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

Minutes of the meeting held on Friday, 8th April 2016 in Aviation House, London.

Present

Chairman:	Professor A Boobis	
Members:	Mr D Bodey Prof J Cade Dr J Coulson Dr R Crevel Dr A Hansell Dr C Harris Prof D Harrison Prof R Harrison Prof B Houston Prof B Lake Dr N Plant Prof R Smith Prof F Williams	
Food Standards Agency (FSA) Secretariat:	Mr B Maycock Dr D Gott Ms H Gbormittah Ms C Mulholland Ms F Hill Ms R Acheampong Ms L Buckley Dr D Hedley Dr J Shavila Mr A Sbaiti Dr L Kent Ms K Sturgeon	
Public Health England (PHE) Secretariat:	Ms F Pollitt	PHE Scientific Secretary

Invited Experts and Contractors:	Dr K Ong	SMCN	Item 5
	Dr R Boyle	Imperial College London	Item 5
	Dr V Garcia-Larsen	Imperial College London	Item 5
	Dr P Turner	Imperial College London	Item 5
	Prof I Kimber	University of Manchester	item 5
	Dr M Perkin	St George's University Hospitals	Item 5
	Dr M Trivella (by phone)	University of Oxford	Item 5
	Dr P Turner	Imperial College London	Item 5
	Mr P Gregory	Deenside Ltd	Item 4
	Prof M Coleman	Aston University	Item 4
Officials:	Dr Halina Garavini	Toxicology Unit, Imperial College London	
	Ms V Lund	PHE	Items 5
	Ms E Kendall	FSA, Food Allergy Branch	Items 5
	Ms M Ige	FSA, Chemical Contaminants and Residues Branch	Items 6 - 8
Assessors:	Prof T Gant	PHE	

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Announcements

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

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

3. The Chair explained that this would be Ms Pollitt's final meeting as the PHE Scientific Secretary as she was retiring. Ms Pollitt had taken over this role following Mr John Battershill's retirement and had previously held the role of Scientific Secretary to the Committee during the 1990s. She had also been Scientific Secretary for the Lowermoor sub-group. The Chairman expressed best wishes to Ms Pollitt on behalf of the Committee and thanked her for her substantial contributions to the work of the Committee over the years.

Item 1: Apologies for absence

4. Apologies were received from Members Prof I Morris, Dr M Graham and Dr J Thompson. Apologies were also received from Dr D Benford (Scientific Secretary) and Dr O Sepai (PHE Secretariat).

Item 2: Draft minutes of the meeting held on 2nd February 2016

5. The minutes were agreed subject to minor amendments. The text in para 35, "only the estimates for exposure to inorganic arsenic should be included in a draft statement as there was currently no health-based guidance value with which the exposures to total arsenic could be compared" would be replaced with "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."

Item 3: Matters arising

Item 3: Matters arising from previous meetings

6. Para 5: Dr Hansell reported that the COT-Committee on Carcinogenicity (COC) Synthesising Epidemiological Evidence Subgroup was currently finalising its document. It was noted that there was considerable external interest in this work.

7. Para 6: The work of the joint COT/Scientific Advisory Committee on Nutrition (SACN) subgroup on the risks and benefits of potassium replacements for sodium chloride and sodium-based additives was ongoing. A teleconference to discuss

progress was arranged for the end of April, and it was intended that the work be completed by the end of the year.

8. Para 8: A draft statement on aluminium in the diet of infants and young children would be considered at this meeting under Item 9.

9. Para 9: The report of the triennial review of the scientific advisory committees had been discussed by the General Advisory Committee on Science (GACS), which had raised a number of reservations. These would be fed into the discussion by the FSA Board which was scheduled for its next meeting on 18th May.

Item 4: Potential future discussion items – horizon scanning

10. Para 19: The review by PHE on cadmium kinetics using Bayesian methods and expanding current radionuclide models was tabled at this meeting.

11. Para 24: The paper on priority setting was to be brought to the next COT meeting, in May.

Item 5: Third draft statement on the role of hydrolysed cows' milk formulae in influencing the development of atopic outcomes and autoimmune disease

12. Para 26 and Reserved Business minutes, para 4: The finalised COT statement had now been published, as had the research report and the study manuscript in the British Medical Journal.

Item 7: Enquiring about Tolerance (EAT) study – a randomised trial of the early introduction of allergenic foods to breastfed infants

13. Para 28: A joint subgroup of the COT and the SACN Subgroup on Maternal and Child Nutrition (SMCN) was being created to bring together the conclusions of the respective groups on infant feeding, primarily the early introduction of allergenic foods and the risk/benefits to the infant. The Chairman noted that Dr Cade had agreed to join this group and asked for another COT Member to volunteer.

14. The Chairman explained that a procedural issue had been raised from the Independent Data Monitoring Committee of the EAT study at the last GACS meeting. There were no concerns with the conduct or conclusion of the study. The FSA was looking into its procedures, though the study had been set up 8 years ago and procedures had changed since then.

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

15. Para 41: A draft statement would be considered at this meeting under Item 7.

Item 9: First draft addendum to the 2013 COT statement on potential risks from lead in the infant diet

16. Para 45: A revised draft statement would be considered at this meeting under Item 8.

17. The Secretariat had no other matters to raise.

Item 4: Follow-up paper on the submission for a reformulation of PAVA irritant spray – TOX/2016/10 [Reserved Business]

18. No interests were declared.

19. Mr Paul Gregory, an incapacitant consultant for the applicant, Deenside Ltd., and Professor Michael Coleman, a toxicologist at Aston University who had prepared a risk assessment of the reformulation for the applicant, attended to answer the Committee's questions.

20. This item was reserved business as it considered commercially sensitive information.

Item 5: Review of risks arising from the infant diet and the development of atopic and autoimmune disease: Systematic Review B – Timing of the introduction of allergenic foods to the infant diet: a systematic review and meta-analysis – TOX/2016/11 [Reserved Business]

21. Professor Ian Kimber (University of Manchester) and Dr Paul Turner (Imperial College London) were both present to offer advice to the committee on this topic. Members of the contractor team were present to answer questions on the review: Dr Robert Boyle and Dr Vanessa Garcia-Larsen in person, and Dr Marialena Trivella was available via teleconference. Dr Ken Ong attended in his role as a representative from the Scientific Advisory Committee on Nutrition's Subgroup on Maternal and Child Nutrition (SMCN).

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

Item 6: Review of potential risks from acrylamide in the diet of infants aged 0 to 12 months and children aged 1 to 5 years – TOX/2016/12

23. No interests were declared.

24. 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. SACN was examining the nutritional basis of the advice. The COT had been asked to review the risks of toxicity from chemicals in the diet of infants 0-12 months, most of which had been completed, and young children aged 1 to 5 years. The reviews would identify evidence that had emerged since the Government's recommendations were formulated, and would appraise that evidence to determine whether the advice should be revised.

25. In 2014, the European Food Safety Authority (EFSA) issued a draft scientific opinion on the risks to public health related to the presence of acrylamide in food. The COT and the Committee on Carcinogenicity (COC) responded to the consultation, noting that they were broadly in agreement with the conclusions and making proposals for clarifications. Since the publication of the finalised EFSA opinion in June 2015, some interim results from the UK 2014 Total Diet Study (TDS) on acrylamide had become available. However, the analysis of acrylamide from the 2014 TDS may have been affected by some analytical issues which were being investigated.

26. This discussion paper provided provisional exposure estimates to acrylamide in infants and young children using the interim concentrations identified in the 27 food groups of the 2014 TDS, and provisional estimates of margins of exposure (MOEs) to the benchmark dose lower confidence limit for a 10% extra incidence of tumours ($BMDL_{10}$) estimated by EFSA. The TDS indicated that potatoes, snacks and miscellaneous cereal groups were the main contributors to total dietary exposure to acrylamide. It was agreed that future exposure estimates conducted using the 2014 TDS should be refined further and expressed in terms of the main contributing subgroups forming each food group. The COT requested further explanations for the types of foods considered by EFSA in their exposure assessment, and whether the submitted data to EFSA was for food as purchased, or as eaten.

27. Members requested that a draft statement include some brief discussion of other sources of exposure. Exposure to acrylamide could also occur from tobacco smoke, including environmental tobacco smoke, but since acrylamide was unstable in soil and water exposure from these sources was unlikely.

28. Members agreed that advice from the COC should be sought about the interpretation of the margins of exposure (MOEs) in infants and young children.

These MOEs were derived from relatively short periods of increased exposure to a genotoxic carcinogen, rather than reflecting average life-time exposure. However, it was also possible that these life stages were of increased susceptibility to acrylamide.

29. Members agreed that a statement should be drafted for consideration at a future meeting.

Item 7: First draft statement on the potential risks from arsenic in the diet of infants aged 0 to 12 months and young children aged 1 to 5 years – TOX/2016/13

30. The Chair, Professor Boobis, declared a non-personal, non-specific interest in this item as he had been a member of the EFSA Panel on Contaminants in the Food Chain (CONTAM) when the scientific opinion on arsenic in food had been adopted in 2009.

31. A discussion paper providing estimates of exposures to total and inorganic arsenic for infants and young children in the UK aged 0 to 5 years had been presented to the Committee at the February 2016 meeting. At that meeting, Members had agreed that a statement should be drafted focusing on the estimated exposures to inorganic arsenic, and had requested that further information be provided on the proportion of inorganic arsenic in breast milk and that consideration be given to the exposures that could arise from the use of private rather than public water supplies. This information was incorporated into a draft statement (TOX/2016/13 Annex A), in addition to some information on the bioavailability of arsenic in soil.

32. At the February meeting, Members had also requested that the exposure estimates from all sources be combined to form aggregate exposures that could be compared to the BMDL. Members had requested that the aggregate exposures be estimated by adding the high level exposure estimate from one source of exposure to the average exposure estimates from all other sources. The aggregate exposure estimates were included in the draft statement.

33. At the current meeting, the Committee agreed that in the absence of consistent data on the proportion of inorganic arsenic in breast milk, it was appropriate to assume that 100% of the arsenic present was inorganic. Members also agreed with the approach taken for the aggregate exposure estimates but asked that the tables be re-formatted.

34. The Committee noted that the United States Food and Drug Administration (FDA) had recently published a detailed risk assessment on exposures to arsenic

from rice and rice products[1]; the Secretariat would determine what impact, if any, this assessment may have on the draft statement.

35. The Committee raised concerns about the age of the data used in the soil exposure assessment. One Member and the Scientific Secretary from PHE indicated that they might be able to supply more recent data on the concentrations of arsenic and other elements in UK soil that could be used instead. Members also raised concerns about the general approach taken in the soil exposure assessments, and suggested that other Members with the relevant expertise be asked to advise on the suitability of the approach.

36. Members understood that the water regulatory agencies did not hold representative data on the concentration of arsenic (and other elements) in private water supplies, but requested that an indication of the proportion of the population using such supplies be provided. One Member and the Scientific Secretary from PHE also indicated that they might be able to supply some data on the concentrations of arsenic and other elements in private water supplies.

37. The Committee requested that the use of the lowest EFSA $BMDL_{01}$ (0.3 µg/kg bw/day) rather than the JECFA $BMDL_{0.5}$ (3.0 µg/kg bw/day) be reconsidered. One Member would assess the critical studies used by each organisation to derive these BMDLs, and would advise the Secretariat as to which study would be the more appropriate to use for derivation of a BMDL. Further consideration would also be given to how to interpret the margins of exposure, and whether the use of the respective BMDL in the characterisation of risks from exposures in 0 to 1 year olds was appropriate. The Committee also requested that clear statements outlining the assumptions made in the exposure assessments and the uncertainties in the statement as a whole be included in future drafts.

38. A second draft statement would be drafted taking into account the aforementioned issues in addition to some minor formatting and editorial amendments.

Item 8: Second draft statement on the potential risks from lead in the diet of infants aged 0 to 12 months and young children aged 1 to 5 years – TOX/2016/14

39. The Chair, Professor Boobis, declared a non-personal, non-specific interest in this item as he had been a member of the EFSA CONTAM panel when the scientific opinion on lead in food had been adopted in 2010.

[1] FDA (April 2016) 'Arsenic in Rice and Rice Products Risk Assessment Report' http://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM486543.pdf

40. A discussion paper providing estimates of exposures to lead and margins of exposure for infants and young children in the UK aged 0 to 5 years had been presented to the Committee at the December 2015 meeting. The secretariat drafted a statement addendum at the request of the Committee which was presented at the February 2016 meeting. Members had requested that a more holistic approach to modelling be used for the exposure scenarios taking into account bioavailability and exposures from private water wells and from the consumption of game. A revised draft addendum had been produced for consideration at this meeting.

41. As per the Committee's comments on the arsenic addendum, Members raised concerns about the age of the data used in the soil exposure assessment. One Member and the Scientific Secretary from PHE indicated that they might be able to supply more recent data on the concentrations of arsenic and other elements in UK soil that could be used instead. Members had raised concerns about the general approach taken in the soil exposure assessment for arsenic, stating that these concerns were also relevant to the lead and aluminium addendums. It was suggested that other Members with the relevant expertise be asked to advise on the suitability of the approach.

42. Members had also raised concerns about how relevant the data were in relation to arsenic levels in private water supplies, stating that these concerns were also relevant to the lead addendum. Whilst Members understood that the water regulatory agencies did not hold representative data on the concentration of lead (and other elements) in private water supplies, they requested that an indication of the proportion of the population using such supplies be provided. One Member and the Scientific Secretary from PHE also indicated that they might be able to supply some data on the concentrations of lead and other elements in private water supplies.

43. Members made a number of editorial comments on the draft statement addendum. In considering the MOEs in the addendum, the Committee requested that the MOEs be presented as ranges. There were a large number of uncertainties and assumptions in the risk assessment and these should be clearly identified. Members noted that uncertainties in the estimates of exposure would be reduced by studying blood lead concentrations.

44. A third draft statement addendum would be prepared for consideration at a future meeting.

Item 9: First draft addendum to the 2013 COT statement on the potential risks from aluminium in the infant diet – TOX/2016/06

45. A discussion paper providing estimates of exposures to aluminium for infants and young children in the UK aged 0 to 5 years had been presented to the Committee at the December 2015 meeting. The Committee had requested that a statement addendum be prepared with information to be included on aluminium uptake in soya plants (and other similar species), and the uptake and potential risks from aluminium nanoparticles. Members had also requested that the bioavailability of aluminium be considered, and that the estimated exposures be revised to include median and 97.5th percentile aluminium concentrations in drinking water. In addition, aggregate exposure tables had been included, to ensure consistency with the reviews of lead and arsenic at the February 2016 meeting.

46. The Committee requested that information be included on the basis for the Provisional Tolerable Weekly Intake (PTWI), and that further explanation be provided of the major contributors to the estimated exposures and the uncertainties associated with this assessment. Members also requested a number of editorial changes.

47. It was agreed that the addendum would be revised and the revised addendum finalised by Chairman's action.

Item 10: Draft 2015 Annual Report - TOX/2016/09

48. Members were asked to consider the draft text of the COT section of the 2015 Annual Report of the Committees on Toxicity, Mutagenicity and Carcinogenicity; to comment on the extent to which COT evaluations in 2015 had complied with the Food Standards Agency's Good Practice Guidelines for scientific advisory committees; and to advise of any changes to their annual declarations of interest.

49. The Committee asked that the section on the COT's response to the EFSA consultation on caffeine be condensed, noting that the COT's comments had previously been published in full as a COT paper.

50. Members were asked to submit any other comments by email.

Item 11: Peer review by EU-ANSA agencies – a reflection paper - TOX/2016/17

51. Due to the there being insufficient time for discussion, Members were requested to send in any comments on this paper by email. If required, this item could be brought back to the next meeting for a full Committee discussion.

Item 12: Update on action taken subsequent to COT advice - TOX/2016/15

52. This paper was provided for information only

Item 13: EFSA Scientific Advisory Committees (SACs) updates - TOX/2016/16

53. This paper was provided for information only.

Item 14: Any Other Business

54. The FSA confirmed that it was unable to provide financial support for COT Members to attend a one-day workshop, “Recent advances in alternative approaches for chemical safety assessment and regulatory perspectives,” being jointly hosted by the Interdepartmental Group on Health Risks from Chemicals (IGHRC) and the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) on 19th May.

55. Members explained that they would like to be notified when all of the papers were available on the electronic system rather than having to check periodically, and that the file names were not all clear. In addition, some Members had been unable to access papers on the system in the run-up the meeting. The Secretariat would investigate this.

Date of next meeting

56. The next meeting would be held on 24th May 2016 in Conference Rooms 4&5, Aviation House, 125 Kingsway, London, WC2B 6NH.