TOX/2025/06

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Potential future discussion items – horizon scanning

Background

1. The Committee Terms of Reference specify *"*To advise at the request of" (……government departments). Therefore, the work of the Committee is primarily reactive and the agendas are set by the Secretariat based upon the need for advice from Government Departments and Agencies particularly, but not exclusively, the Food Standards Agency (FSA) and the UK Health Security Agency (HSA).

2. The Code of Practice for Scientific Advisory Committees (Office of Science and Technology, December 2021), specifies that "committees should ensure that they have mechanisms in place that allow them to consider on a regular basis whether new issues in their particular areas of responsibility are likely to emerge for which scientific advice or research might be needed".

3. Members have agreed that it would be useful to have an annual agenda item to discuss potential future topics. A list of upcoming topics is also displayed on the Committee's website: Forthcoming COT meetings | Committee on Toxicity.

4. As Members are aware, now that the UK has left the European Union the authorisation of regulated products that would have been done by EFSA is being done in the UK. Two Joint Expert Groups (JEGs) have been established to cover the authorisation of regulated products and these will be over seen by the COT who will provide challenge, comment and assurance of their work. The FCMJEG

covers food contact materials and AEJEG covers food additives, enzymes and other regulated products. An additional AEJEG group is working solely on the reauthorisation of smoke flavourings.

5. Details of completed JEG assessments are available on the FSA website Research projects | Food Standards Agency using the Scholastica publication format.

6. Requests for COT advice are also being received from the Nutrition, Labelling Composition and Standards Group which is a risk management group for the 4 countries of the UK and covers legislative areas such as infant formula and follow on foods, food supplements, and nutrient sources where the policy lead is the responsibility if the Department of Health and Social Care in England, FSA Northern Ireland, the Scottish Government and the Welsh Assembly; topics previously raised by NLCS include green tea catechins, fortificants in bread and flour and folic acid hypersensitivity.

7. This has been reflected in the agendas of the Committee, although it is still unclear how much Committee time this will represent in the long term.

Agenda items for 2025

Ways of working

8. The Committee considered horizon scanning as part of their recent discussions on ways of working. It was agreed that while the process could be more effective, and that they would be interested in information on different horizon scanning techniques it was important in considering these to determine what exactly the Committee needed to get out of the process. Members agreed that the results of horizon scanning should be a living document.

9. It was also noted that other Advisory Committees and Regulatory Agencies covering chemicals undertook horizon scanning and it might be useful to learn what they were doing, noting that, for example, the United States Environmental Protection Agency (EPA) or the German Federal Institute for Risk Assessment (BfR) might be a

nearer equivalent than the COC or the COM, whose interests were more focused. Unfortunately, due to resource constraints it has not been possible to develop work on horizon scanning since the Committee discussions on ways of working took place.

Ongoing items

10. There are a number of ongoing items, either on the current agenda or scheduled for further discussion at a future meeting:

- COT input into the Scientific Advisory Committee on Nutrition (SACN) review of the maternal diet.
- Biologically based food contact materials.
- Bisphenol A.
- Emerging marine biotoxins.
- the mycotoxins T2 and HT2.
- per and poly fluoroalkyl substances (PFAS).
- Nanoplastics.
- Antimony with respect to drinking water guidelines.
- Boron with respect to drinking water guidelines.

Upcoming items

11. Upcoming items may include alternatives to BPA, mycotoxins in cat food and acrylamide.

Proposed Workshops

12. The two most recent COT workshops have been held on “Evolving Our Assessment & Future Guiding Principles Workshop” and “Gut Reactions: Xenobiotics and the microbiome” which took place in October 2024.

13. It is proposed that the 2025 workshop cover Artificial Intelligence (AI) in

chemical risk assessment and any workshop would be likely to take place in October 2025. It is intended that the proposed workshop be a first step towards reviewing state of the art AI technologies relevant to chemical risk assessment as well as discussing the opportunities and the challenges associated with application of AI in chemical safety assessment. However, Members will wish to consider other potential topics.

14. The FSA and UKHSA Secretariat are exploring options for holding a joint meeting with other Committees to discuss areas of joint work and ongoing topics.

COC and COM horizon scanning

15. COC and COM have been considering the approach used to horizon scanning for these Committees, which included a joint discussion session in October 2023. This was further investigated by COC in 2024, with discussions at the March and November meetings. In the meantime, there is no further update to activities for COC or COM than was presented in the 2023 COT horizon scanning paper.

Other Updates

FSA-funded Computational Toxicology Fellowship and LIDo PhD student in AI

16. The FSA and COT have been reviewing New Approach Methodologies (NAMs) to scope the best scientific methodologies available to be used in risk assessment of chemicals in foods and the environment and understand how these can be incorporated in a regulatory context with validation approaches.

17. The FSA have recruited a computational toxicology fellow at the University of Birmingham and a PhD Student (London Interdisciplinary Doctoral Program-LIDo-TOX AI) at King's College London. The aims of the projects are to develop *in silico* tools (*i.e.* artificial intelligence machine learning) for toxicological prediction of chemicals through case studies and proof of concept studies. The fellow and student will also work alongside other government departments to understand how NAMs will improve indicative levels of safety in chemical risk assessment.

18. In addition, these new partnerships will help with networking, research collaboration, training opportunities and further our knowledge in this area. The fellowship and studentship also compliment the work set out in our UK Roadmap towards using new approach methodologies in chemical risk assessment.

19. The programme of work in the fellowship consists of (i) scoping the FSA's problem space in chemical risk assessment and mapping this to our computational NAMs solution space, thereby aiding the FSA to develop a strategy for the utilisation of NAMs; (ii) ensuring that the FSA is trained in the use of computational NAMs by delivering training courses, including an introduction to existing and emerging NAM technologies, and topics selected from the FSA's NAM strategy; (iii) developing and evaluating confidence in a new hazard assessment workflow that integrates in vitro omics toxicity data, benchmark dose modelling and PBPK modelling to serve as the basis for quantitative risk assessment for human health, i.e., towards generating human health-based safety thresholds for FSA and other regulators; and (iv) developing and delivering a second case study that fortifies the community-wide acceptance of 21st century methods in risk assessments, to accelerate the successful application of NAMs within the FSA.

20. The postdoctoral fellow case study on a perfluorinated substance, perfluorooctanoic acid (PFOA) has now been completed and published. The NAMs employed include:

- NAMs in relation to the type of testing platform - in vitro hepatic microtissues;
- NAMs in relation to the type of data/read-outs - transcriptomics data, providing an untargeted measurement of extensive gene expression;
- NAMs in relation to data analysis - PBPK modelling.

21. Our recent work on PFOA (Silva et al., 2024) has been presented on several occasions. To list a few, PARC Science Day (poster presentation), NURA Dynamic Discussions (oral presentation, online), HSE's workshop (oral presentation, online), EFSA's workshop (oral presentation, online), EUROTOX 2023 (poster presentation), ASPIS Open Symposium 2023 (poster presentation). The PFOA work was submitted

as a nomination to the Lush Prize under the Young Researcher category and was one of the five projects awarded in 2022.

22. The third case study is now under consideration by the supervisory team, which is keen to work with tropane alkaloids as this class of substances is of high interest to the FSA.

23. The programme of work in the PhD up to the present is composed of three parts: (1) Exploration of dimensionality reduction algorithms, for powering QSAR models of mutagenicity, constructed of simple feed-forward Deep Neural Networks (DNNs) (Kalian et al., 2023, Kalian et al., 2023) (This article belongs to the Collection Artificial Intelligence and Data Mining for Toxicological Sciences and is a Feature Paper and Editor's Choice); (2) Development of Graph Convolutional Networks (GCNs) to improve mutagenicity predictions, via graph classification of molecules, while also allowing for mining of structural alerts (SAs).

24. The PhD student current program of work consists of graph attention networks using knowledge graphs, for predicting novel points of departure for brominated flame retardants (BFRs) by the development of Graph Neural Networks (GNNs) for node classification of molecules, in order to predict toxicological properties of BFRs (Kalian et al., 2024). This won the **Toxics Travel Award 2024** and was presented at Eurotox 2024.

25. The postdoctoral fellow and PhD student are working on a case study together.

FSA Research Programme

26. The FSA research strategy has seen the consolidation of all research in the portfolio into a series of programmes by area of research interest.

27. Current projects in the Chemical, Radiological and Hypersensitivity Research Evidence Programme include:

- A literature review of nitrates and nitrites with a focus on the four food additives sodium nitrate, sodium nitrite, potassium nitrate and potassium nitrite. The aim is to review the literature published since these 4 additives were last reviewed by EFSA.
- Determination of the bioavailability of hydrogen cyanide following consumption. This project aims to determine the bioavailability of hydrogen cyanide from a range of foods.
- Method development for PFAS in fruit and vegetables. The aim of this project is to develop analytical techniques to measure 30 pre-identified PFAS in a range of fruit and vegetable matrices.

Balance of expertise on the Committee

28. It has previously been agreed that the following types of specialist expertise are required by the Committee for some or all of its evaluations:

Analytical techniques
Biochemistry
Bioinformatics
Cell biology
Clinical practice
Dietary exposure assessment
Endocrinology
Environmental exposure assessment
Epidemiology
Human toxicology
Immunology
Mathematical Modelling
Mechanistic toxicology
Molecular biology
Neurotoxicology
Nutrition

Paediatrics
Pharmacokinetics
Pharmacology
Probabilistic modelling
Reproductive toxicology
Respiratory toxicology
Risk assessment
Statistical aspects of experimental design
Statistics
Systems biology
Toxicogenomics
Toxicological pathology
Xenobiotic metabolism

29. It would not be necessary to have an individual member for each listed expertise as some people would have a combination of the required skills. Additional key experts are also invited to attend meetings for specific topics to supplement missing knowledge.

30. As Members are aware recruitment to the FSA Scientific Advisory Committees is now carried out annually by a central team, starting in the Autumn. However, the balance of expertise set out below is used to guide the process.

31. Members are invited to comment on whether this list is still appropriate and if there are important gaps amongst the current membership or in light of possible future developments.

Questions on which the views of the Committee are sought:

32. Members are invited to comment on each of the above areas and also to consider the following questions:

i) Do Members have additional suggestions for future topics for:

- Specific issues to be included as routine agenda items.
- Focussed topics for one-day meetings or workshops.
- Generic issues requiring establishment of a Working Group.

ii) Do Members have any proposals for research that FSA should fund in order to improve future COT risk assessments?

iii) Do Members have any comments on the balance of skills on the Committee? Members are reminded that they may draw particular issues to the attention of the Secretariat at any time.

Secretariat January 2025

References

CoPSAC (2021) Code of Practice for Scientific Advisory Committees and Councils: CoPSAC 2021 - GOV.UK.

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