Meeting

Final Minutes of the 21st May 2024 COT Meeting

Meeting of the Committee at 10:00 on 21st May 2024 at Broadway House, London and on Microsoft Teams

Present

Chair:	Professor Alan Boobis

	Dr James Coulson
	Professor Gary Hutchison
	Professor Thorhallur Halldórsson
	Dr Michael Routledge
	Dr Natalie Thatcher
	Dr Simon Wilkinson
	Professor Philippe Wilson
	Dr Gunter Kuhnle
	Professor Shirley Price
	Dr Cheryl Scudamore
	Dr Stella Cochrane
COT Members:	Dr David Lovell
	Professor Peter Barlow
	Dr Steven Enoch
	Dr Mac Provan
	Professors Maged Younes
	Mr Gordon Burton
	Dr Meera Cush
	Mr Nick Richardson
	Dr Chris Morris
	Dr Andreas Kolb
	Dr Alison Yeates
	Dr Phil Botham (Co-opted)

	Professor Jeanette Rotchell
	Dr Samantha Donnellan
COT Associate Members:	Ms Eimear O'Rourke
	Dr Charlotte Mills
	Dr Tarek Abdelghany

	Ms Cath Mulholland - FSA Scientific Secretary
	Ms Chara Tsoulli
	Ms Abigail Smith
	Dr David Gott
	Dr Alex Cooper
	Mr Michael Dickinson
	Ms Claire Potter
	Dr Barbara Doerr
	Dr Olivia Osborne
	Ms Sabrina Thomas
	Dr Gail Drummond
	Ms Cleanncy Hoppie
	Ms Jocelyn Frimpong-Manso
Food Standards	Ms Michelle Hutchinson
Agency (FSA)	Dr Gaetana Spedalieri
Secretariat:	Mr Thomas Hornsby
	Dr Emily Hudson
	Dr Aaron Bradshaw
	Dr Lorcan Browne
	Ms Natasha Adams
	Dr Katie Schulz
	Ms Katie Wetherall
	Mr Barry Maycock
	Ms Frederique Uy
	Dr Rachel Kerr
	Mr James Metcalfe

UK HSA Secretariat:	Ms Britta Gadeberg - UK HSA Scientific Secretary
Invited Experts and Contractors:	Dr Sarah Bull - Institute for Environmental Health (IEH)
Assessors:	Ms Louise Dearsly - Health and Safety Executive (HSE)
Observers:	Dr Stephen Ruckman TSG consulting
FSA and other Officials:	Mr Allan Shivembe - FSA Mr Tim Chandler - FSA Mr Chris Rundle - FSA Ms Krystle Boss - FSS Ms Rachel Daniels - Health & Safety Executive (HSE)

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Announcements

1. The Chair welcomed Members and other attendees.

2. This was the first meeting for new COT Members - Mr Nick Richardson, Mr Gordon Burton, Dr Andreas Kolb, Dr Chris Morris, Dr Meera Cush and Dr Alison Yeates. Dr Yeates, who had not been able to attend previously as an observer briefly introduced herself to the Committee.

3. This would be the last COT meeting for Associate Members Professor Jeanette Rotchell, Dr Ben-Amies Cull, Dr Samantha Donnellan, Dr Charlotte Mills, Dr Tarek Abdelghany and Dr Eimear O'Rourke as their terms of appointment expire at the end of June. The Chair thanked them for their contributions to the Committee and invited them to reflect on how they had found the experience. It was generally agreed that it had been a very useful experiment and it was hoped that it would be continued in the future.

4. Dr David Gott, ex Scientific Secretary of the Committee and long-standing Member of the Secretariat would be retiring In June after 30 years in the Civil Service as well as many years serving on EFSA panels. The Committee thanked him for all his support for the work of the COT.

Interests

5. 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

6. Apologies were received from COT Members Dr Silvia Gratz and Professor Mireille Toledano and regular observer and FCMJEG Member, Dr Emma Bradley.

Item 2: Draft Minutes from the meeting held on 26th of March 2024

(TOX/MIN/2024/02)

7. The Committee reviewed the draft minutes and the reserved minutes of the 26th March 2024 meeting (TOX/MIN/2024/02).

8. The minutes and reserved minutes were accepted as an accurate record.

Item 3: Matters arising

Joint Expert Groups (JEG) update

Additive and Enzyme Joint Expert Group (AEJEG)

9. The AEJEG met in April and drafted a Committee Advice Paper on RP507, an application for authorisation of Blue Microalgae Extract; another Request For Information (RFI) would be sent to the Applicant. Members were informed that RP1467, an application for authorisation of the substance glycolipids (E 246) (Nagardo, AM-1), would return to the AEJEG to allow a review of the entire dossier, before being presented to COT. A flavouring for a plant-based meat alternative (soy leghemoglbin; RP733) was also reviewed at the AEJEG and it was agreed that an RFI should be issued to the Applicant. The new processes/reforms in the Regulated Products service were presented to AEJEG Members.

10. The next AEJEG meeting will be on the 4th of June. The Smoke Flavourings Working Group will next meet in July to begin phase 3 assessment (conclusion on genotoxicity, assessment of general toxicity and Extended One-Generation Reproductive Toxicity (EOGRT)).

Food Contact Material Joint Expert Group (FCMJEG)

11. The FCMJEG last met on the 10th of April where Members discussed an application for a plastic additive. RFIs for two polyethylene terephthalate (PET) recycling processes were also reviewed and deemed to be satisfactory. Safety advice documents will be prepared for review by the JEG, and these will then come to COT. FCMJEG Members also received a presentation on continuous improvement of the Regulated Products service and were invited to ask questions and make comments.

12. The next FCMJEG meeting is on the 29th of May, where Members will review the first draft of a safety advice document for PET recycling processes. The FCMJEG will also be reviewing two Annex documents prepared to accompany future safety advice documents coming to COT.

Publications

13. Two COT Workshop Reports have recently been published: “Exploring Dose Response and Physiologically Based Pharmacokinetic Modelling (PBPK) for Regulators” and “UK FSA COT Paving the way for a UK Roadmap – Development, Validation, and Acceptance of New Approach Methodologies.” These publications are available online.

14. The COT statements on aircraft cabin air and lead in the maternal diet have now been published.

COT Workshop 2024

15. During discussions at the February meeting, the microbiome was suggested as a potential topic for the 2024 COT workshop. Members had been invited to suggest agenda items and/or speakers. A preliminary structure for the day could include ’current state of play/knowledge’, ‘data we already have’, a roundtable discussion on future themes, and identification of research data gaps that would be important for regulators.

16. Members discussed the proposed workshop topic and noted that the microbiome covered a very broad area. It was suggested that topics including current methodologies and possible mechanisms of action might also be of interest. Members considered that it was important to identify the questions of most relevance to the COT, including how do diet and chemicals affect the microbiome. The kinds of data needed for risk assessment, the relevance of animal models, the interpretation of metagenomic studies, and the forms of possible extrapolation to risks to human health were all considered important areas to discuss.

Subgroups and Working Group updates

17. The joint Advisory Committee on Novel Foods and Processes (ACNFP) and COT Working Group on Cannabidiol (CBD) is continuing to review the different purity groups of CBD products. They will next be meeting on the 22nd of May.

18. The Joint Scientific Advisory Committee on Nutrition (SACN)-COT Working Group on Plant Based Drinks have prepared a second draft of their report, following significant restructuring in response to comments received on the first daft from the main COT and SACN Committees. The second draft would be presented to SACN and COT with the aim of publishing the report for public consultation before the Parliamentary Recess in July. This may require organising an ad hoc COT meeting to discuss the report due to the short time lines.

Item 4: Committee Advice on the safety of the Application to modify the conditions of use of E401 (sodium alginate) for use as a surface treatment in entire fruits and vegetables (Reserved) - Update (TOX/2024/17)

19. No interests were declared.

20. A confidential AEJEG safety advice document on the safety of the application to modify the conditions of use of E401 (sodium alginate) for use as a surface treatment in entire fruits and vegetables was presented to the COT.

21. The item is currently being treated as reserved, as it is developing policy. The minutes will be published once confidentiality agreements have been finalised.

22. Members reviewed and commented on the paper.

Item 5: Fifth draft statement on the safety of Titanium Dioxide (E171) as a Food Additive (TOX/2024/18)

23. Professor Alan Boobis had previously declared an interest that dated back to 2019. He is member on the External Advisory Committee of the Centre for Research on (Food) Ingredient Safety at Michigan State University. One of their research groups had undertaken research on titanium dioxide, (TiO2) published in 2019, which was partly funded by industry. This was not a direct interest and would not preclude Professor Boobis from contributing to the discussions, but the item was chaired by Dr Phil Botham. Dr Stella Cochrane and Dr Natalie Thatcher declared non-personal specific interests as their employers may use titanium dioxide in their products. This interest did not preclude them from contributing to the discussion of this item". Professor Shirley Price was part of the JECFA Working Group on titanium dioxide.

24. In 2021 the EFSA FAF Panel published their Opinion on titanium dioxide (E171), which concluded that it could no longer be considered as safe when used as a food additive.

25. In 2021 the COT published an interim position on TiO2 capturing the outcomes of the discussions and outlining the next steps. Members had been asked to evaluate the EFSA Opinion and comment on whether they agreed with EFSA's conclusions and provide further guidance on the next steps that should be taken by producing an opinion paper following a review of the new EFSA opinion and the extended one generation reproductive toxicity (EOGRT) study data by both the COT and the Committee on the Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM).

26. A draft statement is in preparation and has been presented to the COT on several occasions with amendments to the structure and content being made in response to Members' comments. The drafting of the statement is being supported by a sub-group of COT Members.

27. The draft statement includes the COT conclusions on the following endpoints: absorption, distribution, metabolism, and excretion (ADME), Aberrant Crypt Foci as a marker for Carcinogenicity, Reproductive and Developmental Toxicity, Immunotoxicity and Inflammation, Neurotoxicity and Genotoxicity (the latter being based on the review and conclusions of the COM), together with the establishment of a Health-Based Guidance Value.

28. The focus of the discussion was on the executive summary, which could be published as a standalone document if necessary, as well as the main statement on the safety of TiO2 as a food additive. Comments on the executive summary should also be applied to the main statement. It was suggested that some of the sections in the executive summary should be reorganised for a more coherent structure.

29. The ADME characteristics of TiO2 were also examined. It was noted that TiO2, primarily in microparticulate form, was poorly absorbed, which likely contributed to the absence of observed toxicity in a range of *in vivo* studies. It was suggested that certain sections should be rephrased to clarify the contribution of low absorption to the absence of observed adverse effects.

30. No changes had been made to the neurotoxicity section since the last review, but additional amendments to the wording of the conclusions were suggested to ensure clarity.

31. The carcinogenicity section addressed potential concerns related to aberrant crypt foci, concluding that there was no clear treatment-related effect. The sections on inflammation and immunotoxicity had been reviewed in particular

detail for the latest version of the statement and, therefore, the executive summary. There were inconsistent findings and again it was concluded that there were no significant treatment-related effects associated with TiO_2.

32. The Committee discussed the uncertainty over the toxicological effects of TiO_2 nanoparticles. However, it was emphasised that food-grade TiO_2 contains only low levels of nanoparticles. It was noted that consistency and clarity in the report were crucial, ensuring that statements in the text did not contradict findings regarding nanoparticles and systemic availability.

33. There were no significant changes in the conclusions regarding mutagenicity. However, some additional clarification from the COM was requested.

34. The Committee discussed the proposed health-based guidance value (HBGV) and noted that there will be additional conservatism in applying a conventional uncertainty factor to the critical NOAEL of E171 selected, because 1,000 mg/kg bw per day was the highest dose of TiO_2 tested, thus, the NOAEL could actually be higher. Also, as there is no metabolism of TiO_2 particles, inter-/intra-species kinetic differences are likely to be lower than default. Overall, the COT concluded that food-grade TiO_2 poses no significant health risk.

35. It was suggested that the EU status of TiO_2 and the broader uses of TiO_2 including in medicinal products be included in the introduction.

36. The Committee noted that the main statement contained extensive reviews of mutagenicity, inflammation, neurotoxicity, carcinogenicity, developmental and reproductive toxicity, with the findings of the extended one-generation reproductive toxicity study presented separately. The Committee suggested that it would be clearer if these were discussed within each related endpoint.

37. Members were informed that the report would be edited, to ensure clear referencing and consistency. The final version of the report will be shared for further review, with the aim of publishing the executive summary as soon as possible and publishing the statement soon afterwards.

38. It was agreed that it would be ideal to coordinate with COM to ensure that all the statements were released together.

Item 6: Sixth draft interim position statement on bisphenol A (TOX/2024/19)

39. Professor Thorhallur Halldórsson and Professor Maged Younes of the Committee and Dr David Gott of the Secretariat were Members of the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) and Bisphenol A (BPA) Working Group. They were able to answer questions and provide clarification on the EFSA opinion but could not take part in the discussion. Dr Stella Cochrane and Dr Natalie Thatcher declared non-personal specific interests, as their employers would have an interest in the use of BPA in packaging. No other interests were declared.

40. In April 2023, the EFSA CEP panel established a new Tolerable Daily Intake (TDI) of 0.2 ng BPA/kg bw per day. Following their diverging view from EFSA, the German Federal Institute for Risk Assessment (BfR) published their own full assessment of BPA in 2023, establishing a TDI of 0.2 µg/kg bw per day (equivalent to 200 ng/kg bw per day).

41. Following COT discussion of the EFSA opinion, a draft interim position statement was presented to the Committee in May, September and October 2023. Following the subsequent publication and discussion of the BfR assessment at the December meeting and internal discussions with policy colleagues, an updated draft interim position statement was presented at the February 2024 meeting and the Committee agreed to adopt the BfR TDI. This development was incorporated into a further revision of the interim position statement which was discussed at the March 2024 meeting. Paper TOX/2024/18 presented the updated statement reflecting the changes requested by the Committee at the March meeting.

42. Members also asked for clarification on the no migration rule in coatings and varnishes applied to Food Contact Materials (FCMs) intended for infants and young children, as BPA is prohibited for use in such products. Clarification was also sought on whether the effects of BPA on the male reproductive system (decreased sperm count and mobility, changes to testis histology) identified by the BfR were the only observed effects or whether they were the main ones considered in their assessment. The Committee also asked for clarification on the considerations of the TDI being (100%) protective for any other relevant effects/toxicological endpoints, including intermediate endpoints.

43. Overall, the Committee were content with the changes made but suggested some minor editorial changes to the document.

44. The statement will be amended and cleared by Chairs action.

Item 7: Pinnatoxin - surveillance and exposure (Presentation)

45. No interests were declared.

46. 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.

47. In July 2023, a paper was brought to the committee which provided information and data on the risks associated with pinnatoxins (PnTX) in shellfish (TOX/2023/37). PnTX are not currently regulated in England or Wales. The views of the COT were sought on whether PnTX would pose a risk to UK consumers. The Committee concluded that due to the lack of toxicological and occurrence data it was currently not possible to determine the extent of any public health risk. Members agreed that occurrence data on PnTX would be useful to help fill some data gaps, including whether the UK population would be exposed to PnTX from shellfish consumption.

48. The recent availability of new analytical standards has allowed PnTX to be monitored in UK shellfish. Committee members were informed that LCMS monitoring data for PnTX-G had been provided to the FSA by the Agri-Food and Biosciences Institute (AFBI) in Northern Ireland and by Food Standards Scotland (FSS). The Secretariat provided a presentation summarising the most recent such data.

49. Members queried whether there could be differences between wild shellfish and farmed shellfish and whether that information was available in the dataset. This was not known but could be followed up. The fact that different shellfish may have different feeding mechanisms and therefore accumulate PnTX-G differently was also highlighted.

50. Members asked how cooking or processing might affect the levels of toxin. The Secretariat clarified that the toxins were relatively heat stable but that processes such as cooking or dehydration of the meat during steaming and canning could lead to different levels of PnTX in the final product as compared to the raw shellfish.

51. It was noted that the exposures estimated by EFSA using a 400 g portion size assumed that a consumer would eat 400 g of a single shellfish type and it was questioned how likely this would be for some shellfish species. Members also commented that cultural differences could lead to large differences in the amounts and types of shellfish consumed. It was also noted that the number of respondents for some of the National Diet and Nutrition Survey (NDNS) data were very low and therefore there was significant uncertainty around some of the exposure estimates.

52. Members questioned whether PnTX-G was known to co-occur with other marine biotoxins, however, there did not appear to be any reports of regular co-occurrence.

53. Members asked if it was possible to reduce PnTX-G contamination through methods such as using depuration tanks. It was noted that there were no data available on the efficacy of such an approach, but as they are lipophilic biotoxins this made extraction of the biotoxin into clean water more challenging.

Item 8: COT Ways of working (discussion paper) (TOX/2024/20)

54. Comments from COT Members were provided to the secretariat in advance of the meeting.

55. The workload of the Committee and in particular the Chair has increased over recent years, partly, though not solely, as a result of the UK’s exit from the EU, including the additional activities associated with the authorisation of regulated products. It was therefore appropriate to review the current working practices of the Committee to ensure that it remains sustainable, and that the role of the Chair does not become unmanageable. In addition, due to the increase in hybrid and virtual meetings, it was important to ensure the Committee could work in an effective manner, with members being able to fully contribute and be engaged.

56. Paper TOX/2024/20 set out a number of ideas on ways of working following discussions between the Chair and the Deputy Chair and some senior COT Members.

57. The recent difficulties in recruiting a new Chair were noted and Members were asked for suggestions on the future shape of this role, including

workload. One suggestion was to train current Members over a defined period, initially as Deputy Chair, moving on to sharing the Chair's workload, and finally stepping into the role of Chair, so there was a clear succession planning process. However, it was noted that Chairs were appointed through an open recruitment process so it would not be appropriate to fill the role in that way.

58. The Secretariat explained that the Chair and Members were appointed for 3 year terms with a maximum of 3 terms or 10 years being served. However, appointment for a third term was expected to be exceptional. Members commented that a single 3-year term might be better for the Chair due to the workload, however it was noted that an individual might take time to settle into the role which should be taken into account.

59. It was agreed that, in addition to chairing the meeting when the Chair was unavailable or had a conflict of interest, it could be useful for the Deputy Chair to lead in a particular topic area to reduce the workload of the Chair.

60. Members discussed whether having co-Chairs would be useful, however there was concern it could be confusing in terms of clear leadership.

61. The recent innovation where small groups of Members were attached to particular papers was discussed. Members agreed that the small group working should include more groups attached to discussion papers from an earlier stage and following the process through. The small groups worked best when supported by the Secretariat. It was agreed that small groups should also consider first draft statements. Thought could also be given to including lay members and/or associate members in small groups.

62. It was noted that there was significant learning potential in being part of a small group at an early stage, particularly for new Members: with one new member detailing their positive experience of this. While some new Members felt more comfortable contributing ideas initially in a small group compared to the main meeting, this would depend on the individual.

63. With respect to online meetings, the Committee were asked their views on whether they should remain as a single full day or whether having 2 half day meetings should be explored instead, to reduce the blocks of screen time. Members acknowledged that both options had advantages, with half days spreading out the preparation time needed, while full days could be easier to schedule. Members confirmed that they can easily gain the attention of the Chair in hybrid meetings, if participating online.

64. Members discussed their preference for in person versus online meetings, it was noted that in person meetings reduced distractions and disturbances that some may experience if taking an online meeting at home or in the office. However, online meetings could also be easier to fit into a busy schedule.

65. The audio quality of both hybrid and in person meetings could be poor depending on the venue. It was suggested that this could be improved by the use of roving microphones, however there were financial constraints as the equipment had to be hired. Members noted this but considered that there needed to be a solution if it affected the operation of the Committee.

66. Members were asked if it would be beneficial to have draft statements in the collaboration area of Teams prior to the meeting to allow them to contribute at an earlier stage with a view to speeding up the process. It was agreed that doing this would risk constantly changing versions of documents. It was also raised that some Members may struggle to find the time to consider early drafts of statements along with the other reading. Members also expressed concern that adding comments prior to the meeting might influence the direction of the discussion on the day. Overall, it was agreed that the small groups and subgroups would be a more effective way of commenting on early drafts of statements.

67. Members were reminded that they could provide written comments on agenda items ahead of the meeting, particularly if they were unable to attend. It was noted that extra information potentially useful to discussions could be provided if requested in advance of meetings.

68. It was discussed that lay Members may sometimes find it difficult to participate at meetings due to the very technical content. It was agreed that lay Members from different Committees should meet to share their perspectives. It was suggested that it might be beneficial to recruit lay Members to the Committee at different times so their appointments were staggered.

69. Members were reminded that they were free to suggest ideas on ways of working to the Secretariat at any time.

Item 9: Updated position paper on bamboo composites in food contact materials (TOX/2024/21)

70. No interests were declared.

71. In May 2020, a scoping paper entitled “Alternatives to conventional plastics for food & drinks packaging” (TOX/2020/24), which introduced some of the possible toxicological hazards associated with the use of bio-based food contact materials (BBFCMs), was presented to the COT. A proposed list of BBFCMs for health risk assessment was then presented to the Committee in February 2021 (TOX/2021/01); this included BBFCMs containing bamboo food contact materials.

72. In 2021, the COT considered whether exposure to bamboo bio-composites in food contact materials posed a risk to human health in discussion papers TOX/2021/34 and TOX/2021/54. Overall, the Committee agreed that the migration of formaldehyde and melamine from bamboo composite cups was a potential concern to human health. In 2022, the COT published an interim position paper on bamboo composites in BBFCMs, capturing the outcomes of the discussions and their current position.

73. In March 2024, the COT were provided with an update on the use of bamboo composites in BBFCMs (TOX/2024/09). This discussion paper contained a summary of responses obtained from manufacturers following a 2023 FSA call for information plus additional analytical data.

74. Following the discussion at the March 2024 meeting, an updated position paper on bamboo composites in BBFCMs was prepared and was attached at Annex A to TOX/2024/21. New text was highlighted in yellow.

75. Members suggested a few minor editorial changes to the position paper.

76. It was agreed that the draft position paper could be cleared by Chair's Action

Item 10: Update on the work of other FSA Scientific Advisory Committees - for information (TOX/2024/22)

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

Item 11: Any other business

78. Members were informed about the British Toxicology Society (BTS) skills gap initiative which has been running since 2021 and which was entering into phase three and about to launch its first training module.

Date of next meeting

79. The next meeting of the Committee will be at 10:00 on the 9th July 2024 by Microsoft Teams only.