Meeting

Potential future discussion items – horizon scanning 2023

This is a paper for discussion.

This does not represent the views of the Committee and should not be cited.

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. When discussing horizon scanning (section 6.1), the Code of Practice for Scientific Advisory Committees (Government Office for Science, 2021), notes that "SACs should keep under review potential future threats, opportunities and key developments in their particular areas of responsibility".

3. Members have agreed that it would be useful to have an annual agenda item to discuss potential future topics. The list of topics is displayed on the Committee's website: Forthcoming COT meetings | Committee on Toxicity (food.gov.uk).

4. As Members are aware, now that the UK has left the European Union and the authorisation of regulated products that would have been done by EFSA is being done in the UK. Two Joint Expert Groups (JEGs) cover the authorisation of regulated products; 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. Although a JEG covering animal feed and feed additives was initially established, this was superseded by the reconstitution of the Advisory Committee

on Animal Feedingstuffs (ACAF) who will cover authorisations of animal feed and feed additives and who may, on occasion, seek specialist advice from the Committee.

5. Requests for COT advice in the post EU exit area, 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 of the Department of Health and Social Care in England and the devolved administrations.

6. Requests arising from EU exit activity is starting to affect the agendas of the Committee, although it is unclear as yet how much Committee time this will represent in the long term as the first authorisations are only now being seen by the Committee.

Agenda items for 2023

Ongoing items

7. 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.
- Microplastics -inhalation.
- Dioxins: Following the discussion of the EFSA opinion on dioxins and the COT ’s recommendations to undertake their own review, funding was secured for an external contractor, with work starting in October 2022. The results are expected in late spring 2023.
- Regulated products including smoke flavouring re-authorisations.
- The COT/FSA Roadmap: “Development, Validation and Regulatory Acceptance of New Approach Methodologies (NAMs) in Chemical Risk Assessment”.
- PFAS
- Aircraft cabin air.

8. The FSA has a substantial programme of surveys to monitor the safety and quality of food. Details of these are available on the FSA website: Research projects | Food Standards Agency.

9. Where appropriate, the Committee's advice will be sought on the health implications of the results. The Secretariat is not aware of any surveys likely to be received in the near future.

Working Groups

Plant based drinks

10. The joint COT/SACN Working Group (WG) on plant based drinks is undertaking a risk- benefit assessment of oat, almond and soya drinks using the BRAFO methodology. The draft final statement will be presented to the Committee in the early part of this year.

Cannabidiol (CBD)

A joint Working Group of the COT and the Advisory Committee on Novel Foods and Processes (ACNFP) has been established to review the data on cannabidiol (CBD) submitted as a part of the novel foods applications process. The outcome of the WG will be presented to the Committee.

Codex report on Food Allergen thresholds

11. A Working Group has been established to review the Codex report on Food Allergen thresholds. The outcome of the WG will be presented to the Committee this year.

Upcoming items

2023 Workshop

12. Following discussions at previous meeting, a workshop is planned for May 2023 to initiate planned work on updating the COT guidelines on toxicity testing.

BPA

13. Members will recall that at the end of 2021, EFSA published a draft opinion on Bisphenol A. Members reviewed the draft opinion and detailed comments were forwarded to EFSA. The final opinion was anticipated in December 2022, but has not yet been finalised. However it seems likely that it

will be published early in 2023. It is expected that the final opinion will be presented to the Committee for their comments.

Potential discussion topics

UK HSA

Phosphate-based flame retardants – updated literature search

14. Phosphate-based flame retardants (PFRs), otherwise known as organophosphate esters, show some structural similarity to other classes of organophosphates, such as organophosphate (OP) pesticides, which have been shown to interfere with neurodevelopment by cholinergic and noncholinergic (serotonergic and dopaminergic) pathways (Danish EPA, 2016). In 2019, the COT published a statement on phosphate-based flame retardants (PFRs) and the potential for neurodevelopmental toxicity (2019/04).

15. The conclusion from the 2019 statement (2019/04) was that 'the available evidence indicates that PFRs do not pose a risk of developmental toxicity at anticipated exposure levels. Overall, the Committee determined that the experimental evidence suggested that PFRs were different from other OPs in terms of their chemical and biological activity and therefore PFRs would not be expected, de facto, to show the same neurotoxicological effects as other OPs. No experimental data on the developmental neurotoxicity of PFRs were identified. The experimental data retrieved did not provide evidence in support of any OP-related mode of action for developmental neurotoxicity of PFRs. However, the available epidemiological studies, albeit limited, provided some evidence for neurodevelopmental effects in exposed populations. Limitations in this evidence included study design and a lack of specificity in the relationships identified. The Committee concluded that PFRs were very unlikely to share the neurodevelopmental effects of other OPs but could not exclude the possibility that PFRs could produce neurodevelopmental toxicity by some other mechanism'.

16. In 2021, the COT become aware of new data relating to PFRs and developmental neurotoxicity and consequently replicated previous literature searches to capture this and any other new data published between 2019 and 2021 (TOX/2022/07). The Committee also requested such searches be carried out in subsequent years to capture any new published data. This paper presents data captured using the same literature search as previously presented (TOX/2022/07) that was published in 2022.

Results

17. Two papers addressed the relationship between PFRs and developmental toxicity, including attention-deficit/hyperactivity disorder (ADHD) following maternal and postnatal exposure, respectively.

18. Hall et al. (2022) reported some evidence that gestational organophosphate ester exposure (di-n-butyl phosphate (DnBP) and bis(1,3- dichloro-2-propyl) phosphate (BDCIPP)) may be associated with increased odds of ADHD, although associations were modest in magnitude and did not follow a monotonic exposure response trend.

19. Percy et al. (2022) reported organophosphate esters were not significantly associated with IQ in the main models used for analysis but observed stronger adverse effects on cognitive abilities for children from more disadvantaged socioeconomic status.

20. Although not related to neurodevelopmental toxicity, other papers reported an association between exposure to organophosphate esters during pregnancy and adverse pregnancy outcomes such as infant anthropometric measures (Yang et al., 2023a, 2023b) and anogenital distance (Luan et al., 2023).

Questions for the Committee

21. Does the Committee wish to take this topic forward for further consideration as a discussion paper, with further detail on the studies outlined above? If so, should the scope of the discussion paper focus on neurodevelopmental toxicity or should it be widened to adverse pregnancy outcomes in general?

COC and COM horizon scanning

22. The COC last undertook horizon scanning in November 2021, and the discussion paper is attached at Annex A. The topics of interest flagged at that time were:

- Maintain a watching brief on factors affecting cancer susceptibility including shift work, stress and other lifestyle factors and how that might affect assessment of chemicals and carcinogenicity.

This was subsequently discussed at the joint COC-COM meeting on 2nd March 2022.

- Consider an update to guidance on assessment of nanomaterials, possibly as a joint activity across COC, COM and COT.

Subsequently the latest COM guidance on nanomaterials was provided for information at the joint COC-COM meeting on 2nd March 2022

- Gain awareness of the potential effects of antibiotics and antivirals on the microbiome.
- Consider a joint discussion with COM on thresholds for in vivo mutagens and whether there is new information subsequent to the 2010 COM opinion.
- Endocrine disruption and the link with carcinogenicity, acknowledging that endocrine disruption is also a COT remit.
- Impact of chemicals on potential for metastasis or progression of cancer, in particular with respect to the Hallmarks of Cancer and linking to the tumour microenvironment topic.
- Communication of cancer risk and how COC should be involved with this, especially with the move away from a yes/no decision on whether a substance is a carcinogen, and ensuring consistency in describing risks, possibly starting with a landscape review of terminology across a number of Committees (FSA and UKHSA) and led by Lay Members.
- Ensuring appropriate considerations are made to acknowledging diversity in the population especially where there might be differences in risk between different groups.

23. The COM last undertook horizon scanning in October 2022, and the discussion paper is attached at Annex B. The topics of interest highlighted included:

- iPS organoids as model systems (COM and COC);
- the use of genomics in toxicity testing strategies; and
- whether epigenetics should/can be incorporated into standard toxicity testing.

FSA Research Programme

24. The FSA research strategy has seen the consolidation of all research in the portfolio into a series of programmes by area of research interest. The four key research priorities are “Assuring food and feed safety standards”,

“Understanding consumers and our wider society”, “Adapting to the food and feed system of the future” and “Addressing global grand challenges”, with the first of these most likely to involve matters that COT will be consulted on. Further details can be found at : Areas of research interest | Food Standards Agency.

25. As noted above an external review of dioxins has been commissioned. The results are expected in the late Spring.

Balance of expertise on the Committee

26. 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

Bioinformatics

Clinical practice

Endocrinology

Epidemiology

Immunology

Mechanistic toxicology

Neurotoxicology

Paediatrics

Pharmacology

Reproductive toxicology

Risk assessment

Statistics

Toxicogenomics

Xenobiotic metabolism

Biochemistry

Cell biology

Dietary exposure assessment

Environmental exposure assessment

Human toxicology

Mathematical Modelling

Molecular biology

Nutrition

Pharmacokinetics

Probabilistic modelling

Respiratory toxicology

Statistical aspects of experimental design

Systems biology

Toxicological pathology

27. 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.

28. 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

29. In addition to the questions in paragraph 21, Members are invited to comment on each of the above areas and also to consider the following questions:

a. Do Members have additional suggestions for future topics for:

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

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

31. Do Members have any comments on the balance of skills on the Committee?

32. Members are reminded that they may draw particular issues to the attention of the Secretariat at any time.

Secretariat

January 2023

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