Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Meeting of the Committee at 10:00 on 7th December 2021 on Microsoft Teams

Present		
Chair:	Prof Alan Boobis	
COT Members:	Dr Phil Botham Ms Jane Case Dr Stella Cochrane Dr James Coulson Dr Rene Crevel Dr Caroline Harris Professor Gary Hutchison Professor Thorhallur Ingi Halldórsson Dr Gunter Kuhnle Dr David Lovell Professor Shirley Price Dr Mac Provan Ms Juliet Rix Dr Michael Routledge Dr Cheryl Scudamore Dr Natalie Thatcher Dr Simon Wilkinson Professor Philippe Wilson Professor Matthew Wright Professor Maged Younes Prof Paul Haggarty Prof Ken Ong Prof John O'Brien	 SACN Liaison SACN Liaison Science Council Liaison
Food Standards Agency (FSA) Secretariat:	Ms Cath Mulholland Mr Michael Dickinson Dr Alex Cooper Mr Barry Maycock Ms Claire Potter Dr Barbara Doerr Dr Douglas Hedley Dr Olivia Osborne Ms Emma French Ms Rhoda Aminu Ms Sabrina Thomas Dr Gail Drummond Ms Chara Tsoulli	FSA Scientific Secretary

	Ms Frederique Uy Ms Cleanncy Hoppie Ms Jocelyn Frimpong-Manso Ms Sophy Wells Ms Chloe Thomas Dr Gaetana Spedalieri Mr Thomas Hornsby Mr Lawrence Finn Mr Shaddad Saleh Dr Emily Hudson Dr David Kovacic Dr David Gott	
UK HSA Secretariat:	Ms Britta Gadeberg	UK HSA Scientific Secretary
Invited Experts and Contractors:	Dr Sarah Bull	IEH
Assessors	Ms Valerie Swaine Ms Rachel Elsom Dr Tim Gant Dr Sam Fletcher Mr Ian Martin Ms Susannah Brown Ms Estella Hung	HSE DHSC UK HSA VMD EA DHSC UK HSA
Observers	Dr Arthur de Carvalho e Silva Prof John Colbourne Dr Stephen Ruckman	University of Birmingham University of Birmingham TSG Consulting
FSA and other Officials:	Professor Robin May Dr Amie Adkin Dr Marianne James Mr Vincent Greenwood Tim Chandler Dr Marianne James Ms Nuala Meehan Ms Alana Mcdonald Ms Wendy Dixon Ms Danielle Gazi Ms Aisling Jao Ms Erica Kintz Mr Josh Hunt Dr Ovnair Sepai	FSA FSA FSS FSA FSA FSS FSA NI FSS FSA FSA FSA FSA FSA UK HSA

	Dr Tim Marczylo Mr Will Munro Ms Krystle Boss Ms Lucy Smythe Dr Kerry Broom	UK HSA FSS FSS FSS UK HSA

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Announcements

1. The Chair welcomed Members and other attendees.

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 Sarah Judge and Professor Mireille Toledano.

Item 2: Draft Minutes from the meeting held on 26th of October 2021 (TOX/MIN/2021/06)

4. The draft minutes were agreed without amendment.

Item 3: Matters arising from the meeting held on 26th of October 2021

Topic proposals for a COT workshop in March. TOX/2021/56

5. Members were reminded that, as discussed briefly at the October 2021 COT meeting, the Secretariat was considering setting up a workshop to potentially run alongside the March 2022 COT meeting.

6. The Secretariat included five proposals for Members' consideration: UK benchmark dose (BMD) modelling guidance; Microbiome; Food Contact Materials (FCM); Mixtures; Metabolomics; and 'Chemicals and food regulation in the UK-current structure and future development and divergence'.

7. Members were asked and whether there were any additional topics that they would like to consider. None was suggested. They were then asked to consider each of the proposals provided.

8. Members considered that several of the topics merited a workshop but, on balance, prioritised the workshop on 'Chemicals and food regulation in the UK-current structure and future development and divergence' and considered that this would be a very important topic, which should include policy and regulatory frameworks.

9. Members were also supportive of the proposed workshop topic of food contact materials (FCM). As more alternatives to plastics emerge, such as FCM

coatings, it would be necessary to keep up with industry and developments in this field.

10. The Committee agreed that the topics of Benchmark Dose (BMD) modelling and mixtures might be better addressed in discussion papers at the present time. It was suggested that the COT should be looking to develop guidance for itself and the UK on BMD modelling, and should work alongside COM/COC who also have an interest in this area.

11. Members agreed that whilst the microbiome is an important topic, the scientific field had not advanced sufficiently since the last workshop to support another one at this time, and therefore it would be better to schedule this topic for a later date.

12. The Committee agreed that an '-omics' workshop would be very useful in the future.

13. The Committee recommended that the Secretariat should put together a workshop on chemicals and food regulation in the UK, to be held sometime next year.

JEGs update

14. A summary of the current activities of the FSA's three Joint Expert Groups (JEG) was provided as an update for the COT.

15. It was noted that the JEG on Animal Feed and Feed Additives were currently working on validation of a dossier for a feed additive. In addition, there were several dossiers where authorisation was required for extensions of use, and it was anticipated that the Secretariat would present these items for the COT to review in early 2022.

16. Work by the JEG on FCM included continuous work on FCM applications and responses to enquiries by policy colleagues on various aspects of FCM.

17. The AEJEG is processing a number of applications for the extension of use of various food additives and which the Secretariat will present to the COT in due course.

Item 4: First draft statement on the effects of excess vitamin A on maternal health (TOX/2021/57)

18. No interests were declared.

19. The Scientific Advisory Committee on Nutrition (SACN) last considered the maternal diet and nutrition in relation to offspring's 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 the latter report, the impact of breastfeeding on maternal health was also considered. In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet.

20. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete relevant risk assessments, e.g. in the area of food safety advice. Following a discussion at the COT meeting in September 2020, it was agreed that papers on a number of dietary components should be prioritised and, to this end, papers on iodine, vitamin D, and dietary supplements have been or will be presented to the Committee. The remaining list of compounds were to be triaged on the basis of toxicity and exposure.

21. Following discussion of the first prioritisation paper on substances to be considered for risk assessment, the Committee agreed that vitamin A should be addressed in a separate paper. A discussion paper was brought to the COT in September 2021 and a number of points were raised. This first draft statement was written taking into account the points in question.

22. The Committee made a number of recommendations on the structure of the draft statement and some editorial suggestions to improve clarity.

23. It was noted that there was no evidence of any efficacy of vitamin A supplementation in HIV-positive pregnant women as a public health intervention for reducing the risk of mother-to-child transmission of HIV and this needed to be clarified within the statement.

24. Members pointed out that only one possible mechanism for the protection given by vitamin A against neoplastic transformation was given, however, other possible mechanisms existed and should be mentioned.

25. The Committee requested that more information on the use and effects of the proprietary acne treatment Accutane (isotretinoin) should be provided. Dose levels at which effects are seen should also be included.

26. The paragraph citing the work of Kizar (Western Journal of Medicine, 152:78-81, 1990) on exposure to vitamin A should be updated with a more recent reference.

27. It was suggested that more detail should be given on literature discussions about the teratogenicity of topical retinoids, including information found in the EFSA (2006) Opinion.

28. Members agreed that the disclaimer regarding the theories of Mawson and Croft should be given greater prominence.

29. It was suggested that the interactions between vitamin A and folic acid should be included.

30. Members requested further detail on how the NOAEL of 4500 µg Retinol Equivalents (RE)/ day was derived and how exposure from the consumption of ghee was calculated.

31. The Committee stated that it should be pointed out that the confidence intervals on the beta-carotene CARET study were very large due to the low statistical power of the study.

32. The NHS advice should be deemed “still appropriate”, rather than “still valid”. In general, the paper should reflect UK Government advice.

33. The Committee agreed that a second draft of the statement should be presented to the Committee.

Item 5: Discussion paper for the risk assessment of cows’ milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations–Part 2 (TOX/2021/58)

34. No interests were declared.

35. The Committee had previously been asked to consider the potential for adverse effects arising from the consumption of plant-based drinks by young children (aged 6 months to 5 years) who were following a plant-based diet. The drinks considered were soya, oat and almond; rice drinks were not reviewed since there was existing advice that these should not be given to young children due to their arsenic content. The overarching statement on the consumption of plant-based drinks, setting out the views and conclusions of the Committee, was published in January 2021. A joint working Group had been established between the COT and SACN to bring together the nutritional and toxicological considerations of plant-based drinks.

36. The Committee had agreed, during their meeting in July 2021, that the main comparator for plant-based drinks should be cows’ milk and that a discussion paper should be produced reviewing the potential chemical risks from the consumption of cows’ milk in the population group of interest (children aged 6 months to 5 years). Members had discussed part 1 of this assessment at their October meeting.

37. Members discussed the individual chemicals included in part 2 of the review.

38. Members noted that the evidence base for chlorate and perchlorate was small, although they did agree these were unlikely to be of concern. It was recommended that further detail be provided on the previous COT conclusions on perchlorate.

39. For the risk characterisation of lead, it was noted that for the sake of brevity, information on exposure from dairy products could be removed leaving just the conclusions on cows’ milk.

40. Members requested that the wording regarding the toxicity of arsenic should be clarified.

41. Members requested that minor editorial changes were made to the section on iodine, including further explanation of the previous COT conclusion that ‘iodine in cows’ milk was unlikely to pose a risk to health even in children who are high level consumers’.

42. Members had several recommended changes within the endogenous oestrogen section. Firstly, to reconsider the title of the section to make it clear what was being considered, and particularly what was meant by the term “endogenous”. Also, the term endocrine ’disrupting’ chemicals should be replaced by endocrine ‘active’ chemicals. Secondly, this section should be re-written to focus on the levels of relevant hormones present naturally in humans versus concentrations found in cows’ milk. It should also be emphasised that the use of external hormone supplementation to dairy cows is not permitted in the UK.

43. Members noted, within the endogenous oestrogen section, that a detailed consideration of studies providing evidence of carcinogenicity would also need to include discussion of studies showing the reverse. But Members questioned whether this level of detail was necessary. Where there was any mention of genotoxic potential, it should be emphasised that this was mediated via an indirect mechanism of action.

44. It was noted that for hexabromocyclododecanes, further details should be provided on how the acceptable margin of exposure was calculated.

45. Regarding microplastics, Members requested that a number of additional details be added to this section: the emphasis that microplastics found in milk were likely to be present due to the milk containers/processing rather than from the milk itself; and that microplastic exposure from milk was relatively low compared to that from other foodstuffs.

46. Members requested that some editorial changes be made to the summary and tables and legends regarding occurrence data.

47. Members concluded that there were no health concerns for cows’ milk for any of the contaminant groups based upon the data presented in the paper.

48. Members did not add any further chemical contaminants to the list for evaluation.

49. A COT statement would be drafted encompassing the chemicals reviewed in this paper and part 1 of the assessment. It will capture the COT’s suggested changes, and incorporate their conclusions.

Item 6: Position paper on bamboo composites in food contact materials (TOX/2021/59)

50. No interests were declared.

51. The Committee were asked to consider the potential risks of bamboo composites in food contact materials (FCMs) at their meetings in July and October 2021. The Committee concluded that the migration of formaldehyde and melamine from bamboo composite cups was a potential concern to human health and it would therefore be appropriate to conduct a full risk assessment, once UK data were available. As obtaining the data and providing a full risk assessment would require time, the COT agreed to publish an interim statement to set out their concerns and allow for risk management action. The draft interim position paper on bamboo composites in food contact materials was presented for Members' comments.

52. Members discussed the labelling of bamboo composite FCMs. Members were made aware that some products on the market were labelled as being made from "bamboo" but were actually bamboo bio-composites.

53. It was agreed that relevant text on data gaps and compositional data from the bio-based FCM position paper TOX-2021-33 should be added to the position paper on bamboo composites.

54. It was agreed that paragraph 6 of the paper should be redrafted to reflect that there were currently insufficient UK data to undertake a risk assessment.

55. The Committee concluded that recommendations on bamboo bio-composite FCMs cannot be made until a risk assessment has been conducted with UK data. The Committee were informed that research in this area was ongoing. It was agreed that additional text on when the data will be available should be added to the position paper.

Item 7: Discussion paper on the potential risks from cadmium in the maternal diet (TOX/2021/60)

56. No interests were declared.

57. The Scientific Advisory Committee on Nutrition (SACN) last considered the maternal diet and nutrition in relation to offspring's 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 the latter report, the impact of breastfeeding on maternal health was also considered. In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet.

58. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete relevant risk assessments, e.g. in the area of food

safety advice. A list of chemicals was drawn up by SACN in 2020 and discussed by the COT at their September 2020 meeting where it was agreed that cadmium was one of the contaminants that should be prioritised.

59. Public Health England (now the UK Health Security Agency (UKHSA)) has produced information for the general public on the risk of exposure to cadmium but there are currently no Government dietary recommendations for the maternal diet that relate to this metal.

60. The COT previously considered cadmium in the diets of infants aged 0 to 12 months and children aged 1 to 5 years, publishing a statement in 2018 (TOX/2017/28). The COT has now been asked to consider whether exposure to cadmium would pose a risk to maternal health.

61. Members considered that more information on exposure was needed - especially with respect to maternal dietary intake. Members asked if there were any concerns regarding exposures in subpopulations who consumed larger quantities of certain food groups such as rice.

62. Members agreed that the epidemiological evidence was inconsistent and needed to include additional data, where available, to assess the strength of the study.

63. Members queried what other sources of cadmium, in addition to the diet, led to increased body burden. It was noted that smoking was a significant source of cadmium. Members asked how much cadmium was in bystander/passive smoke and suggested that exposure from cigarette smoke and vaping should be included in the assessment. The direct/indirect effects and synergistic/additive effects of cadmium should also be considered.

64. The Committee suggested that more information was needed on metallothionine and the role it plays in the body and in the placenta, and if cadmium was in the metallic form or the divalent ion.

65. It was noted that the number of pregnancies and deliveries experienced would reduce the cadmium body burden, which would affect interpretation of some of the epidemiology studies.

66. Members raised the issue of the exposure assessment using the Total Diet Study (TDS) in the first instance and asked if there were any studies where individual food commodities had been monitored. Members agreed that this was the best thing to use but background data on occurrence would be needed. A question was also raised as to whether there were UK surveys on heavy metals in the diet that could be incorporated.

67. As rice may have an impact on the risk assessment of sub-populations, Members asked if it was possible to separate the rice from the miscellaneous grouping used in the TDS.

68. Given the lack of sub-population specific information in dietary surveys, Members discussed whether, given the contact pregnant women have with the healthcare system, it be difficult to gather information on their diet in this way. It was, however, noted that even though pregnant women may change their diet during pregnancy, the body burden of cadmium that they had already accumulated before pregnancy might already be high and would not change appreciably with dietary changes over the duration of a pregnancy, given the half-life of cadmium.

69. Members highlighted that the total daily exposure used in the exposure assessment was an appreciable overestimate because the upper bound 97.5th percentile intakes would not be consumed for all commodities. However, some Members noted that this was the standard approach but was conservative and the uncertainties should be recognised in the document.

70. Members suggested including the view of the COT on EFSA's evaluation of the health-based guidance value (HBGV) for cadmium and additional information needs to be added to some of the paragraphs to make it clearer who or what was being referred to.

71. No final conclusion was reached. However, on the basis that at worst, there was only a marginal exceedance of the HBGV at the 97.5th percentile exposure, Members considered that there was no immediate health concern from cadmium.

Item 8: Phthalates: EFSA draft opinion and exposure protocol open for public consultation (TOX/2021/61)

72. Although her employers Exponent have carried out work on phthalates, Dr Caroline Harris has not personally been involved in this. Therefore this was considered a non-personal specific interest and it was agreed that Dr Harris was able to participate in the discussions. No other interests were declared.

73. On the 5th of November 2021, EFSA published a "draft opinion on identification and prioritisation for risk assessments of phthalates, structurally similar substances potentially used as plasticisers in materials and articles intended to come into contact with food" and a "draft protocol for the exposure assessment as part of the safety assessment of phthalates, structurally similar substances potentially used as plasticisers in materials and articles intended to come into contact with food" for public consultation.

74. The new assessment follows on from EFSA's previous update on the risk assessment of five phthalic acid esters (ortho-phthalates), namely di-butylphthalate (DBP), butyl-benzyl-phthalate (BBP), bis(2- ethylhexyl)phthalate (DEHP), di-isononylphthalate (DINP) and di-isodecylphthalate (DIDP) for use in FCMs, in December 2019.

75. The Committee was presented with a short summary paper of the key points from the 2021 EFSA opinion and links to the COT's previous assessment of the 2019 EFSA opinion and the COT's last discussion of phthalates within the scope of

the review of the risk of toxicity of chemicals in the diets of infants and young children aged 1-5 years in 2018.

76. The Committee was informed that the Joint Expert Group on FCMs had reviewed the EFSA opinion and overall agreed with the approach and prioritisation that EFSA were taking.

77. Overall, the Committee agreed that the approaches proposed by EFSA to prioritise phthalates and the corresponding assessment of their exposure were logical and pragmatic.

78. Members were however unclear whether the reference to a hazard assessment protocol in the terms of reference was a proposed third document or included within the identification and prioritisation of chemicals. If the latter, little information had been added since the main EFSA discussion of phthalates in 2019.

79. The current work on phthalates was being undertaken in collaboration with ECHA as part of EFSA's chemical sustainability strategy. Members noted that both organisations had moved some of the low-molecular weight phthalates into an exclusion category, which seemed to be in line with ongoing work on "one chemical one assessment" and the intention to remove these compounds from the food chain, unless beneficial as FCMs.

80. The main toxicological concern for phthalates were adverse effects on reproduction, the mode of action involving fetal testosterone reduction. The COT highlighted the difficulty of grouping phthalates for hazard assessment purposes, given that reproductive toxicity was not the main toxicological outcome for all substances (i.e. DIMP and DIPP). Oher compounds with different toxicities have yet to be assessed, including some higher molecular weight phthalates. EFSA based its current prioritisation list on the previous assessment date of phthalates. However, the COT noted that some of these compounds were currently undergoing further assessment by ECHA, and hence additional data with a focus on genotoxicity and reproductive effects may be forthcoming.

81. While the overall process of identifying and prioritising phthalates was considered to be sensible, the COT noted that until a complete list and toxicological profile for these substances is available, further comment on the (hazard) assessment would prove difficult.

82. Members also noted that the information provided in the draft exposure assessment was limited and not entirely clear. A deterministic approach could result in an overestimation while a probabilistic approach could be potentially more realistic, especially if human biomonitoring was used to validate the findings. Members considered it a positive step that the EFSA approach appears to be integrating human biomonitoring data. However, Members noted that there was very little information provided on how PBPK modelling would be used to interpret the human biomonitoring data.

83. Members highlighted that it may prove difficult to exclude and/or separate occupational exposure within biomonitoring data. Occupational data may also prove to significantly contribute to the overall exposure, potentially more so than the diet. Members suggested a questionnaire on occupational exposure may be beneficial to gather additional information on this.

84. Overall, Members agreed that the exposure protocol was sensible and acknowledged the advantages of including exposure in EFSA's prioritisation process. However, until data are available and estimation of combined exposures is possible, the current approach is mostly theoretical.

85. EFSA will not be considering the UK population as part of their exposure assessment, hence the Committee suggested that the FSA may need to consider how to follow up on EFSA's evaluation from a UK perspective.

86. Members were asked to submit any additional comments they may have by Monday the 13th of December 2021.

Item 9: Discussion paper on vitamin D exposure levels in formula fed infants (reserved) (TOX/2021/62)

87. No interests were declared.

88. This item is currently reserved as draft policy; the minutes will be published in due course.

Item 10: Smoke flavourings reauthorisations (reserved) (TOX/2021/63)

89. Professor Maged Younes was Chair of, and Professor Matthew Wright was a member of, EFSA's Panel on food additives and flavourings (FAF) who issued the guidance on smoke flavourings; they were able to answer questions but did not contribute to the conclusions. Dr Stella Cochrane declared that her employers Unilever uses smoke flavourings in some of their products; as this was not a direct interest she was able to contribute to the discussion. No other interests were declared.

90. This item is currently reserved as draft policy; the minutes will be published in due course.

Item 11: Update on the work of other advisory committees – paper for information (TOX/2021/64)

91. This item was for information and the paper was circulated to Members.

Item 12: Any other business

92. There was no AOB.

93. The Committee were reminded to state via the poll their preference for in-person or hybrid attendance at the next meeting of the Committee.

Date of next meeting

94. The next meeting of the Committee Meeting will be at 10:00 on the 8th of February 2022 via Skype and Teams, based on the post-meeting outcome of the poll of Members.