Minutes

Draft Minutes of the 11th July 2023 COT Meeting

Meeting of the Committee at 10:00 on Tuesday 11th July 2023 via Microsoft Teams

Present

Chair:	Prof Alan Boobis

Dr Phil Botham

Professor Thorhallur Ingi Halldórsson

Dr Michael Routledge

Dr Natalie Thatcher

Ms Juliet Rix

Dr Simon Wilkinson

Professor Mireille Toledano

Professor Philippe Wilson

Ms Jane Case

Professor Gunter Kuhnle

Professor Shirley Price

COT Members:

Dr Cheryl Scudamore

Dr Stella Cochrane

Dr David Lovell

Professor Matthew Wright

Dr Steven Enoch

Professor Peter Barlow

Professor Jeanette Rotchell

Dr Samantha Donnellan

Ms Eimear O'Rourke

Dr Ben Amies-Cull

Dr Charlotte Mills

Dr Tarek Abdelghan

COT Co-Opted Members:	Professor Paul Haggarty	SACN Liaison

Food Standards Agency (FSA)	Ms Cath Mulholland	
Secretariat:	Mr Michael Dickinson	
	Dr David Gott	
	Dr Alex Cooper	
	Mr Barry Maycock	
	Ms Claire Potter	
	Dr Barbara Doerr	
	Dr Olivia Osborne	
	Ms Chara Tsoulli	
	Ms Frederique Uy	
	Ms Rhoda Aminu	
	Ms Sabrina Thomas	
	Dr Gail Drummond	
	Ms Cleanncy Hoppie	
	Ms Jocelyn Frimpong-Manso	FSA Scientific Secretary
	Mrs 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	

UK HSA Secretariat:	Ms Britta Gadeberg	UK HSA Scientific Secretary
Invited Experts and Contractors:	Dr Sarah Bull	Institute for Environment and Health (IEH)
	Dr Ian Kimber	Codex Subgroup
Assessors	Ms Louise Dearsley	Health and Safety Executive (HSE)
	Ms Susanah Brown	Office of Health Improvement and Disparities (OHID)
	Dr Ovnair Sepai	UK Health Security Agency (UKHSA)
	Ms Hannah Jones	Business, Energy and Industrial Strategy (BEIS)
	Mr Ian Martin	Environment Agency
Observers	Mr Joe Brennan	UK Flour Millers
	Mr Alex Costigliola	UK Flour Millers
	Dr Stephen Ruckman	TSG Consulting
	Profession Anna Hansell	Committee on the Medical Aspects of Air Pollution (COMEAP) Member

	Mr Vincent Greenwood	
	Dr Andy Axon	FSA
	Ms Holly Howell-Jones	FSA
	Mr Allan Shivembe	FSA
	Ms Amanda Blacker	FSA
	Ms Ese Hughes	FSA
	Mr William Birkin	FSA
	Dr Joanne Edge	FSA
	Ms Kerry Gribbin	FSA
FSA and other Officials:	Mr Elliot Dews	Food Standards Northern Ireland (FSA NI)
	Ms Coleen Mulrine	FSA NI
	Mr James Isaac	UKHSA (COMEAP Secretariat)
	Ms Alison Gowers	UKHSA (COMEAP Secretariat)
	Ms Krystle Boss	UKHSA (COMEAP Secretariat)
	Ms Lucy Smythe	Food Standards Scotland (FSS)
	Ms Holly Alpren	FSS
	Mr Mark Cairn	Department for Environment Food & Rural Affairs (DEFRA)
		Civil Aviation Authority (CAA

Contents

Item		Paragraph
1	Apologies for absence	5
2	Draft minutes of the 28th May 2023 meeting- TOX/MIN/2023/03	6
	Matters arising	
3	JEG update Update on Panorama	7– 17
4	Interim position paper on Bisphenol A (BPA)– TOX/2023/31	18 – 30
	Titanium dioxide	
5	a) Review of the EFSA opinion on the safety of titanium dioxide as a food additive: Part 2 - TOX/2023/32 b) First draft statement on the safety of titanium dioxide as a food additive - TOX/2023/33	31-45
6	Assessment of the Codex report on food allergen thresholds - TOX/2023/35	46-56
7	Public consultation on draft EFSA opinion on polybrominated diphenyl ethers (PBDEs) -TOX/2023/34	57-70
8	Aircraft cabin Air Environment: first draft statement - TOX/2023/36	71-77
9	Emerging biotoxin report: Pinnatoxins - TOX/2023/37	78-90

10	Sub-statement on the potential risk(s) from exposure to microplastics: Inhalation route (Third draft) – TOX/2023/38	91-104
11	Ergot alkaloids in the maternal diet - TOX/2023/39	105-114
12	Update on the work of other FSA Scientific Advisory Committees - for information – TOX/2023/40	115
13	AOB	116
	Date of the next meeting – Tuesday 5th September 2023 at Broadway House, London and via Teams	117

Announcements

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

2. New Committee Members Professor Peter Barlow and Dr Steven Enoch briefly introduced themselves.

3. Members were reminded that the FSA were trialling an Associate Member Scheme to encourage mid-career researchers to join the Committee for one year and see what Scientific Advisory Committee work was all about, with a view to applying for full Membership in due course. Newly appointed Associate Members Dr Charlotte Mills, Professor Jeanette Rotchall, Dr Samantha Donnelly, Dr Ben Amies-Cull, Dr Tarek Abdelghaney and Dr Eimar O'Rourke briefly introduced themselves.

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 were received from COT Members Professor James Coulson, Professor Gary Hutchison, Dr Mac Provan, Dr Sarah Judge, Professor Maged

Younes and Dr Silvia Gratz. Apologies were also received from Ms Chara Tsoulli of the Secretariat.

Item 2: Draft Minutes from the meeting held on 28th of May 2023 (TOX/MIN/2023/03)

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

Item 3: Matters arising from the meeting held on 28th of May 2023

JEGs Update

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

Additives, Enzymes and other Regulated Products (AEJEG)

8. Members were informed that on the 1st June the AEJEG met online and concluded the risk assessment of RP773, for soy legume haemoglobin as a flavouring precursor for plant-based meat alternatives, and that a second round of Requests for Further Information for other applications had been prepared by the Secretariat.

9. On the 12th of June, the Smoke Flavourings working group of the AEJEG met in person and discussed the weight of evidence (WoE) for a risk assessment of the eight Smoke Flavourings dossiers. The discussions and the points raised on WoE would be compiled in a live document as a guide for future meetings; this would be finalised in September. It was hoped that by December, the Secretariat would have a timeline of when smoke flavourings will be presented to COT.

10. The Secretariat plans to present two new regulated product opinions to the COT before the end of this year.

Food Contact Materials (FCMJEG)

11. The FCMJEG will be having their next meeting on the 23rd August. The FCMJEG were working on recycling plastics, and a paper supporting Members'

understanding of the recycling process would be considered at a meeting at the end of September.

Update on Panorama Programme

12. It was noted that Members may have seen the Panorama programme on Ultra Processed Foods shown in June which mentioned the Committee. The FSA and the COT Chair were given a week to address questions asked by the programme makers and both provided statements correcting and clarifying numerous points; however, much of this information was not included in the final broadcast.

13. The FSA and the Science Media Centre would be responding to the BBC with respect to the misleading content of the programme.

14. Following the programme, the FSA have received a handful of complaints and a Freedom of Information request, though this was for information already in the public domain. The FSA Board strongly defended the integrity of the Expert Committees at their recent meeting.

Interim position statement on PFAS

15. The interim position statement on per and polyfluoryl alkyl substances (PFAS) was published on 29th June 2023.

16. The PFAS Working Group (WG) is in the process of being set up, and Professor Shirley Price has kindly agreed to Chair this group. The COT Chair thanked Members who have already volunteered to join the WG and any additional Members who would be interested were asked to contact the Secretariat.

SACN report on the diet of children aged 1-5

17. The Scientific Advisory Committee on Nutrition (SACN) have published their report on the diet of children aged 1-5. SACN Members thanked the COT for their contribution to this work.

Item 4: Interim position statement on bisphenol A - (TOX/2023/31)

18. Professor Thorhallur Ingi 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 (the CEP) and its Bisphenol A (BPA) Working Group. These are personal specific interests and while they were able to answer questions and provide clarification on the EFSA BPA opinion they could not otherwise take part in the discussion. Professor Matthew Wright is an EFSA panel Member (Food Additives and Flavourings (FAF)) but was not involved in the BPA evaluation and was able to take part in the discussions. 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.

19. No other interests were declared.

20. Following public consultation in December 2021, the EFSA CEP Panel published their final opinion on the re-evaluation of the health risks arising from the presence of BPA in food in April 2023. The Panel established a new Tolerable Daily Intake (TDI) of 0.2 ng BPA/kg bodyweight (bw) per day. This reduction would mean that mean and high level consumers for all age groups would now exceed the new TDI by 2-3 orders of magnitude.

21. Since the COT's discussions of the final EFSA opinion along with diverging opinions by the EMA and the BfR in May 2023, the European Commission (EC) has published a statement announcing a ban on the use of BPA in food contact materials (FCMs). The measures will set out derogations and transitional periods and also address the use of other bisphenols in FCMs to avoid substitution with other harmful substances. No information is yet available on the bisphenols the EC/EU are considering.

22. At the May 2023 meeting, Members considered it possible that the TDI would need to be revised to account for new evidence but noted that the time and resource implications of doing their own review of the database were significant.

23. The Committee agreed with the proposal to take a weight of evidence approach to the relevant endpoints, drawing on the data in the EFSA opinions (2006, 2008, 2015, 2023) and any data published since the cut-off point of the EFSA literature review.

24. Members considered there was a lack of transparency in the EFSA opinion on how the weight of evidence/data integration was performed by EFSA. Therefore, it was agreed that the SETE principles should be applied for data

integration, where applicable, with the aim of identifying key endpoints, gaps and uncertainties and suggest a way forward in establishing a TDI for BPA.

25. Members reiterated that rather than selecting and applying one specific intermediate endpoint for the derivation of a health-based guidance value (HBGV), it would have been more appropriate for EFSA to consider all evidence, or at least a wider range of endpoints/data in their assessment. Hence, Members agreed that to derive a point of departure or rather an endpoint from which to derive a UK health-based guidance value, the COT would consider evidence integration of all relevant endpoints/data and ensure that the weight of evidence and data integration was reflected transparently in their assessment.

26. At the May meeting, it was also decided that an interim position paper, capturing the COT's view and the proposed next steps should be published. Members considered the draft presented in paper TOX/2023/31 and made a number of suggestions on wording and content.

27. The EFSA opinion is a substantial assessment, with an extensive data set. Hence, the Committee will require some time to assess all the relevant information and to conclude on the relevant endpoint(s) to establish a safe level for the UK population. Members stressed that this would need to be clearly reflected in the interim position statement.

28. Members agreed that the interim position statement should also clearly state the reasoning why the Committee were undertaking their own assessment and if possible, provide clarification and explanation on where the Committee's views diverged from those of EFSA, and should outline the COTs proposal on how to take the work forward. It would also be helpful for consumers to know why BPA was considered necessary and what food contact materials it was used in.

29. As a position statement is generally a briefer document and not accompanied by a lay summary, Members highlighted the importance of communicating the concerns and considerations by the Committee in clear and where possible in lay terms, to ensure the statement is accessible to the general public.

30. A second draft interim position statement will be prepared for the September 2023 meeting.

Item 5: Titanium dioxide

31. 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 Dr Phil Botham (in the absence of the Deputy Chair, Dr Sarah Judge).

32. 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 declared a non-personal specific interest as her employers Unilever, 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.

33. EFSA published a revised opinion on the safety of titanium dioxide in food (where it is known as E171) in 2021 which concluded that because some studies suggested a potential for immunotoxicity, neurotoxicity and inflammation, and that as concerns related to genotoxicity could not be ruled out, E171 could no longer be considered as safe when used as a food additive. As a result of the concerns expressed by COT and COM with respect to the conclusions drawn by EFSA, the Committees were undertaking their own review of titanium dioxide. The provisional timeline of the COT/COM review of the safety of titanium dioxide as a food additive following the publication of the EFSA review was shared with Members. It was hoped that the review could be completed by the end of the year.

Item 5a: Review of the EFSA opinion on the safety of titanium dioxide as a food additive: Part 2 – (TOX/2023/32)

34. A discussion paper (TOX/2023/16) was presented to the COT in March 2023 reviewing the EFSA Opinion on the reproductive and developmental toxicity of titanium dioxide as a food additive. This paper covered the data from an Extended One-Generation Reproductive Toxicity Study (EOGRT) as well as relevant information from a literature search covering the period from 2015 - 2020. Based on the EOGRT study, the Committee agreed on a provisional point of departure of 1000 mg/kg/bw for titanium dioxide based on reproductive effects and stated this would be sufficiently robust to establish a health based guidance

value.

35. Paper TOX/2023/32 presented at this meeting, discussed the data underlying the main changes in the EFSA 2021 Opinion's conclusions on the endpoints of immunotoxicity and neurotoxicity, COT's initial conclusions from July 2021 on immunotoxicity and neurotoxicity, and a revised literature search covering the period from 2021-2023 on the following topics: Reproductive Toxicity, Immunotoxicity, Neurotoxicity, Developmental toxicity, considerations including Absorption, Distribution, Metabolism and Excretion (ADME), and other toxicological effects.

36. It was noted that there was some concern about the quality and validity of the additional studies including uncertainty about the physical form of the titanium dioxide used: this is important as the size and shape of titanium dioxide particles can alter their potential toxicity.

37. Members had previously discussed the findings of aberrant crypt foci (ACF) and concluded that TiO2 did not induce ACF in the studies investigating this endpoint. The Committee considered that in the only study where ACF were observed (Bettini et al. 2017), these could not be attributed to TiO2, as ACF were also present in the control groups. A 28 day and a 90 day study by Akagi et al., 2023, conducted in accordance with OECD Test Guidelines 407 and 408, confirmed the absence of aberrant crypt foci.

38. The Committee suggested that the text in paragraph 26 be reworded in future documentation as it was not clear what EFSA had concluded on immunotoxicity.

39. Members noted that the specification for titanium dioxide needed to be clear before any conclusions on the additional endpoints can be made.

40. It was agreed that a small group of Members would be set up to do a more detailed critical evaluation on the additional endpoints. Members requested sight of the template being used by COM to characterise titanium dioxide for their genotoxicity assessment to ensure a consistent approach. Any Members interested in participating in this work should contact the Secretariat.

Item 5b: First draft statement on the safety of titanium dioxide as a food additive. (TOX/2023/33)

41. The first draft statement on the safety of titanium dioxide as a food additive was presented to the Committee annexed to paper TOX/2023/33. The draft statement was in a more preliminary state than would be usual, and so had not been published on the COT website, but the Secretariat wanted to obtain Members' initial thoughts on how the final statement should be structured given the complexity of the topic.

42. Members suggested further consolidation of the text to minimise duplication in the introduction and background.

43. It was also proposed that details of products containing titanium dioxide should be included in both the lay summary and the statement as this was useful information for consumers.

44. It was stated that the different sections needed to be more clearly separated, particularly with respect to ADME.

45. Members agreed that there needed to be more clarification of the characterisation of titanium dioxide in the statement. The EFSA definition of a nanomaterial which was not specifically engineered to be a nanomaterial should be included; this specified that it would contain less than 50% nanoparticles, but without a lower limit being specified. It was suggested that the hazards associated with nanoparticles in E171 needed to be identified; this was something the working group could consider. The percentage of nanoparticles was important as these smaller particles could have different toxicological effects.

Item 6: Assessment of the Codex report on food allergen thresholds TOX/2023/35

46. Non-specific personal interests were declared by Dr Natalie Thatcher and Dr Stella Cochrane, as they are employed by food manufacturing companies. No other interests were declared.

47. Dr Ian Kimber was in attendance for this item, as the Chair of the COT subgroup reviewing the Codex report.

48. Paper TOX/2022/62 was presented to the COT at the December 2022 meeting under matters arising. The paper introduced the need to carry out an assessment of the Codex Expert Committee's report on the 'Risk assessment of food allergens. Part 2: review and establish threshold levels in foods for the priority allergens' to inform decisions by the Food Hypersensitivity Policy Team at

the FSA on whether it would be appropriate for the reference doses recommended in the report to be applied to regulated allergens in the UK.

49. At the December 2022 meeting it was agreed that a subgroup should be established to carry out an assessment of the Codex report. The group comprised several COT members along with other external experts, under the chairmanship of Prof Ian Kimber, and met four times to discuss the report. The Chair of the Codex Expert Committee on allergen thresholds (2nd Joint FAO/WHO Expert Consultation meeting) was invited to attend one of these meetings to clarify and answer some questions about the Codex Expert Committee's report.

50. The Committee were invited to consider the report of the subgroup on their review of the Codex Report which was attached at Annex A to TOX/2023/35.

51. Members of the COT subgroup highlighted that the underpinning data used to derive the eliciting doses (both ED01 and ED05 values) in the Codex Expert Committee report were not made available with the report and were not otherwise available. This made it difficult to confirm the conclusions. It may be useful to request access to the raw data.

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

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

54. Members considered that the reference to "mild anaphylaxis" in the Codex Expert Committee report did not seem appropriate as NICE have a very clear definition that anaphylaxis is always a severe reaction.

55. The Committee agreed with how the assessment has been undertaken by the COT subgroup and with the contents and key conclusions reached by them. However, Members requested that a sense check on clinical terminology was carried out on Annex A and that paragraph 17 of Annex A should be rephrased to clarify the conclusions in the final version of the report.

56. With respect to the question of whether using reference doses based on ED05 as opposed to ED01 values would significantly impact upon public health,

the Committee emphasised that since both values represented effect levels, more people would be affected if the ED05 were used rather than the ED01. The wider implication of using one or the other was more of a risk management issue.

Item 7: Public consultation on draft EFSA opinion on polybrominated diphenyl ethers (PBDEs) (TOX/2023/34)

57. No interests were declared.

58. EFSA had released for public consultation a draft update of its risk assessment of polybrominated diphenyl ethers (PBDEs) in food. EFSA previously published a risk assessment on PBDEs in 2011, which focused on the eight isomers considered most relevant to dietary exposure, based on the composition of technical PBDE mixtures and data on occurrence in the environment and in food. EFSA had been asked to update its 2011 risk assessment, focusing on ten congeners, the same eight as previously and two others (BDE-49 and -138), which had subsequently been included in dietary monitoring.

59. Members were invited to provide comments on the draft opinion, to be submitted to EFSA, and were asked to advise on whether they agreed with EFSA's approach to assessing the risks of PBDEs. Members were also asked whether they agreed with the conclusion that the dietary exposures assessed raise a health concern for toddlers, with >70% certainty at mean exposure and >95% certainty at 95th percentile exposure, and whether they had any other comments.

60. A Member considered the animal data to be generally robust but noted that some significant assumptions had been made. They agreed that neurodevelopmental effects and reproductive toxicity were the critical endpoints. Metabolites had not been taken into account. The available epidemiological studies, though robust, were small and difficult to assess. Another Member added that there was a substantial amount of data from cohort studies but it was inconsistent. Some of the studies were of small numbers of people, and the specificity of the relationships was not clear. Specific PBDEs were not consistently associated with specific endpoints. They noted that some of the endpoints, e.g. on ADHD and IQ, are difficult to assess. Overall, the epidemiological evidence was considered to provide less of a signal than the toxicological data. The recommendations made in the draft opinion seemed pertinent but some appeared to be aimed more at risk management.

61. A Member considered that some of the evidence from animal studies for a substance-related effect was questionable. Concern was expressed that the approach taken appeared to have been to identify an endpoint and then identify a study that could be modelled, and this was not reflected in the uncertainty analysis. Some of the neurobehavioral changes were very minor, which also should be reflected in the uncertainty analysis. There were major inconsistencies in the neurobehavioral changes reported, which lacked biological plausibility. It was also observed that a developmental neurotoxicity study conducted according to OECD test guideline 426 for a technical PBDE product showed no adverse effects at any dose up to 1000 mg/kg bw/day, which contrasted greatly with the point of departure identified for its major constituent congener, but there did not appear to be any discussion of this and it was unclear how different studies had been weighed against each other. This should have been considered in the uncertainty analysis.

62. While it was noted that studies on neurobehavioural effects can be difficult to replicate, it was considered that findings in single studies, in particular those without clear dose-response relationships, should be treated with caution, and especially when an adequate OECD guideline study identifies no adverse effects.

63. Animal studies showed effects on the thyroid and the draft opinion appeared to be trying to link this to thyroid disease in humans but this was considered a step too far as there was no explanation provided and the animal data did not support this. The effects observed in studies in rats were typical of a liver-thyroid effect seen in rats, with microsomal enzyme induction causing increased clearance of thyroid hormones, with a sex difference in the effect. There was also some suggestion of possible dioxin contamination, and dioxins also have the same liver-thyroid effect in rats. The draft opinion did not appear to discuss direct versus indirect effects on the thyroid.

64. A Member noted that it is usual to consider whether epidemiological data are sufficient to identify adverse effects in humans, whereas the approach EFSA had taken appeared to be to consider whether the epidemiological data were sufficient to conclude that adverse effects did not occur in humans.

65. Members found the uncertainty analysis very difficult to interpret. It was not considered useful without a rationale being provided and without further information on how the numbers for percent certainty were generated and what they mean, e.g. why specifically did they conclude that there was >70% certainty of a health concern for toddlers, at mean exposure. Risks may be overestimated

by the body burden approach used when considering the endpoints and susceptible populations and the very long half-lives in humans, which were up to 8 years. It was unclear how this had been taken into account in the uncertainty analysis.

66. Members questioned why the draft opinion described differences in hormone levels which were not statistically significant in a number of places. It was noted that the draft opinion indicated that the induction of biotransformation enzymes was a possible mechanism for decreases in circulating oestradiol, testosterone and T4. A clearer conclusion on the potential for endocrine perturbation (or not) would have been helpful.

67. Members considered that the EFSA draft opinion had reviewed a substantial amount of information but had made a number of assumptions in drawing conclusions; for example, appearing to link developmental neurotoxicity to thyroid effects.

68. It was noted that the draft opinion used the latest EFSA guidance on benchmark dose modelling, taking a Bayesian model averaging approach. There are now 6 or 7 versions of benchmark dose modelling software in use. None give exactly the same values for BMDLs, though the approach now being used by EFSA gives broadly the same BMDLs as the US Environmental Protection Agency (US EPA) software. Benchmark dose modelling had been conducted on small studies, and there should be some consideration of the applicability of the data to benchmark dose modelling.

69. Members questioned the objective of some of the recommendations for those PBDEs that are no longer used, when there is already a significant amount of toxicology and exposure data available, and a risk has been identified. For example, it would be helpful to understand the value of making the development of AOPs a recommendation, for such compounds. The first sentence of the final recommendation was considered to be unclear. Surely the starting point should be observations in humans and then the question asked if there are animal data to support them.

70. Members were asked to submit any further comments on the draft opinion in writing ahead of EFSA’s deadline.

Item 8: Aircraft cabin air environment: first draft statement TOX/2023/36

71. No interests were declared.

72. The first draft statement on aircraft cabin air was being presented following a series of papers on this topic, which were discussed by the Committee between May 2022 and March 2023. The paper presented also outlined the assessment for the potential for mixture effects for volatile organic compounds (VOCs).

73. The question for the current review was confirmed as “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)?”. It was noted that the terms of reference of the current work differed to previous reviews that considered potential causes of ill health experienced by aircrew, particularly the possible effects of oil or hydraulic fluid fume contamination incidents.

74. The Committee noted that most published information on chemical concentrations in cabin air were background levels, while the original and continued concern was more related to fume events leading to peak exposures. However, robust data on such events were still scarce. Members commented that any information obtained using real-time monitoring of aircraft would be invaluable in any future assessments.

75. Members agreed that the draft statement was a succinct representation of all of the Committee’s discussion since May 2022. The inclusion of the hazard index (HI) approach to assess mixture effects of VOCs was considered an appropriate first tier approach, and Members agreed with the HI calculations and the provisional derived no effect level (DNEL) for hexanoic acid, The Committee concluded that as the HI was less than 1, no effects, including mixture effects, would be expected.

76. A number of comments were made with respect to phrasing of the discussion and conclusion sections of the statement to provide clarity on the Committee decision making.

77. It was agreed that the statement would be updated and a second draft would be presented at a future meeting.

Item 9: Discussion paper on the risk of emerging marine biotoxins in British shellfish – Pinnatoxin (TOX/2023/37)

78. No interests were declared.

79. 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.

80. The main purpose of this work is to identify any emerging marine biotoxins in UK waters, including a consideration of the potential increases in occurrence with increasing temperatures due to climate change. The views of the COT were being sought on whether any of these marine biotoxins would pose a risk to human health. A scoping paper providing an overview of emerging biotoxins will be brought to the Committee later in the year, as well as a discussion paper on pectenotoxins.

81. Paper TOX/2023/37 provided information and data on the risks to human health associated with consumption of shellfish from UK waters, in relation to the class of emerging marine biotoxins known as pinnatoxins (PnTXs). The paper considered the toxicological database for PnTXs and whether there were relevant occurrence data with a view to performing a risk assessment. Considerations have also been given to the likelihood of PnTXs becoming more prevalent due to climate change and rising sea water temperatures around the UK.

82. PnTx are not currently regulated in England or Wales, but with the availability of new analytical standards, future monitoring programs of PnTX could aim to include PnTX-G, -E and -F.

83. The Committee noted that the toxicological data base for PnTx was limited. The presence of reactive epoxides as a potential hazard was questioned, and further information on this requested. The chemical reactivity of any such intermediate would make it potentially allergenic. Although some acute toxicity studies existed in mice, there were substantial evidence gaps for both the toxicity of PnTX and exposure data in humans. No human intoxications have been reported to date but while there is no strong evidence to suggest PnTXs are a risk to humans, based on the limited data the Committee was unable to fully exclude a risk.

84. Members highlighted that PnTX toxicity might occur but go unreported as individuals showing signs of PnTX intoxication might not be asked whether they have consumed shellfish recently or might not make the connection themselves, hence making it difficult to link symptoms with PnTX exposure. Members queried whether other seafood, such as shrimp could also contain PnTX and if there could be any data available in veterinary literature on possible animal intoxication from toxic algal blooms. The Committee concluded that further information on shellfish imported into the UK from abroad would be useful regarding the possible regulation of PnTX in other countries.

85. The Committee concluded that no risk assessment relating to chronic exposure of PnTX could be carried out as no chronic exposure data currently existed.

86. Members also discussed the broader question of how to obtain more occurrence data relating to PnTXs in shellfish. One possibility might be to utilise DNA sequence analysis for a broad-based screening of algae to detect populations in water samples from the aquatic environment as a potential alternative to large and expensive algal monitoring programmes. However, Members noted that the available literature often reported detecting PnTX or the toxigenic algae Vulcanodinium rugosum, but not both. This has been suggested to be due to the benthic nature of *V.* rugosum, and hence algae monitoring programmes might not detect the presence of algae in the water column, despite the presence of PnTX. Members also remarked that seaweed could be a potential vector for the toxic algae *V.* rugosum and PnTXs.

87. Members concluded that while there has been no human intoxication reported to date, if the technology was already in place in the UK it may be reasonable to include PnTX in any monitoring programme. While this would ultimately be a risk management decision and outside the remit of the Committee, Members noted that relevant occurrence data for UK waters would be useful to establish possible exposures of the UK population. The Committee however stressed, should a monitoring programme be introduced for PnTX in the UK that they would strongly discourage the use of a mouse bioassay as a detection method for both scientific and animal welfare reasons.

88. Members noted that it was plausible that increasing temperatures in UK waters could lead to an increased occurrence of V. rugosum and PnTXs. However, the toxin has already been detected in Norwegian waters, which presumably have lower or similar temperatures than UK waters. If data were available from other countries demonstrating an increasing trend in algae with increasing ocean

temperatures, then this would provide support for the need of occurrence data. However, the Committee highlighted that their expertise was primarily toxicological and not ecological and hence the question of the effect of climate change might be outside their expertise.

89. Overall, the Committee concluded that due to the lack of toxicological and occurrence data on PnTX it was currently not possible to determine the extent of any public health risk relating to PnTXs. While there are no reports of human adverse effects and no reports to date of any human intoxication, potentially there could be a risk based on the limited information that is available on the mechanism of action of the toxins and their acute effects in mice. Occurrence data on PnTX would be useful to help fill some of the data gaps, indicating whether the UK population would be exposed to PnTX from shellfish consumption. However, the Committee stressed that they were not in favour of using the mouse bioassay to measure PnTX but rather would favour use of chemical analysis for any monitoring.

90. Members suggested several editorial changes that could be included in any future statement.

Item 10. Sub-statement on the potential risk(s) from exposure to microplastics: Inhalation route (Third draft) (TOX/2023/38)

91. Professor Alan Boobis declared an interest as one of the authors of the 2022 WHO report Dietary and inhalation exposure to nano- and microplastic particles and potential implications for human health (who.int). He is also involved in, multi-stakeholder discussions to identify data gaps in the assessment of the risk to human health of microplastics, coordinated by ILSI Europe and by Plastics Europe. Professor Shirley Price also declared an interest as she one of the authors of the 2022 WHO report. No other interests were declared.

92. Dr Alison Gowers and Dr James Isaac of the Secretariat for the Committee on the Medical Effects of Air Pollution (COMEAP) were in attendance along with the COMEAP Chair Professor Anna Hansell.

93. In 2019, as part of horizon scanning, the COT identified the potential risks from microplastics as a topic it should consider to inform FSA discussions (TOX/2019/08). Since then, several discussion papers have been presented to the COT (see Annex A1) and in 2021, the COT published an overarching statement on

the potential risks from exposure to microplastics (COT Statement 2021/02). This document provided a high-level overview of the current state of knowledge, data gaps and research requirements with regards to this topic.

94. There is evidence for the presence of plastic particles in both indoor and outdoor air and thus inhalation is a possible route of exposure to microplastics (Gasperi et al., 2018; Domenech & Marcos, 2021).

95. The purpose of the sub-statement on inhalation is to provide supplementary material to the overarching statement (COT Statement 2021/02) and to consider in more detail the potential toxicological risks of exposure to microplastics via the inhalation route.

96. Colleagues at the Committee on the Medical Effects of Air Pollution (COMEAP) have provided comments on this draft of the statement and a table had been added to give more weight to the study from Jenner et al. 2022 setting out the length and width of the particles measured.

97. COMEAP were supportive of the COT statement and highlighted their concern that there was a lot of public misinformation and a lack of knowledge in this area and so they may also undertake work on this topic in the future. If there was an opportunity to produce a joint statement in future, COMEAP would be happy to collaborate with COT.

98. The definition of microplastics was considered by Members, who advised that the definition be clarified. It was highlighted that the ECHA definition includes both microplastics and nanoplastics. It was suggested that a comment be added at the start of the statement giving the working definition of microplastic being used by the Committee and to be clearer on the reasoning for undertaking this piece of work.

99. The Committee discussed fibres and decided that although they need to be included, but this did not have to be in detail. Fibre fragments were raised as these are now being considered more by researchers, along with the use of analytical methods involving pyrolysis. Members noted that particle size in the environment is dynamic, and that in addition to weathering and fragmentation, processes such as agglomeration may also occur.

100. The Committee recommended that studies should specify what source material is being used in testing, and if material was commercially purchased the specification should be clearly documented. Members highlighted that this basic characterisation of particles is necessary to enable interpretation of studies and

should be included in the Sub-statement as a recommendation. Members also discussed that there are limitations in the analytical methodologies used to characterise micro/nanoplastics, and that there are differences between studies, thus making comparisons difficult.

101. The Committee suggested some restructuring of the statement and to clarify references to food as the inhalation statement has broader relevance.

102. The rankings provided for research recommendations were re-ordered by the Committee and it was suggested that these be tabulated and organised with different headings.

103. Members suggested that consideration of the effects of pathogens on microplastics could be a piece of future work.

104. The redrafted statement would be presented to the Committee later in the year.

Item 11. Ergot alkaloids in the maternal diet – first draft statement (TOX/2023/39)

105. A declaration of interest was made by Dr David Lovell as a member of the 91st JECFA in 2021 cited in the paper. The Committee agreed that he could still participate in the discussion. No other interests were declared.

106. This paper is part of the ongoing programme of work assessing the maternal diet being conducted by the Scientific Advisory Committee on Nutrition to which the COT are contributing. It was agreed that ergot alkaloids were among the priority chemicals for consideration.

107. Ergot alkaloids (EA) are secondary metabolites produced by the fungi families Clavicipitaceae and Trichocomaceae, with Claviceps purpurea being the most widespread producing-species in Europe. They are known parasites affecting more than 400 plant species, including some economically important cereal grains such as rye, wheat, triticale, barley, millet and oats.

108. Due to their structural similarities, EAs have been suggested as agonists or antagonists of noradrenaline, dopamine and serotonin neurotransmitters and have been reported to produce pharmacological effects such as serotonin antagonism or adrenergic blockade, direct effects such as uterotonic action or vasoconstriction and central nervous system (CNS) effects such as induction of

hypothermia and emesis.

109. The Committee discussed the potential risk from ergot alkaloids (EAs) in the maternal diet (TOX/2022/36) at the COT meeting in July 2022. The Committee had asked for any supporting evidence from animal studies on sirenomelia associated with EAs to be included, if available, to clarify the likelihood of a causal relationship in the single case study reported. Further information was also requested on the extent of gastrointestinal absorption and the effect on prolactin levels. The Committee agreed that a statement should be prepared based on the information provided. The draft statement summarises the key safety concerns as well as conclusions from the discussions of the Committee. The requested information has been included in the respective sections of the draft statement.

110. Members suggested adding some historical context into the introduction section of the paper. The Committee discussed the background section and suggested some information on ergot related synthetics (e.g. LSD) should be included in this section.

111. In paragraph 6 it was queried why some peripheral effects on receptors were referred to as ‘indirect’ effects and whether or not EFSA referred to them as ‘indirect’ effects as well.

112. Members queried if the maximum levels established for ergot sclerotia and EAs applied to the United Kingdom (UK) as they were set by the European Union (EU) in 2022 and will be further reduced in 2024.

113. Members highlighted that there needs to be more specificity on the risk, in paragraphs 43 and 44 of the risk characterisation section.

114. Overall, it was agreed that the statement will be brought back to the Committee as a second draft statement.

Item 12: Update on the work of other FSA Scientific Advisory Committees - for information - (TOX/2023/40)

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

Item 13: Any other business

116. There was no other business.

Date of next meeting

117. The next meeting of the Committee will be at 10:00 am on the 5th of September 2023 at Broadway House, London and via Microsoft Teams