Minutes

Draft Minutes of the 25th March 2025 COT Meeting

Meeting of the Committee at 10:00 on the 25th of March 2025 at Clive House, London and via Microsoft Teams.

Present

Chair:	Professor Alan Boobis	Committee on Toxicity

	Dr Stella Cochrane	
Members:	Professor James Coulson	
	Professor Gary Hutchison	
	Professor Thorhallur Ingi Halldórsson	
	Dr Gunter Kuhnle	
	Dr David Lovell	
	Professor Shirley Price (Deputy Chair)	
	Dr Mac Provan	
	Dr Michael Routledge	
	Dr Cheryl Scudamore	Committee on Toxicity
	Professor Mireille Toledano	
	Professor Philippe Wilson	
	Dr Steven Enoch	
	Professor Peter Barlow	
	Dr Chris Morris	
	Dr Meera Cush	
	Mr Gordon Burton	
	Dr Andreas Kolb	
	Mr Nick Richardson	
	Dr Simon Wilkinson	

Liaison Member	Professor Paul Haggarty	Scientific Advisory Committee on Nutrition (SACN)
Science Council Liaison Member	Ms Jacqueline Healing	Science Council (SC)

	Ms Cath Mulholland	
	Dr Alex Cooper	
	Mr Barry Maycock	
	Ms Claire Potter	
	Ms Chara Tsoulli	
Food Standards	Dr Barbara Doerr	
Agency (FSA)	Dr Olivia Osborne	
Secretariat:	Ms Sabrina Thomas	
	Dr Gail Drummond	
	Ms Frederique Uy	
	Ms Jocelyn Frimpong-Manso	
	Ms Sophy Orphanos	
	Dr Gaetana Spedalieri	FSA Scientific Secretary
	Mr Thomas Hornsby	
	Dr Emily Hudson	
	Dr Aaron Bradshaw	
	Ms Natasha Adams	
	Dr Katie Schulz	
	Dr Rachel Kerr	
	Mr James Metcalfe	
	Ms Yoana Petrova	
	Ms Alba Ureña Rusillo	
	Ms Polly Bevan	
	Ms Katie Wetherall	

UK HSA Secretariat:	Ms Britta Gadeberg Ms Sanyukta Pallavi	UK HSA Scientific Secretary
Assessors	Ms Rachel Elsom	Health Improvement Global and Public Health Group. Department of Health and Social Care (DHSC)
Assessors	Ms Neeve Pearce	Health Improvement Global and Public Health Group. (DHSC)
Assessors	Ms Francesca Gauntlett	Department for Business and Trade (DBT)
Assessors	Ms Hannah Jones	Business, Energy and Industrial Strategy
Assessors	Mr Ian Martin	Environment Agency
Invited Experts	Mr Alexander Kalian (presenting item 7)	Kings College London
Invited Experts	Dr Arthur de Carvalho e Silva (presenting item 7)	Birmingham University
Invited Experts	Dr Claire Stephenson	AEJEG Member
FSA and officials from other Government Departments	Ms Pamela Iheozor-Ejiofor Mr Craig Jones (item 8) Ms Elli Amanatidou (item 8) Ms Aisling Jao Ms Laura-Jayne Quinn Dr Mindy Dulai Dr Andy Axon Dr Joseph Shavila	FSA

FSA NI – Food Standards Northern Ireland:	Ms Kerry Gribbin – Tentative Ms Catherine Hardy	FSA NI
	Ms Thahina Liakat	
FSS – Food Standards Scotland:	Ms Krystle Boss	FSS
Observers	Dr Helen Crawley	Lizzie Vann Foundation
Observers	Dr Stephen Ruckman	Head of Human Health, TSG Consulting
Observers	Rev. Professor Lesley Stanley	ACNFP Member and Incoming Chair

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Announcements

1. The Chair welcomed Members and other attendees.

2. This was the last meeting for the current COT Chair, Professor Alan Boobis and a number of Members - Professor Maged Younes, Dr Mike Routledge, Dr Natalie Thatcher, Dr Mac Provan, Professor Gunter Kuhnle and Professor James Coulson, whose terms of appointment expire at the end of March 2025. The Chair and the Secretariat thanked the outgoing Members for all their hard work and their contributions to the Committee over the past years and wished them well for the future. The Chair was also thanked for his contributions to the Committee which is also noted in Item 12 below.

3. A number of external observers were present; Dr Arthur Carvalho and Mr Alexander Kalian presenting Item 7, Rev Professor Lesley Stanley of ACNFP (and incoming Chair), Dr Steven Ruckman of TSG consulting and Dr Helen Crawley of the Lizzie Vann Trust.

Interests

4. The Chair reminded those attending the meeting to declare any commercial or other interests they might have in any of the agenda Items.

Item 1: Apologies for absence

5. Apologies had been received from COT Members: Dr Alison Yeates, Professor Maged Younes, and Dr Natalie Thatcher. Apologies were also received from a number of assessors: Ms Frances Hill (DBT), Ms Louise Dearsley (HSE), Dr Ovnair Sepai (UKHSA), Ms Minako Allan (HSE), Ms Liz Lawton (DEFRA). Apologies were also received from Dr Emma Bradley (FCM JEG: Observer)

Item 2: Minutes of the meeting held on February 4th 2025 (TOX/MIN/2025/01)

6. The Committee reviewed the draft minutes and the reserved minutes of the 4th of February 2025 meeting. It was noted that the main minutes incorrectly gave the date of the next meeting as 26th March 2025. There were no other comments and subject to the above correction, the minutes and reserved minutes were accepted as an accurate record.

Item 3: Matters arising (TOX/2025/09)

Joint Expert Group (JEG) updates

Additives, Enzymes and other Regulated Products - AEJEG

7. The last standard AEJEG meeting was held on the 11th of February 2025 and the following items were presented:

i) The fourth Draft Committee Advice Document (CAD) on the Application for the Authorisation of Blue Microalgae Extract (Blue Galdieria Extract) for use as a new food additive in the “colour” functional class (RP507). It was agreed that the Secretariat would circulate the CAD document to the AEJEG via correspondence for minor amendments and final sign off. It is anticipated that the CAD will be presented to COT in May.

ii) An update paper and cover paper on the Extension of use of phosphates (E-338-341, E343, E450-452) to a new food category “egg analogues” (RP40) were presented to the AEJEG. A Request for Further Information (RFI) was sent to the Applicant. Following a response from the Applicant to the RFI an update paper and cover paper will be presented to the AEJEG in June.

8. The AEJEG Smoke Flavourings Working Group (SFWG) met on the 11th of March 2025 to revise the draft CAD for RP1616 and the summary document for RP1613.

9. The next standard AEJEG meeting will be on the 1st of April 2025. The next meeting of the SFWG will be on the 26th of March 2025, where the last two summary documents (RP1614 and RP1615) will be presented. The Chair thanked Members of the SFWG for all of their hard work on Smoke Flavourings.

Food Contact materials - FCMJEG

10. The last meeting of the FCMJEG was held on the 26th February 2025. The FCMJEG discussed further amendments to the CAD for a plastic additive application (RP1702) and two recycling process applications (RP1741 and RP1862). The next meeting will be held on the 9th of April 2025, where the FCMJEG will be reviewing additional information on two recycling process applications (RP1415 and RP1898).

11. Currently, two plastic additive applications were at the RFI stage (RP2147 and RP2263). One plastic additive and one recycling process application are now in the process of being finalised (RP1702 and RP1741).

Ways of working technical documentation TOX/2025/09

12. No interests were declared.

13. At the September 2024 meeting, paper TOX/2024/33 “Ways of Working-2” was presented to the Committee. One proposal discussed in the paper was to format specific discussion papers as a “State of the Science” paper or a “Science and Research Special Topics Report,” where the paper covered an individual topic rather than being a risk assessment, on which a statement would ultimately be published. Such papers are currently published only in draft, as part of the media for discussion prior to the relevant meeting, and are not citable. The format proposed would include a cover page summarising the paper, research recommendations and any other relevant information. This type of document could form part of the planned COT guidance package, where it was envisaged that the overarching guidance would be complemented by standalone papers on individual topics, as required. Furthermore, citation of such documents would be possible and promote the Committee’s work more widely.

14. At the September meeting, Members had agreed that reformatting some of the discussion papers in this way would be useful and they agreed to review a more developed version of a draft template in due course.

15. Paper TOX/2025/09, on novel bioavailable supplements, had been formatted as a State of the Science report as discussed at the September meeting. The Committee discussed the paper and requested changes to some of the wording and agreed that the Committee's recommendations should be included in the executive summary.

16. Members endorsed both the proposed format and the specific document on novel bioavailable supplements, which could therefore be published as reflecting the views of the Committee.

SAC Recruitment

17. The proposed appointments to the Committee have been confirmed by the FSA Chair and the four Chief Medical Officers of the UK and were currently undergoing right to work checks, before being announced.

Working Group updates

COT Guidance

18. The COT Guidance WG will be having an initial meeting on the 28th March 2025.

PFAS Working Group

19. The Secretariat is continuing to prepare papers for the next PFAS Working Group meeting. The Group have been updated on current progress and a date will be set for the next meeting in due course.

Item 4: COT workshop report- Gut reactions: Xenobiotics and the microbiome (TOX/2025/10) (reserved)

20. The Chair declared an interest as he had been involved in discussions at Joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) Meetings on Pesticide Residues (JMPR), Joint FAO/WHO Expert Committee on Food Additives (JECFA) meetings and an FAO workshop in December 2023 on how to address the effects of chemicals on the microbiome.

21. Dr Stella Cochrane declared a non-specific interest as Unilever has ongoing work in the microbiome area, although she was not currently working on such projects herself. No other interests were declared.

22. Members discussed the draft COT workshop report. This item is being treated as reserved until the report is finalised.

Item 5: Working Group on plant-based drinks: Draft report (TOX/2025/11) (reserved)

23. Dr Meera Cush declared that she had been involved in a project for a manufacturer, where she had provided toxicology information on the safety of isoflavones for use in medical foods for the elderly; the company concerned had commented on the draft report. It was agreed that she could contribute to discussions but should not participate in formulation of the conclusions. No other interests were declared.

24. The draft Working Group report “Assessing the health benefits and risks of consuming plant-based drinks: A Joint Report from the Scientific Advisory Committee on Nutrition and the Committee on Toxicity of Chemicals in food, Consumer products and the Environment” was published for peer review of its scientific content; this process ending on the 17th of September 2024. The comments received from the review were shared with the Committee at their meeting on the 10th of December 2024.

25. At the present meeting, the aim of paper TOX/2025/11 was to allow the COT to review the proposed Working Group responses to the comments, some of which had resulted in amendments to the report. Members discussed the proposed responses to the comments made on the draft report.

26. This item is being treated as reserved until the report and outcome of the peer review are published.

Item 6: Review of the safety of ashwagandha in food, drinks, and food supplements (TOX/2025/12) (reserved)

27. No interests were declared.

28. Members discussed a review of ashwagandha in food, drinks, and supplements. This item is being treated as reserved at this time as it contains commercially confidential information.

Item 7: Update from FSA Fellow and PhD student (TOX/2025/13)

29. No interests were declared.

30. The FSA and COT have been reviewing New Approach Methodologies (NAMs) to scope out the best scientific methods available for use in the risk assessment of chemicals in foods and the environment, and to understand how these can be incorporated and accepted within a regulatory context.

31. In 2021, the FSA provided funding to support a three-year PhD Studentship for Mr Alexander Kalian (London Interdisciplinary Doctoral Program-LIDo-TOX AI), at King's College London and a 4-year computational toxicology postdoctoral fellow for Dr Arthur de Carvalho e Silva, at the University of Birmingham.

32. The PhD student and the Fellow prepared yearly reviews and at this meeting presented their progress to date to COT Members.

33. Mr Alexander Kalian provided an update on his postgraduate research over the last year. This involved 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 by Mr. Kalian, 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).

34. Members discussed whether the models would be capable of predicting endpoint(s) of interest on any given 'data poor' chemical and if the predicted outputs could be complemented and/or confirmed by *in vitro* or *in vivo* work. It was agreed that this should be possible; however, the chemical would need to be in the applicability domain of the model.

35. Dr Arthur de Carvalho e Silva provided an overview of his recent activities. The latest case study is 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.

36. COT Members suggested Organisation for Economic Co-operation and Development (OECD) reporting templates, of which they had already started doing this.

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

38. The COT Members thanked both presenters and wished them well in the next steps of their research.

Item 8: Risk assessment of T2 and HT2 mycotoxins in food (TOX/2025/14)

39. No interests were declared.

40. Dr Claire Stephenson from the AEJEG was in attendance to provide additional support on exposure assessment.

41. This risk assessment for T-2 and HT-2 mycotoxins in food was being conducted due to recent changes in EU legislation, which had lowered the

maximum permitted levels for the sum of these two mycotoxins in several food categories. The new maximum levels came into force in the EU and Northern Ireland in July 2024 but have not automatically been adopted by Great Britain; risk management options are under review.

42. Paper TOX/2025/14 was a follow-up to a previous, provisional exposure assessment, which was presented to the Committee in July 2024 (TOX/2024/24). At that meeting the Committee noted several uncertainties in the assessment. The current paper provided a more refined exposure assessment. The primary focus of the current meeting was the assessment of exposure levels and their relevance to the health-based guidance values (HBGVs), which had been discussed previously.

43. At the start of the meeting, Dr Stephenson provided an expert analysis of dietary exposure assessment of T-2 and HT-2 mycotoxins and offered critical feedback on the draft discussion paper.

44. It was acknowledged that the use of the 97.5th percentile exposure values for chronic exposure assessment was highly conservative. While these values often exceeded the HBGVs, mean exposures tended to remain below them. Members discussed whether the 97.5th percentile should be used in risk characterisation, noting that lifetime exposure at this level was unlikely. However, its inclusion would be relevant for shorter-duration exposures or those affecting specific life stages.

45. A key concern raised by Members was that the mycotoxin levels in the discussion paper exceeded the new EU maximum legislative levels adopted in 2024. Data showed that barley and wheat levels of T2 and HT2 were 1.5 to 2.5 times above these limits, while levels in oats were 15 to 30 times higher. This raised concerns about levels demonstrating a lack of compliance versus the actual risk of the mycotoxins at those levels, particularly given that these new limits have not yet been adopted in Great Britain.

46. The temporal trend analysis of T2 and HT2 residues from 2004 to the present demonstrated an overall decline. However, notable dips were observed in 2007 and 2013. In response to a question from the Committee, the Secretariat suggested that these dips might be attributable to regulatory changes in 2013, and smaller sample sizes assessed in 2007 and 2013. It was recommended that for risk assessment purposes, data from 2014 onwards be prioritised, as this would provide a picture more relevant of recent exposure trends.

47. Concerns were raised about potential double counting in the chronic exposure assessments, as exposure sources were divided into three groups: unprocessed cereal grains (which had not been cleaned or dehulled and would not be consumed in this form), processed cereal grains (which had been cleaned and dehulled, but had not been incorporated into any foods and remained as a commodity), and ready-to-eat foods, and then considered these groups in combination; with a reduction factor being applied to unprocessed oats where relevant. The FSA Exposure Assessment team clarified that the exposure assessment was based on actual dietary patterns and did not involve simple addition of food groups, thereby avoiding double counting.

48. The discrepancy between T2 and HT2 levels in raw commodities and ready-to-eat foods was discussed. It was noted that the samples of ready-to-eat foods had higher levels of T2 and HT2, even when compared to unprocessed oats. This raised questions about data reliability, given the small sample size of ready-to-eat foods. Members highlighted that this dataset might not accurately reflect general exposure levels due to the limited number of data points and potential bias from targeted sampling where, for example, contamination was known or suspected.

49. Further discussion revolved around the potential accumulation of mycotoxins in animal products, if contaminated feed were consumed. The Secretariat confirmed that the data call did not include occurrence data for meat and dairy products, so these had not been included in the assessment. However, the literature did indicate that there was potential for transfer of these toxins to animal tissues. The Secretariat agreed to include additional information on this aspect, particularly concerning unprocessed animal feed.

50. The methodology used for quantifying mycotoxin levels reported by industry was also examined. Members sought clarification on whether Liquid Chromatography-Mass Spectrometry (LC-MS) or Enzyme-Linked Immunosorbent Assay (ELISA) methods were used, with confirmation that LC-MS or Gas Chromatography-Mass Spectrometry (GC-MS) were the primary techniques employed. Questions were raised about whether industry testing could extend to additional ready-to-eat foods to provide a more comprehensive dataset.

51. Revisions to the risk characterisation section were suggested, particularly concerning the wording on high consumption of unprocessed oats leading to exposures close to the reference dose. Members emphasised that the reference dose includes a wide margin of safety, meaning that even exposures below, but close to, this level should not be considered a significant concern. It

was also recommended that greater emphasis be placed on estimates based on processed oats rather than treating processed and unprocessed grains equally.

52. The Secretariat confirmed that the suggested changes and comments would be addressed before developing a draft statement. The discussion concluded with agreement on the next steps for refining the assessment and ensuring that exposure estimates accurately reflect real-world dietary habits and regulatory considerations to the extent possible.

Item 9: Marine biotoxin risk ranking (TOX/2025/15)

53. No interests were declared.

54. The FSA is considering the current advice and monitoring programme for marine biotoxins and whether there is a need to update or change existing legislative standards.

55. The Committee previously reviewed an overview of the available toxicological information, occurrence data, and any additional relevant information, such as proposed or current limits, monitoring data and human case reports on emerging marine biotoxins in the forms of a scoping paper (TOX/2023/59) and a discussion paper (TOX/2024/25). During these discussions, the Committee concluded that there were significant data gaps, including a lack of information on the presence and concentrations of emerging marine biotoxins in UK waters, the potential impact of global warming on the occurrence of these toxins in UK waters, detailed studies on human exposure and health outcomes, and potential combinatory effects from co-occurrence of toxins. Due to these data gaps the Committee was unable to conclude on the potential risks of the emerging marine biotoxins to human health and to establish health-based guidance values (HBGVs).

56. To assist in prioritising the emerging marine biotoxins, the Committee discussed the potential applicability of risk ranking based on a numerical scoring system, similar to that used previously to score the relative risk of mycotoxins. To develop the risk ranking system a small working group of Members was formed, and the resulting approach and outcomes of the risk ranking were discussed in paper TOX/2025/25.

57. The Committee agreed with the overall approach of using a decision tree to clearly depict the underlying considerations and how the data for each biotoxin was weighted. For data gaps, the approach suggested was using a suitable structurally similar analogue, if available, with sufficient data to fill these gaps and assist in assigning ranks for each biotoxin. However, the Committee had reservations about this and noted that using analogues for all scoring categories would be difficult unless there was clear evidence, e.g. the occurrence of biotoxins directly relates to the occurrence of their structural analogues . If this could not be clearly demonstrated, then the use of analogues should be reserved for the hazard categories only.

58. The toxicity category of the risk ranking considered the known adverse effects of each toxin, identified from *in vivo* animal studies. Neurotoxic effects were ranked highest followed by gastrointestinal effects and lastly mild effects such as weakness and general unwellness. Two different schemes for numerical scoring of toxicity were considered in the paper. One was where a numerical score from 1-3 was assigned, according to the endpoints described above, and a second, where scores of 1-5 were used, where consideration was also given to the lethal dose (LD50) of the toxins, to further differentiate toxicity profiles between biotoxins and aid in prioritisation. There were uncertainties with respect to the LD50s as they were based on a limited toxicological database; however, the Committee concluded that the 5-point approach was preferred as it helped to better differentiate the ranks of the biotoxins and took full advantage of the limited data available. Members noted that the category of human case reports was scored 1-3. This meant that the weighting of this category to the overall score was less than that of the other categories. The Committee suggested that consideration should be given to changing this to 1-5, recognising that there were limitations in the available data.

59. The risk ranking successfully differentiated some biotoxins as of higher or lower concern; however, a number of biotoxins achieved identical scores due to the lack of data available. The Committee suggested that biotoxins with identical scores should be prioritised by giving most weight to human data, followed by animal toxicological data and then occurrence. Prioritisation on hazard data was considered the most conservative approach for protecting public health. The Committee suggested that a coloured matrix would be useful to illustrate the breakdown of scores for each biotoxin to easily interpret which categories drove the scores, especially for comparing biotoxins with identical rankings.

60. The regulatory attention/monitoring category was included in the risk ranking to capture the variance in attention that the biotoxins receive across both the EU and UK, not just by authorities but also by unofficial research monitoring programmes. The Committee concluded that considering information on monitoring assisted in risk ranking; however, regulation should be considered separately where there are already UK regulations, as the risk ranking was for emerging biotoxins and different considerations would apply to those that are already regulated in the UK (e.g. saxitoxin).

61. The Committee agreed that the inclusion of a narrative alongside the scoring was essential to clearly explain how the data was weighted, especially where data was extremely limited.

62. Overall, the Committee agreed that the approach was very helpful and that it had succeeded in distinguishing some toxins as high or low priorities. However, due to the gaps and uncertainties in the data it was not possible to derive clear rankings for all emerging biotoxins. Members requested the changes discussed be included in a draft statement.

Item 10 - Citrinin in the maternal diet- first draft statement TOX/2025/16.

63. Due to a lack of time, this item was postponed to a future meeting. However, Members were encouraged to send in any comments so these could be incorporated into the next draft of the statement.

Item 11: Update on the work of other FSA Scientific Advisory Committees - for information (TOX/2025/17)

64. This paper was circulated for information, but Members should contact the Secretariat if they have any questions.

Item 12: Reflections from the Chair

65. As this was his last meeting, Professor Alan Boobis, the COT Chair reflected on his decade-long tenure chairing the COT and prior to that as a COT Member. He reflected on the rigorous and important work undertaken by the

Committee and discussed the breadth of topics reviewed. Thanks were extended by the outgoing Chair to Committee Members and Secretariat for their support and dedicated work throughout his time as Chair.

66. The Members and the Secretariat thanked Professor Boobis for all his hard work as Chair, both on the day-to-day activities of the Committee but also in taking their activities forward to leave a valuable legacy.

Item 13: Any other business

67. There was no other business.

Date of next meeting

68. The next meeting of the Committee will be at 10:00 on the 20th of May 2025 at Broadway House, London. The meeting will be hybrid.

Secretariat

March 2025