SCIENTIFIC COMMITTEE
122nd Plenary meeting – OPEN to observers

21 - 22 November 2024
9:00-17:45 / 09:00-16:30
MINUTES - Agreed on 22 January 2025

Location: EFSA, Parma

Attendees:

- **Panel Members:**
  Susanne HOUGAARD BENNEKOU, Ana ALLENDE, Josep CASACUBERTA, Laurence CASTLE, Tamara COJA, Amélie CREPET, Thorhallur HALLDORSSON, Chris HOGSTRAND (vice-chair CONTAM Panel), Ron HOOGENBOOM, Kostas KOUTSOUMANIS, Claude LAMBRÉ, Søren SAXMOSE NIELSEN, Dominique TURCK, Laurence VERNIS (vice-chair FEZ Panel), Antonio VICENT CIVERA
- **Hearing Experts[1]:**
  Diane Benford (for item 6.1), Baltasar Mayo (for item 6.5) Martin Wilks (for item 7.1); Jean-Charles Leblanc (for item 6.3)
- European Commission and/or Member States representatives:
  Athanasis RAIKOS and Eleni GKANA – DG SANTE E1(online); Veerle VANHEUSDEN- DG SANTE E2 (online for item 6.1 and 6.3); Domenico DESERIO (online) DG SANTE E4 (for item 6.5).
- **EFSA:**
  Executive Director: Bernhard Url (day 1 until coffee beak)

  Head of Risk Assessment Services Department (ENABLE): Nick Kriz

  Head of Risk Assessment Production Department (ASSESS): Guilhem de Seze

  Head of Communication and Partnership Department (ENGAGE): Barbara Gallani (for item 6.4)

  Chief Scientist: Carlos das Neves

  Methodology and Scientific support Unit (MESE): Claudia Roncancio Pena, Daniela Maurici, Maria Bastaki, Irene Cattaneo, Lucian Farcal, Marios Georgiadis, Petra Gergelova, Sara Levorato, Alexis Nathanail, Laura Martino, Alicia Paini, Francesca Riolo

  Feed and Contaminants Unit (FEEDCO): Montserrat Anguita Freixa

  Nutrition and Food Innovation Unit (NIF): Agnès De Sesmaisons

  Pesticides Peer Review Unit (PREV): Arianna Chiusolo

1. Welcome and apologies for absence

The Chair welcomed the participants and the observers.
Apologies were received from Holger Zorn, replaced by Laurence VERNIS (vice-chair Food Enzymes Panel FEZ) and from Helle KNUTSEN, replaced by Chris Hogstrand (vice-chair Contaminants in the Food Chain Panel CONTAM)

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Panel members

[1] As defined in Article 34 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management,[3] EFSA screened the Annual Declarations of Interest filled out by the Scientific Committee (SC) members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

Certain interests were declared orally by Thor Halldorsson, vice-chair of the SC, before the beginning of the meeting. For further details on the outcome of the screening of the Oral Declaration of Interest made at the beginning of the meeting, please refer to the Annex II.

4. Tour de table of SC members and EFSA staff present in the room

The SC members and the EFSA management introduce themselves for the benefit of the observers.

5. Presentation of Guidelines for observers

The observers were reminded about the code of conduct before, during and after open plenary meetings. The Chair may grant observers the opportunity to ask questions either after they have observed a discussion on a given topic or at the end of the open plenary meeting, on other topics which fall within the remit of the Committee. If members of the SC are unable to answer questions from observers during the meeting, they may resubmit their questions to EFSA through the #AskEFSA service on the EFSA website.

6. Scientific output(s) submitted for discussion/adoption

6.1 Draft opinion on bromide (EFSA-Q-2022-00329)

The SC was presented with the draft opinion on the risks to human and animal health from the presence of bromide in food and feed. The Terms of reference (ToR) of the mandate received from the European Commission (M-2022-00105) included the assessment of: a) the toxicity of bromide to humans and animals, and establishing of toxicological reference values; b) risk to animals related to the presence of bromide ion in feed, in particular in algae and seaweed and derived products; c) transfer of bromide from feed to food of animal origin; d) comparison of current Maximum Residue Limits (MRLs) to occurrence data and screening of MRLs safety compared to reference values established. The mandate did not request a human exposure assessment or human risk assessment. The assessment of MRLs safety is atypical for exposure assessments. The draft scientific opinion was endorsed for public consultation at the 119th SC plenary in June 2024. The public consultation closed on 6 September 2024 and the comments received were addressed by the Working Group Bromide with text revisions as appropriate.

Thyroid effects were considered the relevant health effect of bromide on which a Tolerable Daily Intake (TDI) and an Acute Reference Dose (ARfD) were established for humans and maximum safe concentrations in feed were established for food producing and non-food producing animal species. Besides the published literature, evidence reviewed by ECHA in the context of biocides was obtained through interagency collaboration under the one-substance-one-assessment framework. The WG also engaged with experts of the WG on Endocrine Disrupters for assistance in the interpretation of the evidence on the thyroid. A high-level screening of the MRLs instead of

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

a standard dietary exposure assessment was performed according to the ToR. The outcome was compared to the TDI and the ARfD. An additional screening was performed using available monitoring data in place of MRL values. Exceedances of the TDI and ARfD were noted for a few foods and were lower in the latter screening approach compared to the MRL screening. Recommendations were provided for generating relevant data to fill the data gaps identified, including bromide concentrations in drinking water and potentially major contributing foods, such as seafood. Dietary exposure assessment and risk characterisation for food producing and non-food producing animals was not feasible due to lack of sufficient concentration data in feed materials and water for drinking.

The major comments received from the public consultation were related to the benchmark dose modelling approach; the communication of the outcome of the uncertainty analysis; and the rationale for the selection of critical endpoint. Other comments were related to data on bromide occurrence in some food categories; lack of data in fish; and contribution of coffee and tea to the total intake. The technical report of the public consultation was also made available to the SC for information.

The SC adopted the scientific opinion for publication, subject to minor clarifications. The opinion will be published in the beginning of January 2025.

6.2 Draft scientific report on the use of biomarkers of effect in risk assessment EFSA-Q-2024-00128

The SC was presented with the final version of the Scientific Report on the conceptual basis to develop a guidance on the use of biomarkers of effect in risk assessment of chemicals. The project was initiated in 2023 as a self-task mandate (M-2023-00097) of the SC. The main goal of this initial effort was to build a basis and a recommended path to explore the possibility to develop guidance on how to use biomarkers of effect in risk assessment. The work also included the mapping of topic-relevant resources (e.g. projects, publications) and activities in the area.

Several collaboration and engagement activities were established during the development of the Scientific Report (e.g. surveys, workshops, public consultation, bilateral meetings, and participation to different events) that supported the process.

The presentation also contained an overview of Phase 2 plans, especially the development of a draft guidance in collaboration with other organisations (e.g. EU Agencies, MSs, non-EU and international organisations) at varying levels of involvement (e.g. coordination, adoption, drafting, consultation).

The SC provided comments on the draft. The use of biomarkers of effect for the assessment of chemical mixtures and uncertainty factors were also acknowledged as challenges for the guidance. Finally, further clarifications were requested on the expected outputs of Phase 2.

Following the presentation and discussion, the SC endorsed the Scientific Report that will be published in December.

6.3 Draft opinion on fluoride EFSA-Q-2021-00358

The draft opinion on the updated consumer risk assessment of Fluoride in food and drinking water including contributions from other sources of exposure was presented to the SC for possible endorsement for public consultation. Following the discussion held at the last SC Plenary, revised sections on the weight of evidence, selection of the critical endpoints, derivation of reference points, establishment of reference values, and risk characterisation were presented, highlighting changes and clarifications made in response to previous SC comments.

The SC endorsed the draft opinion for public consultation conditional upon specific text modifications to improve clarity, consistency, and transparency. The public consultation will be launched in the beginning of December for 8 weeks, remaining opened until the beginning of February 2025.

6.4 Strategic role of the Scientific Committee

The SC was provided with a presentation from Carlos Das Neves, EFSA chief scientist, on the strategic role of the SC for EFSA.

The majority of the global changes that are taking place at present have links with the food safety. These are, among others, climate changes, loss in biodiversity, depletion of natural resources, etc. In this world of rapid change, the system we have in place to assess the risks in the food chain is probably no longer fit for purpose and we need to find a way to better address the challenges ahead of us.

EFSA performs risk assessment which should be of scientific excellence, transparent, actionable and to be produced as soon as possible. There are difficulties as for example there is sometimes limited data or limited accessibility to data which brings uncertainties in our risk assessment; the complexity of the assessments is also increasing due to the multidisciplinary implications. The "food safety ecosystem" would imply a very good collaboration among all the different actors (risk managers, research scientists, policy makers, risk assessors, EU institutions etc) for the health protection of the EU citizens.

Proposals to improve the risk assessment paradigm and to produce risk assessment that is more fit for purpose and at the forefront in Europe have been presented and are summarised below. In all of them, the strategic role of the SC would be essential:

- Strategic work on guidance documents and on structure of scientific opinions. It is important to develop guidance documents that are more fit for purpose, that can help applicants to submit dossiers of good quality and assessors to produce risk assessment that is actionable for risk managers. Consideration to improve the structure of EFSA's opinions in relation to length and readability, also making use of new tools for their development is important for EFSA to be at the forefront in its area of work;
- Strategic foresight: to analyse signals of emerging risks or threats identified for example by the stakeholders platform for the identification of emerging risks. More consideration of innovative tools is another topic to be addressed, to be prepared for future challenges;
- Strategic preparedness: considering results of the roadmaps that have been developed to address gaps in areas which are key for EFSA's future risk assessment (e.g. roadmap on OMICS, NAMS, microbiome). This is important also in the view of the launching of the new research framework programme of the Commission, the FP 10, that will start in 2028.

The SC welcomed the presentation and proposed to have a closer look into each of the topic, providing enough time for a meaningful discussion. Consideration of changing the way of working has been also discussed and some proposals were put forward that will be further addressed. The SC agreed to plan more time to discuss its strategic role in future plenary meetings.

6.5 Draft Guidance on the characterisation of microorganisms in support of the risk assessment of products used in the food chain (EFSA-Q-2024-00438)

The SC was presented with a draft guidance on the characterisation of microorganisms used in the food chain. The draft document has been prepared by the FEEDAP Panel WG on microbiology and was subject to the endorsement of eight EFSA Scientific Panels[4]

The guidance focuses on the requirements to characterise the microorganisms and, to some extent, their products. It provides the basis for the risk assessment of microorganisms intentionally used in the food chain. In particular, it establishes the requirements to: i) taxonomically identify the microorganism, ii) investigate the presence of genes of concern involved in resistance to antimicrobials, production of antimicrobials of therapeutical interest, and the virulence potential of the microorganism, iii) establish the presence of viable cells of the microorganism, genetic material and/or substances of concern that may remain in the product made from or produced with the microorganism, and iv) conduct the environmental risk assessment and study the impact of products containing living microorganisms and products made from microorganisms, genetically modified or not, on the gut and food/feed microbiome. The guidance covers bacteria, yeasts, filamentous fungi, microalgae and other protists, and viruses (including bacteriophages and their host strains), genetically modified or not.

The document was presented to the SC and some discussion took place. The SC endorsed the document for public consultation5.

7. Feedback from the Scientific Committee/ Scientific Panels/EFSA/ EC

7.1 Overview of the Plant Protection Products and their Residues (PPR) panel work-program and update on the opinion on the use of historical control data

An overview of the work-programme (Nov 2023-Nov 2024) of the PPR panel was provided to the SC. Summary information was presented on the ongoing and finalised mandates for both generic requests or in support of the peer review of pesticides or dietary cumulative risk assessment.

The SC was updated on the PPR mandate for the development of the opinion on the use and reporting of historical control data (HCD) in regulatory studies. Setting of criteria and methodology for the collation, evaluation and use of HCD is an urgent need for the Pesticides regulated area (HCD submission is a data requirement), however the horizontal nature of the topic was also acknowledged. The draft opinion was published for public consultation until the 29th April 2024 and it is currently under revision considering the comments received. Feedback from testing the methodology with Pesticides data (through ongoing outsourcing) is also considered to develop the final draft that will be considered for possible adoption in June 2025.

7.2 Overview of the Food Contact Materials (FCM) panel work-program

The FCM Panel, its origin and the activities of its five Working Groups (on FCM substances, Recycling Plastics, Re-evaluation of phthalates, structurally similar substances and replacement substances, Extraction solvents, and the Evaluation of substances used to reduce microbial contamination from products of animal origin) were presented to the SC.

[4] Document endorsed by BIOHAZ, CONTAM, FAF, FCM, FEEDAP, FEZ, GMO and NDA EFSA Panels.
[5] Publication date 2 December 2024, available HERE.

- Summary information were presented on the ongoing and finalised mandates for both applications and generic mandates. A specific update was provided for the mandate on the re-evaluation of styrene considering that the final opinion may have an impact on other EFSA's ongoing assessments (Flavourings, Contaminants); on the technical report indicating the need to re-evaluate the safety of hexane as an extraction solvent. Some of the expected challenges and mandates for the future were also presented, such as the future aassessment of natural compounds to be used in FCM, of materials other than plastics as FCM, the revision of the FCM Regulation and drafting of the related FCM guidance, the assessment of novel recycling technologies, and a shared mandate with ECHA requesting consolidation and assessment of exposure related data on substances used as plasticisers.

7.3 Draft scoping paper for the revision of the guidance on genotoxicity testing strategies

The SC has agreed to revise the Scientific Opinion on genotoxicity testing strategies applicable to food and feed safety assessment (EFSA Opinion, 2011) and the additional follow-up guidance documents used by EFSA and relevant stakeholders, namely the 2017 opinion 'Clarification of some aspects related to genotoxicity assessment', the guidance on the 'Genotoxicity assessment of chemical mixtures' published in 2019, the 'Guidance on aneugenicity assessment' published in 2021 and in the end the technical report 'Harmonised approach for reporting reliability and relevance of genotoxicity studies' published in 2023.

The aim of the revision is to produce a single guidance document, considering the state-of-the-art methods and approaches in the area of genotoxicity assessment. EFSA is interested to implement a transparent process by reaching out to relevant stakeholders to provide feedback on the proposed revision, outlined in a scoping paper drafted by experts of the cross-cutting WG on Genotoxicity. The scoping paper includes background information on EFSA's genotoxicity framework, the proposed areas of revision, as well as the work plan and tentative timelines, and was presented at this open SC plenary meeting for discussion and endorsement. For the preparation of the scoping paper, feedback was also gathered from relevant Units and Panels dealing with genotoxicity assessments.

The purpose of the SC discussion was to receive feedback on the scoping paper and potentially an endorsement for Public Consultation in order to refine and finalise the terms of reference for the guidance revision.

The scoping paper was endorsed by the SC for Public Consultation that will be launched in the beginning of December and will run for 6 weeks. During the Public Consultation stakeholders will be invited to provide comments related to:

1. The proposed areas of revision of existing guidance documents on genotoxicity assessment
2. The work plan proposed
3. Engagement activities

7.4 Discussion on Terms of Reference for the revision of the guidance on the Margin of Exposure approach

The Terms of Reference (ToR) for the revision of the opinion on an "Harmonised approach for the risk assessment of substances that are both genotoxic and carcinogenic", (related to the Margin of Exposure (MoE) approach) published by EFSA in 2005 (link here) were presented. The presentation included reflections and feedback collected from the EFSA units and the outcome from the preparatory meeting with SC members (See 10.1). This resulted in the following proposed ToR:

- ToR.1. Draft SC statement providing the definitions of MoE and Margin of Safety (MoS), clarifying which definitions EFSA and other EU/international agencies use, and providing general principles as introduction to the MoE/MoS approach.
- ToR.2. Revision of the 2005 opinion as guidance for substances that have both genotoxic and carcinogenic properties, following the areas of revision proposed.
- ToR.3. Guidance on the Margin of Exposure for chemicals with other modes of action/endpoints, excluding those that are both genotoxic and carcinogenic, in collaboration with Default Values working group mandate M-2024-00067.

After a brief discussion on the ToR and clarifications and encouragement to work closely with the working group revising the guidance on Default Values to be used in risk assessment in the absence of actual data (EFSA Journal 2012, available here) and the Working Group on the use of the Benchmark Dose (BMD), the ToR were endorsed by the SC. The discussed topics included:

- importance of defining the MoE and MoS in EFSA's work and clarifying which definitions are used by other EU/international agencies,
- clarification on the cut-off at 10,000 for substances with both genotoxic and carcinogenic properties,
- low dose extrapolation with BMD modelling,
- terminology regarding "low concern",
- combined Margin of Exposure (MOET), and
- use of MoE for chemicals with other modes of action/endpoints.

7.5 Feedback from panel consultation on the draft read across guidance

The SC was provided with an update on the draft "Guidance on the use of read-across in food safety assessment" (EFSA-Q-2020-00413). The collaboration efforts related to dissemination as well as the comments received during the targeted consultation were briefly described. The consultation was addressed to EFSA Units and Panels, but also to sister agengies and international organisations (e.g. EChA, EC-JRC, OECD). More than 600 comments were received that included scientific and technical clarifications, editorial changes and some general comments or suggestions. These are now being incorporated where appropriate into the draft guidance, with the aim to present and discuss the updated version for endorsement for public consultation, during the next SC plenary in February 2025.

The SC was also informed of a workshop planned on this topic (estimated to be organised at the end of March 2025), aligned with the public consultation.

7.6 Consultation on the possible topics for guidance development to build the SC work-program 2026-2027

The Units and the Panels were consulted on possible topics to be included in the draft SC work-programme for 2026-2027. Proposals were received from the FAF Panel, FEZ Panel and the NDA Panel. The PPR Panel will submit its proposal in December.
Member States will also be consulted on possible topics to be included in the SC work-programme and an updated list will be shared with the European Commission for final comments before agreeing on prioritisation of topics to be included in the SC work-programme until 2027. As usual, the list will be revised at the end of the year for possible amendements. More disucssion will take place at the next meeting.

8. Questions from and answers to Observers (in application of the guidelines for Observers)

Questions from observers submitted at the time of the registration to the meeting and answers from EFSA

Few questions were received upon registration:

Q1: *Update on assessments for recycled polyolefins & food contact*

A1: EFSA has not received any mandates for the assessment of recycling technologies for polyolefins for the manufacture of food contact materials and articles. If such a mandate is received, a guidance document will be developed by EFSA to set the scientific criteria necessary to support the risk assessment process.

Q2: *For complex foods (e.g., spirulina powder, chlorella powder) that are not soluble and biological substances that may contain fractions of small particles below < 250 nm, what are EFSA's specific safety concerns?*

A2: As detailed in the 2021 EFSA Nano Guidance documents, nanoparticles (including small particles <250nm that may retain properties characteristics of the nanoscale) may have different toxicokinetic and toxicodynamic properties than their non-nano counterpart, and therefore they might need a specific assessment.
It should be considered that the EFSA Guidance on Particle (available here) proposes several appraisal routes to assess if a nano-specific assessment is needed, or to confirm that a conventional risk assessment approach is sufficient.

Q3: *To confirm the metabolites produced by microbial species using whole genome sequencing results, we need to use bioinformatics tools. Is it sufficient for us to use the gene clusters that encode metabolites from available databases such as MIBiG and NCBI?*

A3: The search of genes coding for known virulence factors (e.g. toxins, invasion and adhesion factors) and/or to identify the presence of known metabolic pathways involved in toxigenicity or production of clinically relevant antimicrobials should be done by comparison of the Whole Genome Sequencing (WGS) against specific up-to-date databases. The choice of the databases will depend on the metabolites the requestor refers to. EFSA will be in the position to know if the data is sufficient once the information is submitted and assessed.

Q4: *I would like to know if the future trend in food contact materials (FCMs) are positive/negative lists like it is now or entirely different concept is in preparation*.

A4: The decision on the approaches to apply in the management of food contact materials authorisations is within the remit of the European Commission not of EFSA. The Commission is currently working on a revision of the FCM Regulation; therefore, changes can be expected. For a better and more detailed information on this subject, it would be better to address directly the Commission.

Q5: *How is the Committee involved in the Commission's roadmap to transition to animal-free regulatory systems? There are immediate steps that can be taken to reduce animal testing that are aligned with EFSA Strategy 2027. This includes updates and/or new guidance for several endpoints, for example, acute dermal toxicity, eye irritation, skin sensitization, and the oral 90-day dog study. What have been the developments in these areas (e.g., when will waivers for the 90-day dog study be accepted)?*

A5: EFSA Staff from a range of units are involved in the preparation of the EC road map and are members of the change management, human health and environmental risk assessment working groups. EFSA's contribution particularly focuses on reviewing data requirements across jurisdictions within its remit to identify potential alternatives to animal testing as short term, mid-term and more long-term solutions. In addition, EFSA is also working with EChA and EMA to identify common endpoints in data requirements and alternatives to harmonise the formulation of recommendations and RA approaches as much as possible.

There is an ongoing EFSA working group, dealing with the preparation of a Scientific Opinion of the PREV Unit, to assess the possibility of phasing out dog studies as a data requirement in the authorization process of pesticides. This scientific opinion will include a retrospective analysis on the impact of dog studies and will propose a decision scheme for the exclusion of the dog.

***Q6**: Regarding the terms of reference of the mandate for the update of the risk assessment of fluoride, specifically the exposure assessment which includes contribution from other known sources of exposure, how were these other known sources (for example toothpastes) calculated? Were other experts such as the Scientific Committee on Consumer Safety consulted?*

A6: There is extensive description in the Methods section for the calculation of sources of exposures.
The method used for assessing fluoride exposure from non-dietary sources are described in detail in sections 2.2.3, 2.3.8 and 3.9.3 of the draft opinion.
For toothpaste, the amount of fluoride ingested was calculated using four variables:

- the fluoride concentration of toothpaste,
- the amount of toothpaste used,
- the daily frequency of tooth brushing and
- the amount ingested after brushing and rinsing the teeth.

Values used for these variables were extracted from relevant literature and calculations are described in Section 3.9.3. A hearing expert was also interviewed when discussing this part

Questions submitted during the meeting and answers from EFSA:

Q1: Regarding the guidance on microorganisms (agenda point 6.5)

In the previous version of the guidance, in vitro cytotoxicity test with VERO cells was recommended for bacillus strains. Are these cells also suitable for testing other microorganisms? The test indicator strains are limited to ATCC strains or other well documented in house strains are in as well? Then for other species, the phenotypic test for toxigenicity will be? If there are gene clustered identified involved in the toxigenicity with WGS, the guidance referred to phenotypic test, what phenotypic test is here? For MIC test and antimicrobial production analysis, ATCC strains are mentioned as examples?

A1: The guidance provides examples of strains (e.g. ATCC strains) that can be used to study the capacity of the strain under assessment to produce antimicrobial substances. Other well-documented strains from the literature can also be used. The applicants should provide the rationale for their choice. If in-house strains are being used, the suitability of the collection to demonstrate the susceptibility of the strains to several antimicrobial classes should be documented and reported.

For bacteria, the whole genome sequence data should be analysed for the presence of coding for known virulence factors; further phenotypic testing may be needed in those cases. For certain taxonomic units (e.g., Bacillus) for which safety can be established by specific tests like the one mentioned in the question, there is no need to conduct the search of the WGS for known virulence factors.

Q2: *Can you disclose the timelines for the public consultation?*

A2: The public consultation will be open until the 7th of February 2025, available HERE

Q3: *This question refers to the EFSA statement on the requirements for whole genome sequence analysis of microorganisms intentionally used in the food chain. The statement mentioning the ANI values "usually reaching >94%" is ambiguous. It is unclear whether this threshold has been lowered compared to the previous document to include closely related species in the analysis or if it specifically applies to species identification criteria.*

A3: For the purpose of the assessments and when using WGS data for the identification at the species level, digital DNA-DNA hybridisation (dDDH) should usually reach >70% identity and ANI should usually reach >94%; for ANI values, it is considered that a strain belongs to a species if it is higher than 94%. The references cited have a scope (species separation) different to the one of the statements and therefore a different threshold is applied.

Q4: *One question regarding the MetaPath database and its upcoming inclusion of mammalian toxicological metabolism (ADME). I am eager to hear about its implementation and public availability?*
A4: The MetaPAth is publicly available under Pesticide evaluation: Tools | EFSA

Q5: *Regarding the revision of the guidance on genotoxicity testing strategies, is there a discussion planned on the presence of a threshold for genotoxic effect? When will be launched the public consultation of the scoping paper?*
A5: For the revision of this guidance and the related ones (see also point 7.3), all the latest developments in the field will be considered and discussed for the revision. The public consultation of the scoping paper will be launched in the beginning of December and will last until the beginning of February 2025.

Q6: *Is there consideration to conduct genotoxicity risk assessment using in vitro results combined with PBPK modelling to support NAM?*

A6: Consideration on use of PBPK modelling data for genotoxicity assessment of substances and potential inclusion of specific guidance on the matter will be made in the forthcoming Genotoxicity Testing Strategies Guidance revision. In fact, EFSA is currently funding research activities (such as the ADME4NGRA project) for use of in vitro kinetics data and PBPK modelling within safety assessments, including for genotoxicity. Regarding the use of in vitro data in general, genotoxicity is one of those hazard classes already heavily relying on in vitro assays, and this will continue to be part of the guidance also by expanding into newer state-of-the-art in vitro approaches.

Q7: *Are you considering the evaluation of the human relevance (Mode of Action - MoA) of the animal results in the definition of the Point of Departure for the MoE calculation?*

A7: Given possible differences in chemicals' MoA between species, discussion on the relevance of animal data for defining a Point of Departure in humans for MoE calculations will be considered by the working group.

Q8: *EFSA has since longer been busy in updating the Compendium of Botanicals. Would there be more news on when the updated Compendium will be published*?

A8: The update and the revision of the database is almost complete, and the new version will be published in the beginning of 2025.

Q9: *In line with the Commission's roadmap to transition to non-animal regulatory systems, will there be guidance documents on endpoints in which there are validated non-animal methods readily available (for example, skin sensitisation)?*

A9: As stated in its strategy for 2027, EFSA is committed to implement the use of New Approach Methodologies (NAMs) in the risk assessment of food and feed products, with the aim of minimising animal testing while ensuring a high level of protection for citizens. The development of a guidance on the use of NAMs in EFSA's risk assessment is not foreseen for the moment, nevertheless provisions are already available within EFSA's sectoral guidance documents to guide applicants on possibilities to integrate the use of NAMs within specific regulatory frameworks on a case-by-case basis. Furthermore, many projects on the topic are ongoing, and EFSA is actively contributing to the European Commission's efforts to prepare a roadmap for the phasing out of animal studies.

9. AoB

The SC was informed about a new EC mandate to develop guidance on critical appraisal of evidence as part of the systematic literature review methodology applicable for all food and feed assessments **(EFSA-Q-2024-00584)**. A WG is in the process to be established and will be chaired by EFSA. The guidance will be completed in 2026.

Annex 1: Preparatory meeting/s with risk assessment

Since the last 121st Plenary meeting, 1 preparatory meeting chaired by EFSA staff was held as follows:

10.1 Preparatory meeting on the Terms of Reference of the guidance on Margin of Exposure, 4 November 2024.

10.1a Scientific Committee members attending the meeting:

LAMBRÉ Claude, KNUTSEN Helle, HOOGENBOOM Ron,CASTLE Laurence,

COJA Tamara,TURCK Dominique, VILLA Roberto, HOUGAARD BENNEKOU Susanne.

10.1b **Declaration of Interest of Panel/Scientific Committee members**

In accordance with EFSA's Policy on Independence[6] and the Decision of the Executive Director on Competing Interest Management[7], EFSA screened the Annual Declarations of Interest filled out by the SC members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process.

10.1c **Discussion points**

In order to align, clarify, and prepare the Terms of Reference (ToR) for the revision of the opinion, published in 2005, presenting an harmonised approach for the risk assessment of substances that both genotoxic and carcinogenic (Margin of

6 http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
7 http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Exposure (MoE) Approach), which will take place during the 122nd open SC Plenary, EFSA organised a preparatory meeting with some members of the Scientific Committee (SC). EFSA presented and discussed the following steps:

1. Clarification of the definitions of Margin of Exposure (MoE) and Margin of Safety (MoS).

   The need for establishing clear definitions of MoE/MoS and understanding of how EFSA will use the approach will be published as a statement.

2. Revision of the 2005 opinion on the use of MoE for chemicals which have both genotoxic and carcinogenic properties.

   The areas of revision have been identified in a scoping paper. The scoping paper was published for public consultation in summer 2024. The areas of revision were presented and discussed at the last SC plenary, however, the SC asked for more discussion to better frame the ToR. EFSA discussed internally with its Units and during the preparatory meeting with experts. The need was expressed for including in the revision (i) the use of human data, (ii) low dose extrapolation by Bayesian benchmark dose (BMD) modelling, and (iii) clarification on the scientific rationale for the cut-off at 10.000 for genotoxic carcinogens and the cut-off from sub-chronic to chronic.

3. Extension of the use of MoE to other substances and endpoints.

   There was a discussion about extending the use of the MoE to chemicals with other modes of action (MoA), excluding those that are both genotoxic and carcinogenic. The need was highlighted to align this step with the guidance on default values.

It was agreed to present the revised Terms of references at the 122nd SC plenary that will be held on 20-21 November 2024 for final agreement.

10. 2 Next meeting

The next SC plenary meeting will be held on 19-20 February 2025, in Parma.

Annex II

Interests and actions resulting from the Oral Declaration of Interest done at the beginning of the meeting

NO CONFLICT: With regard to this meeting, Dr Thor Halldorsson declared the following interest:

"I have been invited by the Danish Ministry of Environment and Gender Equality to participate as an independent expert at the international expert group for the evaluation of the parametric value for nitrate in drinking water. The work does not entail any risk management actions/decisions."

In accordance with EFSA's Policy on Independence[8] and the Decision of the Executive Director on Competing Interest Management[9], and taking into account the specific matters discussed at the meeting in question, the interest above was not deemed to represent a Conflict of Interest for the expert concerned.

Annex III List of Observers

Online registered observers:

Observer	Organization
Abbas Hanna	dsm-firmenich
Afghan Abdul	Bureau of Chemical Safety, Health Products and Food Branch
Agersoe Yvonne	Novonesis
Alavrez Pablo	Lallemand
Baldwin Nigel	BaldwinAdvice (Baldwin Advisory Services Ltd)
Bali Anne pihl	Novonesis
Basualdo Najera Karla	Digesa
Belletti Sara	-
Blomberg Martin	Agteria
Bocquet Laetitia	Lesaffre
Bru Audrey	Lallemand
Bucher John	NTP US
Buckle Benjamin	Salus Animal Health
Celorio Ricard	FoodDrinkEurope
Cluzelle Cécile	Synpa, the French specialty food ingredients association
Coppens Patrick	Food Supplements Europe
De Bourayne Valerie	KEMIN HUMAN NUTRITION & HEALTH
De Marta Flavia	Pen & Tec Consulting (Argenta)

[8] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[9] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

De Oude Wim	Eastman Chemical Company
Elbassuny Malak	National Food Safety Authority
Falcioni Ornella	MAFA- Animal Health and Welfare Department
Flores Vidal Rosalia	Atova Regulatory Consulting SL
Gaiofatto Donatella	Meda Pharma S.p.A.
Geiser Stefanie	EAS Strategies
Giner Marta	Devreg Consulta
Gruszecka-Kosowska Agnieszka	AGH University of Krakow
Guillaumot Laurence	Novonesis
Hafellner Martin	Spar
Halimaa Pauliina	Biosafe - Biological Safety Solutions Ltd
Helbig Rainer	dsm-firmenich
Herzog Michaela	Feed and Additives GmbH
Hignard Malorie	Foodchain
Honkila Anna-Kaarina	Self-employed
Hooper Jeremy	MARS WRIGLEY
Jin Qiwen	Syngenta
Koukoulanaki Marina	COSMETICS EUROPE
Kucharska Katarzyna	Amcor Flexibles
Latino Alessio	Perfetti van Melle S.p.A
Lauritsen Ida	Novonesis
Lensch Alexandra	Evonik
Lepretre Christophe	Keller and Heckman LLP
Luque Pedro	Colgate-Palmolive Europe
Magby Jason	Colgate-Palmolive
McConochie Carmen	European Chemical Industry Council
Melton Emily	IFF
Merino Ana	Atova Regulatory Consulting SLU
Michel Erwin	Lallemand Specialty Cultures
Pappas Maria	Democritus University of Thrace
Perrot Tifenn	ALL4FEED
Pescador Paula	Biosafe Ltd Oy

Petersen Annika Boye	Technical University of Denmark
Poláčková Soňa	National Institute of Public Health
Post Jan Dirk	Coca-Cola GmbH
Prasad Meera	Novonesis
Radogna Flavia	LBMCC
Renahan Tess	PETA Science Consortium International e.V.
Rey Caroline	Cellular Agriculture Europe
Rooney Andrew	NTP US
Ross Daniella	Colgate-Palmolive
Rouault Marie	Nutraveris
Scardurzio Aurora	ssica
Schrenk Dieter	RPTU Kaiserslautern-Landau
Shima Anxhela	Ministry of Agriculture and Rural Development
Šumberová Hana	National Institute of Public Health, CZ
Suthar Dipen	Syngenta
Tangianu Silvia	University of Konstanz
Taylor Kyla	NTP US
Thomann Marlies	Tetra Pak
Trapp Judith	Syngenta
Trovato Marinella	SISTE
Vaughan Mark	Haleon
Wenio Iwona	Warsaw University of Life Sciences
Wiebrock Lars	Chr. Hansen GmbH
Worrad-Andrews Tamsin	Unilever
Wu Yu-Chen	oceanBASIS
Wulf-Andersen Linda	Novonesis
Zhu Hua	BaseClear
Zuskova Eva	National institute of Public Health

Onsite participants:

5 people registered, but only 4 observers attended.

Observer	Organization

Caroline Idowu	Atova Regulatory Consulting SLU
Heike Scheffler	Procter&Gamble
Corrado Galli	Retired (University of Milan)
Marina Marinovick	University of Milan