using theoretical food consumption data (25% of all solid foods and beverages containing the sweetener) at the proposed MPLs and assuming that a typical 3-year old child, weighing 15 kg, consumes daily 1.5 L of beverages and 94 g of solid foods, containing the steviol glycosides).

- Scenario 2: Exposure was also calculated using consumption data of relevant food categories from Member States whilst assuming presence of steviol glycosides in these food groups at the MPL.

11. Exposure estimates for the second scenario were based on consumption data submitted from Belgium, France, the Netherlands, Spain, Czech Republic, Italy, Finland, Germany, Greece, Sweden (ages 1-10) and Cyprus (ages12-14). The exposure estimates included data submitted by UK for 1.5-4.5-year-old children from an older National Dietary and Nutrition Survey (NDNS).

12. Exposure data as reported in the 2010 evaluation for children aged 1-14 years old are presented below:

Table 7: Steviol glycoside exposures to children aged 1-14 years

| | **Exposure** | |
|---|---|---|
| | Mean Exposure (mg/kg bw/d) | 95$^{th}$ percentile (mg/kg bw/d) |
| Scenario 1 | n/a | 37.0[a] |
| Scenario 2 | 0.7-7.2 | 3.7-17.0 |

[a] Maximum exposure calculated
*Exposures rounded to 2 SF

13. In 2011 these were corrected to reflect the revised levels of used proposed by applicants. For European children (aged 1-14) exposure ranged from 1.7 to 16.3 mg/kg bw/day (EFSA, 2011).

**Conclusions**

14. The exposures calculated by EFSA in 2010 and 2011 were based on conservative estimates for inclusion of the steviol glycosides at the MPL, due to the lack of analytical data for actual inclusion levels in food. Based on the revised calculations of 2011, children who are high consumers of foods containing steviol glycosides would be exceeding the ADI by up to 4 times. Prolonged exposures above the ADI are undesirable, however considering that it is unrealistic that steviols would be present at the MPL in all products, across all food categories, it is unlikely that actual exposures are at the levels as calculated based on the available information.

**Questions on which the views of the Committee are sought**

i) Do the Members agree that the exposures presented are conservative and what are their thoughts on the possible implications of this exceedance?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

## References


- EFSA (2010): Scientific Opinion on the safety of steviol glycosides for the proposed uses as a food additive, EFSA Panel on Food Additives and Nutrient Sources added to Food, *EFSA Journal,* 8 (4),1537.

- EFSA (2011): Revised exposure assessment for steviol glycosides for the proposed uses as a food additive, EFSA Panel on Food Additives and Nutrient Sources added to Food, *EFSA Journal, 9(1):1972*

- JECFA (2008): Compendium of Food Additive Specifications. Monograph 5. Steviol glycosides. Available at: http://www.fao.org/ag/agn/jecfa-additives/details.html?id=898

- JECFA (2016): Evaluation of certain food additives, Eighty-second report of the Joint FAO/WHO Expert Committee on Food Additives, *WHO Technical Report Series no.1000.* Available at: https://apps.who.int/iris/bitstream/handle/10665/250277/9789241210003-eng.pdf?sequence=1#page=66%22%3E

- Maki KC, Curry LL, Carakostas M, Tarka S, Reeves MS, Farmer MV, McKenney JM, Toth PD, Schwartz SL, Lubin BC, Dicklin MR, Boileau A and Bisognano JD (2008): The hemodynamic effects of rebaudioside A in healthy adults with normal and low-normal blood pressure, *Food and Chemical Toxicology* 46, S40-S465.

- Nunes APM, Ferreira-Machado SC, Nunes RM, Dantas FJS, De Mattos JCP, Caldeira-de-Araújo A (2007): Analysis of genotoxic potentiality of stevioside by comet assay, Food and Chemical Toxicology 45, 662-666.

- Toyoda K, Matsui H, Shoda T, Uneyama C, Takada K, Takahashi M (1997): Assessment of the carcinogenicity of stevioside in *F344 rats, Food and Chemical Toxicology*,35, 597-603.

# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## Sorbitol and Xylitol

### Background

1. Sorbitol and xylitol are polyols, referred to as bulk sweeteners. Both sorbitol and xylitol naturally occur in some fruits and vegetables and xylitol is also formed as part of the pentose phosphate shunt during carbohydrate metabolism in humans. (Mortensen, 2006)

2. They are currently on EFSA's call for data list and will be re-evaluated.

3. Polyols have been subject to review by both the SCF (1985) and JECFA (1983).

### Toxicity

4. Both sorbitol and xylitol have been allocated an ADI "not specified" following review of the available safety information in both animals and humans. Both Committees acknowledged that excessive consumption of polyols could produce a laxative effect and recommended that the consumption of polyols from all sources should be limited to levels below those shown to induce diarrhoea.

*5.* Their laxative effect is attributed to a disturbance in osmosis across the intestinal wall due to the poor digestibility of polyols and their metabolites. Tolerability in humans varies greatly and there are also indications that younger children are more susceptible to the laxative effects than adults. At the time of the evaluation, it was concluded that consumption of up to 20 g/polyols/day would be unlikely to cause any undesirable symptoms (SCF, 1985). They noted that for both xylitol and sorbitol intake of doses ≥ 50g/day induced diarrhoea in humans. In children doses below 30g/day are unlikely to cause gastrointestinal discomfort (Rapaille *et al., 2003).*

### Exposure

6. Apart from their natural presence in the diet and their use as sweeteners, polyols are being used in dental products as they have been shown to promote general dental health by preventing tooth decay and decreasing tooth demineralisation (EFSA, 2011). Information on aggregate polyol intakes from all sources could not be located, neither on occurrence in breastmilk.

7. A study reporting potential intake of total polyols in children based on the UK National Dietary and Nutrition Survey data (2012) was identified. The exposures were based on reported use levels of polyols in the relevant food

categories and it was felt that it would be more relevant to express intakes on a per meal occasion basis in relation to the development of gastrointestinal discomfort. (Tennant, 2014)

8. The results are tabulated below:

Table 8: Total Polyols Intake per meal

| **Age group** | **Mean Intake (g/meal)** | **95$^{th}$ Percentile (g/meal)** |
|---|---|---|
| 1-2 years | 1.3 | 3.6 |
| 3-9 years | 1.6 | 4.7 |

*Exposures rounded to 2 SF

9. Total daily polyol intakes (both adults and children) were 3.5g/day (mean) and 10.4g/day (95$^{th}$ percentile).

**Conclusion**

10. Based on the available information the main safety concern for polyols is gastrointestinal discomfort due to their laxative properties. It is unlikely that this will occur based on a regular diet, and in cases of excess the nature of these effects cause discomfort however they are transient and not severely detrimental to human health.

**Questions on which the views of the Committee are sought**

i) Do Members agree with the conclusions presented in this document?

ii) Do the Members have any other comments?

iii) Do the Members agree for a brief summary of the safety of aspartame in the diet of infants and young children to be included in the overarching statement?

**Secretariat**
**June 2019**

## References


- Tennant D (2014): Potential intakes of total polyols based on UK usage survey data, *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*, 31(4): 574–586.

- EFSA (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*, 9(4):2076

- Rapaille A, Goosens J, Heume M (2003): Sugar Alcohols, Encyclopedia of Food Sciences and Nutrition (Second Edition), 5665-5671.

- SCF (1985): Sweeteners, Reports of the Scientific Committee for Food (Sixteenth Series), EUR 10210 EN, Commission of the European Communities, Luxembourg.

- WHO (1983): Evaluation of certain food additives and contaminants, *WHO Technical Report Series* 696, Twenty Seventh Report of the Joint FAO/WHO Expert Committee on Food Additives, Geneva.

- Mortensen A (2006): Sweeteners permitted in the European Union: Safety aspects, *Scandinavian Journal of Food and Nutrition,* 50(3), 104-116

## Abbreviations

| | | |
|---|---|---|
| 1,6-DCF | - | 1,6-dichloro-1,6-dideoxyfructose |
| AceK | - | Acesulfame K |
| ACF | - | Scientific Panel on Food Additives, Processing Aids and Materials in Contact with Food |
| ADI | - | Acceptable Daily Intake |
| ANS | - | EFSA Panel on Food Additives and Nutrient Sources added to Food |
| COC | - | Committee on Carcinogenicity |
| COT | - | The Committee on Toxicity in Food, Consumer Products and the Environment |
| DKP | - | 5-benzyl-3,6-dioxo-2-piperazine acetic acid |
| ERF | - | European Ramazzini Foundation |
| FDA | - | US Food and Drug Administration |
| IARC | - | International Agency for Research in Cancer |
| INFID v4 | - | Irish National Food Ingredient Database v4 |
| JECFA | - | Joint FAO/WHO Expert Committee on Food Additives |
| mg/kg bw | - | Milligram per kilogram bodyweight |
| NOAEL | - | No Adverse Effect Level |
| NOEL | - | No Effect Level |
| NPNS | - | National Pre-School Nutrition Survey |
| PKU | - | phenylketonuria |
| SACN | - | Scientific Advisory Committee on Nutrition |
| µM | - | Micromolar |