Scientific Committee ongoing work-programme 2025-2027 for cross-cutting guidance development

This document summarises the ongoing work-programme of the Scientific Committee, providing the link to the published mandates. It also presents the latest topics recently included in the work-programme for the development of new cross-cutting guidance documents.

The present work-programme covers the years 2025 until 2027. Towards the end of 2026, a new consultation with Panels and Units will be initiated to gather ideas to be discussed to be possibly included the work-programme 2027-2029.

Title of the guidance	Mandate number with link to OPEN EFSA	Comments
Guidance on the use of biomarkers of effect in regulatory risk assessment of chemicals	M-2023-00097	New cross-cutting guidance
Guidance on critical appraisal of evidence as part of the systematic review methodology	M-2024-00115	New cross-cutting guidance
Guidance on selected default values to be used by the EFSA Scientific Committee, Panels and Units in the absence of actual measured data	M-2024-00067	Guidance revision
Guidance on the use of the Margin of Exposure approach for chemicals which are both genotoxic and carcinogenic	M-2023-00167	Guidance revision
Guidance documents for risk assessment of nanomaterials and materials containing nanoparticles in the food chain	M-2024-00062	Guidance revision

Guidance on genotoxicity assessment in the food and feed chain	M-2024-00152	Guidance revision

New guidance to be developed, included in the Scientific Committee work-programme 2026-2027

1- **Guidance on the establishment/application of relative potency factors** (RPFs).

Consumers are exposed daily to a wide mix of chemicals originating from various sources. However, the safety of chemicals in the EU is often assessed through the evaluation of single substances and of mixtures intentionally added for particular uses, but it is to an increasing degree considering the combined exposure to mixtures of structurally related chemicals, e.g., analogues, modified forms, congeners. Relative potencies of these compounds may be very different.

Relative Potency Factors (RPF) have been established in a number of Opinions of the Panel on Contaminants (CONTAM panel), whereas in some other, the data were insufficient/not robust enough to derive RPFs. For dioxins and Dioxin-Like Polychlorinated Biphenyls (DL-PCBs), criteria for deriving RPFs have been developed by WHO to set toxic equivalency factors (TEFs) for these compounds.

The CONTAM panel identified the need to develop guidance and harmonised criteria for deriving RPFs across EFSA Panels. Such criteria should take into account elements such as: the type and quality of the studies to be used, structural similarity, persistence, similarity in mode of action and observed effects, toxicokinetic data, dose-response modelling, etc.

The Scientific Committee discussed this proposal in 2025 and agreed to include it in its work-programme. The activity will be probably initiated in the end of 2025 or beginning of 2026. A scoping paper will be drafted to describe the background and the reasoning to undertake the activity, including also draft terms of reference. A public consultation will be launched on the scoping paper to gather feedback from different stakeholders. Comments will be considered before initiating the development of the guidance. Another public consultation is foreseen on the draft guidance before finalization.

2- **Guidance defining a tiered approach for an ADME (Absorption, Distribution, Metabolism and Excretion) testing strategy and on the use of kinetic data and qualification/validation of Physiologically based kinetic (PBK) models in human and environmental risk assessment.**

Physiologically-based models (PBK) include biologically realistic descriptions of processes involved in the absorption, distribution, metabolism, and excretion (ADME) of a compound.

Such models have been applied in the derivation of Health Based Guidance Values (HBGV) for humans in EFSA Opinions.

PBK models can have a significant role in the derivation of HBGVs and impact on the outcome of a chemical risk assessment. For chemicals for which data are unavailable, PBK models can be used in combination with quantitative structure-activity relationship (QSAR) approaches, read-across, and in vitro data, to predict toxicity, allowing assessment of safety/risk of the chemical. Models for quantitative *in vitro* to *in vivo* extrapolations (QIVIVE) have also been developed and coupled to PBK models to make use of *in vitro* data and New Approach Methodologies (NAMs) in risk assessment. As NAMs are increasingly used in risk assessment across EFSA panels, there is a necessity for harmonized QIVIVE methodologies. It is important that the predictive values of such models are assessed/qualified/validated as much as possible with regard to the robustness of the models.

The Scientific Committee discussed and agreed to include the development of this guidance in the ongoing work programme. The activity will be probably initiated in the end of 2025 or beginning of 2026. A scoping paper will be drafted to describe the background and the reasoning to undertake the activity, including also draft terms of reference. A public consultation will be launched on the scoping paper to gather feedback from different stakeholders. Comments will be considered before initiating the development of the guidance. Another public consultation is foreseen on the draft guidance before finalization.

Revision of existing guidance in the process to be initiated

1- Revision and merging of guidance on the weight of evidence approach in scientific assessment and guidance on the assessment of biological relevance of data in scientific assessment.

The cross cutting guidance for the use of Weight of Evidence in scientific assessment (link here) and the guidance on the assessment of Biological Relevance of data in scientific assessment (link here) were both published in 2017. The aim was to provide guiding principles for improved risk assessments by using harmonised, systematic, consistent and transparent methodologies. Weight of Evidence, Biological Relevance together with the Uncertainty assessment were the three priority areas identified of such methodology needs.
EFSA's 2017 Weight of Evidence guidance shares key elements with similar guidance documents developed by other organisations and agencies, including ECHA, US EPA, ANSES (2016), OECD (2019), EU SCHEENIR and SCHEER.
A key aspect of the Weight of Evidence process pertains to the assessment of the relevance of the available evidence together with assessment of the reliability and consistency of the evidence. Assessment of the relevance of evidence in this process results in substantial overlap with the guidance on Biological Relevance. In addition, several standard elements in the guidance on Biological Relevance overlap with the respective elements in the Weight of Evidence guidance.

Possibility to develop one single guidance document is under discussion. This guidance will incorporate the evaluation of Biological Relevance into the assessment of overall

relevance of the evidence in the Weight of Evidence process. Considering inter-dependencies of the evidence assessment processes, cross-reference will be made to other EFSA guidance for standard aspects of the risk assessment process, such as protocol development and systematic literature review, to avoid redundancy.
The new guidance will include consideration of and coherent and consistent integration in risk assessment of evidence from alternative data sources, such as read-across, use of biomarkers of effect, NAMs data and toxicokinetics, along with or in the absence of traditional sources of evidence used to identify a critical effect.

A scoping document is in preparation to describe the background and the reasoning to undertake the activity, including also draft terms of reference. It will be published for public consultation in autumn 2025 and comments received will be considered to refine the terms of reference of the mandate. Work will be initiated in the beginning of 2026, with a tentative deadline by the end of 2027 for the revised-merged guidance to be published.

2. Revision of the guidance for the safety assessment of botanicals and botanical preparations.

The cross-cutting guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements (EFSA 2009) provides indications on the scientific data needed to carry out a safety assessments of a botanical or a botanical preparation. It also proposes a two-tiered scientific approach for the safety assessment depending on the available knowledge on a given botanical and the substance(s) it contains. The guidance also provides a set of criteria to help prioritise the safety assessment of botanical ingredients which are in use.

In addition to the guidance, EFSA has compiled the available information on a large number of botanicals which have been reported to contain substances that may be of health concern. The resulting compendium, which has been recently updated (link to the database here), is intended to assist manufacturers and food safety authorities by highlighting possible safety issues which may require further consideration. The Compendium of Botanicals is an open-source database used to facilitate the hazard identification of plant-derived substances of potential concern. The new version of the database contains information obtained from an extensive literature for approximately 2,700 plant species and 1,500 naturally occurring substances of potential concern.

Revision of the guidance on botanicals published in 2009 has been identified as a priority in order to consider new development in the area, and to provide more indication for the assessment of botanicals not only as food supplements, but also in other areas like flavourings and feed additives.

A mandate is in preparation and will be finalised in autumn 2025. Work will be initiated in the beginning of 2026, with a tentative deadline by the end of 2027 for the revised guidance to be published.