2023 Draft Annual Report - Other Committee Activities: Joint Expert Groups, Presentations and Workshop

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This is a paper for discussion.

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

Presentations

Presentation from the LIDo-TOX AI PhD Student

1.188 The FSA and COT have been considering New Approach Methodologies (NAMs) in order to understand the best scientific methodologies available for use

in the risk assessment of chemicals, and to consider how these can be incorporated and accepted in a regulatory context.

1.189 In 2021, the FSA started funding a PhD Student at King's College London as part of their Interdisciplinary Doctoral Program (LIDo-TOX AI).

1.190 The PhD student has been working to understand how NAMs will improve indicative levels of safety in chemical risk assessment.

1.191 In addition, these new partnerships have helped with networking, research collaboration, training opportunities and other activities. The studentship also complements the work set out in the COT FSA UK Roadmap towards using new approach methodologies in chemical risk assessment.

1.192 The PhD student presented a yearly review to the Committee, updating them on his progress to date using Artificial Intelligence and in silico tools for the assessment of food safety.

1.193 The main work so far comprised three parts: (1) Exploration of dimensionality reduction algorithms, for powering Quantitative Structure Activity Relationship (QSAR) models of mutagenicity, constructed of simple feed-forward Deep Neural Networks (DNNs); (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); (3) Development of Graph Neural Networks (GNNs) for node classification of molecules, in order to predict toxicological properties of brominated flame retardants (BFRs), starting with acute toxicity and comparing to predictions from the Toxicity Estimation Software Tool (TEST) of the United States (US) Environmental Protection Agency (EPA).

1.194 The COT Members were impressed with the progress to date and gave feedback to the PhD student.

Opportunities and outlook for United Kingdom Food and Chemicals regulation post European Union Exit-COT Workshop Report

1.195 The COT, UKHSA and FSA organised a workshop in July 2022 on "Opportunities and outlook for UK food and Chemicals regulation post EU exit".

1.196 A report of the workshop was considered by the Committee in 2023.

1.197 The participants were from industry, academia and regulatory agencies and the day was divided into three sessions:

- The landscape of regulation post EU exit: UK stakeholder perspectives, international perspectives, opportunities and challenges for UK divergence;
- Major drivers for change and potential impact on chemical regulation; and
- Indirect Effects: food prices, food security, supply chain, fraud (Food regulation/human health).

1.198 Each of the sessions consisted of presentations followed by a roundtable discussion and included interactive sessions.

1.199 The workshop report is now available online and PDF.
(DOI: https://doi.org/10.46756/sci.fsa.ebr546)

Evolving Our Assessment & Future Guiding Principles Workshop

1.200 The COT held a workshop in May 2023 to start work on updating their guidance on toxicity testing and its supporting principles. The starting point for the process was to use existing frameworks and guidance but with the aim of introducing innovative improvements where appropriate.

1.201 The workshop aimed to identify areas where guidance needed to evolve and included reviewing fundamental risk assessment principles, current guidance on risk assessment and what can be learned from it, integration of new approach methodologies, exploring hazard vs risk and weight of evidence. The overall objective of the workshop was to discuss how the Committee moves forward in a new era of risk assessment.

1.202 Members discussed the output of the workshop, considering “must, could and should” priorities to be taken forward. It was emphasised that the most important aim was to have applicable guidance to ensure public safety.

1.203 The assessment of benefits was not within the terms of reference of the COT, but thought should be given as to how COT advice can be best aligned for this to be undertaken when needed or appropriate.

1.204 Members noted that to take the guidance forward, establishing an initial framework would be important; this could then be expanded and linked to other guidance as necessary. There were two parts to the work, to codify what the

Committee currently do and then to provide guidance on areas where the approach was not yet codified such as benchmark dose modelling.

1.205 A sub-group would be formed in 2024 to take forward the next steps in updating the guidance. It was agreed that it would be important to work with the policy colleagues from the relevant Government Departments and not to re-invent the risk analysis process. In particular, the required levels of protection needed for consumers should be considered.

1.206 The finalised report will be published next year.

Horizon Scanning

1.207 The COT undertake horizon scanning at their February meeting, where they review the work anticipated for the coming year; this includes ongoing topics, the annual workshop, current or planned working groups and the skills balance of the Committee. However, Members are also encouraged to suggest topics for discussion throughout the year.

1.208 In 2023, In addition to the items outlined above, Members considered the following:

General horizon scanning

1.209 The COT terms of reference include advising, at the request of many different government departments, on a wide variety of chemicals and routes of exposure, making them very broad, and potentially overlapping with those of a number of other Scientific Advisory Committees. Thus, while the Committee’s work is mostly reactive, the terms of reference also include advising on important general principles and scientific discoveries in relation to toxic risks, which was more proactive. The Committee is constrained by a heavy workload, but it is important that it is proactive where it can be, taking a lead on advances in the application of novel science in the risk assessment of chemicals. The work on new approach methodologies and evidence integration are examples of this.

1.210 It is important that the Committee is aware of emerging topics and a databank of potential areas of interest could be created as it would be useful to know whether there were topics being discussed elsewhere, such as by EFSA and ECHA, that may be relevant to topics that should be addressed by the Committee.

Phosphate based flame retardants

1.211 In 2019, the COT published a statement on phosphate-based flame retardants (PFRs) and the potential for neurodevelopmental toxicity. The Committee concluded that PFRs were very unlikely to share the neurodevelopmental effects of other organophosphate compounds, but they could not exclude the possibility that PFRs could produce neurodevelopmental toxicity by some other mechanism.

1.212 In 2021, the COT became aware of new data relating to PFRs and developmental neurotoxicity and a literature search was carried out to capture any additional data published between 2019 and 2021. The Committee also requested such searches be carried out in subsequent years to capture any new published data.

1.213 The Committee reviewed the most recent update and considered that unless the Department of Health and Social Care (DHSC) requested another review, there was insufficient new information to justify taking this topic further at this time. However, the literature should continue to be monitored, though there was no need for an update every year, unless significant (in terms of toxicology or amount) new information became available.

The microbiome

1.214 It was agreed that the microbiome should remain under consideration by the Committee, with a view to re-examining the topic when new data become available.

Joint Expert Groups

Assurance of Joint Expert Group opinions

1.215 The Joint Expert Groups (JEGs) were established by the FSA to assess applications for the authorisations of regulated products that were previously authorised by the European Food Safety Authority (EFSA). The two JEGS are the FCM JEG which covers food contact materials and the AEJEG which has responsibility for food additives, enzymes and other regulated products. In 2023 the COT provided support, challenge and assurance to the work of the two JEGS for assessments as set out below.

AEJEG assessments

1.216 The COT considered Risk Assessments prepared by the Joint Expert Group on Additives, Enzymes and other Regulated Products (AEJEG) regarding the following regulated product applications:

- For the modification of specifications to include fermentation by Yarrowia lipolytica as a production method for steviol glycosides.
- For the modification of specifications to include fermentation by *Saccharomyces cerevisiae* as a production method for steviol glycosides.
- For the modification of specifications to include production from stevia leaf extract by enzymatic conversion as a production method for steviol glycosides.
- The authorisation of a new flavouring 2-Hydroxy-4-methoxybenzaldehyde.

1.217 All items are currently reserved as they cover draft AEJEG Committee Advice Papers not currently published.

1.218 AEJEG Committee Advice Papers will be published in 2024.

FCMJEG assessments

1.219 The COT considered Risk Assessments prepared by the Joint Expert Group on Food Contact Materials (FCMJEG) regarding the following regulated product application:

- On the safety of the use of 2-hydroxyethyl methacrylate (HEMAP) as a component in the manufacture of kitchen countertops and sinks. This assessment is for HEMAP only, and not the final reaction mixture used in the manufacture. This item is currently reserved as the Committee Advice Paper is not currently published. Publication of the final assessment is expected in 2024.
- On the safety assessment on the evaluation of the recycled poly(ethylene terephthalate) decontamination process operated by PETUK Ltd. for use in manufacture of articles in contact with food. The COT endorsed the assessment made by the FCM JEG. This item is currently reserved as the Committee Advice Paper is not currently published. Publication of the final assessment is expected in 2024.

Working Groups

Joint ACNFP/COT Working Group on Cannabidiol (CBD)

Cannabidiol (CBD)

1.220 A joint Subgroup of the ACNFP and COT was formed to address a series of questions in relation to the safety of CBD-containing and hemp-derived ingredients. The overarching aim of the Subgroup is to enable the FSA to perform risk assessments for CBD in food. The group established an ADI for pure form CBD (>98% purity) of 0.15 mg/k bw/day (10 mg/day for a 70 kg adult) as set out in a joint statement. Work continues on the assessment of novel products containing a lower proportion of CBD.

1.221 The joint position paper from the Advisory Committee on Novel Foods and Processes (ACNFP) & Committee on Toxicity (COT) on establishing a provisional acceptable daily intake (ADI) for pure form (≥98%) cannabidiol (CBD) in foods, based on new evidence can be found using this link Joint position paper from ACNFP & COT on establishing provisional ADI for pure form CBD in foods | Advisory Committee on Novel Foods and Processes.

Plant-based drinks

1.222 Plant-based drinks have become increasingly popular in the United Kingdom (UK) both for individuals with an allergy to cows' milk or lactose intolerance and those who wish to avoid dairy products for other ethical or cultural reasons. Three such drinks were reviewed by the Committee, with a statement being published in 2022.

1.223 The Scientific Advisory Committee on Nutrition (SACN) have also considered these drinks from a nutritional perspective. To bring these two strands together, a joint Working Group was established to undertake a benefit risk-assessment of soya, oat and almond drinks as replacements for cows' milk. To support this work, a risk assessment of the components and contaminants, potentially present in cows' milk was conducted (see paragraph?). The Working Group started work in December 2021 and it is hoped that a draft report will be published for consultation in 2024.

PFAS

1.224 Following publication of the COT Interim position on per- and polyfluoroalkyl substances, a COT subgroup on PFAS has been formed.

1.225 The terms of reference for this subgroup are:

1.226 To provide guidance to UK Government Departments and Agencies to support human health risk assessments of per- and poly-fluoroalkyl substances (PFAS) where exposures to existing and legacy PFAS is occurring through food, drinking water and other environmental media. This will include:

- Undertaking an independent review of toxicological and epidemiological data, focusing on a number of critical endpoints, and considering the biological relevance of the endpoints assessed.
- Considering the toxicokinetics of PFAS.
- Determining whether different PFAS can be grouped for assessment and how this can be done.
- Deriving a HBGV or a number of HBGVs as the data allow

1.227 The subgroup will endeavour to follow the guidance from the Joint COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence (SETE) subgroup in undertaking this assessment.

1.228 The subgroup held two meeting in 2023, which considered papers on animal and in vitro data on thyroid effects of PFAS and animal data on liver effects of PFAS. Further papers on these endpoints as well as papers on other endpoints will be considered in the future.

Codex report on food allergen thresholds

1.229 The Committee were asked to carry out an assessment of the Codex Expert Committee's report on establishing threshold levels for allergen of global importance (Part 2: review and establish threshold levels in foods for the priority allergens) to inform decisions by the FSA on whether it would be appropriate for the Eliciting Dose (ED) reference doses recommended in the Codex report to be applied to regulated allergens in the UK.

1.230 The assessment was carried out by a subgroup comprising of several COT members along with other external experts, under the chairmanship of Prof Ian Kimber. The COT subgroup met virtually on four separate occasions. The Chair of the Codex Expert Committee on allergen thresholds (2nd Joint FAO/WHO Expert Consultation meeting) was invited to attend one of these meetings to clarify and

answer some questions about the Codex Expert Committee's report.

1.231 In addressing questions posed in the Terms of Reference, the COT subgroup reached the following conclusions:

- There is no reason to suggest that the data are not sufficiently representative of the UK population.
- There are uncertainties regarding the way in which ED values have been derived – and, as a consequence, the accuracy of these values. Given the available data upon which derived ED values are based this is a limitation that must – at present – be acknowledged. However, there are no key gaps that can be filled using the published literature.
- There is insufficient evidence to demonstrate that using reference doses based on ED05, as opposed to ED01 values would not significantly impact on public health.

1.232 The report of the subgroup was then presented to the Committee. The following comments were made:

1.233 It was noted that the underpinning data used to derive the EDs (both ED01 and ED05 values) in the Codex Expert Committee report were not made available with the report and were not otherwise available. This made it difficult to confirm the conclusions and access to the raw data would have been beneficial.

1.234 The report contained few graphs showing the modelling used and those that were included did not give confidence that the proposed eliciting doses were of appropriate values. The benchmark approach used was not the same as that normally used in toxicology. It was further noted that no safety factors were included.

1.235 However, the Committee acknowledged that while the dataset for some of the allergens was based upon very small numbers, there probably were no other data available in the literature to refine the dataset.

1.236 It was also noted that the reference to "mild anaphylaxis" in the report did not seem appropriate as NICE have a very clear definition that anaphylaxis is always a severe reaction.

1.237 The Committee agreed with the way the assessment of the report had been undertaken by the COT subgroup and with the contents and key conclusions reached by them.

1.238 The Committee also emphasised that since both ED01 and ED05 values represented effect levels, more people would be affected if the ED05 were used rather than the ED01 but the decision on which value to use will need to take into account additional considerations and was for risk managers to make rather than the COT.

1.239 The COT subgroup's report can be viewed at: COT Codex Subgroup Report on Codex Allergen Thresholds Report FINAL SO ACC V_0.pdf (food.gov.uk).