SCIENTIFIC PANEL ON MESE

116th Plenary meeting

20-21-22 November 2023
14:00-18:00 / 9:00-13:00 / 9:00-12.30
MINUTES - Agreed on 9 January 2024

Location: EFSA, Parma

Attendees:

- **Panel Members:**
  Simon MORE, Vasileios BAMPIDIS, Diane BENFORD, Susanne HOUGAARD BENNEKOU, Claude BRAGARD, Thorhallur HALLDORSSON, Antonio HERNÁNDEZ-JEREZ, Kyriaki MACHERA, Josef SCHLATTER, Dieter SCHRENK, Kostas KOUTSOUMANIS*, Dominique Turck*, Maged YOUNES*, Ewen MULLINS*, Søren SAXMOSE NIELSEN*, Claude LAMBRÉ*

  * ONLINE ATTENDANCE

- **European Commission:**
  Eleni GKANA, Athanasios RAIKOS

- **EFSA:**
  Executive Director: Bernhard URL (only day 1 until coffee break)

  Head of Department ENABLE - Nikolaos KRIZ

  Head of Department ASSESS – Guilhem DE SEZE (only day 3)

  Chief Scientist: Carlos DAS NEVES

  Methodology and Scientific Support (MESE) unit: Claudia RONCANCIO PEÑA, Daniela MAURICI, Maria BASTAKI, Maria Chiara ASTUTO, Djien LIEM, Lucian FARCAL, Irene CATTANEO, Sara LEVORATO, Petra GERGELOVA, Marios GEORGIADIS

  PLANTS Unit: Agnès RORTAIS

  BIOHAW Unit: Pietro STELLA, Andrea GERVELMEYER

1. Welcome and apologies for absence

The Chair welcomed the participants.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Panel members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group 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/adoption

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

4.1 Draft guidance on Epidemiological studies

The new chapter 4.4 of the draft guidance document has been submitted to the SC for discussion. The SC has been asked to provide feedback regarding any needs for further developing the different sections, to indicate whether the level of detail of the guidance/explanations provided is sufficient, if clarifications need to be added to the existing explanations, and if additional questions should be addressed in chapter 4.4. The general feedback was positive and the WG has received very useful indications on how to further develop the guidance document. Specifically, it was suggested to explain in which cases Benchmark Dose (BMD) modelling using human epidemiological evidence could be applied and to expand the guidance regarding alternative modelling approaches for dose-response relationships.

4.2 Draft guidance on risk benefit assessment (EFSA-Q-2022-00211)

The revised draft guidance on risk-benefit assessment (RBA) was presented to the SC for discussion. The SC was invited to review the EFSA 2010 guidance on Risk Benefit Assessment (RBA) of foods and other related publications as context in which to review the updated guidance. The SC was asked to provide general and specific feedback on the draft guidance; specifically, the SC was asked if the guidance stands as an authoritative document for assessment of risks and benefits in contexts of high complexity, such as considering multiple compounds, different health endpoints and different populations; if it provides sufficient and clear guidance to produce clear outputs to risk managers; if it presents appropriate methodological options in addition to the DALY (disability-adjusted life years) for assessing all possible and relevant (positive and negative) effects over a range of potential food intakes when Health Based Guidance Values are exceeded and Dietary Reference Values (DRVs) are not met; if it emphasises transparency in and justification of the selection of relevant compounds for comparable outcomes of different RBAs of the same food. The guidance also aims to strike a balance between providing an overview of relevant methods and providing practical guide for their implementation, and templates for reporting the results of the RBA. Based on the feedback to these questions, the document will undergo further revision and the timing of launching a public consultation will be determined accordingly.

4.3 Draft opinion on Bromide (EFSA-Q-2022-00329)

The SC was presented with new sections of the draft opinion for discussion, specifically the section on the characterisation of critical effects of bromide in humans, the revised section on the evidence available in target species of food-producing and non-food producing animals, and revisions to the sections related to the screening of exposure based on the Maximum Residue Levels (MRLs) for bromide. The SC was asked to provide feedback on the selection of the evidence upon which to establish a reference value for bromide. Considering the sources of bromide exposure, primarily as a naturally occurring substance and as a contaminant, the reference value will be expressed as a tolerable daily intake (TDI). The SC agreed to allow additional time for the WG to discuss the interpretation of the evidence and to complete sections of the draft opinion that are still under development including the characterisation of critical effects for target species of food-producing and non-food producing animals, the uncertainty analysis, the conclusions and recommendations. The time of the public consultation on this draft opinion was therefore postponed to early 2024.

5. Other scientific topic for discussion

5.1 The future of Risk Assessment: holistic approaches, challenges, and possibilities

The SC was provided with a series of presentations to pave the discussion on holistic risk assessment, considering the idea of One substance One assessment (1S1A) as presented in the Chemicals Strategy for Sustainability (CSS). As an example, the mandate on Azole was presented (EFSA-Q-2022-00040; **https://open.efsa.europa.eu/questions/EFSA-Q-2022-00040?search=)**.

In 2022, the European Commission submitted an interagency mandate on "Impact of use of azole fungicides (other than as human medicines) on the development of azole-resistant *Aspergillus spp.",* involving five EU Agencies. The deadline to deliver the report linked to this mandate is July 2024. The Agencies involved are EFSA (overall coordination), ECDC, ECHA, EMA, EEA; contribution of JRC is also foreseen. The topics covered by the mandate are the following: collecting data on use of azole fungicides, identify links to environmental use- resistance, epidemiology of human infections, risk assessment, prevention and control, studies to be provided by applicants in the future, data gaps and research needs. Responsibilities linked to the terms of reference were split among the five agencies. The assessment is ongoing and the final conclusions and recommendations will be prepared and discussed once the work is finalised. The fact that five agencies were involved makes this mandate a very good example and will give the chance to analyse scientific and administrative aspects of interagency collaboration in a One Health mandate and make recommendations to improve them in the future.

The SC discussed the pros and cons of the holistic risk assessment and tried to define what should/could be done to make this concept operational. Several proposals were put forward as for example asking each agency to describe in a document its own way to perform risk assessment and then to compare the approaches for deciding one common way to proceed. This would also include development of joint methodologies for the risk assessment. Other members suggested the creation of a pool of experts/EFSA staff with different competences in order to cover the different areas of the assessment and being able to integrate the evidence.

Critical points were identified in the legislation, as different legal frameworks sometimes ask for different data requirements and this should be changed before being able to go in the direction of 1S1A. The role of the risk managers is essential to build capacity, methodologies and partnership with the other agencies and the Member States competent authorities. We need to build trust in the work of others to build synergies and avoid duplication of efforts.

The SC also suggested to include the socio-economic impact in the holistic approach to risk assessment, as already done for example by ECHA, where the socio-economic impact is weighing the pros and cons of an action for society as a whole and plays a vital role in the restrictions and authorisation processes.

In the end, the issue of the speed of the risk assessment was also discussed, as speeding up the risk assessment process will allow for more innovative approach to be tested and then implemented.

5.2 TKPlate 1.0: An Open-access platform for Toxicokinetic and Toxicodynamic modelling of chemicals

The SC was presented with an update on the TKPlate 1.0, an Open-access platform for toxicokinetic and toxicodynamic modelling of chemicals to implement new approach methodologies in chemical risk assessment.

The TKPlate 1.0 platform has been published online on November 14th within the EFSA R4EU tools (link here) together with an EFSA editorial, an external scientific report on the platform's development and two technical reports. These consist of a user guide and case studies providing practical advice and real-life examples in using the platform in the chemical risk assessment area. TKPlate 1.0 contains a series of models for humans, test species (rat, mouse, rabbit, dog), farm animals (cattle, sheep, pig, chicken) and species of ecological relevance and is constituted of a workflow with seven modules:

1) An input module to select the model, the chemical-specific data, the exposure patterns and related time scales,

2) A forward dosimetry module to predict kinetic parameters and concentrations in blood plasma and relevant organs (liver, kidney, etc. ...),

3) A reverse dosimetry module to calculate external exposure from internal dose profiles (i.e., blood and urine),

4) A toxicodynamic module for benchmark dose modelling on an internal dose basis,

5) A dynamic energy budget module allowing to quantify the impact of chemicals on the life cycle of individuals and populations of species of ecological relevance,

6) A module (MIXTOX) for deterministic risk characterisation of combined exposure to multiple chemicals using the component-based approach and dose addition assumption as detailed in EFSA Scientific Committee Guidance for the risk assessment of combined exposure to multiple chemicals published in 2019 (link here), and

7) An automated report summarising the inputs provided by the user and the outputs, graphs and datasets.

The SC was also informed that trainings are in preparation.

6. Feedback from the Scientific Panels/EFSA/EC

6.1 Ongoing work-programme of the Panel on Genetically Modified Organisms (GMO)

The SC was presented with an update on the main ongoing activities of the GMO Panel. The panel is developing an Opinion on risk assessment of protein safety in applications (Regulation EU 503/2013 provides specific requirements for assessing toxicity and allergenicity of proteins) and the publication is expected by end of 2024. A public consultation will be launched in summer 2024. The Opinion will reflect the current practice, challenges and future opportunities of protein safety in GMOs, considering experience gained in the assessment including more complex recent applications, and also developing complementary/alternative testing strategies
The chair of the Panel also mentioned the GMO Panel opinions on the New Genomic Techniques (NGTs) that have provided a key scientific contribution for the Commission legislative proposal on plants obtained by certain NGTs that was published in July 2023.

To conclude, in the last year the panel has worked on 4 new mandates and on 7 new applications.

6.2 Ongoing work of the Panel on Plant protection Products and their Residues (PPR)

The remit of the PPR Panel is to develop and review guidance documents on the risk assessment of pesticides, to provide advice on the risk assessment of pesticides in support of the Peer Review of pesticide active substances. Moreover, on an ad-hoc basis,

the PPR Panel can be involved in applications, i.e. risk assessment of pesticide active substances.

The SC was updated on the Panel activities (recently finalised or ongoing), including the development of: i) Adverse Outcome Pathways (AOPs) relevant for the identification of substances having endocrine disruptors properties, ii) AOP for Voltage Gate Sodium Channel inhibition leading to Developmental Neurotoxicity Adverse Outcome, iii) a statement on the design and conduct of groundwater monitoring studies supporting groundwater exposure assessments of pesticides, iv) an opinion on the use and reporting historical control data for regulatory studies. In addition, a mandate to EFSA for scientific and technical assistance on the toxicological properties and MRL of acetamiprid and its metabolites has been received.
In addition, the SC was updated on the activities the PPR Panel is supporting, such as the ongoing project on dietary Cumulative Risk Assessment of pesticide residues, and in the activities for the identification of the specific effects in kidneys and liver.

6.3 Update on WG Activities:

WG Fluoride:
The WG on Fluoride is currently reviewing and discussing the available evidence on three prioritised endpoints, neurodevelopment and neurotoxicity, and effects on the thyroid and bone, from human epidemiological and experimental animal studies. Data reported on other endpoints have been extracted and are pending expert review.
The exposure assessment section has been updated to include information received from national authorities of EU countries on the use of oral fluoride tablets as dental health preventive treatment through a survey disseminated in coordination with the European Medicines Agency (EMA); consideration on possible contribution of fluoride-containing materials in contact with water under the remit of the European Chemicals Agency (ECHA); and refinements using fluoride concentrations in specific food subcategories. The draft opinion will tentatively be presented for the second reading at the February 2024 SC Plenary.

WG Nanotechnologies:
The cross-cutting WG on Nanotechnologies has recently finalised various requests for assistance on feed additives and novel foods.
In addition, the WG is currently analysing the lessons learnt from the first two years of implementation of the Nano Guidances to reflect on possible revision. Targeted surveys will be launched to the EFSA NanoNetwork, EFSA Panels and Units, and applicants to collect additional feedback.
Lastly, the SC was informed on additional activities on the topic, such as the update of the EFSA Webpage on Nanotechnologies[3] and a recent call for experts launched with the aim to increase expertise on the topic in EFSA WGs. Work is also ongoing with the EFSA NAMs4NANO Project[4] to promote implementation of New Approach Methodologies (NAMs) for nano-specific risk assessment. Ongoing cooperation with the DG JRC is joining forces for capacity building on the topic, and efforts in monitoring the experiences from international activities and other agencies aim to ensure alignment and integrate new relevant knowledge into EFSA guidance documents as appropriate.

WG Genotoxicity:

[3] https://www.efsa.europa.eu/en/topics/topic/nanotechnology
[4] https://www.efsa.europa.eu/it/art36grants/article36/gpefsamese202201-nams4nano-integration-new-approach-methodologies-results

The cross-cutting WG on Genotoxicity is currently dealing with two assessments on an active substance of a pesticide and on a food additive.

WG Biomarkers of effect:
The newly established WG held its first meetings. The WG implements the self-task mandate (EFSA-Q-2023-00583) on the "*Guidance on the use of biomarkers of effect in regulatory risk assessment of chemicals*". The first deliverable of the WG is a feasibility study, while the first meetings were focused on defining and refining the scope of the study, the outline of the first report and discussions on the definitions, description and examples of biomarkers of effect in the regulatory risk assessment context. These discussions will be reflected in a Scientific Report to be finalised by October 2024.
In addition, the WG is consulted on the collaboration and engagement activities to be established towards co-creating the guidance within an EU/international partnership in the next phase of the project.

WG Read Across:
The work is ongoing focusing on transferring and integrating the knowledge from an ongoing procurement contract, and in the environmental scanning to ensure full understanding of parallel activities. The plan for 2024 includes internal and external consultations, ensuring that the guidance considers all relevant aspects for this topic.

WG MUST B :
An overview of the progress made by the WG on the definition and selection of environmental scenarios for the honey bee colony model ApisRAM (link here) was provided to the SC. This included the presentation of baseline and case scenarios. Baseline scenarios include the setting of initial conditions for colony and environmental attributes presenting varying levels of ecological quality. The case scenarios correspond to the conditions set for the testing of specific Plant Protection Products/use. Increasing exposure modification factors can be applied to the case scenarios combined with various levels of baseline scenarios (going from most favourable to least favourable ecological quality). This factorial design defines a risk matrix and margins of safety. Preliminary conclusions and recommendations from this work were presented to the SC.

6.4 Discussion on Scientific Committee 2024-2025 Work programme

The SC was provided with an overview of the achievements of 2023 and the draft work programme for 2024. In relation to achievements, the guidance on protocol development was finalised and published in October 2023 (link here).

Work is ongoing for the development of guidance on read across and on risk benefit assessment. With regard to guidance on default values, a survey was made with the EFSA Units and Panels and the results have been summarized in a report. The SC will be requested to review the proposals made and to advice on the possible revision of the guidance.

Work is also ongoing and will be finalised in 2024 for the risk assessment of bromide and fluoride. The SC was also reminded about the list of possible guidance to be developed that was drafted in the end of 2022 after consultation with Panels, Units, and the Advisory Forum and the EC-DG Sante. A similar process will start in 2024 to build the work programme for 2025-2026.

A new mandate was presented to the SC in relation to the risk assessment of microorganisms that are used in the food chain for different purposes. The assessments are linked to requests for authorisation of the products under the applicable Regulations. The products evaluated may contain the microorganism, be prepared from, or obtained

with the microorganism, and the microorganisms can be genetically modified or not. EFSA considers it necessary to have one scientific guidance document detailing the requirements for the risk assessment of microorganisms that could be applied across sectors. As the SC plays a major role in harmonising practices across areas, it was proposed that the SC prepares a guidance document on the risk assessment of microorganisms used in the food chain to be applied across sectors. The SC agreed on the proposal and a self-task will be prepared. At this regard, it is intended that the WG on Microbiology from the FEEDAP Panel with experts from other Panels will prepare the draft guidance for the consideration of the relevant EFSA Panels and finally for the endorsement and adoption by the Scientific Committee.

7. Any other business

8. Preparatory meetings

Since the last Plenary meeting, a preparatory meeting chaired by EFSA staff was held on the 14 November to discuss the agenda items.

9. Next meeting

The next plenary meeting will be held on 5-6 February 2024 via teleconference**.**