Other Committee Activities: Joint Expert Groups, Presentations and Workshop

In this guide

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Presentations FSA Postdoctoral Fellow and PhD student

1.108 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 to understand how these can be incorporated and accepted in a regulatory context.

1.109 In 2021, the FSA started funding a 4-year computational toxicology postdoctoral fellow at the University of Birmingham and a four-year PhD Student (London Interdisciplinary Doctoral Program-LIDo-TOX AI) at King's College London.

1.110 The fellow and PhD student have been working alongside other government departments to understand how NAMs will improve indicative levels of safety in chemical risk assessment.

1.111 In addition, these new partnerships have helped with networking, research collaboration, training opportunities and furthering our knowledge in this area. The fellowship and studentship also compliment the work set out in the COT FSA UK NAMs Roadmap towards using new approach methodologies in chemical risk assessment.

1.112 The Postdoctoral Fellow and PhD student prepared a yearly review and gave a presentation to the Committee on their progress.

1.113 The PhD student provided an update on his research over the last year which involves the development of novel Quantitative Structure-Activity Relationship (QSAR) models using innovative artificial intelligence approaches. The aim of these models is to reliably predict the toxicological properties of molecules found in food and drink over a diverse range of endpoints of interest. Several case studies were presented which aimed to predict: 1) *in vivo* doses relevant to neurotoxicity, developmental toxicity and reproductive toxicity of brominated flame retardants; 2) Drug-Induced Liver Injury, Drug-Induced Renal Injury and Drug-Induced Cardiotoxicity of selective androgen receptor modulators and 3) the neurotoxicity and other toxicological effects of tropane alkaloids (TAs).

1.114 The postdoctoral fellow provided an overview on the latest international case study focusing on plant alkaloids of three large classes: tropane alkaloids (TAs), pyrrolizidine alkaloids (PAs), and glycoalkaloids (GAs). The first objective of this case study is to support the UK FSA's policy need to determine which TAs are the most potent (neuro)toxicants to prioritise specific substances and inform decisions on the UK's monitoring of these alkaloids in foods. An integral part of this aim is to confirm that neurotoxicity is the primary mode of action of these alkaloids. The second objective of this case study is to derive a HBGV for human exposure for the top priority, i.e. most potent substance within the class of TAs. This will utilise physiologically-based pharmacokinetic (PBPK) modelling and quantitative *in vitro* to *in vivo* extrapolation (QIVIVE). From a methodological perspective, a broader third objective of the case study is to evaluate and attempt to build confidence within the FSA in the application of a

series of relevant NAMs that have been integrated in a manner to address policy needs. These NAMs are tiered and incorporate existing human *in vivo* data as well as new testing on human *in vitro* cell lines. The method in which to carry out this prioritisation is to utilise a tiered-testing strategy of *in silico*, *in vitro* and 'omics NAMs and use the outputs of this to derive a health-based guidance value to maximise the relevance and accuracy to human food safety.

1.115 The COT Members suggested the use of Organisation for Economic Co-operation and Development (OECD) reporting templates that provides a standardized structure for documenting PBPK models; it was noted that the fellow and PhD student had already started doing this.

1.116 The COT Members appreciated the work carried out and were impressed by the varied outputs.

Safety of Nitrates and Nitrites as Food Additives – Presentation from RSM UK Consulting LLP

1.117 Sodium and potassium nitrate, and sodium and potassium nitrites are salts commonly used as food additives for their antimicrobial properties, as well as their ability to maintain properties such as colour, texture and flavour. The safety of nitrates and nitrites as food additives was last evaluated by EFSA in 2017. In 2023, following an assessment on the safety of nitrosamines, the EU announced a decision to change the maximum permitted levels of nitrites and nitrates used as food additives to levels lower than those allowed in GB due to concerns regarding the additives' contribution to the formation of nitrosamines. This prompted a review of the current understanding of the safety of these additives in food sources in the context of GB legislation.

1.118 The RSM UK Consulting team delivered a presentation on the FSA-funded literature review of the safety of nitrates and nitrites as food additives. The presentation covered topics such as the research questions explored, the methodology used and the scope applied, as well as the findings resulting from the literature review and a brief discussion around these findings. RSM highlighted the uncertainties of the project, advised on ideas for future research and summarised the main conclusions of the literature review. The review had specifically focussed on the human and in vitro data.

1.119 The Committee made a number of comments on the review and thanked RSM for their hard work on this project and for delivering an insightful presentation.

AI in Risk Assessment Workshop

1.120 The COT held a workshop on AI in Chemical Risk Assessment in October 2025 in London, United Kingdom. The workshop included themed sessions consisting of short flash presentations followed by roundtable discussions. There was attendance from multiple stakeholders including academia, government and industry.

1.121 The workshop set out to explore the complex readiness of the data ecosystem and state of the art AI technologies. Opportunities as well as challenges associated with application of AI in chemical safety assessment were reviewed. The aim was to enable new insights and initiate discussions to determine how to best harness these technologies in future.

1.122 The finalised report will be published in due course.

Gut reactions: xenobiotics and the microbiome workshop

1.123 The COT held a workshop in October 2024 in London, United Kingdom on xenobiotics and the microbiome. The workshop included themed sessions consisting of short flash presentations followed by roundtable discussions. There was attendance from multiple stakeholders including academia, government and industry.

1.124 The workshop set out to explore the complex current state of the science of the microbiome pathophysiology and the possible impact of xenobiotics on host microbiome interactions and vice versa, including possible mechanisms and health implications, with a particular emphasis on the gut microbiome and dietary exposure. In addition, the aim was to enable new insights, review the science, initiate discussions to determine where the data gaps are in research, what effects are of concern, and how might xenobiotics be evaluated practically for such effects in the future.

1.125 The four sessions were: Interactions of the host microbiome system; Gut microbiome and xenobiotics; Assessing the impact on the microbiome;

Possible ways to evaluate in the short to medium term and microbiome interventions for maintaining health and treating disease and Future Directions

1.126 The workshop report is now available as HTML format and as a PDF. (DOI: https://doi.org/10.46756/sci.fsa.hew928)