UPDATE ON THE RE-EVALUATION OF SWEETENERS

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EUROPEAN FOOD SAFETY AUTHORITY

OUTLINE OF PRESENTATION

Re-evaluation of sweeteners: state of play

Re-evaluation of polyols: current status and tailored protocol for toxicological assessment

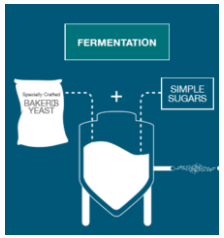
Revision of protocol on hazard identification and hazard characterisation of sweeteners

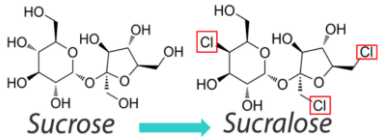
RE-EVALUATION OF SWEETENERS AS FOOD ADDITIVES

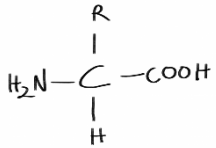
E Number	Food additive(s)
E 420	**Sorbitols**
E 421	**Mannitols**
E 950	Acesulfame K
E 951[(a)]	Aspartame[(a)]
E 952	**Cyclamates**
E 953	**Isomalt**
E 954	Saccharin and its Na, K and Ca salts
E 955	Sucralose
E 957	Thaumatin
E 959	Neohesperidine dihydrochalcone
E 961	Neotame
E 962	Salt of aspartame-acesulfame
E 965	**Maltitols**
E 966	**Lactitol**
E 967	**Xylitol**
E 968	Erythritol

(a) In May 2011, EFSA was asked by the European Commission to bring forward the full re-evaluation of the safety of aspartame (E 951). That re-evaluation was completed by EFSA in 2013 (EFSA ANS Panel, 2013).

- Thaumatin (E 957): 2021
- Neohesperidine DC (E 959): 2022
- Erythritol (E 968): 2023
- Saccharins (E 954): 2024
- Acesulfame K (E 950): 2025
- Neotame (E 961): 2025
- Sucralose (E 955): 2025 (published Feb 2026)
- Salt of aspartame acesulfame (E 962): to be published in September







TWO PROTOCOLS DEVELOPED AND IMPLEMENTED

- Protocol on hazard identification and characterisation of the sweeteners (2020)
- **Revised Protocol** on Hazard Identification and Characterisation of Sweeteners | Zenodo **(2023)**
- Protocol for the exposure assessment of the sweeteners (2020)
- Revised protocol on exposure **(2024)**

Problem formulation	• Is there a dose-response relationship between the dietary exposure to sweeteners and adverse effects in humans/experimental animals?
Extensive Literature Searches	• Open-ended searches; from last SCF/EFSA opinion • Refinement if needed
Screening the studies for relevance	• Two steps: Ti/Ab_full text • Setting of inclusion/exclusion criteria
Evaluation of the Risk of Bias/Data extraction	• Adapted from the OHAT rating tool (NTP, 2019); 3 tiers • Modified from the EFSA BPA protocol, 2017
Weighing the body of evidence	• Modified version of the OHAT (NTP, 2019) and EFSA Guidance on WoE (2017) • Grouping animal/human studies on the same endpoint
Synthesis of the evidence and uncertainties	• EFSA Guidance on WoE, 2017 • EFSA Guidance on Uncertainties, 2018

A further revision of the protocol on HI and HC: *to be published during summer*

SALT OF ASPARTAME-ACESULFAME (E 962)

- Adopted ***1 July 2026***
- **Publications** foreseen later in **September**

- Communication activities planned:
  - ✓Carousel at the end of the open plenary
  - ✓Plain language summary (PLS) together with scientific opinion
  - ✓News linked to the PLS

NEXT SWEETENER: CYCLAMATES (E 952)

- Foreseen to be finalized ***by June 2027***
- Work has started at the beginning of 2026

✓**Technical assessment**: first discussion with WG sweeteners (12 June); next meeting in autumn

✓**Exposure assessment**: **Open call for food additives analytical data and use levels in food and beverages intended for human consumption:** launched on 4 March 2026, closing end August 2026;

  ✓exposure assessment ready beginning of 2027

✓**Toxicological assessment**: ongoing (ADME, genotoxicity, WoE animal and human data)

  ✓foreseen to be finalised beginning 2027

UPDATE ON THE RE-EVALUATION OF POLYOLS

EUROPEAN FOOD SAFETY AUTHORITY

ERYTHRITOL (E 968): ADOPTED IN OCTOBER 2023

- **Re-evaluation** of erythritol (E 968) as a food additive and an **application for its exemption from the laxative warning label** requirement as established under Regulation (EU) No 1169/2011
- Dataset evaluated: **human interventional studies**
- **ADI of 0.5 g/kg bw per day**: protective for the immediate laxative effect as well as potential chronic effects, secondary to diarrhoea (electrolyte imbalance)
- Exposure estimates for both **acute** and **chronic dietary exposure** to erythritol (E 968) **above the ADI:** individuals with high intake may be at risk of experiencing adverse effects after single and repeated exposure
- Both dietary exposure assessments are an **overestimation**
- The **warning** '*excessive consumption may produce laxative effects*' **remains appropriate:** available data do not support the applicant's proposal for the exemption of erythritol from the current laxative warning requirement under Regulation (EU) 1169/2011 for food containing more than 10% erythritol (100,000 mg/L or mg/kg)

ERYTHRITOL (E 968): FOLLOW UP AFTER ADOPTION

The Panel recommended the European Commission to consider:

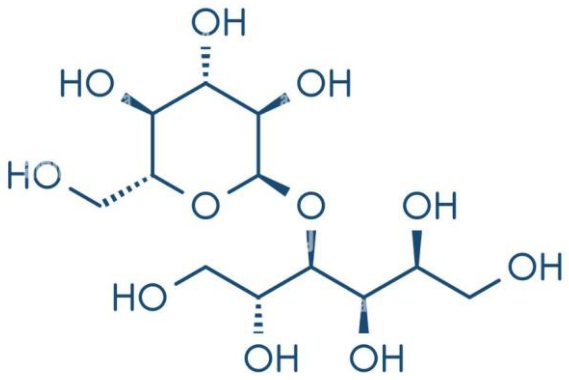
- *requesting more detailed occurrence data (use levels and analytical data) and label information, in order to be able to refine the exposure assessment*

- **Refined exposure assessment for erythritol**:
  - included in the EFSA 'Call for analytical data and use levels on food additives – 2026': https://www.efsa.europa.eu/en/call/open-call-food-additives-analytical-data-and-use-levels-food-and-beverages-intended-human
  - 3 most relevant food categories (and their relevant FoodEx subcategories) for refining the exposure assessment

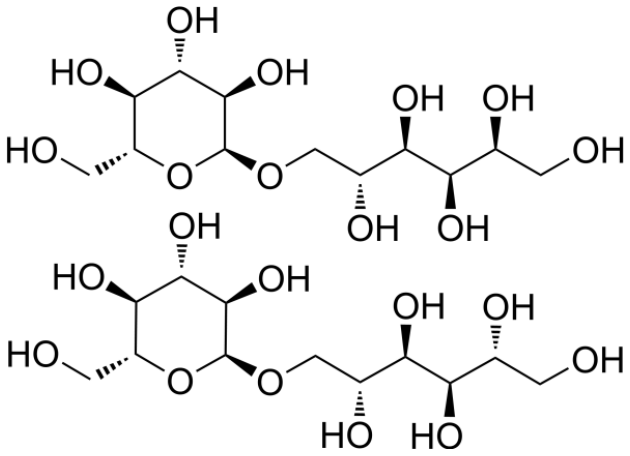
- 03. Edible ices
- 07.2 Fine bakery wares
- 14.1.4 Flavoured drinks

The list of foods (FoodEx2 codes from the MTX catalogue) belonging to these food categories are available in the following file: 'FoodEx2 codes_Erythritol.xlsx'

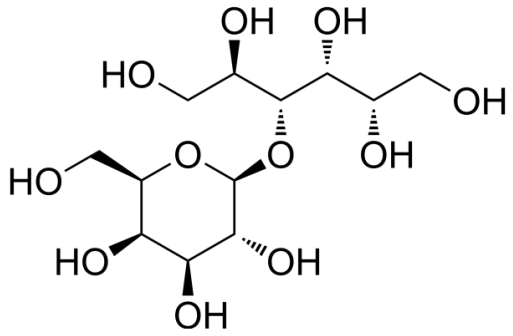
CHEMICAL STRUCTURES OF POLYOLS



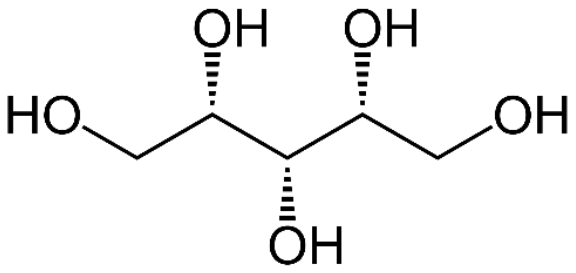
maltitol



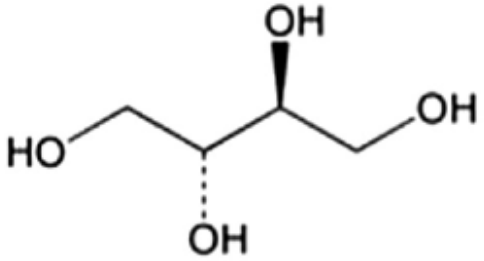
isomalt



lactitol

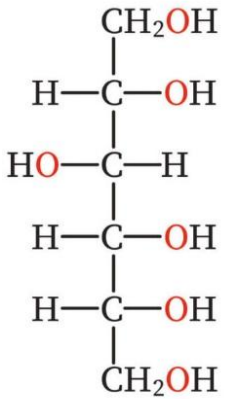


xylitol

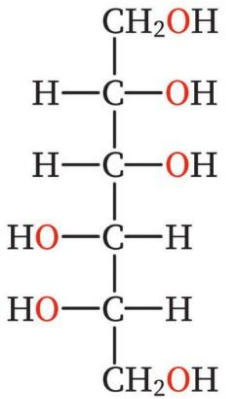


erythritol

Sorbitol



Mannitol



$C_6H_{14}O_6$

ONGOING WORK

Technical part:

- compilation of in-house data following previous calls for data (data submitted from IBOs for all the polyols);
- drafting of the technical sections of the opinions;
- assessment of technical information: identity, specifications, purity, impurities, manufacturing processes, stability, analytical methods for quantification in food matrices,…;
- Consideration of relevant manufacturing aspects, including fermentation-based production and production microorganism when applicable;

Xylitol (E 967): to be considered jointly with a **new application** (amendment of specifications);

- Confidentiality check: ongoing

ONGOING WORK

Exposure part:

- **Open call for food additives analytical data and use levels in food and beverages intended for human consumption:** launched on 4 March 2026
- Deadline for submission: **30/06/2026**
  Deadline for validation and acceptance of data: **31/08/2026**
- Exposure assessment will start early 2027
- Old data received from the previous call used for the exposure assessment, if confirmed to be still valid
- Both **acute** (if relevant) and **chronic** exposure considered

Mannitols (E 421): the only sweetener permitted in **foods for infants and young children**, as a carrier for vitamin B12

ONGOING WORK

Biological and toxicological part:

- **Tailored protocol** for the evaluation of the six polyols, under development (during 2026)
- **Public consultation**

- Preliminary considerations related to:
  - chemical structure
  - ADME properties
  - overlapping studies among different polyols
  - potential shared mode of action

may support a **grouped approach** to the toxicological assessment

- either for all polyols or for specific subsets

ONGOING WORK

Preliminary considerations on the tailored protocol for polyols:

- Prioritisation of **ADME** (grouping) and **genotoxicity** assessment
- Prioritisation of **certain health outcome categories** (e.g. laxative effects for human,…)
- Prioritisation of **human studies** *vs* animal studies
  - Mapping of animal data available
  - Consider whether animal and human data can be linked (in terms of HOCs); for each identified HOC for human it will be checked whether relevant animal data are available.
- Prioritisation of certain **types of human studies** for the main health outcomes (e.g. HCT, ..)

CALL FOR DATA ON GENOTOXICITY (2021 AND 2023)

Isomalt (E 953)

Lactitol (E 966)

Xylitol (E 967)

Data from the basic battery of in vitro tests, i.e. **bacterial reverse mutation assay** (OECD TG 471) and an ***in vitro* micronucleus assay** (OECD TG 487)

Maltitols (E 965i)

Sorbitols (E 420i)

***In vitro* micronucleus test**, performed following the more recent version of the relevant OECD guideline (TG 487)

RESOURCES INVOLVED

- **WG Sweeteners enlarged** (28 members, covering different expertise)

- **FAF Team colleagues:**
  - Chemistry: Fabio Alfieri, Paula Podea, Ana Rincon, Panagiota Zakidou
  - Toxicology: Stefania Barmaz, Costanza Bonnici, Consuelo Civitella, Federica Lodi, Elena Mazzoli, Josef Daniel Rasinger, Camilla Smeraldi

- **Other EFSA Units:** MESE (Exposure: Claudia Cascio, Petra Gergelová, Zsuzsanna Horvath, Francesca Riolo, Alexandra Tard); Library (Lit searches and Distiller; AI tools); ccWG Genotoxicity,…; i-DATA; COMM (Plain Language Summaries and other media requests); ENREL (Info-session stakeholders meeting); RAL.

- **Outsourcing activities:** 1 Procurement, 2 Tasking Grants, Several ISA contracts (e.g. Gabriele Gagliardi, ongoing).

REVISION OF THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

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EUROPEAN FOOD SAFETY AUTHORITY

UPDATES TO THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

Number	Sub-question
1a	What is the ADME of sweeteners in humans?
1b	What is the ADME of sweeteners in mammalian animal species?
1c	How do the human and animal ADME data correlate?
1d	Are there any biomonitoring data that contribute to the assessment of ADME?
2	Do any of the substances included in the assessment show a genotoxic potential?
3a	Is there a dose-response relationship between the dietary exposure to sweeteners and adverse effects in humans (observational and interventional studies)?
3b	Is there a dose-response relationship between exposure to sweeteners and adverse effects in toxicological studies conducted in experimental animals?
4	Which could be the potential mode(s) of action for the relationships found, if any, between sweeteners intake and the adverse health outcomes?

Revised to reflect the current approach described in the technical report on the harmonised approach for reporting reliability and relevance of genotoxicity studies (EFSA, 2023)

Introduction of an overview of HOCs and associated endpoints or outcomes assessed in previous opinions. Additional clarifications on inclusion and exclusion criteria on both animal and human studies are provided.

UPDATES TO THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

Problem formulation	• Is there a dose-response relationship between the dietary exposure to sweeteners and adverse effects in humans/experimental animals?
Systematic Literature Searches	• Systematic searches; from last SCF/EFSA opinion • Refinement if needed
Screening the studies for relevance	• Two steps: Ti/Ab, Full Text • Setting of inclusion/exclusion criteria
Evaluation of the Risk of Bias/Data extraction	• Adapted from the OHAT rating tool (NTP, 2019); 3 tiers • Modified from the EFSA BPA protocol, 2017
Weighing the body of evidence	• Modified version of the OHAT (NTP, 2019) and EFSA Guidance on WoE (2017) • Grouping animal/human studies on the same endpoint
Synthesis of the evidence and uncertainties	• EFSA Guidance on WoE, 2017 • EFSA Guidance on Uncertainties, 2018

Introduction of the cut-off date

- Clarification on downgrading and upgrading elements.
- Clarification on the integration of the human and animal evidence
- New section on the hazard characterisation and identification of a reference point
- Revision of uncertainties section

UPDATES TO THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

Systematic Literature Searches

- A *cut-off date* for the update of the literature search is established for each assessment.
  - This is a common practice in systematic review methodology, allowing for sufficient time to perform all the subsequent steps of evidence appraisal, synthesis and weighing.
  - *Studies published after the cut-off date are not considered in the assessment*

Weighing of the body of evidence

Synthesis of the evidence

- An *overview of the HOCs and associated endpoints or outcomes* assessed in previous opinions has been added.
- Clarifications on the *downgrading and upgrading elements* have been added
  - Downgrading elements: risk of bias, relevance, unexplained inconsistencies, imprecision
  - Upgrading elements: magnitude of effect, presence of dose-response, consistency across study designs/species/population, residual confounding (human studies only)

UPDATES TO THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

Integration of human and animal data

- Clarifications on the *integration of human and animal data* have been provided.
  - The integration process should be informed by the outcome of the WoE. Where appropriate, considerations of biological plausibility, mode of action and conclusions of previous evaluations will be taken into account.

Hazard characterisation and identification of a reference point

- A new section describing the hazard characterisation and reference point selection has been added.
  - Overview on the level of likelihood of an association between the sweetener intake and an adverse effect on health
  - Considerations on the HOCs for which a hazard has been identified as “likely” or “very likely”
  - Identification of a reference point and derivation of an ADI.

UPDATES TO THE PROTOCOL ON HAZARD IDENTIFICATION AND CHARACTERISATION OF SWEETENERS

Uncertainties

- The section has been revised to reflect the uncertainty analysis approach applied in the sweeteners assessment.
  - Identification and reporting of all sources of uncertainty
  - In more data-rich cases with more diverse sources of uncertainty qualitative characterisation of the direction of that uncertainty and/or a qualifier for the magnitude will be reported
- The uncertainty analysis for the exposure assessment is conducted separately.

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