Research in Food Safety

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The re-evaluation of sweeteners by the European Food Safety Authority (EFSA)

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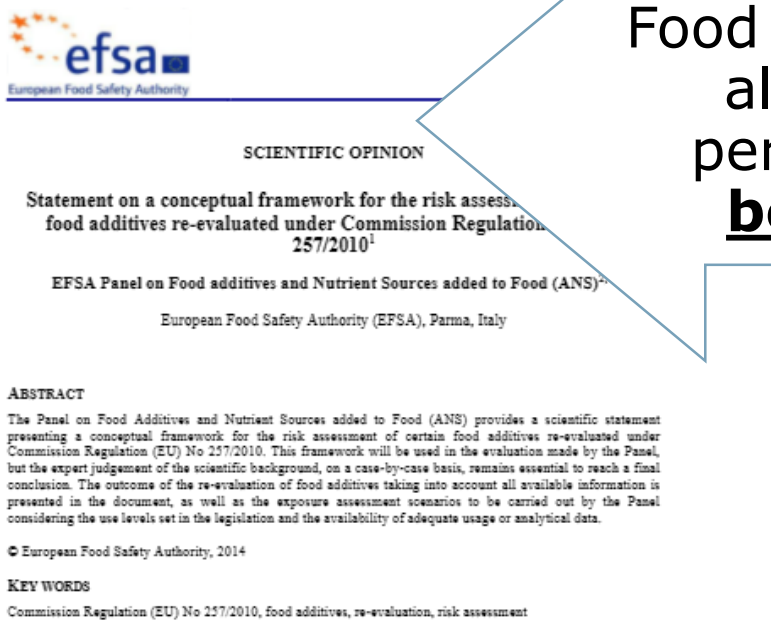
Outline of presentation

- Food additives re-evaluation
- Re-evaluation of sweeteners
- Protocol on hazard identification and characterisation
- Working Group Sweeteners

Re-evaluation *vs* New Application

Re-evaluation



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European Food Safety Authority

SCIENTIFIC OPINION

Statement on a conceptual framework for the risk assess… food additives re-evaluated under Commission Regulation… 257/2010[1]

EFSA Panel on Food additives and Nutrient Sources added to Food (ANS)[2]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The Panel on Food Additives and Nutrient Sources added to Food (ANS) provides a scientific statement presenting a conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010. This framework will be used in the evaluation made by the Panel, but the expert judgement of the scientific background, on a case-by-case basis, remains essential to reach a final conclusion. The outcome of the re-evaluation of food additives taking into account all available information is presented in the document, as well as the exposure assessment scenarios to be carried out by the Panel considering the use levels set in the legislation and the availability of adequate usage or analytical data.

KEY WORDS

Commission Regulation (EU) No 257/2010, food additives, re-evaluation, risk assessment

Food additives already permitted **before**

20 Jan 2009

Food additives authorised **after**

efsa

EFSA Journal 2012;10(7):2760

SCIENTIFIC OPINION

Guidance for submission for food additive evaluations[1]

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

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 16 August 2012, replaces the earlier version published on 18 July 2012.[4]

ABSTRACT

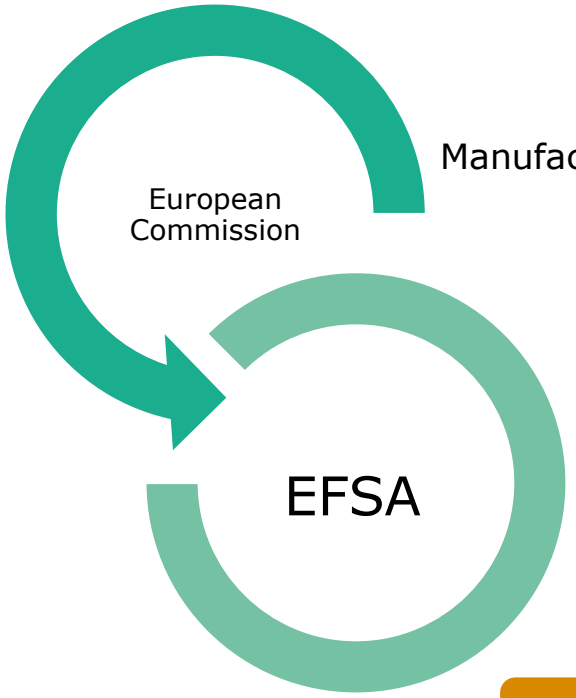
This guidance document refers to the applications for authorisation of a new food additive or to a modification of an already authorised food additive, combining in a single document the description of the data requirements and their context, and also a description of the risk assessment paradigm applied. The document is arranged in four main sections: chemistry and specifications, existing authorisations and evaluations, proposed uses and exp… assessment, and toxicological studies. Assessment of the exposure to food additives is based on info… on known or anticipated human exposure to the proposed additive or toxicologically relevant com… the additive from food, and any other potential dietary sources. For the toxicological studies, this guid… …s a tiered approach which balances data requirements against the risk, taking into con… welfare by adopting animal testing strategies in line with the 3-Rs (replacement, …his tiered approach for toxicological studies consists of 3 tiers, for which the testing …d triggers are described. According to this tiered approach, a minimal dataset …been developed under Tier 1, while Tier 2 testing, generating more extensive …ds which are absorbed and/or demonstrate (geno)toxicity in Tier 1 tests. Tier …case basis taking into consideration all the available data, to elucidate …ation of findings in Tier 2 tests. This guidance document replaces the …Committee for Food published in 2001.

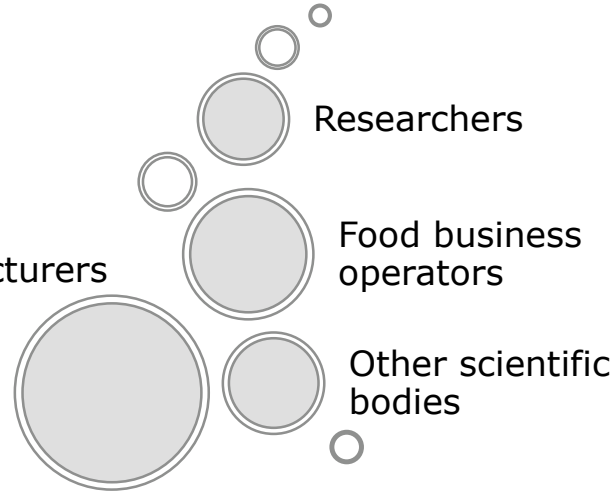
…ation, Tiered approach, Risk assessment, Toxicological studies

New applications

Re-evaluation *vs* New Application

Single mandate





Calls for data:
Technical, exposure, biological/toxicological

All available data

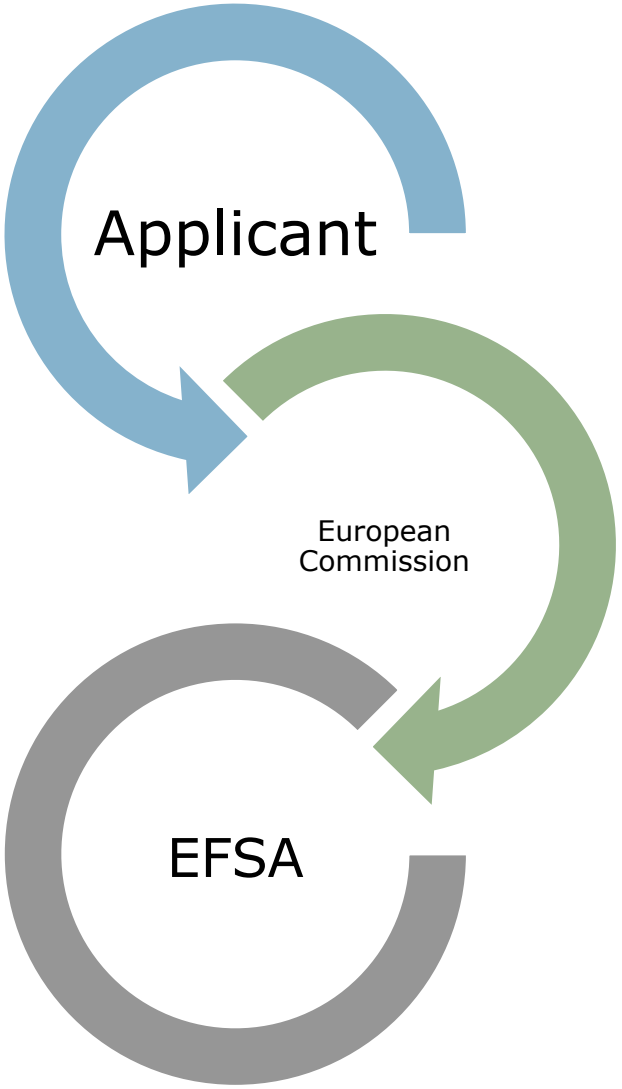
- Published literature
- Previous evaluations
- Unpublished reports

20 Jan 2009

Dossier

- Scientific information

9 months
(+ stop-the-clock) from receipt of a valid application



Scientific Assessment

Technical part

- Identity of the substance
- Specifications
- Analytical results
- Manufacturing process
- Methods of analysis in food
- Stability and fate in food

Questions

- What is the food additive?
- Are we talking about the same substance that it was assessed at the time of the initial authorisation?
- What are residuals/by products resulting from manufacturing process/storage/interaction with food?

HAZARD IDENTIFICATION

Scientific Assessment

Biological and toxicological data

- ADME (absorption, metabolism, distribution, excretion)
- Genotoxicity (in vitro, in vivo)
- General toxicity (short-term, sub-chronic, chronic, carcinogenicity)
- Reproductive toxicity
- Immunotoxicity
- Other studies

Questions

- What happen to the additive once it is ingested with the diet? Is it absorbed? To what is it metabolised?
- Are adverse effects identified from the available studies?
- If yes: can a dose response be identified?
- If no: true lack of effect or lack of data?
- Are the data available still reliable compared to today's standards?

HAZARD CHARACTERISATION

Re-evaluation of sweeteners: list of substances

- Sweeteners to be re-evaluated under Regulation (EC) No 257/2010

E Number	Food additive(s)		Substance
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 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 953	Isomalt		
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		
E 965	Maltitols	E 965(i) E 965(ii)	Maltitol Maltitol syrup
E 966	Lactitol		
E 967	Xylitol		
E 968	Erythritol		

Deadline:

by end December 2020

(a) Aspartame: re-evaluation already completed by EFSA in 2013

Re-evaluation of sweeteners: calls for data

- **Technical/Biological and toxicological data**: closed in June 2018
  - Procurement contract (ended June 2019): inventory and synthesis

- **Occurrence data**: Call for food additives usage level and/or concentration data in food and beverages intended for human consumption (Batch 7) closed in October 2018

- **2nd call for Technical data:** information on particle size and particle size distribution launched on 13 May 2019- deadline 13 September 2019

Re-evaluation sweeteners: new literature search

- New procurement contract: started on 28 October 2019

→to perform extensive literature searches in order to identify and retrieve all related information on both technical and biological/toxicological data on the 15 sweeteners, published after the last evaluation of the SCF or EFSA.

Re-evaluation of sweeteners: protocols for RA

- Background information:

As outlined in Regulation (EC) No 257/2010 on the re-evaluation of food additives, in the course of the re-evaluation procedure "*EFSA shall:*

a) examine the original opinion and the working documents of the Scientific Committee on Food ('SCF') or EFSA;

b) examine, where available, the original dossier;

c) examine the data submitted by the interested business operator(s) and/or any other interested party;

d) examine any data made available by the Commission and Member States;

e) identify any relevant literature published since the last evaluation of each food additive".

- Two protocols have been developed:
  - One framing the scope of the assessment from the general mandate from EC (for all steps of RA, except exposure)
  - One focussing on exposure assessment

Protocols for risk assessment

Principles and process illustrated in the EFSA PROMETHEUS project (PROmoting METHods for Evidence Use in Scientific assessments) (EFSA, 2015)

- Aim:

To define as much as possible beforehand the strategy applied for collecting and selecting data, appraising the relevant evidence, and analysing and integrating the evidence in order to draw conclusions that will form the basis for the scientific opinions.

- Iterative/ Planning phase

✓ **Impartiality & methodological rigour along the process**

Re-evaluation of sweeteners: target population

- General European population: the following age groups will be considered a priori:

  - Infant below 16 weeks of age, only for Mannitol (E 421), which is the only sweetener permitted in foods for infants and young children, as a carrier for vitamin B12
  - Infants ≥ 4 to < 12 months
  - Toddlers (young children) ≥ 1 to < 3 years
  - Other children ≥ 3 to < 10 years
  - Adolescents ≥ 10 to < 18 years
  - Adults ≥ 18 to < 65 years
  - Elderly adults ≥ 65 years

- Sub-populations with anticipated high levels of intake (i.e. diabetics) and sub-population with distinct vulnerabilities to the intake of sweeteners (e.g. individuals with inborn errors of phenylalanine metabolism) will be considered during the assessment.

Protocol for assessment of hazard identification and characterisation of sweeteners

- Sub-questions to be addressed in the 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?

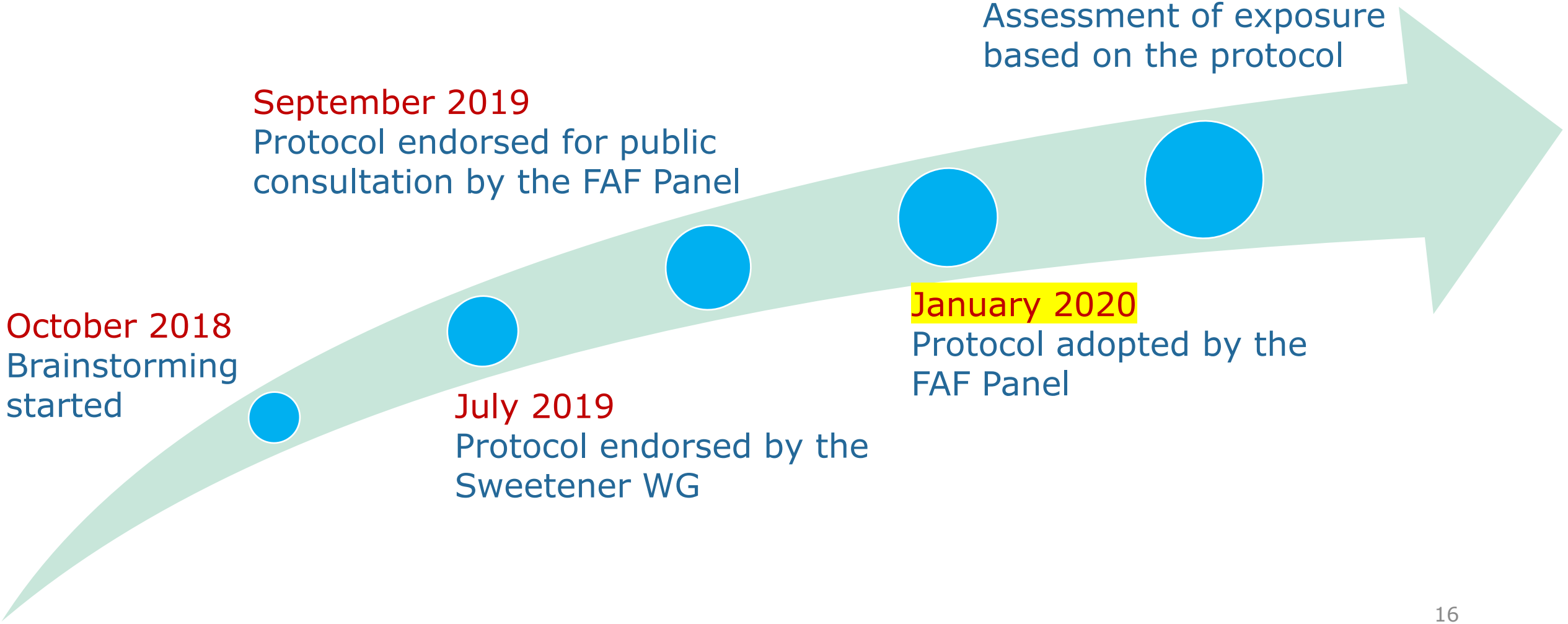
1 (a-d), 2 and 4 (ADME, genotoxicity, MoA): narrative approach
3 (a, b) (animal and human studies): systematic review

Protocol for assessment of hazard identification characterisation of sweeteners

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 • Refinment 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, 2015); 3 tiers • Modified from the EFSA BPA protocol, 2017
Weighing the body of evidence	• Modified version of the OHAT (NTP, 2015) 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

Steps and timeline: protocol for assessment of hazard identification and characterisation of sweeteners

Steps and timeline: protocol on exposure assessment



Re-evaluation of sweeteners

Impartiality and Methodological rigour along the process

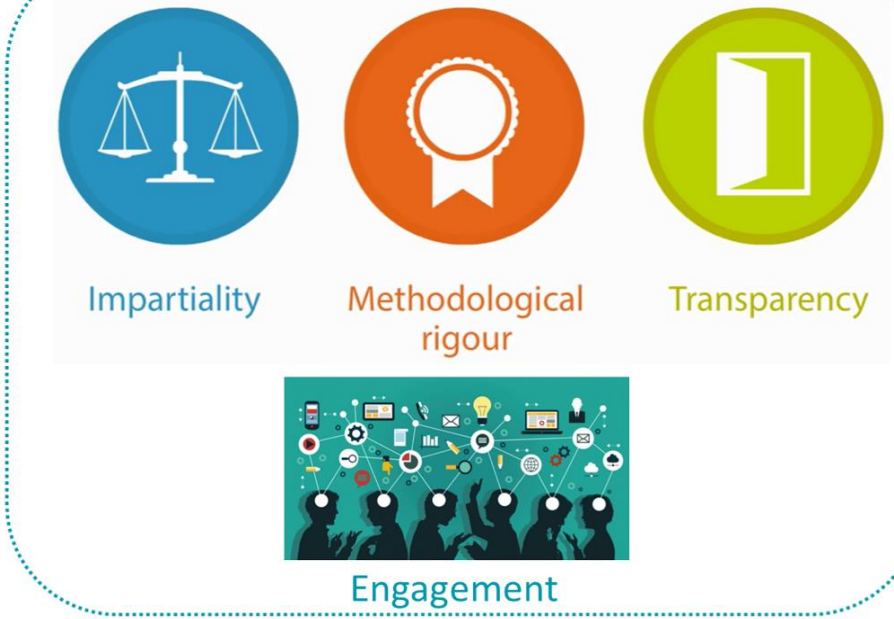
- Plan ahead: protocol development
- Systematic review process

Engagement and transparency along the process

- Open FAF Plenary (26-28 March, 2019)
- Public consultations (2nd part 2019)
- Stakeholder event: food additive re-evaluation with focus on sweeteners, Paris, 3 December 2019:

https://www.efsa.europa.eu/en/events/event/technical-stakeholder-event-re-evaluation-authorised-food-additives

PRINCIPLES
for the scientific assessment process



Re-evaluation of sweeteners: current way of working

- Current organisation of Working Group on sweeteners:
  - *Sub-group for overall strategy for the assessment*
  - *Sub-group for technical part*
  - *Sub-group for exposure assessment*
- Interaction between the three subgroups

Implementation of protocol: future way of working

✓Working Group Sweeteners enlargement

- Will evolve in a fully multidisciplinary WG with all areas of expertise:
  - Chemistry
  - Exposure,
  - Subchronic/chronic toxicity, genotoxicity, reproductive/developmental toxicity, general toxicology, epidemiology, etc….
- Engage with Art.36 organizations (but not only): attract experts to be part of this WG, according to their expertise

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