Scientific Committee

Minutes of the 101st Plenary meeting

Held on 11-12 November 2020
WEB - conference

(Agreed on 3 December 2020)

Participants

- Panel Members

  Simon More (chair), Diane Benford (vice chair), Susanne Hougaard Bennekou (vice chair), Vasileios Bampidis, Claude Bragard, Thorhallur Halldorsson, Antonio Hernandez-Jerez, Kostas Koutsoumanis, Kyriaki Machera, Miguel Miranda Chueca (1st day), Hanspeter Naegeli, Søren Saxmose Nielsen (2nd day), Josef Schlatter, Dieter Schrenk, Vittorio Silano, Dominique Turck, Maged Younes.

- Hearing Experts[1]:

  Christer Hogstrand (for item 4.6)

- European Commission and/or Member States representatives:

  Marina Marini (DG SANTE Unit D1, Farm to Fork Strategy)

  Frans Verstraete (DG SANTE Unit E3) for agenda item 4.2

- EFSA:

  Executive Director: Bernhard Url (day 1)

  Executive Directorate: Marta Hugas

  Risk Assessment and Scientific Assistance Department (RASA): Juliane Kleiner

  Scientific Evaluation of Regulated Products Department (REPRO): Guilhem De Seze

  Scientific Committee and Emerging Risks Unit (SCER): Tobin Robinson, Daniela Maurici, Maria Chiara Astuto, Maria Bastaki, Bernard Bottex, Jean-Lou Dorne, Raquel Garcia Matas, Georges Kass, Christina Kyrkou, Djien Liem, Angelo Maggiore, Caroline Merten, Agnes Rortais, Reinhilde Schoonjans, Rositsa Serafimova, José Tarazona.

[1] As defined in Article 15 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/sites/default/files/corporate_publications/files/expertselection.pdf

Science Studies and Project Identification & Development Office (SPIDO): Claudia Heppner (for agenda item 7.a)

FEED Unit: Paola Manini (for agenda item 6.a)

1. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Søren Saxmose Nielsen for 11 November, who was replaced by Miguel Miranda Chueca, vice chair of the Animal Health and Animal Welfare Panel.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Scientific Committee/Scientific Panel/ Members

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 Panel 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, and no interests were declared orally by the members at the beginning of this meeting.

4. Scientific outputs submitted for discussion and/or possible adoption

4.1 A systems-based approach to the environmental risk assessment of multiple stressors in honey bees EFSA-Q-2018-00645.

This agenda item was chaired by Diane Benford since the chair of the Scientific Committee (SC), Simon More, is also the chair of the WG (MUST-B) assigned to this mandate.

The SC discussed the draft scientific opinion on a systems-based approach to the environmental risk assessment of multiple stressors in honey bees.

[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

This scientific opinion follows a request from the European Parliament ENVI Committee.

First, an overview was provided by EFSA to the SC in order to introduce the mandate, including background, scope and timeline in the context of another mandate that EFSA received in March 2019 from the EC DG-Santé on bee health (i.e. the Review of the Bee Guidance on the risk assessment of Plant Protection Products (PPP) on bees (honey bees, bumble bees and solitary bees – the "bees guidance" Document (GD)). This overview was provided to show the differences between these 2 documents that are currently developed in parallel in EFSA and the need for tight coordination and clear communication to avoid any potential confusion between the 2 activities.

The "bees guidance" is constrained by a legal framework and focused on the 3 types of bees for the risk assessment of PPP, while the opinion tabled for discussion and possible endorsement for public consultation is focused on honey bees for the risk assessment of PPPs in combination with multiple stressors. The last one is therefore a prospective document, putting forward ideas and concepts for future risk assessment. This work is aligned to aspirations outlined in the EU Green Deal and the EFSA strategy 2027 on environmental risk assessment.

After this introduction, the SC was presented with the key scientific challenges linked to these two outputs and the possible issues that also needed further consideration. The SC discussed how to build on these challenges to reinforce clarity and communication on these 2 documents. In this respect, it was highlighted that the finalisation of the scientific opinion before the "bees guidance" would bring more clarity on the "bees guidance" prerogatives and therefore, the public consultation of the scientific opinion should be launched as planned. In the end, the SC was presented with details on how the scientific opinion was amended after the comments received at the last Plenary meeting in September.

The SC recommended maximising the clarity on the regulatory readiness of the scientific methods/tools available and engagement to ensure consistency among the 2 documents. In conclusion, the SC found that the new version of the scientific opinion was greatly improved, and it endorsed it for public consultation. The consultation will be launched in January 2021.

4.2 Update on the draft EC mandate on "Risk benefit assessment of fish consumption in relation to the presence of dioxin (PCDD/FS) and dioxin-like PCBs"

EFSA received and elaborated the draft mandate from the European Commission to provide a risk-benefit assessment of fish consumption in relation to the presence of dioxins (PCDD/Fs) and dioxin-like PCBs and to assess the influence of the presence of other contaminants in fish such as methylmercury, brominated flame retardants and perfluoroalkyl substances (PFAS) on the outcome of the risk-benefit assessment.

In the context of SANTE's working group on Persistent Organic Pollutants (POP) in Food with risk managers of the Member States (MSs), EFSA was able to exchange views with the EC and MSs, who need EFSA's advice in defining dietary advice for fish consumers at national level.

A draft workplan was presented to the SC with four work packages to address the full complexity and to prepare updates of databases and (guidance) documents that are needed for the assessment.

The SC endorsed the proposed workplan and made some suggestions that will be further discussed with the European Commission.

4.3 Update on the finalisation of the guidance for risk assessment of nano substances and the nano technical guidance. EFSA-Q-2020-00269

The risk assessment of nanomaterials is described in the EFSA 2018 Draft Guidance on risk assessment of nanoscience and nanotechnologies in the food and feed chain (link here).

This Guidance has been in a 2 years pilot phase and is being reviewed with improvements and clarifications based on stakeholders' feedback, experience from the application of the Guidance to actual EFSA cases, updated scientific knowledge and the new guidance on Particle-TR in development (EFSA Guidance on Technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles). The focus of this document for applicants is on how to prepare dossiers and adequate safety studies for legally defined nanomaterials/nanoforms.

The SC was informed about where the document has been substantially modified over the last 2 years and asked to provide feedback on the proposed updates. The scope has been clarified by the EC and revised due to more specific insights gained in the context of the new mandate by the EC on the Guidance on Particle–TR. Chapter 4 is new and elaborates on the materials subject to this guidance. It is expected that this will facilitate the appropriate and correct implementation of this guidance by applicants.

The connectivity with other guidance documents is further clarified for risk assessors. There are changes regarding the physicochemical

characterisation and simplifications, and adaptation of structure of hazard assessment chapters. Scientific principles and details have been updated with recent results from scientific research projects and further elaborated in line with the latest progress in science, e.g. current capacity of *in vitro* test models or the application of mixture principles in the risk characterisation, regarding the nano aspects of the material, if toxicokinetics and toxicodinamics for nano and non-nano fractions are different.

The feedback of the SC is welcomed before presenting the final Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain for possible adoption in April or June 2021. In parallel, the SC will be presented for adoption the "Guidance on technical requirements of regulated food and feed product applications to establish the presence of particles at the nanoscale".

The SC Panel chairs are asked to provide input from the respective Panels by end 2020 as comments on the document where necessary.

4.4 Draft opinion on Non Monotonic Dose Response (NMDR) EFSA-Q-2019-00530

Previously, the SC was invited to comment on the draft opinion on biological plausibility of non-monotonic dose responses and their impact on the risk assessment. These, as well as the comments from the bisphenol A (BPA) WG, were addressed in the updated version that was presented to the SC for endorsement for public consultation. The work assesses the biological relevance on the *in vivo* datasets, with apparent non-monotonic dose responses as identified in the external report produced under GP/EFSA/SCER/2014/01. The draft opinion concludes that there is no gold standard method that will give a unanimous assessment for non-monotonicity in the dose response curve. The assessors therefore need to consider the full range of information/methods available, e.g. the checkpoint approach as well as the probabilistic (statistical) methodology (since both may yield different results).

In addition, the draft opinion includes a proposal for addressing the biological relevance of the NMDR. Several important evaluation points are explained in the opinion, e.g. the importance of determining whether the data represent an early (molecular) event, an intermediate effect or an apical effect, and the consistency with the available mechanistic information. Taking into account such evaluation points, a process to be followed for addressing NMDR in the risk assessment process is proposed in the opinion. This approach is recommended for application in cases of

apparent non-monotonicity and was already applied (in the appendices of the opinion) to two case studies: bisphenol A (BPA) and phthalates.

The draft was endorsed for public consultation for a duration of 8 weeks.

4.5 Draft statement on the derivation of Health Based Guidance Values (HBGV) for regulated products that are also nutrients EFSA-Q-2019-00505

Some nutrients are used in various "regulated" products subject to regulatory risk assessment, e.g. phosphates or chlorates as food additives, and copper in pesticides and feed additives. Such an assessment of the risk for consumers should consider all sources of dietary exposure and establish a HBGV taking into account that the regulated product is a nutrient. It is important to consider the overall exposure and the contribution related to the use of the nutrient as a regulated product in the advice to risk managers, for their decision making on the use level of each regulated use.

A statement has been prepared, wherein an integrated and harmonised approach for setting the HBGV is described for assessments of nutrients conducted in the context of regulated products. The statement has incorporated improvements upon feedback from the public consultation launched in July and was presented to the SC.

The scope of the statement has now been clarified and in recommendation number 5 it was clarified whether the HBGV is equivalent to an Upper level (UL) or only applies to the regulated product under evaluation (ADI).

The importance of this statement is to establish the internal procedure for ensuring consistency in EFSA assessment of nutrients as regulated products. A decision tree with regard to the need to revise established HBGV for nutrients used in regulatory products was provided.
The SC acknowledged the quality of the document and considered that additional clarifications should be introduced regarding the description of "general population" and recommendation number 5. The SC requested the WG to address these points supported by three additional SC members and postponed the adoption of the statement to the SC plenary in February 2021.

4.6 Draft guidance on scientific criteria for grouping chemicals into assessment groups for human risk assessment of combined exposure to multiple chemicals. EFSA-Q-2019-00517

The Chair of the WG, Vice-Chair of the CONTAM Panel, Christer Hogstrand, presented to the SC the latest modifications performed in each chapter of the document, already presented at the last plenary.

The problem formulation chapter was shortened to only provide context to the reader and introduce the relevance of grouping into the problem formulation as well as to briefly introduce the chapters on hazard-driven criteria (chapter 3) and prioritisation methods (chapter 4). Chapter 3 (hazard-driven criteria) has been further clarified particularly to highlight the use of mechanistic information on toxicity (mode of action (MoA)/adverse outcome pathways (AOP)) when available, or to use specific effect on target organs or a common adverse outcome when MoA/AOP data are lacking. Hazard-driven criteria also include the use of toxicokinetic data and applying a weight of evidence approach as exemplified in an annex.

The prioritisation methods (risk-based and exposure-driven) have been modified upon the recommendations from the SC and CEP Panel. The SC suggested further improvements to better illustrate the applicability of the framework for identifying low priority chemicals and reduce the numbers of chemicals per group. It has been suggested to be pragmatic in the view of resources available and to contextualise and clarify the use of probability of co-exposure for the exposure-driven approach, which is currently not applied by EFSA Panels and is mostly relevant to research questions or specific biomonitoring questions in National Agencies. The overall scheme for the prioritisation methods has been further clarified and examples of its use are provided for both the risk-based and exposure-driven approaches in Annexes.

The SC provided further comments that will be addressed by the WG prior to consulting sister agencies (i.e. ECHA) and submitting the document for possible endorsement for public consultation at the SC plenary in February 2021.

5. Feedback from the Scientific Committee/Scientific Panels, EFSA, the European Commission

5.1 EFSA including its Working Groups /Task Forces

5.1.1 Cross-cutting WG Genotoxicity

The WG Genotoxicity is engaged to full capacity in the mandate on re-evaluation of food additive E 171 (titanium dioxide) based on new evidence available since 2016 and the EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health risk assessment (EFSA, 2018). Around 100 papers related to genotoxicity, containing around 150 studies

were retrieved and provided to the experts of the WG for evaluation. The final advice of the WG Genotoxicity to the Units requested support for this task is expected by March 2021.

Other requests for advice are under discussion, however they have not been allocated to the WG yet due to the heavy workload already allocated to the WG.

5.1.2 Cross-cutting WG Uncertainty

The guidance document on uncertainty in risk assessment has been implemented for the first time in the development of the new sectoral guidance document (GD), namely, in the scientific guidance for the preparation of applications on smoke flavouring primary products (EFSA FAF Panel EFSA-Q-2019-00687). The smoke flavourings GD includes a chapter on uncertainty analysis and is currently under public consultation until end of November 2020.

A workshop will be organised next year with risk managers from DG SANTE on the application of the guidance on uncertainty in scientific assessments. Now that the uncertainty GD is nearly fully implemented in the Department of Risk Assessment (RASA) with additional examples from the Department of Regulated Products (REPRO), practical examples can be drawn from these experiences to illustrate at the workshop the usefulness of the guidance also for the risk managers. The workshop is currently scheduled for autumn 2021.

In addition, the guidance on Expert Knowledge Elicitation (EKE) (EFSA, 2014, link here) has been used extensively to implement the uncertainty GD. The following needs have been identified by the WG Uncertainty which are currently not covered by the EKE GD: (1) a simplified EKE procedure has been identified as a priority; (2) to include elicitation of 2D distributions (quantifying variability as well as uncertainty); (3) to include elicitation of functions (x-y relations); (4) to add the IDEA protocol to the three methods already in the guidance, as it appears to offer a method that combines benefits of the Sheffield method (which is most often used in EFSA currently) and the Cooke method; (5) to add the recent literature on EKE for bias analysis.

BIOHAZ and AHAW Panels confirmed the need for informal EKE procedure as resources are often too limited for a full formal EKE. The EKE GD will be discussed in the SC in a dedicated session at the February 2021 plenary with the idea of start a review of the GD.

5.1.3 Cross-cutting WG Benchmark Dose (BMD) EFSA-Q-2020-00137

The WG received the mandate to update the SC guidance on the use of the benchmark dose approach in risk assessment in order to align EFSA's guidance with chapter 5 on dose response assessment of WHO IPCS EHC240. The EFSA Platform for BMD analysis needs to be updated accordingly. Some of the development needs, such as the implementation of Bayesian model averaging as the preferred approach, have been contracted out. The activity has accumulated four months delay due to an ongoing discussion among the partners on some statistical issues. A meeting will be organised by the end of the year with the various partners to clarify these issues and agree on the way forward.

5.1.4 WG Copper EFSA-Q-2020-00399

The WG has started its activities on the mandate to revisit the HBGV for copper (based on old as well as new evidences) and to make a complete exposure assessment aggregating all routes of exposure to copper. The WG is now identifying the sources of exposure and the information for quantifying the levels. A protocol is also being developed for this activity.

5.1.5 WG Read across (RaX) EFSA-Q-2020-00413

The kick-off meeting of the WG took place in September. A guidance for read across approaches in EFSA is under development, taking account of the experience gained by ECHA with their Read-Across Assessment Framework (***RAAF***).

5.1.6 Nano Network

The Nano Network has reached its 10th year of existence and the Advisory Forum (AF) reports provide yearly an overview of its achievements: e.g. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2020.EN-1784

The Terms of Reference (ToR) of the Nano Network have been renewed twice and expire again end 2020. Per default the ToR will remain valid until further notice. It is expected that the EFSA Management Board and the AF will decide on renewal of EFSA Networks in general and possible adjustments of the tasks. The SC is asked to share views on (1) the operation and functionality of this network and (2) its activities and contributions to the work of the SC. New ideas/topics for supportive activities by this network are invited per written procedure.
Further to the annual reports, useful background docs are published in the microsite of the network such as list of members, terms of references, agendas and minutes (https://www.efsa.europa.eu/en/cross-cutting-issues/networks).

6. Other scientific topics for information and/or discussion

a. Applicability of Margin of Exposure (MoE) in the risk assessment of botanicals and botanical preparation used as feed additives

The FEEDAP Panel presented to the SC the issue of risk assessment of botanical preparations containing natural compounds that are both genotoxic and carcinogenic. In line with the SC recommendation of 2005, the EFSA FEEDAP Panel established in 2015 that "*the intentional addition of such substances to the food chain via feed additives is not acceptable. This applies independently from the origin of the substances (chemical synthesis or botanical origin)".* The FEEDAP Panel has been requested to assess the safety for the target species of botanical preparations containing compounds that are both genotoxic and carcinogenic. The methodology proposed would be the application of the MOE. For substances for which the MOE is not applicable, the FEEDAP Panel proposes an approach based on the comparative intake of the same substances via feed of plant origin. Three specific methodological questions were discussed with the SC and endorsed for the further work strategy by the FEEDAP Panel.

b. Draft planning for agenda item "Feedback from Panels" in 2021 and draft planning for discussion on cross-cutting guidance implementation in 2021-2022

As agreed at the previous plenary, this agenda item has been redesigned and a plan for 2021 was drafted to have two Panels providing feedback on cross-cutting issues at each plenary meeting. This planning allows enough time for more in-depth discussion and reserves some time for other Panel Chairs to report cross-cutting issues that came up recently, e.g. new mandate of horizontal nature received. This annual planning setting should allow the Panel Chairs to prepare well in advance with their supporting EFSA Unit.

The SC was very positive about the scheme, as it also allows to plan for important issues that come up during the work from the Panels and that need solutions of cross-cutting nature. Future possibilities include ad hoc raising of urgent issues, as well as systematic feedback on the applicability of selected cross-cutting guidance documents in the various Panels that are discussed in every plenary, focussing on one guidance at the time. The aim is to review the implementation of each guidance, highlighting possible problems and gaps identified during its use. The discussion could bring to the decision to review the selected guidance in order to have a document more fit for purpose.

Vittorio Silano, Chair of the CEP Panel, brought to the attention of the SC the mandate received from EC on styrene, where EFSA is asked to re-

evaluate the safety of styrene (FCM No 193) for use in plastic food contact materials (FCM), following the classification by the International Agency for Research on Cancer (IARC) as 'probably carcinogenic to humans'. The IARC Monograph (Vol 121) pertains to hazard identification, based on studies on high-dose occupational exposures by inhalation and also animal studies, mainly by inhalation exposure. The Panel considered that the IARC conclusions cannot be directly applied to the evaluation of risks for consumers from the oral exposure to styrene, but also concluded that, based on the data provided in the IARC Monograph and by the industry, a concern for genotoxicity associated with oral exposure to styrene cannot be excluded. A first opinion was published in October 2020 (link here). Taking the human exposure data into account, the Panel concluded that a systematic review of genotoxicity and mechanistic data, comparative toxicokinetics and analysis of species differences, is required for assessing the safety of styrene for its use in FCM. This second step of the analysis is ongoing.

The CONTAM Panel offered cooperation and it was suggested the possibility that this topic could be scheduled for the upcoming 103rd SC plenary early next year (14-15 April 2021).

Hanspeter Naegeli, Chair of the GMO Panel, informed the SC about the initiation of one of the general biotech mandates. Now that 3 opinions (on Synthetic Biology plants, one SDN1 and SDN3, and on gene drives) are ready for publication (or are already published), the GMO Panel has started working on the draft opinion on in vitro random mutagenic techniques, which are currently exempt from GMO legislation. The EC mandate asks the differences and consequences of in vivo and in vitro mutagenesis, the former using whole plants and the latter plant cells, using physical or chemical mutagenic agents. The consequences of this mandate for plant breeding in general may be significant. Therefore, the GMO Panel found it necessary to embark on a thorough protocol development first, so that an agreement can be reached on the level of detail requested under the seemingly easy Terms of Reference relating to possible differences between in vivo and in vitro mutagenesis.

7. Any other business

a. SPIDO update-Open call for tender: Roadmap for action

In order to address the requirements of the Transparency Regulation (EU) 2019/1381 (Art. 32d), EFSA has established a Science Studies and Project Identification & Development Office (SPIDO). Four identified scientific

themes paper have now gone through an extensive consultation process with DG-SANTE, JRC, EU Agencies, the EFSA's Scientific Committee, and Member States at the EFSA Advisory Forum. The launch for an open call for tenders to develop three roadmaps for action providing recommendations for future multi-annual, multi-partner studies or projects on:

i. Risk assessment of combined exposure to multiple chemicals,
ii. New approach methodologies in risk assessment,
iii. Building a European Partnership for next generation, system-based environmental risk assessment

is foreseen to open end of November for a duration of three months. The SC members are asked to disseminate this call for roadmaps into their networks to attract the right talents. The call will be made available at EFSA webpage; LinkedIn and EU e-tender.

The development of the 4th roadmap for action on "Artificial Intelligence for evidence management in risk assessment" will be outsourced using a reopening competition through and available EFSA framework.

b. Results of the expert mutual assessment

Results from the expert survey as well as from the expert assessment are overall very positive. Response rates ranged from 50% to 100% and are correlated to the level of experience. The details of the responses have been analysed to inform action points for improvements in the expert-EFSA collaboration. Suggestions for long term scientific quality, collaboration with other panels and increased effectiveness were noted, such as simplification and better accessibility of harmonized cross-cutting guidance documents. As a follow up of this expert mutual assessment, seventeen proposals have been formulated and will be discussed in detail at the next SC plenary meeting. In the meantime, a prioritisation of the proposals will be organised.

c. Draft agenda next SC Plenary

The SC was presented with an overview of the topics that will be on the agenda of the next meeting scheduled for the 17-18 February 2021.

d. General matters arising

The Scientific Committee was provided with a document summarising relevant activities that took place since the last plenary meeting with focus on the activities of the EFSA Advisory Forum (AF), interagency and international scientific cooperation and EFSA Stakeholders Meetings.

e. List of published opinions since September 2020

The Scientific Committee was provided with a document containing the list of published opinions from 1 September 2020 to 30 October 2020 produced by the different Panels and Units, including those on applications for food contact materials, enzymes, flavourings, GMOs, health claims, novel foods and food additives. The list also provides a list of published conclusions on pesticides and ongoing public consultations.