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

Minutes of the meeting held on Tuesday, 2nd February 2016 in Aviation House, London.

Present

Chairman:	Professor A. Boobis		
Members:	Mr D Bodey		
	Dr R Brimblecombe		
	Dr J. Coulson (for items1-4)		
	Dr M Graham		
	Dr A Hansell		
	Dr C Harris		
	Prof B Lake		
	Prof I Morris		
	Dr J Thompson		
	Prof F Williams		
Food Standards Agency (FSA) Secretariat:	Dr D Benford		
	Ms R Acheampong		
	Ms L Buckley		
	Ms H Gbormittah		
	Dr D Gott		
	Dr D Hedley		
	Ms F Hill		
	Dr L Kent		
	Mr B Maycock		
	Ms C Mulholland		
	Ms C Potter		
	Ms K Sturgeon		
	Mr A Sbaiti		
	Dr J Shavila		
Public Health England (PHE) Secretariat:	Dr Ovnair Sepai	PHE	
Invited Experts and Contractors:	Prof P Aggett	SMCN	Items 5-7
	Dr Robert Boyle	Imperial College London	Items 5-7
	Dr V Garcia-Larsen	Imperial College London	Items 5-7
	Prof Ian Kimber	University of Manchester	Items 5-7
	Dr M Perkin	St George's University Hospitals	Items 5-7
	Dr M Trivella	University of Oxford	Items 5-7
	Dr P Turner	Imperial College London	Items 5-7

Officials:	Ms Rachel Elsom	PHE	Items 5-7
	Ms Elizabeth Kendall	FSA, Food Allergy Branch	Items 5-7
	Ms Erin Oliver	FSA, Food Allergy Branch	Items 5-7
	Mr P Tossell	FSA, Food Allergy Branch	Items 5-7
Assessors:	Prof Tim Gant	PHE	
	Mr Scott Samuels	Health & Safety Executive (HSE)	

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Announcements

1. The Chairman welcomed Members and Assessors to the meeting.

2. The Chairman reminded those attending the meeting to declare any commercial or other interests that they might have in any of the agenda items.

Item 1: Apologies for absence

3. Apologies were received from Members Professors B. Houston, R. Harrison, R. Smith, D. Harrison and J. Cade, Dr R. Crevel and Dr N. Plant. Dr Ovnair Sepai of PHE attended in place of Ms Frances Pollitt.

Item 2: Draft minutes of the meeting held on 8th December 2015 – TOX/MIN/2015/06

4. The minutes were agreed subject to a minor amendment.

Item 3: Matters arising

Item 3: Matters arising from previous meetings

5. Para 5: The COT-Committee on Carcinogenicity (COC) Synthesising Epidemiological Evidence Subgroup. Unfortunately, the planned third meeting of the sub-group had to be cancelled and will be rescheduled; however, a draft document would be discussed via email. It was noted that the international Society of Environmental Epidemiologists was proposing a symposium in the summer to link in with the Cochrane group and was interested in the work of the sub-group.

Item 6: Potassium replacements for sodium chloride and sodium based additives

6. Para 35: A meeting of the joint COT/SACN sub-group was held on the 14th January 2016. The group agreed to undertake a risk-benefit assessment of potassium.

Item 7: Review of potential risks from lead in the diet of infants and young children

7. Para 46: The Secretariat had explored the possibility of using probabilistic modelling for addressing variability in the levels of lead from all routes of exposure. In view of the composite nature of food groups analysed in the TDS, it would not be possible to use modelling to take full account of variability in levels from this type of dietary study. Probabilistic modelling was a viable option for refining the contributions from other routes of exposure; however, it was likely to involve complex assessments that also need to take account of dependency of each route on overall exposure. This was likely to involve additional resources and a considerable extension of the period needed for finalising the review. A draft statement on lead was considered under item 9 of the current agenda.

Item 8: Review of potential risks from aluminium in the diet of infants and young children

8. Para 50: A draft statement will be on the agenda of the April meeting of the COT

Review of scientific committees

9. The triennial review of the Scientific Advisory Committees was currently under way. The Chairman informed members that the draft report would be circulated to members and would be discussed by the FSA board in the near future.

Item 4: Potential future discussion items – horizon scanning – TOX/2016/01

Agenda items for 2016

10. Members noted a list of agenda items for 2016 that were planned or underway, and discussed several other topics that might also be considered.

11. The COT input into the Scientific Advisory Committee on Nutrition (SACN) review on complementary and young child feeding focussing on age 1 to 5 involved a comprehensive review of 16 substances which was still ongoing; due to the size of the task it was unlikely to be finalised in 2016

Potential discussion topics

Consultations of the European Food Safety Authority (EFSA)

12. Members were informed that a review of Weight of Evidence based approaches to risk assessment was ongoing and the Committee's views were likely to be sought when the draft Opinion was published for public consultation.

Items carried forward from the 2015 horizon scanning

Emerging non-animal methods

13. Amongst a number of important initiatives in the US, the Tox21 and ToxCast programs were well underway, while in Europe the SURAT 1 project had recently concluded. A large Horizon 2020 project in this area, called EU-ToxRisk had recently started, coordinated by the Netherlands.

14. The Committee considered that since there was much current research activity in read across and predictive toxicology which was likely to influence the future of toxicity testing a workshop in this area would be useful.

15. COT wished to be kept appraised of related topics such as new test guidelines and tiered approaches and the activities of the Interdepartmental Group of Health Risks from Chemicals (IGHRC) which was coordinated by Cranfield University. It was noted that the IGHRC would be organising an awareness day that would link in with work by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs). It would be useful for the COT to be included in this.

16. The Committee noted there was a need for an international consensus on how best to determine the validity of *in vitro* methods for risk assessment since the current validation process was increasingly considered to be too slow. Members wished to be kept informed about this topic.

17. The Committee agreed that presentations on *in vitro* methodologies should be sought, including SEURAT 1, Tox21 and the OECD adverse outcome pathway program, possibly in the form of a workshop.

Modelling Kinetics

18. The Committee noted that the application of physiologically based toxicokinetic modelling (PBTK) in risk assessment had shown little recent progress, although there were some developments, such as a tool for non-expert use, and in-house modelling by the pharmaceutical industry. It was agreed that the COT would keep a watching brief on this topic.

19. A review by PHE on cadmium kinetics using Bayesian methods and expanding current radionuclide models had recently been conducted. This was not yet published but PHE agreed to circulate this review to Members.

Analysis of the evidence gap for postulated human health effects of Endocrine Disrupting Chemicals

20. Members agreed that a systematic review of the health effects of Endocrine Disrupting Chemicals (EDCs) would be useful but recognised that this would be a major task. A similar task had been conducted by the WHO but more focussed questions would have been helpful. Without a coordinated systematic review to understand the evidence base (possibly an "umbrella" review of reviews to obviate author selection bias) the impact of EDCs was uncertain. In the first instance, Members agreed that a paper on the evidence gaps would be helpful; this would be prepared by PHE.

Possible human health effects of 'E-cigarettes'

21. The Chair expressed a personal, non-specific interest as he was a member of the WHO Study Group on Tobacco Product Regulation (TobReg).

22. The Committee decided that it would be timely to review the toxicity of both nicotine-containing and nicotine-free electronic delivery systems. The Medicines and Healthcare Products Regulatory Agency (MHRA) has licenced at least one nicotine-containing product. However, most products are currently largely unregulated, but this would change with implementation of the Tobacco Products Directive, in May 2016. The aspects related to carcinogenicity could be worked on jointly with COC and COM, while COT could consider the added flavourings and exposure to vapours and particulates, including bystander exposure. A risk-benefit assessment of E-cigarettes would not be within the COT remit.

Update on the COT 2008 Trans and multigenerational toxicity statement

23. Members noted that the knowledge base on this topic had moved on since the last COT statement was published in 2008. The Committee agreed that the statement should be updated, with input from PHE as appropriate.

Role of chemicals altering the microbiome and potential human health effects

24. The Committee agreed that since the importance of the microbiome in many areas of health and disease was becoming increasingly apparent, the effects of xenobiotics on the

microbiota and of the microbiota on xenobiotics should be considered in a short discussion paper. Both the makeup of the microbiological population, i.e. the species of bacteria and other microorganisms present, and its functional makeup, i.e. the biochemical pathways contributed by the total mass of microorganisms, would be taken into account, along with other potential interactions, for example between air pollution, microorganisms in the respiratory tract and the development of asthma.

Priority setting

25. PHE would provide a short paper on priority setting for discussion at the next meeting.

Balance of expertise on the Committee

26. It was agreed that the range of expertise given in the paper reflected that provided by the current COT Members. It was noted that some new members would be required in the short term, since some current Members' terms would be ending shortly. An expert in epigenetics could be a useful addition to the Committee.

Item 5: Third draft statement on the role of hydrolysed cow's milk formulae in influencing the development of atopic outcomes and autoimmune disease - TOX/2016/04 [Reserved Business]

27. The minutes of this item are currently reserved as they include pre-publication data. They will be published as soon as practicable.

Item 6: Minutes of the Committees discussion of the Review of risks arising from the infant diet and the development of atopic and autoimmune disease: Systematic Review C Part II – Dietary exposures during pregnancy, lactation and/or infancy for reducing risk of allergic or autoimmune outcomes: a systematic review and meta-analysis – TOX 2016/02 [Reserved business]

28. The minutes of this item are currently reserved as they include pre-publication data. They will be published as soon as practicable.

Item 7: Minutes of the Committees discussion of the Enquiring about Tolerance (EAT) Study – A randomised trial of the early introduction of allergenic foods to breastfed infants TOX/2016/03

29. Professor Ian Kimber from the University of Manchester and Dr Paul Turner from Imperial College London were present to provide additional expertise on allergy and atopic disease. Dr Michael Perkin from St George's Hospital, London was available to present details of the EAT study, including the main findings and to answer any questions from the Committee. The item was discussed as "Reserved business" as the EAT study was unpublished at the time of the meeting.

30. The per-protocol (PP) data showed a significant reduction in food allergy in the early introduction group compared with the standard weaning group. The results from the Intention to Treat (ITT) analysis were not significant.

31. Members were impressed with the quality and robustness of the study design; they agreed that it was difficult to see how this could have been improved. The study population was discussed in detail and the Committee agreed that whilst participants did not entirely reflect the UK population, this did not detract from the results.

32. The Committee agreed that early introduction of allergenic foods does not appear to increase the risk of developing allergic or autoimmune disease. The results from EAT will be considered as part of systematic review B from Imperial College London at the COT meeting in April, and hence it would be premature to make recommendations on the basis of this study alone. A number of other trials are currently ongoing in this area and members felt that they would like to see the results of these before reconsidering any advice on the introduction of allergenic foods into the diets of infants. These trials may also provide information on the safety of introducing food to already sensitised individuals. Members also requested a focussed review on the timing of introduction of peanut into the infant diet.

Item 8: Review of the potential risks from arsenic in the diet of infants aged 0 to 12 months and young children aged 1 to 5 years – TOX/2016/05

33. The Chair, Professor Boobis and the FSA Scientific Secretary, Dr Benford, both declared a non-personal, non-specific interest in this item as they had both been members of the European Food Safety Authority's (EFSA) Panel on Contaminants in the Food Chain (CONTAM) when the scientific opinion on arsenic in food had been adopted in 2009. In addition, Dr Benford had been a member of the Working Group (WG) that had drafted the EFSA's scientific opinion, and had also been a member of the WG that had prepared the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives' (JECFA) addendum on arsenic.

34. The Scientific Advisory Committee on Nutrition (SACN) was undertaking a review of scientific evidence that would input to the Government's dietary recommendations for infants and young children. The SACN was examining the nutritional basis of the advice and the COT had been asked to review the risks of toxicity from chemicals in the diet of infants and young children aged 0 to 5 years. The reviews would identify evidence that had emerged since the Government's recommendations were first formulated, and would appraise that evidence to determine whether the advice should be revised.

35. This discussion paper provided estimates of exposures to total and inorganic arsenic for infants and young children in the UK aged 0 to 5 years. In line with previous requests from the Committee, the exposures to arsenic from water had been taken into account using a number of scenarios that had been developed to obtain a reasonable estimate of the possible range of exposures. Where appropriate, exposures based on median and 97.5th percentile concentrations for arsenic in water had been incorporated into the total dietary exposures for each age group.

36. The Committee agreed that while the estimates for exposure to total arsenic provided useful context, only the estimates for exposure to inorganic arsenic should be included in the draft statement as there were benchmark dose levels against which exposure to inorganic arsenic could be compared.

37. To allow a conclusion about the exposures to inorganic arsenic to be reached, the Committee requested that a range of aggregate exposure estimates be calculated by adding the high level exposure estimate from one source of exposure (e.g. soil) to the average exposure estimates from all other sources.

38. Members discussed the assumption that <10% of the total arsenic present in breast milk was inorganic arsenic, and requested that further information be provided regarding the species of arsenic present in breast milk. Members suggested that total and inorganic arsenic exposures should be assessed in women, as it was unlikely that the proportion of total arsenic as inorganic arsenic in breast milk would be greater than that to which mothers were exposed. Data on the level of arsenic in blood could also help resolve this issue.

39. Particular attention had been paid to the potential exposures to inorganic arsenic that could arise from the consumption of rice drinks as the FSA advised that rice drinks should not be used as a *substitute* for breast milk, infant formula or cows' milk, while NHS Choices advised that rice drinks should not be consumed by those <5 years. Members concluded that the current exposure estimates for arsenic supported the FSA advice not to use rice drinks as a *substitute* for breast milk, infant formula or cows' milk, and that this advice should therefore remain in place. However, Members agreed that consumption of 50 mL of rice drink per day by infants and young children aged 1-5 years would not make an appreciable difference to total dietary exposure to inorganic arsenic, contributing less than 10%; this information could be used to supplement the current FSA advice.

40. Concern had been raised about exposures to inorganic arsenic from the consumption of rice cakes as these could contain high levels of inorganic arsenic. Rice cakes were a common snack food for infants and young children, and were available in infant-specific and non-infant specific (i.e. 'adult') forms; as of January 2016, adult rice cakes were subject to a different maximum limit for inorganic arsenic to those marketed for infants. The Committee would be able to reach a conclusion about the exposures via infant and adult rice cakes once the aforementioned aggregate exposure calculations were completed.

41. Members requested that consideration be given to exposures to arsenic from water from private supplies, as the information considered to date by the Committee was for public water supplies. Information about arsenic in private water supplies would be requested from the relevant drinking water regulators and provided to the Committee if possible.

42. A draft statement taking into account the discussion and above requests would be prepared for a future meeting.

Item 9: First draft addendum to the 2013 COT statement on potential risks from lead in the infant diet – TOX/2016/07

43. The Chair, Professor Boobis and the FSA Scientific Secretary, Dr Benford, both declared a non-personal, non-specific interest in this item. Professor Alan Boobis had been on the EFSA CONTAM panel when the Opinion had been adopted in 2010 and also chaired the EFSA lead working group. Dr Diane Benford declared that she had been on the EFSA CONTAM panel that had adopted the Opinion on lead in 2010 and also on the JECFA panel.

44. The Scientific Advisory Committee on Nutrition (SACN) was undertaking a review of scientific evidence that will input to the Government's dietary recommendations for infants and young children. SACN is examining the nutritional basis of the advice. The Committee on Toxicity in Food, Consumer Products and the Environment (COT) has been asked to review the risks of toxicity from chemicals in the diet of infants 0-12 months, most of which has been completed, and young children aged 1 to 5 years. The reviews will identify evidence that has emerged since the Government's recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised.

45. This addendum to the 2013 COT statement on potential risks from lead in the infant diet provided estimates of lead exposures for children in the UK aged 1 to 5 years and also an updated exposure assessment for infants aged 0 to 12 months. Different scenarios had been detailed which included exposure from water using the highest median and highest 97.5th percentile occurrence data.

46. Members requested that a more holistic approach to modelling be used for the exposure scenarios. The bioavailability of lead from soil, air, food and water would need to be taken into account to provide more accurate exposures. It was also requested that lead exposures from water from private wells be considered assuming that it was possible to obtain occurrence data. In addition the Committee requested that a paragraph be included on lead exposure from game, reflecting its previous conclusions on this.

Item 10: Paper for information: FSA Scientific Advisory Committees (SACs) update – TOX/2016/09

47. This paper was provided for information only.

Item 11: Any other business

48. Members' views were sought on using the online system to access committee papers. Members requested that the possibility of adding all the papers in a zip file be investigated, in addition to the individual files, so that all the papers could be downloaded in one go if wished, and asked to be informed when the complete set of papers was available.

49. The Secretariat would email to Members an electronic version of the claims form together with instructions on returning the completed form and receipts electronically.

50. Some of the meeting dates were to be changed, including the next meeting in April due to clashes with other meetings. Members would be consulted on possible alternative dates.

Item 11: Date of next meeting

51. Date of next meeting. This meeting will be rescheduled. The Secretariat will confirm the new date with Members as soon as possible (post-meeting note, this meeting has been re-scheduled for 8 April, 2016).