SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

Scientific Committee

Minutes of the 98th Plenary meeting

Held on 22-23 April 2020

(Agreed on 15 May 2020)

This meeting, originally scheduled as a physical meeting, was converted into a teleconference to avoid traveling to EFSA in line with the measures established to reduce the risk of coronavirus infection.

Participants

- **Scientific Committee 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, Hanspeter Naegeli, Søren Saxmose Nielsen, Josef Schlatter, Dieter Schrenk, Vittorio Silano, Dominique Turck, Maged Younes.

- **European Commission:**

  Marina Marini (DG SANTE DDG.2.D1)

- **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 (REPRO):** Guilhem De Seze
  - **Communication Engagement and cooperation Department (COMCO)**:
  - **Scientific Committee and Emerging Risks Unit (SCER):** Tobin Robinson, Daniela Maurici, Bernard Bottex, Andrea Gervelmeyer, Caroline Merten, Agnes Rortais, Reinhilde Schoonjans, Justyna Slodek–Wahlstrom, Jose Tarazona, Ana Afonso (for agenda item 11), Hans Verhagen.
  - **Transformation Services Unit (TS)**: Marco Conterbia

- Others:

  Hearing experts: NA

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1. Welcome and apologies for absence

The Chair welcomed the participants. No Apologies were received.

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[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the 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 topic(s) for discussion

4.1. Draft opinion on Non Monotonic Dose Response (NMDR)(EFSA-Q-2019-00530)[3]

Following up on an EFSA Scientific Colloquium from 2012 and 2 procurement outsourced by EFSA in 2014 and 2016 on non-monotonic dose response, the SC was self-tasked in 2019 to assess the biological relevance as past assessments did focus mainly on visual or statistical analysis. To this end, the Terms of reference for the WG were to prepare a scientific opinion on the biological relevance of the *in vivo* non-monotonic dose responses identified in the visual/statistics-based analysis.

In case biologically relevant non-monotonic dose responses are identified, the WG needs to address the possible consequences for the human health risk assessments conducted by EFSA.

Considering the time and resource limitations, the SC suggested to use information from the OpenFoodTox database, other EFSA assessments, and the expertise available at the SC and EFSA Panels and Units. More specifically the WG tasks are: (1) To assess the biological relevance of the non-monotonic dose responses identified *in vivo* in the EFSA external report (Beausoleil et al., 2016) and the follow up probabilistic assessment (Chevillotte et al. 2017a,b), based on visual/statistics/probabilistic considerations; (2) To further analyse the non-monotonic dose-responses assessed as biologically plausible, grouping them, if appropriate, and to evaluate their potential link with adverse effects, considering if the response induction/increase and response inhibition/decrease are associated with the same or with different adverse outcomes; (3) To assess the biological plausibility for opposite responses at different dose levels for the adverse effects that are pivotal for EFSA assessments and usually lead the health risk assessment outcome, in order to evaluate the impact of any biologically relevant endpoint showing a non-monotonic dose response *in vivo* on EFSA risk assessment outcomes; (4)To recommend follow up actions in case biologically

[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
[3] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2019-00530

relevant non-monotonic dose responses impacting the risk assessment outcomes are identified. These recommendations should address priorities within EFSA, as well as priorities for international cooperation. Issues encountered so far by the WG in the assessment were discussed with the SC for its feedback. The following issues were discussed in more detail:

(1) Proposed approach for addressing NMDR in the risk assessment process: The approach is based on the consideration on where in the range of available doses the non-monotonicity is observed (upper or lower end of the dose -response curve), and whether the observed effect is an apical, early or intermediate event. It also provides indications for additional testing and signal that New Approach Methodologies (NAMs) may help identifying a mechanistic sequence of events.

The SC agreed with the general approach but indicated that in certain cases it will be realistically difficult to get additional data on doses at a lower range. Attention needs to be drawn on the required quality of the data as some studies did not follow OECD test guidelines and some findings may just have been incidental. On the other hand, a valid study conducted following OECD test guidelines may be sufficient to conclude that the response is non-monotonic when a sufficient number of doses has been tested.

(2) Implications for the BMD approach: The BMD tools are currently not available to evaluate non monotonicity. The available software should not drive the way how risk assessment should be done. If agreement is reached by the SC that non monotonicity exist for relevant endpoints, the update of the SC guidance for the use of the benchmark dose approach in risk assessment, and of the mathematical models used for BMD analysis should be prioritised. In any case, international agreement would be needed on how to take account of non-monotonic dose-response data in regulatory risk/benefit assessment. It was advised to keep the discussion on the BMD modelling separated from the discussion on whether monotonicity is present or not. The SC agreed in passing these considerations to the BMD WG.

4.2. Draft statement on "EFSA approaches for the Derivation of Health Based Guidance Values (HBGV) for food additives, other regulated products and nutrients" (EFSA-Q-2019-00505)[4]

Some nutrients are also used in products subject to regulatory assessment, e.g. phosphates or chlorates as additive, copper in pesticides and feed additives.

When EFSA receives and application using a nutrient as regulated product, the assessment of the risk for consumers should consider all sources of dietary exposure. It is important to consider also the implications regarding the advice to risk managers, for their decision making on each regulated use, as well as for enforcement.

At the February plenary, a technical report reviewing current EFSA approaches for setting Health Base Guidance Values (HBGV) was presented and discussed. Following the SC decision, the information will be incorporated as an annex of the Statement under development.

An integrated and harmonised approach for setting the HBGV is needed for assessments of nutrients conducted in the context of regulated products. A draft statement discussing the recommendations on how EFSA Panels should derive health-based guidance values in a harmonised/consistent manner for these substances was presented to the SC for first discussion.

[4] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2019-00505

The Scientific Committee went through the sections of the statement on risk characterisation and the draft recommendations. A decision tree with regard to the need to revise established HBGV for nutrients used in regulatory products was discussed. It was clarified that deficiency was not covered explicitly in the current sections of the statement, but the particular considerations in terms of benefit and deficiency for nutrients will be covered in other sections of the statement. In addition to the overall approach, a set of specific questions requiring SC feedback were posed. In particular, expressing the HBGV in absolute amount and relative to body weight may be needed for facilitating the communication to and use by risk managers and stakeholders.

Suggestions by the SC were provided to improve the decision tree, clarifications to the questions posed were proposed and some feedback to the draft recommendations in the statement were given. Additional written suggestions by the SC to the draft recommendations may be sent by end of April.

The draft statement is expected to be ready for consultation with EFSA units and panels in May 2020. The draft statement will be presented to the SC for possible endorsement for public consultation at the June Plenary.

4.3. Draft guidance on appraising and integrating evidence from epidemiological studies: chapter 4.3. (EFSA-Q-2019-00199)[5]

Section 4.3 on appraisal of epidemiological studies was presented to the SC. The SC was asked to provide feedback on the usefulness of the overview of critical appraisal tools provided in this section, whether more practical guidance would be needed, and to indicate if any parts should be expanded or better explained.

The SC agreed that the balance between the more generic/background sections (such as 4.3.1 and 4.3.2) and those giving more specific guidance (such as 4.3.3.1-2) was acceptable. It was suggested to provide more examples for identification of biases in 4.3, including examples of studies that were initially judged (or could be judged) low risk of bias while it later turned out to be different, and vice versa. Examples of complete risk of bias appraisals for different study designs (e.g. of one Randomised Controlled trials and another for observational study (cohort)) and using different Risk of Bias tools should be developed and placed in an annex.

The WG was requested to expand the subsection on scoring and give examples, e.g. on how to deal with a study that is appraised to have a "high probability of bias" in the overall assessment. Regarding the topic of evidence integration, it was suggested to keep a good balance between description of approaches and examples without being prescriptive. Finally, it was highlighted that a short conclusive paragraph or sentence at the end of each subchapter would be very useful.

4.4. Draft Guidance on appraising and integrating evidence from epidemiological studies: chapter 4.1 and 4.2

An update was provided to the SC on recent revisions based on past comments by the SC on sections 4.1 (introduction on epidemiological studies) and 4.2 (key epidemiological concepts relevant for evidence appraisal) which intend to explain the principles to understand the concepts relevant for appraising and integrating evidence from epidemiological studies.

The Scientific Committee was asked to provide additional comments and suggestions on the parts that needed to be expanded or better explained.

[5] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2019-00199

Finally, a recent change of project plan was introduced to the SC. Due to a change of resources between EFSA units it is proposed to publish chapters 4.1 to 4.3 as an intermediate report by mid-2020. Panels should start gathering experiences with evidence appraisal and related tools. It was proposed that the final section 4.4 on the Use of epidemiological evidence for specific scientific assessment questions will be developed in a later stage in 2021/2022. This proposal was accepted by the SC.

4.5. Draft technical guidance on nanotechnologies (EFSA-Q-2020-00269)[6]

The SC was presented with the first draft on the "Guidance on technical requirements of regulated food and feed product applications to establish the presence of particles at the nanoscale". 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). The current technical guidance under discussion applies to conventional materials that do not meet the legal definition but may contain particles in nanoform (e.g. due to their production process and, in particular, micronisation of powders). Usually not sufficient information is submitted in the applications of such conventional material, either to be placed on the market or already on the market and subject to renewal of authorisation. The possibility that the material may consist of, or contain nanoparticles, so far became apparent during EFSA assessments or by enforcement authorities after the material has been authorised. Depending on the material, particles may not retain the specific physico-chemical properties of the non-nanoform even if their external dimensions are at the nanoscale. Therefore, having sufficient information in the applications to be assessed by EFSA is essential.

To address this challenge EFSA was tasked by the EC to develop a technical guidance setting out the information requirements for applications in the regulated food and feed product areas of conventional materials which do not meet the definition of engineered nanomaterial set out in the Novel Food Regulation (EU) 2015/2283, in order to demonstrate whether a portion or the whole of the material is in the nanoscale. For those materials which have been determined to contain a fraction of small particles, including particles at the nanoscale, the European Commission asks EFSA to include in the guidance the information requirements demonstrating that the nanoscale fraction of the material was properly evaluated in the safety studies of the material. Only when the particles have the specific properties of the nanoscale, the recommendations in the EFSA 2018 Guidance should be applicable.

The draft technical guidance was presented to the SC for its feedback. It was clarified that the guidance will be applicable to new applications and re-assessments. The SC suggested to make the level of obligation to apply the guidance clearer in the current draft and to get feedback from DG SANTE regarding the implementation time of the guidance after publication.

It was clarified that although not part of the mandate, elements of the guidance could also be applicable to non-regulatory assessment and on particles not necessary in the nanoscale such as micro plastics but with potential nanoscale properties. This means also that particles above the regulatory cut off value of 100nm may require consideration, and a scientifically driven value of 250nm is proposed. The approach proposed was supported by the SC, and several proposals for improvement were discussed. Additional feedback by the SC can be provided until 5th of May.

SC comments on the draft will be considered by the WG and a consultation of the updated version with the relevant panels and units is planned. Endorsement for public consultation is planned for the June SC Plenary. The original deadline in the EC mandate was December 2020. However, this deadline is under reconsideration.

[6] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2020-00269

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

5.1 Update on WGs activities

- **Cross-cutting WG Nanotechnologies**

This agenda item was postponed due to lack of time.

- **Cross cutting WG Benchmark Dose**

In addition to its function to provide assistance to EFSA Units and Panels on BMD-related difficulties, the working group 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: further guidance to set the benchmark response will be provided, the set of models to be fitted to the data will be updated, and Bayesian model averaging will be introduced. The Scientific Committee appointed Dr. Josef Schlatter as Chair of the working group for this new mandate. A number of possible additional needs were identified, pending finalisation of other ongoing EFSA activities, and depending on the resources available: use of the benchmark dose approach with non-monotonic dose response data, benchmark dose modelling of epidemiological and omics data, database of priors for Bayesian benchmark dose modelling. The importance of international cooperation on all these issues was underlined.

- **Cross-cutting WG Mixtox 2**

The working group has made progress on the MIXTOX 2 scientific opinion: "Scientific criteria for grouping chemicals into assessment groups for human health risk assessment of combined exposure to multiple chemicals". Schemes for both hazard-driven criteria and prioritisation tools using exposure-driven and risk-based criteria were discussed during the last meeting. These schemes have been further modified and will be discussed during the next teleconference.

- **Cross-cutting WG Genotoxicity (M-2019-0091)**

The public consultation on the draft guidance on aneugenicity assessment was launched on 30th March it will be closed on 31st May. The comments received will be addressed by the WG to prepare the final guidance hopefully by the end of the year of beginning of 2021. The timelines were slightly revised as other priorities have emerged for the WG.

The WG has also received requests for advice from the PPR Panel on *Pseudomonas chlororaphis* MA342 and from the Peer Review Unit (PREV) on 3,5,6-trichloro-2-pyridinol.

From the Food Ingredients and Packaging Unit (FIP), a request was received to support the genotoxicity assessment of styrene, in response to an EC mandate.

- **Cross-cutting WG Uncertainty**

The WG had their most recent meeting on 10 March 2020. The WG discussed in detail the plan for implementing the guidance document on uncertainty in scientific assessment and uncertainty analysis for two mandates for regulated products:
(1) Scientific Opinion of the PPR Panel on "Developing Integrated Approaches to Testing and Assessment (IATA) on developmental neurotoxicity (DNT)". To develop adverse outcome pathway (AOP) informed IATA case studies using a DNT risk assessment-based problem formulation. This can be done using selected active substances as examples and considering the level of uncertainties associated with the available evidence to integrate the outcomes of a new in-vitro testing battery for DNT (outsourced by EFSA) in the AOP informed IATA case studies. In the end the uncertainty can be re-analyse to guide on the use and interpretation of the in-vitro DNT testing battery. Two case studies were selected: Deltamethrin and Flufenacet using DNT and focusing on the hazard assessment only. This work is still in progress.
(2) New mandate of FAF panel on updating the guidance document for submission of applications on smoke flavouring primary products. The WG recommended to ask for information that can support the characterisation of uncertainty (including variability) when asking for data, which may include errors of estimates (or sufficient statistics to be able to estimate this) of toxicity and, information about how samples have been selected in assessments of batch to batch variability, and uncertainty in parameters supporting the exposure assessment.

- **Beeswax WG (M-2019-0061)**

This agenda item was postponed due to lack of time.

- **WG MUST-B and EU Bee Partnership (M-2018-0155)**

EFSA presented the mandate received from the European Parliament of the MUSTB working group to the PPR Panel on 01/04. The last MUSTB WG was held on 15-16/04 to discuss (i) the structure of the report, (ii) the inclusion of the results of the working group of the Social Research Methods and Advice on the beekeepers' perspectives, (iii) a discussion with risk assessors on the system approach developed under this opinion and (iv) clarifications on the objective and format of this scientific opinion. On the latter issue, more details will be provided by the chair, Simon More, at the SC Plenary in September, when presenting the draft Scientific opinion to the Scientific Committee.

- **WG Compendium of Botanicals (M-2012-0145)**

The working group started reviewing the composition and toxicity/adverse effects data for the last group of 900 plants. The transfer of the 1600 already validated plants is still pending due to problems for updating the EFSA data model. Regarding the characterisation of the toxicity of the substances identified as of possible concern for human health in the above-mentioned 1600 plants, the working group started reviewing the validity of existing QSAR models with 50 substances existing both in the compendium and in openfoodtox, i.e. for which experimental toxicity data exist to validate the predictions obtained from the QSAR models.

- **WG on Synthetic Biology**

Upon endorsement at the last plenary meeting, EFSA launched the Public consultation on the draft Scientific Committee opinion "Evaluation of existing guidelines for their adequacy for the microbial characterisation and environmental risk assessment of micro-organisms obtained through synthetic biology". From 31 March until 26 May, the public will be able to submit comments via the online tool http://www.efsa.europa.eu/en/consultations/call/public-consultation-draft-efsa-scientific-committee-opinion. This public consultation is accompanied by the publication of the outsourced technical report "Horizon Scan of Synthetic Biology Developments for Microorganisms with application in the Agri-Food Sector" (http://www.efsa.europa.eu/en/supporting/pub/en-1664). In parallel, and with the same

timelines, the GMO Panel's draft opinion on synthetic biology in plants was opened for public consultation, and accompanied by the publication of the technical report "Mapping of plant SynBio developments in the agri-food sector" (https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2020.EN-1687). The comments will be addressed in the forthcoming working group meetings, scheduled for the end of June. Finalisation is expected in autumn.

6. Other topics for information and discussion

6.1 Update on COVID 19

The SC was informed about the emergency measures in place for EFSA staff since the onset of the COVID 19 crisis. All staff have been teleworking since the onset of the crisis. The EFSA staff and EFSA experts were acknowledged for their commitment and engagement to continue doing their work in the present difficult situation. The crisis has also shown some opportunities to explore new ways of working that could be reconsidered also in the near future. Increase virtual meeting will also help to reduce impact of commuting and travelling on the environment.

An EFSA task force will consider lessons learnt during this recent period of exceptional teleworking. This analysis will provide useful insights to update the Strategy 2021-2017 document, informing a possible alternative way of delivering the EFSA work. Opportunities are explored for EFSA to be better prepared for future crisis.

6.2 Update on the EFSA strategy 2021-2027

The SC was presented with a short update on the EFSA Strategy 2021-2027. The revised strategic objectives and related work areas were briefly presented: (SO1) Deliver trustworthy scientific assessment and communication of risks from farm to fork; (SO2) Build partnerships for the scientific advice of the future; (SO 3) Empower people and inspire a culture to realise EFSA's strategy.

The initial plan was to have a public consultation during the month of April 2020, and to submit the EFSA 2027 strategy for possible endorsement by the Management Board in June 2020. A strategy detailed implementation and monitoring plan was planned to be prepared for endorsement by the Management Board in December 2020. The SC was informed that, due to the ongoing COVID 19 crisis, this plan and related implementation is now on hold. A discussion on the next steps will be held in June 2020 with the Management Board and future timelines defined.

6.3 Update on the future of risk assessment (RA) in EFSA

The SC held a high-level discussion on a document summarising three reflection papers developed by an EFSA internal Task Force aiming at contributing to the development of the EFSA Strategy 2021-2027. The three reflection papers were prepared in the areas of chemical, environmental and biological risk assessment, focussing on scientific considerations: What are the existing challenges, what risk assessment capabilities is EFSA missing and what will be needed in the future?

The Scientific Committee was consulted on these three documents and the related summary document in March prior to this plenary meeting. Comments received from the EC and the SC were presented and discussed.

The SC was reminded about the context of this work. This activity supports the development of future EFSA strategies to anticipate future challenges for which EFSA need to invest special attention and more efforts. These efforts should be linked to address also more regional and global challenges such as climate change, sustainability, response to crisis etc. Alignment and further harmonisation with international and other EU and MS risk assessment bodies will be sought for along with collaboration with overarching European research projects relevant for EFSA's work such as HBM4EU (Human Biomonitoring for EU). The ideas presented in these internal documents will be used as inspiration for the forthcoming EFSA strategy and its implementation plan, and the SC will be given the additional opportunities to comment. The breadth of ambition covered is greater than EFSA's capacity, so there will be a prioritisation step during the integration of this material into the strategy to pick out the more important aspects for EFSA. These documents are evolving documents which may be updated when necessary.

6.4 Working in TEAMS: brief explanation on the main features for using the digital collaboration

The SC was provided with an introduction on how Microsoft TEAMS will be used in EFSA to improve collaboration on the development on outputs. In particular, the co-authorship features were presented in a DEMO to the SC. All future communications could also be done in TEAMS to avoid email overload.

It was clarified to the SC that the present document management system (DMS) will remain the EFSA repository and should be available to the EFSA experts until spring 2021, when EFSA will move to a new repository system. Currently EFSA is in a transition period in which all its WGs and Panels are migrated to TEAMS.

7. Any Other Business

7.1. General matters arising

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

7.2. EFSA survey on the use of cross cutting guidance documents

The SC was informed that a survey is currently being prepared to monitor how a selection of cross cutting guidance documents are used by the EFSA scientific staff and experts. The survey link has been sent to the EFSA WG coordinators, all the Panels and distributed also to the EFSA units. The SC is encouraged to promote the survey to their respective panels. The survey is open until 18th of May. It was clarified that the survey should be filled in only once by a Panel /WG member even if the survey participant is collaborating in multiple WGs.

7.3. List of published opinions

The Scientific Committee was provided with a document containing the list of published opinions from 30 January to 06 April 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 includes published conclusions on the peer review of pesticides and ongoing public consultations.

7.4. Draft agenda next SC plenary, open to observers

The SC was presented with an overview of the topics that will be on the agenda of the June meeting. The meeting is scheduled for the 23 June – 24 June via web conference. This meeting will be open to observers.

99th SC Plenary: 23 June – 24 June, telemeeting OPEN to observers
100th SC Plenary: 16 Sep (full day) – 17 Sep (9.00-13.00)
101st SC Plenary: 11 Nov (full day) – 12 Nov (9.00-13.00)

SC Plenary dates in 2021: dates will be finalised by the last week of April. Any pending issue with proposed dates for 2021 should be highlighted to SC coordinator by 27 April.

END OF THE MEETING