

Minutes

# **Final Minutes of the 17th October 2023 COT Meeting**

**Meeting of the Committee at 10:00 on 17<sup>th</sup> October 2023 at  
Broadway House, London and on Microsoft Teams**

## **Present**

Chair:

Prof Alan Boobis

Dr Phil Botham

Professor Thorhallur Ingi Halldórsson

Dr Michael Routledge

Dr Natalie Thatcher

COT Members:

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

Dr Steven Enoch

Professor Gary Hutchison

Dr Mac Provan

Dr Sarah Judge

Professor Mireille Toledano

Professor Jeanette Rotchell

Dr Samantha Donnellan

Ms Eimear O'Rourke

Dr Ben Amies-Cull

Dr Charlotte Mills

Dr Tarek Abdelghany

COT Associate Members

Food Standards Agency

Ms Cath Mulholland (FSA Scientific  
Secretary)

Food Standards

Agency (FSA)

Secretariat:

Mr Michael Dickinson

Dr David Gott

Dr Alex Cooper

Mr Barry Maycock

Ms Claire Potter

Dr Barbara Doerr

Dr Olivia Osborne

Ms Frederique Uy

Ms Rhoda Aminu

Ms Chara Tsoulli

Ms Sabrina Thomas

Ms Cleanncy Hoppie

Ms Jocelyn Frimpong-Manso

Mrs Sophy Orphanos

Dr Gaetana Spedalieri

Mr Thomas Hornsby

Dr Emily Hudson

Ms Kaitlyn Jukes

Dr Aaron Bradshaw

Dr Lorcan Browne

Ms Natasha Adams

Ms Abigail Smith

Dr Katie Schulz

Ms Katie Wetherall

Dr Joseph Shavila

Ms Emma French

UK Health Security Agency (UKHSA) Secretariat:	Ms Britta Gadeberg (UK HSA Scientific Secretary)
Institute for Environment and Health (IEH)	Dr Sarah Bull
Kings College London	Mr Alexander Kalian
Office of Health Improvement and Disparities (OHID)	Ms Susanah Brown
	Ms Rachel Elsom
UK Health Security Agency (UKHSA)	Dr Ovnair Sepai
	Ms Liz Lawton
Department for Environment, Food and Rural Affairs (DEFRA)	Ms Annabell Hill
	Ms Hannah Jones
Business, Energy and Industrial Strategy (BEIS)	Mrs Francis Hill
Environment Agency	Mr Ian Martin
	Dr Emma Bradley
Observers	Fera and Food Contact Material Joint Expert Group (FCM JEG)
	Dr Stephen Ruckman TSG consulting
	Mr Vincent Greenwood
Food Standards Agency (FSA)	Dr Andy Axon
	Ms Ese Hughes
	Ms Helen Twyble
Food Standards Scotland (FSS)	Ms Krystle Boss

## Contents

Item	Paragraph
1 Apologies for absence	3
2 Draft minutes of the 5 <sup>th</sup> September 2023 meeting- TOX/MIN/2023/05	4 – 8
3 Matters arising	9 –
- JEG updates	14
4 Third draft interim position statement on bisphenol A – TOX/2023/50	15 – 28
5 Microplastics inhalation sub statement (Fourth Draft)- TOX/2023/51	29 – 34
6 Evolving our assessment and future guiding principles – Workshop Report (2023) - TOX/2023/52	35 – 43
7 Presentations from the FSA Fellow and PHD Student -TOX/2023/53	44 – 52

	53 –
	62
Potential risks from arsenic in the maternal diet: Additional information on Epigenetic Effects- TOX/2023/54	
8	
First Draft Statement on the Potential Risks from Arsenic in the Maternal Diet - TOX/2023/55	
	63 –
	74
10	75 –
Draft statement on the reproductive toxicity of titanium dioxide as a food additive - TOX/2023/56	89
11	
Update on the work of other FSA Scientific Advisory Committees - for information - TOX/2023/57	92
12	
Any other business	93
Date of the next meeting - Tuesday 12 <sup>th</sup> December 2023 at Broadway House, London and via Teams	94

## 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, Professor Maged Younes and Dr James Coulson. Apologies were also received from Dr Gail

Drummond of the Secretariat and Professor John O'Brien, Science Council liaison.

## **Item 2: Draft Minutes from the meeting held on 5<sup>th</sup> of September 2023 (TOX/MIN/2023/05)**

### **Item 3:**

4. It was noted that Professors Maged Younes and Paul Haggarty should have been listed in the apologies section.
5. The title for item 11 should be changed to 'second draft statement'.
6. The study referred to in paragraph 39 was Paul et al (2017).
7. In paragraph 5, "vegan status" should be replaced with "vegan trademark".
8. The remaining minutes and the reserved minutes were accepted as an accurate record.

## **Matters Arising**

### **JEGs Update**

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

### **Additives, Enzymes and other Regulated Products (AEJEG)**

10. The AEJEG working group for smoke flavourings (SFs) met on the 5<sup>th</sup> of October for their first Phase 2 meeting; this was a deep dive discussion of RP1616 where the genotoxicity data and the information received via Requests for Further Information (RFIs) were discussed. Members were unable to reach a conclusion and additional information will be requested from the applicant. There will be a second Phase 2 SFs meeting on the 24<sup>th</sup> October which will be a deep dive discussion on RP1523.
11. On the 19<sup>th</sup> of October there will be a Standard AEJEG meeting where two dossiers (RP 733 and RP1330) will be presented to the Members; it is hoped these items will be concluded and can be presented to COT shortly.



## **Food Contact Materials (FCMJEG)**

12. The FCMJEG met on the 3rd October. They discussed the first draft opinion/safety advice of a plastic additive (RP1702), additional information on a recycling process (RP1741) and the additional data received through a call for evidence for ocean bound plastics.

13. The next meeting will be on 6<sup>th</sup> Dec and the JEG will be discussing the second draft opinions/safety advice of a plastic additive (RP1702) and a recycling process (RP94), and potentially additional information received on recycling process dossiers.

## **Publications**

14. The COT Workshop Report: Opportunities and Outlook for UK Food and Chemicals Regulation post EU Exit Workshop (2022) has now been published on the COT website.

## **SAC Recruitment**

15. The recruitment for the FSA Scientific Advisory Committees closes on the 23<sup>rd</sup> October with starting the on-line application closing on the 20<sup>th</sup> October. Members were asked to notify the Secretariat if they had any final suggestions for possible candidates.

## **Joint COT/SACN WG on plant-based drinks**

16. Following a pause in the activities of this Working Group due to competing priorities, the WG met on the 4<sup>th</sup> October to continue their discussions. It is hoped that an initial draft of the report will be presented to the Committee in December.

## **Item 4: Third draft interim position statement on bisphenol A - TOX/2023/50**

17. Professor Thorhallur Ingi Halldórsson and Professor Maged Younes of the Committee and Dr David Gott of the Secretariat were Members of the EFSA CEP panel and Bisphenol A (BPA) Working Group. They were able to answer questions and provide clarification on the EFSA BPA opinion but could not otherwise take

part in the discussion.

18. Professor Matthew Wright is an EFSA panel Member but was not involved in the BPA evaluation and was able to 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 and were also able to take part.

19. No other interests were declared.

20. 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. This would mean that mean and high level consumers of all age groups would exceed the new TDI by 2-3 orders of magnitude. The final EFSA opinion, along with diverging opinions by the European Medicines Agency (EMA) and the German Federal Institute for Risk Assessment (BfR), were discussed by the Committee in May 2023.

21. Since that time, the European Commission (EC) has published a statement imposing a ban on the use of BPA in food contact materials (FCMs). The measures will set out derogations and transitional periods and will 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. The Committee have expressed a number of concerns about the TDI and the method used to establish it. First and second drafts of a position paper setting out the views of the Committee were discussed in July and September 2023, respectively. Paper TOX/2023/50 was a third draft of the interim position paper, addressing comments made by the Committee in September. The paper also included additional information on health-based guidance values (HBGVs) established by other European and international authorities.

23. The Secretariat also provided a brief verbal update on information available to policy colleagues on the current use of BPA; this information is currently reserved as it is commercially confidential. The Secretariat informed Members on the current legislative status of BPA. In the UK, Annex II of retained regulation 2018/213 on the use of bisphenol A in varnishes and coatings intended to come into contact with food and amending Regulation (EU) No 10/2011 as regards the use of that substance in plastic food contact materials set out the current specific migration limit (SML) for BPA of 0.05 mg/kg. The same SML

applies to varnished and coated food contact materials.

24. The previous EFSA TDI, which is the current UK TDI, is substantially higher than the new EFSA TDI and was based on changes in kidney weights in rodents. The toxicological endpoint used to establish the new TDI for BPA was a change in the number of Th17 cells. Th17 cells are involved in the development of inflammatory conditions, but the change 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.

25. The Committee noted that the recent assessment of BPA by the BfR established a TDI lower than the previous EFSA TDI but higher than the new one. It would therefore be useful to consider the BfR approach in more detail as it was based on the same literature/data available to EFSA, and to establish how it differed from the approach taken by EFSA. The Committee also asked for further details on the TDI established by Health Canada. The Secretariat noted they would contact the Dutch National Institute for Public Health and the Environment (RIVM) to see whether Part 2 of a report evaluating the scientific knowledge on BPA and discussing possible health risks could be made available.

26. The Committee highlighted that the exposure data included in the most recent assessments was from 2015 and was unlikely to reflect current exposure levels in the EU and UK since the use of BPA had been restricted; this uncertainty was noted in both the BfR and EFSA assessments. The Committee emphasised that once a UK TDI had been established, up to date exposure data would be required to fully assess realistic exposures in the UK population and undertake a complete risk assessment.

27. Members were informed that the Secretariat would prepare a discussion paper providing additional information on the establishment of the TDI by the BfR and EFSA, with a specific focus on the BMDL and uncertainty modelling. Members interested in modelling who were willing to assist were asked to contact the Secretariat.

28. A fourth draft interim position statement would be prepared following further discussion of the different approaches taken by EFSA and the BfR. This new draft would include conclusions by the Committee with respect to a possible interim TDI, applicable until the full COT assessment had been undertaken. The new draft would also include recommendations by the Committee regarding the requirement for new exposure data.

## **Item 5: Microplastics inhalation sub statement (Fourth Draft) - TOX/2023/51**

29. Professor Alan Boobis declared an interest as one of the authors of the 2022 World Health Organization (WHO) report “Dietary and inhalation exposure to nano- and microplastic particles and potential implications for human health”. 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 the International Life Sciences Institute (ILSI) Europe and by Plastics Europe. Professor Shirley Price also declared an interest as she one of the authors of the 2022 WHO report. These interests did prevent them taking part in the discussion of this item. No other interests were declared.

30. Dr Alison Gowers and Dr James Isaac of the Secretariat for the Committee on the Medical Effects of Air Pollutants (COMEAP) were in attendance. They informed Members that COMEAP had held a microplastics workshop on the 12<sup>th</sup> of October 2023 which included presentations from some researchers working on microplastics in air and on tyre wear emissions. This was to inform discussion on the scope of a possible COMEAP statement. The intention was that COMEAP’s statement could draw on the conclusions of existing reports such as the COT statement and the recent WHO report on dietary and inhalation exposure to microplastics, without duplicating their content. The focus would be on where COMEAP can add most value to reviews that are already available.

31. 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 on this area (TOX/2019/08). Since then, several discussion papers have been presented to the COT and in 2021, the COT published an overarching statement on the potential risks from exposure to microplastics (COT Statement 2021/02). This provided a high-level overview of the current state of knowledge, data gaps and research requirements with regards to this topic. A more detailed sub-statement on exposure via the oral route has also been published.

32. 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. The purpose of the sub-statement on inhalation was to provide supplementary material to the overarching statement on this route of exposure and to consider the potential toxicological risks of exposure to microplastics via the inhalation route in more detail.

33. The Committee was content with the overall structure and contents of the sub-statement as well as the new revisions. Members suggested any text on tyre wear and occupational exposure be omitted as it is out of scope of the statement. The Committee suggested that the table on research priorities be merged with opportunities for improved study design and research needs. The revised table would be circulated to Members for comment.

34. Members agreed that the rest of the statement, with some suggested editorial changes, could be cleared via Chairs action.

## **Item 6: Evolving Our Assessment & Future Guiding Principles - Workshop Report (2023)**

### **TOX/2023/52**

35. No interests were declared.

36. The COT held a workshop in May 2023 to start work on updating their guidance on toxicity testing and its supporting principles. The starting point for the process was to use existing frameworks and guidance but with the aim of introducing innovative improvements where appropriate.

37. The workshop aimed to identify areas where guidance needed to evolve and included reviewing fundamental risk assessment principles, current guidance on risk assessment and what can be learned from it, integration of new approach methodologies, exploring hazard vs risk and weight of evidence. The overall objective of the workshop was to discuss how the Committee moves forward in a new era of risk assessment.

38. The Committee were content with the structure, layout and content of the draft workshop report. Members congratulated the Secretariat on putting a useful report together. It was agreed that the recommendations should be grouped and expanded in places.

39. Members discussed the “must, could and should” priorities to be taken forward. It was emphasised that the most important aim was to have applicable guidance to ensure public safety.

40. The assessment of benefits was not within the terms of reference of the COT and thought should be given as to how COT advice could be best aligned for this to be undertaken when needed or appropriate.

41. Education and training of toxicologists would be important in the future and should be emphasised in the conclusions.

42. Members noted that to take the guidance forward, establishing an initial framework would be important; this could then be expanded and linked to other guidance as necessary. There were two parts to the work, to codify what the Committee currently do and then to provide guidance on areas where the approach was not yet codified such as benchmark dose modelling.

43. Some minor editorial changes were suggested, which would be cleared by Chairs' action. A sub-group would be formed in 2024 to take forward the next steps in updating the guidance. It was agreed that it would be important to work with the policy colleagues from the relevant Government Departments and not to re-invent the risk analysis process. In particular, the required levels of protection needed for consumers should be considered.

## **Item 7: Presentations from the FSA Fellow and PHD Student - TOX/2023/53**

44. No interests were declared.

45. The FSA and COT have been considering New Approach Methodologies (NAMs) to understand the best scientific methodologies available for use in the risk assessment of chemicals, and to consider how these can be incorporated and accepted in a regulatory context.

46. In 2021, the FSA started funding a computational toxicology postdoctoral Fellow at the University of Birmingham and a PhD Student at King's College London as part of their Interdisciplinary Doctoral Program (LIDo-TOX AI). Paper TOX/2023/53 introduced the work of the student and the Fellow.

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

48. In addition, these new partnerships have helped with networking, research collaboration, training opportunities and other activities. The Fellowship and studentship also complement the work set out in the COT FSA UK Roadmap towards using new approach methodologies in chemical risk assessment.

49. Unfortunately, the Fellow was unable to present his update at this meeting and will present it at a later date.

50. The PhD student had prepared a yearly review and gave a presentation to the Committee on his progress to date using Artificial Intelligence and in silico tools for the assessment of food safety.

51. The main work so far comprised three parts: (1) Exploration of dimensionality reduction algorithms, for powering Quantitative Structure Activity Relationship (QSAR) models of mutagenicity, constructed of simple feed-forward Deep Neural Networks (DNNs); (2) Development of Graph Convolutional Networks (GCNs) to improve mutagenicity predictions, via graph classification of molecules, while also allowing for mining of structural alerts (SAs); (3) Development of Graph Neural Networks (GNNs) for node classification of molecules, in order to predict toxicological properties of brominated flame retardants (BFRs), starting with acute toxicity and comparing to predictions from the Toxicity Estimation Software Tool (TEST) of the United States (US) Environmental Protection Agency (EPA).

52. The COT Members were impressed with the progress to date and gave feedback to the PhD student.

## **Item 8: Arsenic in the Maternal diet**

### **Potential risks from arsenic in the maternal diet: Additional information on Epigenetic Effects - TOX/2023/54**

53. No interests were declared.

54. Following review of the discussion paper on arsenic in the maternal diet at the Committee's March 2023 meeting, Members asked for a review of the epigenetic effects associated with exposure to arsenic. The Committee had stated that although generalised effects were included in the discussion paper, they would like to see the inclusion of the mechanisms that underpin these effects in the general population and in terms of the maternal diet. The aim of the paper was to review the current knowledge in this area to allow Members to decide what would need to be included in the final statement.

55. The Committee agreed that the paper was a helpful review of the area and made a number of comments.

56. Members stated that they would like the section on sex-dependent epigenetic changes to be expanded, and for the research into the male phenotype and targets that perturb male development to be considered.

57. The Committee further requested that changes linked to reactive oxygen pathways in the placenta be considered and the impact on steroidogenesis be reviewed, particularly in males, and the subsequent restriction in fetal growth. Members also asked for additional information to be included regarding genetic reprogramming in utero.

58. It was suggested that for the statement the information presented should be condensed with a focus on pathways that result in adverse outcomes rather than on associations. Members noted that more emphasis should be provided on the importance of the endpoint in each case and that the size of the effect should be given and its link to an adverse effect.

59. Members noted that a lot of work has been completed in this area prior to 2020, however there did not appear to be many new publications after that date. Members considered whether this area of research required a greater length of time for new evidence to be published and noted that this could result in the omission of findings that are more current. The Committee asked the Secretariat to determine whether any follow up had been completed on adverse changes reported in the earlier studies (10 years prior), as although clear findings had been reported relating to associations with arsenic, these did not appear to have been followed up.

60. It was proposed that a new paragraph be introduced before the main bulk of the literature review to provide context on the topic of epigenetics.

61. Members stated that the information contained in paragraph 33 and 34 regarding changes in Long Interspersed Nuclear Element (LINE)-1 function should be explained further as such elements made up a large part of the human genome.

62. Members requested that terminology for the arsenic species included in the final statement be harmonised.

## **First Draft Statement on the Potential Risks from Arsenic in the Maternal Diet - (TOX/2023/55)**

63. No interests were declared.



64. The Scientific Advisory Committee on Nutrition (SACN) last considered maternal diet and nutrition concerning offspring health in its reports on 'The influence of maternal, fetal and child nutrition on the development of chronic disease in later life' (SACN, 2011) and on 'Feeding in the first year of life' (SACN, 2018). In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health including the effect of certain contaminants. From this, arsenic was prioritised and selected as one of the chemicals of interest to be reviewed.

65. The COT most recently reviewed arsenic in 2016 as part of the programme of work with SACN on the diets of infants and young children. A discussion paper on arsenic in the maternal diet was presented to the Committee on 28th March 2023. Paper TOX/2023/55 was a first draft of a statement setting out the views of the Committee. In addition to minor editorial changes, Members made a number of comments on the structure and contents of the draft statement.

66. Members asked for the newly reviewed epigenetic effects to be included by endpoint rather than as a separate subsection in the statement and for an additional paragraph providing context to the review to be added. It was agreed that only studies that linked arsenic exposure directly to adverse outcomes be included in the statement. Members added that effects relating to effects on LINE-1 following arsenic exposure should be documented in the statement.

67. The Committee asked for clarification of paragraph 29 regarding arsenosugars, as it was unclear in which biological systems these would be found.

68. Members stated that in paragraph 30, they would like discussion of the studies that did not reach the conclusion that arsenic exposure was related to adverse pregnancy outcomes to be included to ensure the evidence was balanced.

69. It was agreed that clarification was needed on the study described in paragraph 47 and the comparison used to determine the association between arsenic in well water and cancer risk, with a trend test being used to determine this in the paper.

70. A Member suggested that the review paper could be utilised as metadata for the development of an adverse outcome pathway (AOP); however, it was deemed that the work involved would be outside the scope of the Committee.

71. It was noted that exposure to arsenic is more usually associated with an increased risk of skin cancer, but the BMD modelling used data on lung cancer as this resulted in the lowest BMDL. The genotoxic effects of arsenic might have a threshold as it was thought to be a secondary effect due to the formation of reactive oxygen species causing genomic instability.

72. Members asked for paragraph 52 and 82 to be removed from the statement and asked that paragraph 15 be moved into the conclusions.

73. Members asked for paragraph 67 to include a reference to the most recent COT paper published on pica and for a description of the main sources of iAs to be included in paragraph 89.

74. Members stated that they would like to wait until EFSA publish their new opinion on arsenic, and for a summary to be provided in the statement, before reviewing a second draft statement at a future Committee meeting.

## **Item 9: Draft statement on the reproductive toxicity of titanium dioxide as a food additive - TOX/2023/56**

75. 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.

76. Professors Matthew Wright and 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.

77. COT Members were informed the COM had discussed the not yet complete review of *in vitro* and *in vivo* genotoxic data for titanium dioxide, conducted by a COM sub-group, on the 12<sup>th</sup> October 2023. It was noted that the current COM view was that approximately half of the *in vitro* studies indicated a positive genotoxic response, and it was therefore difficult to rule out *in vitro* genotoxicity, particularly clastogenicity, although this would not necessarily reflect what happens *in vivo*. The data were complex and there were a lot of data gaps and few high quality studies and the implication of the quality scores for each paper on the potential conclusions still needed to be considered by the COM sub-group. Members were informed that the *in vitro* and *in vivo* genotoxic data would be further reviewed at the next COM meeting in December 2023. It was noted that a concluding statement on the genotoxic potential of titanium dioxide would be finalised by March 2024. The sub-group would be considering potential mechanisms and whether the effects were linked to the nanoparticle fraction.

78. Paper TOX/2023/56 was a preliminary version of a statement which covered the COT conclusions to date on the following topics and endpoints: Absorption, Distribution, Metabolism, Excretion (ADME), Aberrant Crypt Foci, Reproductive and Developmental Toxicity and the establishment of a potential Health-Based Guidance Value, dependent on the outcomes of the review by COM. An earlier version had been discussed at the September meeting with amendments being requested following consideration of the accompanying discussion paper, which covered the remaining endpoints reviewed in the EFSA 2021 opinion. It also included the subsequent sub-group work on the additional endpoints. The draft also included the titanium dioxide exposure assessment for the UK population. It was noted that a statement would not normally be presented while discussion was still taking place, but the aim was to finalise the statement as soon as possible after the Committees reached their conclusions. In addition to minor editorial suggestions, the Committee made a number of comments.

79. The scope and approach of the evaluation should be set out in the introduction.

80. The Committee suggested that the text in paragraph 5 should include the wording 'potential evidence of immunotoxicity, inflammation and neurotoxicity'.

81. Members noted the conclusions in paragraph 29 should be checked to ensure they fitted with the data described in the ADME section.

82. Members discussed the Aberrant Crypt Foci section of the statement and noted that once the COT clarified their findings, they could be compared to those of EFSA and Health Canada; this would apply to other endpoints also reviewed by Health Canada.
83. It was suggested that paragraph 48, which discussed the form in which titanium dioxide had been administered, should be reworded.
84. Members suggested that paragraphs 52, 53 and 54 discussing the Health Canada review be reorganised and all the studies that were referred to in their review, fully cited.
85. It was noted that there should be focus on data obtained from studies using food-grade titanium dioxide rather than titanium dioxide nanoparticles.
86. Members discussed the inflammation section of the statement and suggested that paragraph 59 be clarified with regards to the immunotoxicity and inflammation associated with E171 (titanium dioxide as used on the study).
87. It was agreed that paragraph 69 on the potential effects on the gut microflora should be rephrased.
88. A Member offered to supply an additional study to include in paragraph 71, which discussed effects on white blood cell counts.
89. Members discussed the exposure assessment section and noted that there was likely to be a significant overestimation in the exposure assessment as many manufacturers were likely to be using alternatives to titanium dioxide. It was suggested that the values for total exposure in Table 2 should be placed in a separate table. Members were informed that the conclusions in paragraphs 114 and 120 would be re-checked and updated.
90. The Committee also suggested that the review carried out by the COT titanium dioxide subgroup should be included in the statement.
91. Overall, it was agreed that a third draft of the statement along with the genotoxicity conclusions from the COM should be presented at the March 2024 meeting.

## **Item 10: Update on the work of other FSA Scientific Advisory Committees - for information**

## **- TOX/2023/47**

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

### **Item 11: Any other business**

93. There was no other business.

### **Date of next meeting**

94. The next meeting of the Committee will be at 10:00 am on the 12<sup>th</sup> of December 2023 at Broadway House, London and via Microsoft Teams.