Meeting

Final Minutes of the 5th September 2023 COT Meeting

Meeting of the Committee at 10:00 on 5th September 2023 at Broadway House, London and on Microsoft Teams

Present

Role	Name	Affiliation
Chair:	Prof Alan Boobis	COT

COT Members:

Dr Phil Botham

Professor Thorhallur Ingi Halldórsson

Dr Michael Routledge

Dr Natalie Thatcher

Ms Juliet Rix

Dr Simon Wilkinson

Professor Philippe Wilson

Ms Jane Case

Professor Gunter Kuhnle

Professor Shirley Price

Dr Cheryl Scudamore

Dr Stella Cochrane

Dr David Lovell

Professor Matthew Wright

Dr Steven Enoch

Professor Peter Barlow

Professor James Coulson

Professor Gary Hutchison

Dr Mac Provan

Dr Sarah Judge

Professor Maged Younes

	Professor Jeanette Rotchell	
	Dr Steven Enoch	
COT Associate Members	Dr Samantha Donnellan	COT
	Ms Eimear O'Rourke	
	Dr Ben Amies-Cull	
	Dr Tarek Abdelghany	

	FSA Scientific Secretary
Food Standards Agency (FSA) Secretariat:	Ms Cath Mulholland
	Mr Michael Dickinson
	Dr David Gott
	Dr Alex Cooper
	Mr Barry Maycock
	Ms Claire Potter
	Dr Olivia Osborne
	Ms Frederique Uy
	Ms Rhoda Aminu
	Ms Sabrina Thomas
	Dr Gail Drummond
	Ms Cleanncy Hoppie
	Ms Jocelyn Frimpong-Manso
	Ms Sophy Orphanos
	Dr Gaetana Spedalieri
	Mr Thomas Hornsby
	Dr Emily Hudson
	Mr David Kovacic
	Ms Kaitlyn Jukes
	Dr Aaron Bradshaw
	Dr Lorcan Browne
	Ms Natasha Adams
	Ms Abigail Smith
	Dr Katie Schulz

UK Health Security Agency (UKHSA) Secretariat:	Ms Britta Gadeberg	UK HSA Scientific Secretary
Invited Experts and Contractors:	Dr Sarah Bull	Institute for Environment and Health (IEH)
	Dr Ruth Bevan	IEH
	Dr Jo Wilding	Independent consultant
	Ms Louise Dearsley	Health and Safety Executive (HSE)
	Ms Susanah Brown	Office of Health Improvement and Disparities (OHID)
Assessors	Dr Ovnair Sepai	UKHSA
	Ms Hannah Jones	Business, Energy and Industrial Strategy (BEIS)
	Mr Ian Martin	Environment Agency
Observers	Dr Emma Bradley	FCM JEG
	Dr Stuart Adams	FCM JEG
	Dr Jenny Odum	FCM JEG
	Dr Michael Walker	FCM JEG

Food Standards Agency Officials (FSA)	Mr Vincent Greenwood	FSA
	Dr Andy Axon	
	Ms Holly Howell-Jones	
	Mr Allan Shivembe	
	Ms Amanda Blacker	
	Ms Ese Hughes	
	Mr William Birkin	
	Dr Joanne Edge	
Other Officials:	Ms Kerry Gribbin	FSA NI
	Mr Elliot Dews	FSA NI
	Ms Coleen Mulrine	FSA NI
	Ms Krystle Boss	Food Standards Scotland (FSS)
	Ms Lucy Smythe	FSS
	Ms Holly Alpren	DEFRA
	Mr Mark Cairns	Civil Aviation Authority (CAA)

Contents

Date of the next meeting – Tuesday 17th October 2023 at Broadway House, London and via Teams

Announcements

1. The Chair welcomed Members, Associate Members and other attendees to the meeting.

Interests

2. 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

3. Apologies were received from COT Members Dr Silvia Gratz and Professor Mireille Toledano and COT Associate Member Dr Charlotte Mills. Apologies were also received from Dr Barbara Doerr and Dr Gail Drummond of the Secretariat.

Item 2: Draft Minutes from the meeting held on 11th of July 2023 (TOX/MIN/2023/03)

4. It was agreed that the wording at the end of paragraph 56 should be amended from ‘The wider implication of using one or other was more of a risk management issue’ to read ‘but the decision on which value to use will need to include additional considerations, and this is beyond the terms of reference of the COT.’

5. The remaining minutes were accepted as an accurate record.

Item 3: Matters arising from the meeting held on 11th of July 2023

JEGs Update

6. Members were updated on the current work of the Joint Expert Groups (JEGs)

Additives, Enzymes and other Regulated Products (AEJEG)

7. Members were informed that the next meeting of the Additives, Enzymes and Other Regulated Products JEG (AEJEG) would be held on 7th September. This meeting would further consider the applications for smoke flavouring product renewals and the weight of evidence document that had been prepared at the previous smoke flavourings AEJEG meeting.

8. A regular AEJEG meeting was scheduled for the 8th September to consider all other dossiers and authorisations. As the request of the JEG, Dr Phil Botham of the COT would be in attendance to provide additional support regarding the interpretation of short-term animal studies.

Food Contact Materials (FCMJEG)

9. Members were informed that the Food Contact Materials Joint Expert Group (FCMJEG) met on 23rd August to discuss three plastic recycling processes. A further FCMJEG meeting would be held on the 3rd October to discuss a plastic additive application and two recycling processes applications. A call for information on ocean bound plastics was underway and the topic was likely to return to the COT for their views later in the year.

Publications

10. The COT Workshop Report: Opportunities and outlook for UK Food and Chemicals regulation post EU Exit Workshop (2022) has been published on the COT website.

SAC Recruitment

11. Members were advised that the annual recruitment round for the the FSA Scientific Advisory Committees (SACs) and JEGs will be starting shortly. It is hoped that new Members with expertise in clinical toxicology, neurotoxicology, and cellular toxicology can be recruited. Members were asked to let the Secretariat know if they had any suggestions for suitable places where the recruitment could be promoted or suitable individuals that could be approached directly.

Item 4: Draft Opinion 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 (Reserved)

12. No interests were declared.

13. Dr Emma Bradley, Dr Stuart Adams, Dr Jenny Odum and Dr Michael Walker. from the FCMJEG were in attendance for this item.

14. The FCMJEG had been requested to provide an assessment on the safety of post-consumer recycled poly(ethylene terephthalate) (PCR-PET) pellets produced from a recycling process that utilises PCR-PET flakes as the raw input material.

15. This item is currently being treated as reserved, as the data are commercially confidential.

16. Members reviewed and commented on the draft opinion.

Item 5: Assessment of the risk of allergic reaction from fortification of non-wholemeal wheat flour with folic acid – (TOX/2023/41)

17. Dr Stella Cochrane declared a non-personal, specific interest as she was employed by a food manufacturing company that sells vitamin products. This interest did not preclude the Member from contributing to discussion of this item. No other interests were declared.

18. The number of neural tube defect-affected pregnancies (e.g. spina bifida and anencephaly) in the UK remains of concern to UK Health Departments. Advice to women to take folic acid supplements prior to conception and up to the 12th week of pregnancy has been in place for many years, but it remains a public health issue as there is limited uptake of the advice. There is particular concern with respect to unplanned pregnancies where a woman may not find she is pregnant until well into the crucial 12-week period when the neural tube is closing.

19. The UK Health Department's plan to implement a public health intervention that will involve fortifying non-wholemeal wheat flour with folic acid at a level of 250 µg per 100 g of flour to help prevent an estimated 200 neural tube defects in fetuses per year.

20. The fortified flour will be used in a wide range of food products, which in turn will increase folic acid consumption across the UK, including by pregnant women, thereby reducing the risk of neural tube defect-affected pregnancies. The proposal will affect an estimated 22 billion units of food sold in the UK annually.

21. The Committee have previously contributed to the wider discussion on folic acid fortification, particularly with respect to the derivation of a Tolerable Upper Level for the vitamin.

22. The fortification of non-wholemeal wheat flour needs to be reflected in labelling. This responsibility falls within the purview of Defra in England, FSA in respect of Wales and Northern Ireland and FSS in respect of Scotland.

23. Concerns have been raised that there will be difficulties in the timely changing of the labelling and it has been suggested that there could be transitional arrangements to facilitate the change, which could mean that for a period of up to 3 months the presence of folic acid would not be reflected on the label.

24. Paper TOX/2023/41 introduced the need to carry out an assessment of the risk of allergic reaction arising from fortification of non-wholemeal wheat flour with folic acid if it were not labelled on final products (or in the case of food sold loose, not conveyed by other means) during a 3-month derogation period. This assessment will inform risk management decisions by policy teams at the FSA and FSS.

25. The Committee were invited to consider the risk assessment, which was attached at Annex A to TOX/2023/41.

26. Members agreed with the approach used to undertake the risk assessment, considering it to be pragmatic and protective of consumer health.

27. The Committee were content with the estimates given to the frequency of adverse reactions to folic acid, the severity of illness in relation to adverse reactions to folic acid, and the level of uncertainty in the risk assessment. However, it was suggested that the risk assessment should better highlight that the proposed derogation period was for a period of only 3 months.

28. Members noted the lack of evidence of allergic reactions to folic acid in food and suggested that the Medicines and Healthcare Regulatory Products Agency. (MHRA) yellow card reporting system should be checked for any folic acid allergic reactions.

29. It was noted that the risk assessment should refer to food hypersensitivity rather than food allergy with respect to folic acid, and there should be more clarity around the difference between allergy and hypersensitivity. Members suggested adding clear definitions into a new section setting out the mechanisms of action. In this new section the structure of synthetic folic acid compared to naturally occurring folate should also be provided to better explain the possible different mechanism of actions and the data gaps should be highlighted.

30. It was suggested that additional uncertainties should be added to the risk assessment. One of these uncertainties was the lack of validation for skin tests/intradermal tests for folic acid, which were cited as evidence in several of the reported case studies. It was noted that folic acid had been tested in validation studies for skin sensitisation testing and the results were negative, adding further weight to this point. A second uncertainty was the lack of patient history in cases reporting anaphylaxis, making it unclear whether folic acid was the constituent in food responsible for the reactions. It was also suggested noting that some sources of uncertainty may have led to an overestimation of the risk of hypersensitivity to folic acid, such as using data and side effects from higher doses of folic acid in supplements where data on folic acid in food was lacking.

31. As a follow up to this piece of work, it was agreed it would be helpful to find the source of the statement on the NHS website that folic acid could potentially cause anaphylaxis.

Item 6: Systematic review of the literature on dioxins and dioxin-like polychlorinated biphenyls (PCBs) – (TOX/2023/42)

32. No interests were declared.

33. In 2018, the European Food Safety Agency (EFSA) published a tolerable weekly intake (TWI) for dioxins and dioxin-like polychlorinated biphenyls (PCBs) of 2 pg TEQ/kg bw/week. This TWI was 7-fold lower than EFSA’s previous TWI and would mean that, from the current situation in which dietary exposure for most of

the UK population was considered to be below a level of concern, exposure would instead be considered to be at a potentially harmful level. This would also suggest that current risk management measures for dioxins and dioxin-like PCBs in food, which include regulatory limits and precautionary advice to consumers and are based on the previous tolerable intake, may not be sufficiently protective.

34. Following the publication of the 2018 EFSA opinion and the proposed reduction in the TWI, the COT published an interim Position Statement in 2021. This noted that due to uncertainties and inconsistencies in the description and evaluation of the key studies in EFSA's assessment, the COT could not agree with the proposed TWI and further considered the 7-fold reduction in the TWI inconsistent with the current database. The Committee further noted that the European Commission (EC) has not yet adopted EFSA's new TWI due to ongoing work at the international level reviewing the basis and values of the World Health Organisation (WHO) toxic equivalent factors (TEFs) for dioxins. Hence, the Committee felt unable to comment on the dietary exposures and whether they should be compared to the EFSA proposed TWI. The Committee further recommended undertaking a review of the evidence base on dioxins to derive a health-based guidance value (HBGV), focusing on the relevant toxicological endpoints.

35. Paper TOX/2023/42 contained the final report of the commissioned systematic review of the literature on dioxins and dioxin-like PCBs, which covered the literature from 2017 to 2021 and updated the EFSA review. The review and subsequent report focused on male reproductive toxicity and immunotoxicity as recommended by the Committee. Literature on, and assessment of, the mechanism of action of dioxins via the aryl hydrocarbon receptor (AhR) had also been included to investigate species differences related to male reproductive toxicity and immunotoxicity, where possible.

36. The review also included a non-systematic consideration of the data on the potential carcinogenicity of dioxins and dioxin-like PCBs and whether this involved a genotoxic mechanism. Finally, the report provided to the FSA also included evidence integration and visualisation of the conclusions following the SETE guidance.

37. Members considered that the paper was detailed and provided a large amount of data for review. They noted that the tables were useful for interpreting results. However, it would be beneficial to set out the conclusions from this literature review alongside those reached by EFSA. Members also considered that it would be useful if a summary table of endpoints could be included to allow

different endpoints and conclusions to be more easily compared.

38. A Member questioned the conclusions reached by one of the papers considered in the review on how detectable the reported signal of a CYP1 mutation would have been in a 90-day study, given that this would have been an effect in hepatic stem cells, with a very slow turnover. This led Members to query if the plausibility of the findings in the published papers was considered in the review, as this would be required for evidence integration. The Secretariat noted that this was only the first stage of the process, where only an overview of the literature had been provided, and that plausibility will be considered at a later stage when everything was brought together.

39. The Committee discussed the paper on semen parameters in the Russian children's study by Minguez-Alarcon et al. (2017) which was used by EFSA to revise the TWI, and questioned why a second study with different results by Paul et al (2017) hadn't been taken into account. It was stated that the results from the latter study were compelling and it should be made clear about why it wasn't used by EFSA.

40. The reproductive toxicity section was considered to be very detailed, but it would be useful to know the methodology used and the exposure period, as this was confused in some places. There are two clear time windows for male reproductive effects, so including this may improve clarity. The Committee discussed the variability in human fertility and the known factors that differed from study to study, differences being attributable partly to variability and partly to uncertainty. Members asked for assessment of what variability would be expected in the parameters discussed.

41. The Committee stated that it was not clear how the totality of the evidence, including that prior to the start of the current review, had been weighed and integrated. It was premature to apply the SETE approach to the evidence integration without considering all the available data. Members noted that focussing only on recently published papers might not identify concerns in areas that had been already studied extensively but the original research would be excluded by the time limited search criteria, leading to an unbalanced conclusion. Before evidence integration could occur, the current review and reviews previously completed on dioxins would need to be combined to allow consideration of the totality of the data.

42. Members discussed the information on immune responses presented in paragraphs 223 and 224 of the summary section and considered that these

paragraphs did not align with the information provided in the immunotoxicity section. Members asked for additional content and context for this information. They further requested an extended table showing the evidence for immunotoxicity, to present a clearer overall view. Members suggested that the information in the table could be presented in sections for each part of the immune system to show the evidence for each area.

43. It was suggested that paragraph 222 be removed from the review as the correlation between PCBs and dioxins exposure is relatively high and hence the effects of these compounds would not be easily separated.

44. The interpretation of results where there had been mixed exposures, such as in epidemiology studies following Seveso would be complex, making comparisons in different areas of the world difficult. A number of congeners were also weak antagonists.

45. The Committee discussed the use of the Newcastle scoring system used to assess the quality of the papers; it was noted that only high scoring papers were included in the literature review. Members raised concerns that using this system could lead to papers of lesser quality but still with relevant information being omitted; this was a concern also discussed by the SETE sub-group. Members considered that it would be of value to see the relevant information from the papers that did not meet the quality criteria included in the next review. Members noted that the SETE diagrams should indicate the level of uncertainty through differences in symbol size.

46. Additionally, Members asked for a list of uncertainties to be included for the high scoring of the animal and human data presented. Members asked for consideration of plausibility that may affect the interpretation of findings, and for critiques of the studies to be included.

47. Members agreed that the most critical effects from this review and previous reviews should be identified. Converting the doses to body burden should also be considered.

48. The Committee agreed that following the systematic literature review, there currently was not sufficient evidence to identify a key study or studies on which to establish a health based guidance value and further consideration would be required.

Item 7: Chitosan 2nd Draft Statement – (TOX/2023/43)

49. No interests were declared.

50. 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. Subsequently, a proposed list of BBFCMs for health risk assessment was presented to the COT in February 2021 (TOX/2021/01); this included BBFCMs containing chitosan.

51. Paper TOX/2023/43 followed on from the first draft position paper on the potential allergenicity of chitosan in food contact materials (FCMs), which was presented to the COT in September 2022 (TOX/2022/45). As requested by the Committee, information on how to interpret life-cycle assessment (LCA) studies regarding chitosan in the environment was provided in the cover paper. Changes suggested by the Committee had been made to the draft position paper attached at Annex A to TOX/2023/43. This included additional context and background on allergen reference doses, the other allergenic proteins present in crustacea in addition to tropomyosin, and how the migration limit of 10 mg/dm2 in the Plastics Regulation was derived.

52. The Committee agreed that a brief synopsis of the information provided on life-cycle assessments should go into the position paper.

53. Members were content that the position paper sufficiently outlined and summarised the discussions thus far on the allergenicity of chitin and chitosan based BBFCMs, but noted that the paper needed to be clear that the main concern of the COT was contaminating proteins, and the species from which chitin and chitosan is derived.

54. The Committee agreed that research on the protein content (quantification and characterisation) at different stages of production (including the final product), and possible migration into packaged food was needed. This view should be included as a final sentence in the position paper.

55. The Committee considered how chitosan-based BBFCMs, derived from metazoans, might be received by vegans. The Committee noted that vegan and vegetarian labelling is not regulated; as such, manufacturer would not receive the ‘vegan’ or ‘vegetarian’ trademark from the various accrediting bodies. However,

this was not within the remit of the Committee.

56. In paragraph 2, it was not clear how the citation provided fully supported the statement that “chitosan has antimicrobial and antioxidant properties which make it ideal for extending the shelf-life of packaged foods”. Additionally, the information in paragraph 16 could be moved to paragraph 2.

57. In paragraph 6, it was worth noting that very few molluscs contain chitin as, in general, it is crustaceans that contain it. Therefore, it should be noted that allergies to shellfish would not be very relevant to possible cross-over effects based only on the presence of chitosan. It needed to be clarified that it was protein contamination that could cause a problem for people with allergy to molluscs if there was cross-reactivity.

58. In paragraph 29 (point c) which discussed ED01 and ED05, the wording needed to be revised slightly to more closely reflect the conclusions that the COT reached following the deliberations of the working group on allergens, where the choice of which allergen reference dose to use (ED05 or ED01) would include additional considerations.

59. Paragraph 49 contained quoted text from the National Aspergillosis Centre that was no longer available on their website. This text would be deleted from the position paper.

60. It was agreed that the draft position paper could be finalised by Chair’s action.

Item 8: Exposure to titanium dioxide in the UK population – (TOX/2023/44)

61. Professor Alan Boobis declared an interest that dated back to 2019. He is a 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, published in 2019, which was partly funded by industry. This is not a direct interest and would not preclude Professor Boobis from contributing to the discussions, but the item was chaired by the Deputy Chair, Dr Sarah Judge.

62. Professor Matthew Wright and Professor Maged Younes were Members of the EFSA Scientific Panels that reviewed the safety of titanium dioxide for the 2021 Opinion. They were available to answer COT Member’s questions and offer

clarifications on the EFSA Opinion, however they did not participate in the COT's discussion or conclusions. Professor Shirley Price declared an interest as she is a member of the JECFA group on titanium dioxide and will be attending the next JECFA meeting in October 2023 to discuss it. Dr Stella Cochrane and Dr Natalie Thatcher declared non-personal specific interests as their employers may use titanium dioxide in their products. These interests did not preclude the Members from contributing to the discussion of this item. No other interests were declared.

63. Paper TOX/2023/44 is part of the ongoing COT review of titanium dioxide and is the latest in a series of papers presented to the Committee, which have considered toxicokinetics, endpoints including immunotoxicity, reproductive toxicity and aberrant crypt foci, along with an early draft of the statement. The paper presented data on the potential exposure to titanium dioxide in the UK population.

64. Members noted that as many manufacturers are no longer using titanium dioxide in their products, the exposure estimates presented in Tables 2 and 3 might be a significant overestimation of the actual exposure levels; however a conservative risk assessment would need to assume that titanium dioxide was being used at the permitted levels in the absence of other information. It was agreed that all uncertainties from the exposure assessment should be noted. However, titanium dioxide levels in medicines, toothpaste and other non-food sources were not included in the assessment. However, it was important to acknowledge these other sources of exposure existed and include a recommendation that these should be considered in a future assessment.

65. Members discussed the provisional health-based guidance value (HGBV) which had been based on the Extended One-Generation Reproductive Toxicity study previously discussed by the Committee. Members agreed that, subject to the outcome of the COM discussion on genotoxicity, the NOAEL of 1000 mg/kg bw per day would be a suitable basis for the HBGV and the application of an uncertainty factor of 100 would be appropriate, resulting in a HBGV of 10 mg/kg bw/day.

66. It was highlighted that the potential for inhalation exposures to titanium should be acknowledged.

67. A Member suggested that body weights (mg/kg) for all the different age groups should be included. It was also suggested that there should be some further explanation on why the distribution of individual total exposure data were used in Table 2.

68. Members were informed that a draft statement would be prepared for the October 2023 meeting.

Item 9: Interim position paper on Bisphenol A (BPA) – (TOX/2023/45)

69. Interests were declared by Professor Alan Boobis as he is a member of the External Advisory Committee of the Centre for Research on (Food) Ingredient Safety at Michigan State University. Two of the scientists from the Centre had published an opinion piece on EFSA's scientific opinion on BPA . Dr Stella Cochrane and Dr Natalie Thacher also declared personal non-specific interests as their employers use BPA; neither of these interests precluded them taking part in the discussion of this item.

70. Professor Thorhallur Ingi Halldórsson and Dr David Gott of the Secretariat declared direct personal interests as they were members of the EFSA working group on BPA. They were able to answer questions and provide clarification on the EFSA opinion but could not otherwise contribute to the discussion. No other interests were declared.

71. In April 2023, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) established a new tolerable daily intake (TDI) of 0.2 ng BPA/kg bw per day for BPA, which is significantly lower than the current TDI and meant that exposure in mean and high level consumers for all age groups would exceed the new TDI by 2-3 orders of magnitude.

72. The COT discussed the draft EFSA opinion at their extraordinary meeting in February 2022 and submitted comments to EFSA for their public consultation. The final EFSA opinion and diverging opinions by the EMA and the BfR were discussed at the May 2023 COT meeting. A first draft of a position paper setting out the views of the Committee was discussed in July 2023.

73. Paper TOX/2023/45 was a second draft of the interim position paper, following comments made by the Committee in July. Additional text had been added to expand on the background on BPA and why it is used, the concerns raised by the COT on the selection of the endpoint used by EFSA to establish the TDI and the recommendations of the COT on how to take the work forward to establish a UK tolerable daily intake.

74. The toxicological endpoint used to establish the new TDI for BPA was a change in Th17 cells. These cells are involved in the development of inflammatory conditions, but a change in these cells is an intermediate effect and the exact role of the cells in adversity is uncertain, so the Committee did not consider this to be an appropriate endpoint.

75. The current UK TDI is substantially above the new TDI established by EFSA and was based on changes in kidney weights. The Committee agreed that it could not conclude on whether it this endpoint should still be used while BPA was being evaluated as, although there were concerns about the endpoint selected by EFSA, effects were apparent in other endpoints, which were less contested, suggesting the current TDI might no longer be appropriate.

76. Members asked how much BPA exposure was avoidable and requested further detail on the regulatory aspects. It was noted that the Committee had already reviewed one of the potential substitutes for BPA and could be considering further alternatives in the future.

77. The Secretariat informed Members that they would identify the HBGVs used elsewhere for BPA and advise the Committee; a revised version of the draft position paper would be presented at a future meeting. Due to resource constraints, a review of BPA would need to be externally commissioned and would not return to the Committee before the middle of 2024

Item 10: Public consultation on EFSA’S 2023 re-evaluation of the risk to public health from inorganic arsenic in food – (TOX/2023/46)

78. In July 2023, the EFSA Panel on Contaminants in the Food Chain (CONTAM) published a draft opinion re-evaluating the health risks arising from the presence of inorganic arsenic (IAs) in food. EFSA considered it appropriate to update their assessment as new studies have become available on the toxic effects of iAs, as well as new information on occurrence and exposures.

79. EFSA had applied a margin of exposure (MOE) approach as iAs is considered a genotoxic carcinogen with additional epigenetic effects. While the MOEs raised a potential health concern for skin cancer, supported by the uncertainty analysis, EFSA concluded that they were unable to derive a level of low concern due to the use of a human cancer endpoint and the absence of EFSA guidance on the use of such an endpoint.

80. The draft opinion had also been circulated to Members of the Committee on Carcinogenicity of chemicals in Food, Consumer Products and the Environment (COC) who had provided comments.

81. Members agreed that the document was comprehensive and clearly laid out.

82. The relationship between arsenic and skin lesions was well established, though the mechanism was unclear, and further information was needed in this area. It was noted that the paper by Diamond-Gilbert referred specifically to invasive squamous cell carcinoma. A lot of the data came from human studies in Bangladesh where there were high levels of arsenic in drinking water. It was possible that UV radiation was a co-carcinogen.

83. A Bayesian BMD modelling approach had been used and differed from the methods previously used by EFSA. It was noted that the output did not comply with the EFSA Scientific Committee recommendations so may not be appropriate, possibly as the model was extrapolated appreciably beyond the observable effect range. The modelling implied that adverse effects would occur at low levels of exposure but this was not apparent in the individual epidemiology studies.

84. Members noted that IAs was genotoxic and carcinogenic but not necessarily a genotoxic carcinogen, as there could be a secondary mechanism for the effect such as inhibition of DNA repair, which would have a threshold. Based on animal data an MOE of ≥10,000 would be of low concern for a genotoxic carcinogen but that could be mechanistically inappropriate in this case, which has been reflected in previous COT assessments of iAs, where an MOE of <10 was considered an appropriate level of concern.

85. The Committee did not accept the EFSA view that they were unable to identify an MOE of low concern as there was no precedent for using human epidemiology data, noting that human data had been used by EFSA in this way for other compounds with a presumed linear dose-response relationship, such as lead.

86. Members considered that the uncertainty analysis was difficult to understand and the nomenclature used confusing, as the “P values” for experts’ estimated probability could be misinterpreted for statistical “p values”. The opinion needed to be very clear where expert elicitation had been used to give a probability that the exposure exceeded the limit value. It was suggested that

different nomenclature could be used to reduce confusion. Uncertainty usually related to the risk assessment rather than the probability of exceedance of a limit value.

87. Members were asked to send any additional comments to the Secretariat by 6th September.

Item 11: Aircraft cabin Air Environment: Second draft statement – (TOX/2023/48)

88. No interests were declared.

89. The second draft statement on aircraft cabin air was presented following a series of papers on the topic being discussed by the Committee between May 2022 and March 2023 and the first draft statement being presented in July 2023. This second draft statement incorporated the amendments suggested during the meeting in July, predominantly in the discussion and conclusion sections.

90. It was reiterated that the question for the current review was “Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level exposures including mixtures, e.g., of volatile organic compounds (VOCs)?”. This differed from previous reviews that considered the potential causes of ill health experienced by aircrew. It was also noted that the current review was considering both fume events and background exposure in the aircraft cabin environment, but there were data gaps with respect to peak exposures resulting from fume events.

91. Members agreed the amendments made to the discussion and conclusion sections of the draft statement following the July meeting. Some minor changes were suggested with respect to the format of the statement, with an executive summary and a table of contaminants assessed requested.

92. It was agreed that the statement would be updated and finalised by Chair’s action.

Item 12: Update on the work of other FSA Scientific Advisory Committees - for information - (TOX/2023/47

93. This paper was circulated for information. Members were invited to contact the Secretariat for any additional information.

Item 13: Any other business

94. There was no other business.

Date of next meeting

95. The next meeting of the Committee will be at 10:00 am on the 17th of October 2023 at Broadway House, London and via Microsoft Teams.