Revised protocol for assessing exposure to sweeteners as part of their safety assessment under the food additives re-evaluation programme

EFSA Panel on Food Additives and Flavourings (FAF)

**Table of contents**

[1. Introduction and scope of the protocol 4](#_Toc181606776)

[2. Background and rationale of the mandate 4](#_Toc181606777)

[3. Terms of reference as provided by European Commission 4](#_Toc181606778)

[4. Interpretation of the Terms of Reference 4](#_Toc181606779)

[5. Data and Methodologies 5](#_Toc181606780)

[5.1. Data 5](#_Toc181606781)

[5.1.1. Food additive occurrence data availability 5](#_Toc181606782)

[5.1.1.1. Information on use levels submitted 6](#_Toc181606783)

[5.1.1.2. Information on analytical data submitted 6](#_Toc181606784)

[5.1.2. Food consumption database 7](#_Toc181606785)

[5.1.3. Food labelling data 8](#_Toc181606786)

[5.2. Methodologies 8](#_Toc181606787)

[5.2.1. Food classification systems 8](#_Toc181606788)

[5.2.2. Food categories used for the assessment of exposure 9](#_Toc181606789)

[5.2.3. Chronic exposure assessment of sweeteners under re-evaluation 11](#_Toc181606790)

[5.2.3.1. Regulatory maximum level exposure assessment scenario 12](#_Toc181606791)

[5.2.3.2. Refined exposure assessment scenario 12](#_Toc181606792)

[5.2.3.3. Other exposure assessment scenarios 14](#_Toc181606793)

[5.2.4. Acute exposure assessment of sweeteners under re-evaluation 14](#_Toc181606794)

[5.2.5. Uncertainty analysis 15](#_Toc181606795)

[5.3. Comparison with human urinary biomonitoring studies 16](#_Toc181606796)

[References 16](#_Toc181606797)

[Abbreviations 18](#_Toc181606798)

[Appendix A – Link between the FoodEx2 classification system and the food sub-categories used in Mintel GNPD 19](#_Toc181606799)

[Appendix B – Percentage of products within the food sub-categories used in Mintel GNPD labelled to contain at least one sweetener 19](#_Toc181606800)

[Appendix C – Food consumption statistics (consumers only) per country and age class (in g/day) 19](#_Toc181606801)

[Appendix D – Percentage of eating occasions and in quantity for which at least one relevant facet was reported 19](#_Toc181606802)

Please note that the blue font text corresponds to text revised compared with the published EFSA draft protocol for assessing exposure to sweeteners as part of their safety assessment under the food additives re-evaluation programme (EFSA, 2020).

Editorial changes, rewording and updated figures/link are not traced in blue.

**Annex to**:

EFSA (European Food Safety Authority), 2020. Technical report. Outcome of the public consultation on a draft protocol for assessing exposure to sweeteners as part of their safety assessment under the food additives re-evaluation programme. EFSA supporting publication 2020: EN-11913. 52 pp. doi:10.2903/sp.efsa.2020. EN-1913

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Amendments to the protocol

The original draft protocol was approved by the FAF Panel on 23 July 2020 and published as an EFSA supporting publication on 11 August 2020.

During the revision of the current protocol, the following amendments and further elaborations were added:

* **Section 4:** a description of the two types of sweeteners considered in the sweeteners re-evaluation programme (intense sweeteners and polyols).
* **Section 5.2.3:** a clarification on the exposure approach developed for sweeteners.
* **Section 5.2.3.2:** a clarification on how facets are considered in the different exposure scenarios, including a description of an additional refined exposure scenario.
* **Section 5.2.4:** description of the acute exposure assessment method.

These updates have already been applied in previously published opinions on the sweeteners re-evaluation programme.

1. Introduction and scope of the protocol

This document outlines the protocol for the exposure assessment of sweeteners[[1]](#footnote-2) for their safety re-evaluation in the context of Regulation (EC) No 257/2010[[2]](#footnote-3) by the European Food Safety Authority (EFSA) Panel on Food Additives and Flavourings (FAF Panel). It is supported by the FAF Working Group on the re-evaluation of sweeteners. This draft protocol has been developed with the aim of defining as much as possible the strategy applied for cleaning and selecting data, appraising the relevant evidence, and analysing and integrating the evidence in order to perform exposure assessments that will be used for the safety assessment of each sweetener.

This protocol is a current best practices document and may be amended as the assessments proceed, and such amendments will be clearly documented and justified.

1. Background and rationale of the mandate

Regulation (EC) No 1333/2008[[3]](#footnote-4) of the European Parliament and of the Council on food additives requires that food additives are subject to a safety evaluation by EFSA before they are permitted for use in the European Union. In addition, it is foreseen that food additives must be kept under continuous observation and must be re-evaluated by EFSA.

For this purpose, a programme for the re-evaluation of food additives that were already permitted in the European Union before 20 January 2009 has been set up under the Regulation (EU) No 257/20102. This Regulation also foresees that food additives are re-evaluated whenever necessary in light of changing conditions of use and new scientific information. For efficiency and practical purposes, the re-evaluation should, as far as possible, be conducted for groups of food additives according to the main functional class to which they belong.

1. Terms of reference as provided by European Commission

The Commission asks EFSA to re-evaluate the safety of food additives already permitted in the European Union before 2009 and to issue scientific opinions on these additives, taking especially into account the priorities, procedures and deadlines that are enshrined in the Regulation (EU) No 257/20102 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with the Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives.

1. Interpretation of the Terms of Reference

Under the current mandate which covers the re-evaluation of all food additives under Commission Regulation (EU) No 257/2010, this exposure protocol will be applied for the re-evaluation of sweeteners listed in Table 1.

Scientific evaluation will be conducted for individual sweeteners. Should evidence emerge that two or more substances lead to the same adverse effects, in particular through the same Mode of Action (MoA), a group risk assessment will be considered.

It is outside the scope of the scientific re-evaluations of the sweeteners to address their possible beneficial health effects.

This protocol deals with the exposure assessment step of the safety assessment. Hazard identification and hazard characterisation will be assessed following a separate protocol. The safety assessment will be performed based on the outcome of hazard characterisation and exposure assessment.

1. List of food additives, classified as sweeteners, to be re-evaluated under Regulation (EC) No 257/2010

| E Number | Food additive(s) |  | Substance | |
| --- | --- | --- | --- | --- |
| Polyols | | | |
| E 420 | Sorbitols | E 420 (i)  E 420(ii) | Sorbitol  Sorbitol syrup | |
| E 421 | Mannitols | E 421(i)  E 421(ii) | Mannitol by hydrogenation  Mannitol manufactured by fermentation | |
| E 953 | Isomalt |  |  |
| E 965 | Maltitols | E 965(i)  E 965(ii) | Maltitol  Maltitol syrup |
| E 966 | Lactitol |  |  |
| E 967 | Xylitol |  |  |
| E 968 | Erythritol |  |  |
| Intense sweeteners | | | |
| E 950 | Acesulfame K |  |  | |
| E 951(a) | Aspartame(a) |  |  | |
| E 952 | Cyclamates | E 952(i)  E 952(ii)  E 952(iii) | Cyclamic acid  Sodium cyclamate  Calcium cyclamate | |
| E 954 | Saccharin and its Na, K and Ca salts | E 954(i)  E 954(ii)  E 954(iii)  E 954(iv) | Saccharin  Sodium saccharin  Calcium saccharin  Potassium saccharin | |
| E 955 | Sucralose |  |  | |
| E 957 | Thaumatin |  |  | |
| E 959 | Neohesperidine dihydrochalcone |  |  | |
| E 961 | Neotame |  |  | |
| E 962 | Salt of aspartame-acesulfame |  |  | |

1. In May 2011, EFSA was asked by the European Commission to bring forward the full re-evaluation of the safety of aspartame (E 951). Re-evaluation already completed by EFSA in 2013 (EFSA ANS Panel, 2013; <https://www.efsa.europa.eu/it/efsajournal/pub/3496>)

Sweeteners for re-evaluation include polyols and intense sweeteners (see Table 1). Intense sweeteners are usually added to food for their high sweet potency in order to replace sugar. Polyols, on the other hand, are bulk sweeteners. They have a lower sweet potency (equivalent to the one of sucrose) and can also be used in foods for purposes other than sweetening e.g. flavour enhancer (as mentioned in the Regulation No 1333/2008).

Although the re-evaluation of aspartame (E 951) was completed in 2013 (EFSA ANS Panel, 2013), an update of the dietary exposure to aspartame (E 951) will be performed. A dietary exposure assessment of total aspartame from the use of the salt of aspartame-acesulfame (E 962) and aspartame (E 951) will also be performed.

In general, concurrent exposure to impurities and by-products, e.g. toxic elements and process contaminants, will not be estimated by default.

1. Data and Methodologies
   1. Data
      1. Food additive occurrence data availability

In the framework of the re-evaluation programme of food additives that were already permitted in the European Union before 20 January 2009 set up under Regulation (EU) No 257/2010, EFSA has issued several public calls for use levels and/or analytical data (concentration data) on food additives to be re-evaluated since 2013.[[4]](#footnote-5) In particular, batch 7 was launched in January 2018 to collect concentration data on food sweeteners by October 2018[[5]](#footnote-6).

As part of batch 7, national authorities/organisations of the Member States and any interested business operators and other interested parties (e.g. individual food manufacturers, food manufacturer associations, research institutions, academia, food business operators and other stakeholders) were invited to submit concentration data of sweeteners in food and beverages intended for human consumption.

Analytical data of sweeteners are also collected annually via the open call for food additive occurrence data in food and beverages intended for human consumption.

An additional call on concentration data on aspartame (E 951) was launched to collect new data that will be used to update the exposure assessment of aspartame (E 951)[[6]](#footnote-7), as well as to assess the total aspartame exposure from the use of the salt of aspartame-acesulfame (E 962) and aspartame (E 951).

In the sections 5.1.1.1 and 5.1.1.2, the data that were submitted through batch 7 will be discussed.

* + - 1. Information on use levels submitted

The amount of information received for each sweetener through batch 7 varied considerably, ranging from few data (e.g. lactitol, salt of aspartame-acesulfame) to data covering nearly all authorised uses (e.g. acesulfame K, sucralose) laid down in Annex II to Regulation (EC) No 1333/2008 on food additives.

The majority of the information provided was made available by food industry associations that collect use levels from their members.

Use levels are validated; this includes cleaning steps and going back to data provider if clarification is needed.

Typically, very limited information is provided about the representativeness of the use levels submitted with respect to their market share. The only information that may be provided by data providers from the industry is that a level refers to a niche product. A niche product is commonly identified as a specific or unique product or as a product for a certain target subset of the population. The aim of this information is to obtain an indication about whether a reported use level is representative for the whole food category to which the niche product belongs. When the use level for a niche product clearly differs from those for other foods belonging to the food category and the niche product presents unique characteristics compared to those foods, the use level of the niche product will be exclusively assigned to a specific corresponding FoodEx2 code. When this is not possible, use levels related to niche products are not considered in the exposure assessment, unless no more representative levels are available for the overall food category. Whether data are to be considered more representative or not will be decided on a case-by-case basis (see section 5.2.3).

* + - 1. Information on analytical data submitted

The collection of analytical data was undertaken according to the requirements of the EFSA Guidance on Standard Sample Description for Food and Feed (EFSA, 2010) using the data model ‘Standard sample description’ (SSD1 or SSD2) (EFSA, 2010; EFSA, 2013). Analytical data on sweeteners were mainly submitted by European national authorities/organisations.

The number of analytical data provided per sweetener varied from no data (e.g. thaumatin, salt of aspartame-acesulfame) up to several thousands of analytical data (e.g. acesulfame K, saccharin). Analytical results are thoroughly validated; this includes cleaning steps and going back to data provider if clarification is needed. Following the EFSA Standard Operating Procedure (SOP)[[7]](#footnote-8) on data collection and validation, the initial data set was carefully evaluated applying several steps to guarantee an appropriate quality of the data used in the exposure assessment. Special attention is paid to the identification of duplicates and to the accuracy of different parameters such as ‘Sampling strategy’, ‘Sampling method’, ‘Sampling year’, ‘Sampling country’, ‘Analytical methods’, ‘Reporting unit’, ‘limit of detection (LOD)/limit of quantification (LOQ)’. Also, the codification of the different samples under the FoodEx2 classification system and the food categorisation of Annex II, Part D (Reg (EC) No 1333/2008) is evaluated and corrected, if needed.

A number of analytical results submitted to EFSA may report occurrence of sweeteners in food and beverages for which their use is not authorised according to Annex II to Regulation (EC) No 1333/2008. In this case, the presence of the sweetener in those foods (positive results i.e. greater than LOD or LOQ) could, for instance, be due to carry-over, or to natural occurrence (for the polyols only).

Furthermore, products in which sweeteners have not been added, despite being authorised, might have been analysed within the monitoring programmes. A number of monitoring programmes conducted by the data providers used multi-analyte methods in which two or more (and often several) sweeteners are analysed together. As a consequence, a large number of left-censored data (i.e. either below the LOD or LOQ) submitted relate to food categories in which the sweetener is not permitted. Similarly, some left-censored data submitted will be for food categories in which the sweetener is permitted but was not added to the particular product tested. It is therefore expected that a significant part of the analytical results submitted to EFSA is left censored. As described in section 5.2, the methodology used for the exposure assessment of sweeteners is based on the identification of the food categories which are assumed to contain sweeteners (from the dataset). In this context, the concentration of the sweetener present in the product is derived from the quantified analytical results only and the left-censored data will be excluded in order not to bias the results.

Only authorised uses with quantified analytical results at or below the Maximum Permitted Level (MPL) are considered because results above the MPL are outside the scope of risk assessment and subject of risk management measures, e.g. non-compliance purpose. These results will only be considered in specific cases as appropriate (e.g. in case of natural occurrence for polyols). This is in line with the dietary exposure assessments of food additives[[8]](#footnote-9). However, any non-compliant case will be reported in the opinions, if relevant. In case of a significant (based on expert judgement) number/frequency of analytical data exceeding the MPLs and/or a significant presence of a sweetener in foods in which it is not authorised, the Panel might perform an additional exposure assessment scenario including these data.

* + 1. Food consumption database

The dietary exposure to sweeteners will be calculated using food consumption data from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database). This database provides a compilation of existing national information on food consumption at individual level. Details on how the Comprehensive Database is used in exposure assessments are published in the Guidance of EFSA (EFSA, 2011). The food consumption data in the Comprehensive Database are the most complete and detailed data currently available in the European Union (EU). The latest version of the Comprehensive Database is used in the re-evaluation of the sweeteners[[9]](#footnote-10).

The age classes considered in the exposure assessment are the following:

* Infants: from 16 weeks to <12 months old
* Toddlers: ≥12 months to <36 months old
* Children: ≥36 months to <10 years old
* Adolescents: ≥10 years to <18 years old
* Adults: ≥18 years to <65 years old
* The elderly: ≥65 years.

Mannitol (E 421) is the only sweetener permitted in foods for infants and young children (food category 13.1 which covers foods for infants during the first months of life). However, its authorised use is limited as carrier for vitamin B12 (according to Annex III, Part 5, section B, to Regulation No 1333/2008). The FAF Working Group on the re-evaluation of sweeteners, jointly with the FAF Working Group on the re-evaluation of food additives permitted for use in foods for infants below 16 weeks of age, will evaluate in the course of its assessment, this special application of mannitol (E 421) according to the guidance on the risk assessment of substances present in food intended for infant below 16 weeks of age (EFSA Scientific Committee, 2017).

The Comprehensive Database is regularly updated. When for one country and age class, two different dietary surveys are available, only the most recent one will be used.

Consumption data in the Comprehensive database were collected using single or repeated 24-h or 48-h dietary recalls or dietary records covering from 3 to 7 days per subject. Due to differences in the methods used for data collection, direct country-to-country comparisons may not be appropriate. Detailed information on the different dietary surveys available in the Comprehensive Database can be found on the dedicated EFSA website page [[10]](#footnote-11).

* + 1. Food labelling data

EFSA has access to the food label database developed by Mintel, the Global New Products Database (GNPD).[[11]](#footnote-12) This database is an online database, which observes product introductions in consumer-packaged goods marketed worldwide. The GNPD contains data of EU food markets since 1996 and currently 24 of its 27 member countries, Norway and UK are represented in the GNPD.[[12]](#footnote-13) New foods are regularly added to the database. Foods that are no longer on the market are not removed from the database.

For the purpose of the exposure assessments of the sweeteners, the GNPD is used to check food product labels for sweeteners as GNPD shows the compulsory ingredient information on product labels. Only food additives authorised according to Annex II to Regulation (EC) No 1333/2008 are mandatory to be labelled. When information on a sweetener is available in the GNPD, the number (and percentage) of foods labelled with the sweetener per food sub-category of GNPD during the last five years will be reported.

The information in the GNPD is used to compare the food categories for which use levels and/or analytical data were reported to EFSA with the foods labelled to contain the sweetener, together with the authorised uses by the EU legislation. GNPD can provide qualitative information on the use or on the absence of use of a food additive in a food category, but the percentage of foods labelled with a food additive within a food category does not represent the percentage of foods consumed containing a food additive within a food category. The main aim of using the GNPD is to support the identification of the food categories in which the sweetener is used and to evaluate a possible under/overestimation of the calculated exposure.

* 1. Methodologies
     1. Food classification systems

Data on use levels are reported by the data provider according to the food categories (FCs) of Annex II, Part D to Regulation (EC) No 1333/2008, including the original name of each product.

Analytical data on sweeteners are reported according to the FoodEx2 food classification system, as prescribed in the standard sample description (SSD) data model. In addition, for a part of the analytical results, the relevant FCs of Annex II, Part D to Regulation (EC) No 1333/2008 are also reported. When the classification according to the FCs of Annex II, Part D to Regulation (EC) No 1333/2008 is not provided, EFSA will classify the foods accordingly.

Consumption records in the Comprehensive Database are codified according to the FoodEx2 classification system. To assess the dietary exposure to sweeteners, the nomenclature from the FoodEx2 classification system was linked to the FCs of Annex II, part D, to Regulation (EC) 1333/2008 using the lowest FoodEx2 level. To link all consumption events coded with FoodEx2 to the FCs of Annex II, Part D to Regulation (EC) No 1333/2008, the original food descriptor was occasionally used, especially for the dietary survey data provided to EFSA before 2018.

The link between the FoodEx2 classification system and the food sub-categories used in GNPD is reported in Appendix A. The link between the FoodEx2 classification system and the food categories from Regulation (EC) 1333/2008 is available in Zenodo (<https://zenodo.org/records/4461577>).

In FoodEx2, facets are used to add further descriptions of the foods consumed, in relation to different properties and aspects of the foods. The following facets can be used to identify products that could contain sweeteners: “Without added sugar”, “Sugar free”, “Low / Reduced sugar” and “Light”. These FoodEx2 facets are however not always related to the reduction of sugar/addition of sweetener(s), and a case-by-case decision is needed to select the sweetener related facets. For example, “Light” for certain foods, is related to the reduction of fats rather than sugar. In addition, the presence of artificial sweetener(s) among the ingredients of a given food can be reported by means of an ad-hoc facet. Facets are used to identify eating occasions of foods containing sweeteners in the Comprehensive Database (see section 5.2.2).

* + 1. Food categories used for the assessment of exposure

According to the available literature on the dietary exposure to sweeteners in different EU countries, Non-alcoholic beverages and Table-top sweeteners are expected to be the main contributors to the exposure for most sweeteners (Garnier-Sagne et al., 2001; Ilbäck et al., 2003; Arcella et al, 2004; Le Donne et al., 2017). Food Supplements, Desserts and Confectionery (e.g. chewing gum, candies, etc.) could as well represent a signiﬁcant source of exposure (Arcella et al, 2004; Vin et al., 2013; Le Donne et al., 2017). Alcoholic beverages have been mentioned by Le Donne et al. (2017) as an additional potential source.

The percentage of products within the food sub-categories used in GNPD labelled to contain at least one sweetener is reported in Appendix B. This search was performed in the first half of 2019. The five GNPD food sub-categories presenting the highest percentage of products labelled to contain at least one sweetener are Artificial Sweeteners (99%), Gum (89%), Meal Replacements & Other Drinks (58%), Sports Drinks (57%) and Medicated Confectionery (49%). When looking at the food categories from the legislation (Annex II, Part D to Regulation (EC) No 1333/2008) that are expected to be main contributors to the exposure according to the literature, at least one sweetener is reported on the label for 31% of Carbonated Soft Drinks, 32% of Energy Drinks and 21% of Vitamins & Dietary Supplements. The percentage of products with sweeteners on the label is lower for Cakes, Pastries & Sweet Goods (17%), Desserts (GNPD food sub-categories: Frozen Desserts (10%), Shelf-Stable Desserts (10%), Soft Cheese Desserts (9%), Chilled Desserts (9%) and Dessert Toppings (5%)) and confectionary other than gums (GNPD food sub-categories: Other Sugar Confectionery (14%) and Other Chocolate Confectionery (2%)). The percentage of products with sweeteners on the label is negligible for Cold cereals and Savoury Biscuits/Crackers (< 1%) and Alcoholic beverages: Beer (2%), Cider (1.4%), Liqueur (0.2%), and Wine (0.02%).

The FAF Panel proposes to use the FoodEx2 facets to identify eating occasions of foods containing sweeteners in the Comprehensive Database for the assessment of exposure. In practice, when an eating occasion refers to a food for which a FoodEx2 facet (see section 5.2.1) was reported specifying the presence of sweetener(s), the food is assumed to contain the sweetener under evaluation and the eating occasion is included in the assessment of exposure. Of course, this is done only if the sweetener under consideration is authorised in the specific food category, and MPLs, adequate use levels and/or analytical results are available (see in sections 5.1.1 and 5.2.3.2).

The FoodEx2 facets are based on information obtained during the dietary survey from the participants if the survey protocol required the collection of data at a higher level of detail. The reliability of using these facets to identify the possible presence of sweeteners in food categories varies between dietary surveys and food categories. The information reported through facets (e.g. percentage of foods reported with facets and respective consumption amounts of foods with and without facets of interest) and, consequently, the availability of the consumption data related to products containing sweeteners, was evaluated using information on 1) food consumption statistics (consumers only) per country and age class for each FoodEx2 category and corresponding GNPD food sub-category (see Appendix C); and 2) the percentage of eating occasions and quantity consumed for which at least one of the above-mentioned facets (see section 5.2.1) was reported (see Appendix D). The analysis was carried out on the FoodEx2 categories expected to be main contributors to the exposure to sweeteners according to the literature.

In the case of the FoodEx2 categories Chewing gum and Gum drops (linked to the GNPD food sub-category Gum and Medicated confectionary, respectively), the percentage of eating occasions for adults associated with the facets ranged from 50 to 100%, with Austria, Czech Republic, Finland, Romania, Spain and Sweden never reporting any facet. Facets were never reported for FoodEx2 categories linked to the GNPD categories Other Sugar Confectionery and Other Chocolate Confectionery.

In the case of FoodEx2 category Energy drinks (linked to the GNPD food sub-category Energy drinks) the percentage of eating occasions for adults presenting the facets ranged from 0.1 to 17%, with 10 countries out of 17 never reporting any facet.

In the case of FoodEx2 categories linked to the GNPD food sub-category Vitamins & Dietary Supplements, only in Italy and Germany were facets used to identify products containing sweeteners (10% and 0.4% of Vitamin only supplements, respectively).

In the case of FoodEx2 categories related to desserts, facets used to identify products containing sweeteners were reported for Compote of fruit / vegetables (6 countries, from 9 to 38% of eating occasions), Starchy pudding (4 countries, from 3 to 14%), Custard (3 countries, from 1 to 15%), Fruit or fruit-vegetable purée (2 countries, from 26% to 100%), Other desserts spoonable (2 countries, from 31 to 50%), Dairy desserts spoonable (1 country, 40%) and Rice pudding (1 country, 5%).

FoodEx2 categories Diet soft drink with caffeine, Diet soft drinks with fruit juice and Diet soft drinks with flavours (linked to the GNPD food sub-category Carbonated Soft Drinks) are always implicitly associated with at least one of the facets used to identify products containing sweeteners. Caffeine containing Cola beverages are the most largely consumed FoodEx2 category within Carbonated Soft Drinks. The percentage of eating occasions in adults for this FoodEx2 category presenting the facets ranged from 2 to 60%, with 10 countries out of 17 never reporting any facet. But in most of these 10 countries the category Diet soft drink with caffeine was used instead of Caffeine containing Cola beverages (with facets), suggesting still a relatively good identification of soft drinks products containing sweeteners.

The GNPD food sub-category Artificial Sweeteners (e.g. Table-top sweeteners formulations, Table-top sweeteners in liquid form, Table-top sweeteners in powder form and Table-top sweeteners in tablets) contains by definition sweeteners. All eating events under the food category Table-top sweeteners (FC 11.4 and children) will be considered in the exposure assessment scenarios.

In addition, based on an analysis of the percentage of eating occasions presenting at least one of the facets used to identify products containing sweeteners, the FAF Panel noted a likely underestimation of eating occasions of products containing sweeteners for Chewing gum, Gum drops, Energy drinks and Vitamin and mineral supplements. Since these categories are expected to be major contributors to the exposure according to the literature and present a relatively high percentage of products labelled to contain at least one sweetener, the FAF Panel decided to always include these food categories in the exposure assessment regardless of the presence of facets. In order not to underestimate the exposure, foods in these categories are assumed to always contain the sweetener under evaluation, if authorised and if MPLs, adequate use levels and/or analytical data are available. The facets used to identify products containing sweeteners are considered more reliable for the FoodEx2 categories linked to the GNPD food sub-category Carbonated Soft Drinks. In order not to overestimate the exposure, the FAF Panel decided to use the facets to identify the eating occasions of carbonated soft drinks containing the sweetener under evaluation.

Some of the sweeteners are also authorised as flavour enhancer (e.g. neotame and thaumatin in FC 12.6 sauces and FC 15.1 snacks) and this type of use might not be captured with the FoodEx2 facets. This might lead to an under-estimation of exposure that will be considered in the uncertainty section of the opinion, if relevant.

The FAF Panel also decided to apply the same approach, i.e. sweetener considered only present based on facet information, to all other food categories which are not expected to be a signiﬁcant source of exposure to the sweetener, based on the literature and on the low percentage of products labelled to contain sweeteners in the GNPD. In these cases, the uncertainty related to the reliability of the facets is not expected to lead to a considerable underestimation of the exposure.

* + 1. Chronic exposure assessment of sweeteners under re-evaluation

The Panel estimates the chronic exposure to sweeteners. Exposure assessments of sweeteners under the re-evaluation programme are carried out by the FAF Panel based on two different sets of concentration data: (a) MPLs of use as set down in the EU legislation (used in a scenario defined as *regulatory maximum level exposure assessment scenario*) and (b) use levels and/or analytical data provided through the calls for data (used in a scenario defined as *refined exposure assessment scenario*).

These scenarios will be used for single substances and for co-occurring substances. Co-occurrence exists in the case of the salt of aspartame-acesulfame (E 962), which liberates aspartame and acesulfame on disassociation. This should be taken into account together with the single use of these two sweeteners as such. Should evidence emerge that two or more substances lead to the same adverse effects, in particular through the same Mode of Action (MoA), the use of a cumulative assessment group will be considered.

In case other cumulative effects need to be considered within the re-evaluation or by a separate mandate, these scenarios may be adapted.

In the exposure assessment scenarios, the concentration levels considered by the Panel are extracted from the whole dataset received (i.e. reported use levels and analytical data) and are pooled together assuming a European market.

All reported use levels and analytical data will be summarised in the appendices of the scientific opinion for acknowledgment and information.

Sweetener concentration values (MPLs, use levels and/or analytical data) are combined with national food consumption data at individual level from the EFSA Comprehensive Database considering the six different population groups mentioned above (see section 5.1.2).

A use level referring to a niche product will be considered as described in section 5.1.1.1. The possible under/overestimation of the contribution of the food category to which the niche product belongs to the overall exposure will be discussed in the uncertainty section of the opinion.

Use levels reported by food additive producers will not be considered with the same priority as those provided by food industry. The FAF Panel considered that food additive producers might recommend use levels to the food industry, but the final levels used might, ultimately, be different. Therefore, unless food additive producers confirm that the recommended levels are used by the food industry, they will not be considered in the refined exposure scenario. Data from food additive producers will be used in the *maximum level exposure assessment* scenario in case of QS authorisation and when no use levels from food industry or analytical data are available. In this way, the most comprehensive exposure estimates will be calculated.

For the risk assessment of sweeteners, the FAF Panel uses a consumers only exposure approach. This approach differs from a general population approach which is used for other food additives (EFSA ANS Panel, 2017). A consumers only approach is used, because it is likely that consumers choose their foods based on label information concerning the presence of sweetener(s) in a consistent manner and represent the most relevant population for the dietary exposure assessment of sweeteners. For example, diabetics choose products containing sweeteners for health reasons.

Therefore, all exposure scenarios described below (see sections 5.2.3.1., 5.2.3.2 and 5.2.3.3.) refer to consumers only of foods containing sweetener(s). Mean and 95th percentile exposure results will be calculated for consumers only of at least one food category containing the sweetener under evaluation according to Annex II to Regulation No 1333/2008 and will be reported for each dietary survey and population group. The main food categories of Annex II, Part D to Regulation (EC) No 1333/2008 contributing to the total mean exposure to the sweeteners will be provided in each opinion for each scenario.

In addition, exposure results will also be calculated for consumers only for each food category separately and will be included in an Annex to the respective re-evaluation.

Due to limited number of consumption data for diabetics, it is not possible to perform an exposure assessment for this specific population sub-group. Nevertheless, it is expected that diabetics are exposed to sweeteners at levels in the same range as for subjects at the right side (higher end) of the exposure distribution for consumers only of at least one food category containing the sweetener under evaluation.

* + - 1. Regulatory maximum level exposure assessment scenario

The *regulatory maximum level exposure assessment scenario* is based on MPLs of use as set in Annex II, Part E, to Regulation No 1333/2008. Therefore, it includes all food categories authorised according to this Annex or any other legislation clearly defining the food or food category in which the sweetener might be added and for which a numerical MPL has been set (e.g. Annex III of the same Regulation).

Under the *regulatory maximum level exposure assessment* scenario, all FoodEx2 codes belonging to an authorised food category will be assumed to contain the sweetener, unless Annex II to Regulation No 1333/2008 indicates that the sweetener can only be added under specific restrictions/exceptions, e.g. “only energy reduced or with no added sugar”. In that case, the food selection approach based on facets described in section 5.2.2 applies.

For sweeteners authorised according to *quantum satis* (QS) in all or part of the food categories, a *maximum level exposure assessment scenario* will be performed based on the maximum reported use levels provided by industry or on the highest reliable percentile different from the maximum (depending of the number of observations[[13]](#footnote-14)) of analytical data provided by Member States (MSs), whichever is highest or available, as described in the EFSA Conceptual framework (EFSA ANS Panel, 2014). Food categories authorised at QS and for which use levels or analytical data are not available or adequate (e.g. unreliable analytical methods) are not considered in this scenario.

The exposure estimates derived following this scenario are based on the assumption that the population group will be exposed to a sweetener present in food at the MPL, or maximum reported use level or the highest reliable percentile different from the maximum of the analytical level in case of QS authorisation, over a long period of time.

The *regulatory maximum level exposure assessment scenario* is the only scenario which will not be influenced by future changes of sweetener use in the market.

* + - 1. Refined exposure assessment scenario

The *refined exposure assessment scenario* is based on information on reported use levels and/or analytical data, and can only be carried out if sufficient and adequate data have been reported. The refined scenario should be performed taking into account the authorised food categories according to Annex II, Part E, to Regulation No 1333/2008.

Regarding intense sweeteners, the facets will be considered in the refined exposure assessment as described in section 5.2.2. For the polyols, facets will only be considered for food categories with the restriction/exception “only energy-reduced or with no added sugar”, as for the *regulatory maximum level exposure assessment scenario* (see section 5.2.3.1 and Table 2 below). The reason for a different approach is that polyols may also be added for purposes other than sweetening (see section 4).

If both use levels and analytical data are available for the same food category, the highest reliable value (based on expert judgement) for the food category under consideration will be used.

Considering the specific food consumption patterns of foods containing sweeteners, the refined exposure assessment will be based on the brand-loyalty principle. In practice, estimates will be based on the assumption that an individual is a long-term brand-loyal consumer of one food category containing the sweetener at the highest reported use level/highest reliable percentile different from the maximum level analysed and non-brand loyal to the other food categories in the diet, which contain the sweetener at the mean/median of typical reported use level or analytical data. This exposure estimate will be calculated as follows:

* Combining food consumption with the maximum reported use level (or highest reliable percentile different from the maximum level analysed) available for the food category having, at the individual level, the highest contribution to the total individual mean exposure,
* Using the mean of the typical reported use levels or the mean/median of analytical results for the remaining food categories.

As mentioned previously, food categories for which no or inadequate information regarding the use/occurrence of a sweetener is available (obtained from industry or from MSs) cannot be included in the refined scenario. Consequently, this scenario will be limited to those food categories for which information is available. Exclusion of food categories for which data is not available might result in underestimation of the true exposure.

Overall, the *refined exposure assessment scenario* is suitable to calculate the most realistic exposure estimates of sweeteners given the available data. Moreover, assigning the mean concentration of the food additive to food consumed by a given population (with the exception of the food category selected based on the brand-loyalty principle, as described above), is consistent with general chronic exposure approaches.

As the refined exposure assessment scenario may cover less food categories depending on the availability of the concentration data and on the use of the facets for intense sweeteners (see Table 2), the underlying population of consumers only may not be the same as in the *regulatory maximum level exposure assessment scenario*. Therefore, the results of the refined exposure assessment scenario cannot be meaningfully compared to those of the *regulatory maximum level exposure assessment scenario*. For this reason, also a *refined regulatory maximum level exposure assessment scenario* may be performed based on the same population included in the refined exposure assessment scenario.

1. Description of how facets are considered in the different exposure assessment scenarios:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Intense sweetener** | | **Polyols** |
| **Food category (FC) example** | **REGULATORY MAXIMUM LEVEL** | **REFINED MAXIMUM LEVEL and BRAND LOYAL** | **General scenario for chronic and acute scenarios (regulatory maximum level and refined maximum level and brand loyal)** |
|  | **The principle of conservativism** is respected and therefore all authorised food categories are taken without facets unless the restriction/exception indicates, 'only energy-reduced or with no added sugar' | **The principle of refinemen**t is respected and performed through using the facets, with exception of five food categories: gum drops, chewing gum, table-top sweeteners, energy drinks and vitamin and mineral supplements (for which it is assumed that they always contain the sweetener and therefore no facets are applied) | Considering the facets for a food category with restriction/exception ‘only energy-reduced or with no added sugar’ |
| Any FC without restriction (e.g., “12.6 Sauce”) | No facets applied | Facets applied | No facets applied |
| Any FC with restriction (e.g., "12.6 Sauce" + restriction "only energy-reduced or with no added sugar") | Facets applied | Facets applied | Facets applied |
| Gum drops, chewing gum, table-top sweeteners, energy drinks and food supplements in solid form (no restriction) | No facets applied | No facets applied | No facets applied |
| Gum drops, chewing gum, table-top sweeteners, energy drinks and food supplements in solid form + restriction 'with no added sugar' | No facets applied | No facets applied | No facets applied |

* + - 1. Other exposure assessment scenarios

If concentration levels are made available to EFSA for food categories which are not authorised according to Annex II to Regulation No 1333/2008 and in order to consider the presence of sweeteners due to carry-over (Annex III to Regulation No 1333/2008) or due to natural occurrence (relevant only for polyols), additional exposure scenarios may be performed considering the availability of data.

* + 1. Acute exposure assessment of sweeteners under re-evaluation

If acute effects are considered to be relevant for specific sweeteners, the Panel will estimate acute dietary exposure (short-term exposure) per single day and/or per meal. Concentration data used to assess the acute exposure are the same as those used in the refined chronic exposure assessment scenarios (see Section 5.2.3.2).

Acute exposure per day will be assessed for each reporting day by multiplying the total daily consumed amount for each relevant food by its concentration. First, the mean concentrations will be used to determine the two food categories contributing most to the exposure for a single day. Then, the maximum use level/highest reliable percentile for these two food categories, and the mean/median concentrations for the remaining food categories will be used to estimate the acute exposure. This approach considers that for the acute exposure, it is likely that the same person will consume foods from more than one food category with the highest concentration of sweetener on a single day especially consumers following dietary restrictions. The exposures from all foods will then be summed up and either reported as mg per person per day and/or as mg per kg body weight per day, using the individual body weights from the EFSA Comprehensive database.

Acute exposure per meal will be assessed similarly. Meals in the Comprehensive database are defined as breakfast, lunch, dinner, and snacks in between. ‘Unclassified’ eating events are those that are not assigned to any meal during a day. The exposure from these ‘unclassified’ foods are added to the meal having the highest exposure on that day. After this, the two main food categories contributing to the exposure for a meal are identified as described above. Then, the maximum reported use level/highest reliable percentile of analytical data for these two food categories, and the mean/median concentrations for the remaining food categories will be used to estimate the acute exposure. When no information on any meals is available for a certain day, the consumption of the foods reported on that day is not taken into consideration.

The 95th, 97.5th and 99th percentiles of exposure per day and meal will be calculated to express a high level of acute exposure. The food categories having the most important contribution to the acute dietary exposure to sweeteners will be determined across age classes and dietary surveys based on the high percentiles of exposure.

These percentiles are only statistically robust if based on a sufficiently large number of observations (EFSA, 2011), thus it will not be possible to calculate these percentiles for all surveys.

Acute exposure assessment refers to consumers only of at least one food category containing the sweetener and will be reported for each dietary survey and population group.

Details of acute exposure assessment per survey per meal or per day will be made available in annexes.

* + 1. Uncertainty analysis

In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the sources of uncertainties considered are summarised in each opinion in a table in the uncertainty section. They are related to the food consumption data and to the concentration data (use levels or analytical data) used, and to the dietary exposure assessment scenarios presented in the opinions.

An uncertainty paragraph summarises the uncertainties and indicates whether the exposure estimates can be considered as under- or overestimations of the true exposure.

In order to evaluate a possible maximum underestimation related to the use of the FoodEx2 facets, an additional refined exposure scenario is performed and reported in the uncertainty section. It follows the same methodology described in section 5.2.3, but it will include all eating events of foods authorised to contain a sweetener irrespective of the facets.

The GNPD will be used as a qualitative tool to evaluate the uncertainty related to the available use levels/analytical data. As mentioned in section 5.1.3, for each specific sweetener, a table will be produced listing the numbers and percentages of products labelled to contain the sweetener per food sub-category according to the GNPD food classification and in total across all food sub-categories. This should give information on the use of sweeteners in products as available in the market. Based on this information, the following observations are possible:

* There is consistency between the reported use levels/analytical data for foods and beverages with presence information from the GNPD: low uncertainty.
* There is no consistency between reported use levels/analytical data for foods and beverages with presence information from the GNPD: high uncertainty.

The approach on how to include the food categories with or without facets (see section 5.2.2.) could introduce the following uncertainties:

i) For food categories for which all eating occasions are assumed to contain the sweetener (without considering FoodEx2 facets): from low to high uncertainty depending on the sweetener. The uncertainty section should acknowledge a possible overestimation of the exposure if relevant.

ii) For food categories for which FoodEx2 facets are used to identify eating occasions of foods containing a sweetener, the direction and magnitude of the uncertainty depends on the quality of the dietary survey and can hardly be assessed. However, the uncertainty will be acknowledged in the opinion.

As indicated in section 5.2.2, some of the sweeteners are also authorised as flavour enhancer (e.g. neotame and thaumatin in FC 12.6 sauces and FC 15.1 snacks). This use might not be captured in the consumption data with FoodEx2 facets and might lead to an underestimation of exposure. This will be considered in the uncertainty section, if relevant.

* 1. Comparison with human urinary biomonitoring studies

Exposure estimates from published human urinary biomonitoring studies may be used as a cross-check of the estimates made using the scenarios described above, as well as for estimating external exposure.

Some of the sweeteners are either not metabolised or are metabolised only poorly. So they are excreted completely or almost completely unchanged in the urine. Examples are acesulfame-K, saccharin and cyclamates (as reviewed in Lewis & Tzilivakis, 2021). This gives the possibility to estimate exposure to sweeteners using human urinary biomonitoring, whereby the concentration in urine can be used to estimate the exposure of that person in the relevant period of time prior to urine collection.

It may also be the case that even if metabolism is extensive, the metabolites of a sweetener may be unique and could be ascribed to the parent substance. In such a case, if the molar fraction of the urinary excreted metabolite can be related to the parent substance without too much uncertainty (e.g. inter- or intra-person variability), then measurements of the metabolite(s) could be used to derive estimates of exposure to the parent sweetener.

This would require that the biomonitoring data available are suitable and kinetic models are available to allow the conversion of biomonitoring data (internal exposure) into external exposure.

Human biomonitoring data comprises a picture of the tested individual(s) at the moment/period of measurement and their use is based on extrapolation of the derived results to the general population. Human biomonitoring also captures exposure to a substance from all sources, not only dietary. For these reasons, the cross-checking shall be performed to look for a general alignment of the different estimates of exposure rather than requiring any exact agreement. This shall be described in a narrative approach.

References

Arcella, D et al., 2004. Dietary estimated intake of intense sweeteners by Italian teenagers. Present levels and projections derived from the INRAN-RM-2001 food survey. Food and Chemical Toxicology, 42(4), 677-685.

EC (Commission of the European Communities), 2001. Report from the Commission on dietary food additive intake in the European Union (542 final).

EFSA (European Food Safety Authority), 2007. Scientific opinion of the Scientific Committee related to uncertainties in dietary exposure assessment. EFSA Journal 2007;5(1):438, 54 pp. doi:10.2903/j.efsa.2007.438

EFSA (European Food Safety Authority), 2010. Standard sample description for food and feed. EFSA Journal 2010; 8(1):1457, 54 pp. doi:10.2903/j.efsa.2010.1457.

EFSA (European Food Safety Authority), 2011. Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment. EFSA Journal 2011;9(3):2097, 34 pp. doi:10.2903/j.efsa.2011.2097

EFSA (European Food Safety Authority), 2013. Standard Sample Description ver. 2.0. EFSA Journal 2013;11(10):3424, 114 pp., doi:10.2903/j.efsa.2013.3424

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources), 2014. Statement on a conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010. EFSA Journal 2014;12(6):3697, 11 pp. doi:10.2903/j.efsa.2014.3697

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2017. Statement on approach followed for the refined exposure assessment as part of the safety assessment of food additives under re-evaluation. EFSA Journal 2017;15(10):5042, 9 pp. <https://doi.org/10.2903/j.efsa.2017.5042>

EFSA Scientific Committee, 2017. Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age. EFSA Journal 2017;15(5):4849, 58 pp. <https://doi.org/10.2903/j.efsa.2017.4849>

EFSA Scientific Committee, 2018. Scientific Opinion on the principles and methods behind EFSA’s Guidance on Uncertainty Analysis in Scientific Assessment. EFSA Journal 2018;16(1):5122, 235 pp. <https://doi.org/10.2903/j.efsa.2018.5122>

Garnier-Sagne I and al., 2001. Calculation of the intake of three intense sweeteners in young insulin-dependent diabetics. Food and Chemical Toxicology, 39, 745-749.

Ilback NG et al, 2003. Estimated intake of the artificial sweeteners acesulfame-K, aspartame, cyclamate and saccharin in a group of Swedish diabetics. Food Additives and Contaminants; 20(2), 99-114.

Le Donne, C et al., 2017. Assessment of dietary intake of 10 intense sweeteners by the Italian population. Food and Chemical Toxicology, 102, 186-197.

Lewis KA and Tzilivakis J, 2021. Review and synthesis of data on the potential environmental impact of artificial sweeteners. EFSA External Scientific Report, EFSA supporting publication 2021:EN-6918. 127 pp. doi:10.2903/sp.efsa.2021.EN-6918.

Vin K et al, 2013. Estimation of the dietary intake of 13 priority additives in France, Italy, the UK and Ireland as part of the FACET project. Food Additives and Contaminants; 30(12), 99-114.

Abbreviations

|  |  |
| --- | --- |
| EC | European Commission |
| EFSA | European Food Safety Authority |
| EU | European Union |
| FAF Panel | EFSA Panel on Food Additives and Flavourings |
| FCs | Food Categories |
| GNPD | Global New Products Database |
| LOD | Limit of detection |
| LOQ | Limit of Quantification |
| MoA | Mode of Action |
| MPL | Maximum Permitted Level |
| MSs | Member States |
| QS | Quantum satis |
| SOP | Standard Operating Procedure |
| SSD | Standard Sample Description |

1. Link between the FoodEx2 classification system and the food sub-categories used in Mintel GNPD
2. Percentage of products within the food sub-categories used in Mintel GNPD labelled to contain at least one sweetener
3. Food consumption statistics (consumers only) per country and age class (in g/day)
4. Percentage of eating occasions and in quantity for which at least one relevant facet was reported

1. Sweeteners may be evaluated individually or in group. [↑](#footnote-ref-2)
2. Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19–27 [↑](#footnote-ref-3)
3. Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16–33. [↑](#footnote-ref-4)
4. http://www.efsa.europa.eu/en/calls/data [↑](#footnote-ref-5)
5. https://www.efsa.europa.eu/en/consultations/call/180122 [↑](#footnote-ref-6)
6. https://www.efsa.europa.eu/sites/default/files/consultation/callsfordata/Call\_for\_data\_on\_food\_additives\_2020.pdf [↑](#footnote-ref-7)
7. Standard operating procedure 008 for the data collection and validation: <https://www.efsa.europa.eu/en/corporate/pub/sops> [↑](#footnote-ref-8)
8. See EFSA statement: <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.5042> [↑](#footnote-ref-9)
9. See EFSA webpage: https://www.efsa.europa.eu/en/data-report/food-consumption-data [↑](#footnote-ref-10)
10. <http://www.efsa.europa.eu/en/food-consumption/comprehensive-database> [↑](#footnote-ref-11)
11. http://www.gnpd.com/sinatra/home/ [↑](#footnote-ref-12)
12. Missing Cyprus, Luxembourg and Malta. [↑](#footnote-ref-13)
13. For the 99th percentile, the minimum number of observations is 298; for the 95th percentile, the minimum number of observations is 118; for the 95th percentile, the minimum number of observations is 59; for 90th percentile, the minimum number of observations is 29; for the 75th percentile, the minimum number of observations is 11; for the 50th percentile (median), the minimum number of observations is 5. [↑](#footnote-ref-14)