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

Minutes of the meeting held on Tuesday, 8th December 2015 in Aviation House, London.

Present

Chairman:	Professor D Harrison (Deputy Chairman) (Mr D Bodey acted as Deputy Chairman for Items 1 – 4)		
Members:	Mr D Bodey Dr R Brimblecombe Prof J Cade Dr R Crevel Dr M Graham Dr A Hansell Dr C Harris Prof B Lake Prof I Morris Dr N Plant Prof R Smith Dr J Thompson Prof F Williams		
Food Standards Agency (FSA) Secretariat:	Dr D Benford Ms R Acheampong Ms L Buckley Ms H Gbormittah Ms F Hill Mr B Maycock Ms C Mulholland Ms C Potter Mr A Sbaiti Dr J Shavila		
Public Health England (PHE) Secretariat:	Ms F Pollitt	Scientific Secretary	
Invited Experts and Contractors:	Dr Robert Boyle Prof Ian Kimber	Imperial College London University of Manchester	Item 5 Item 5

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

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Announcements

1. The acting Deputy Chairman, Mr Bodey, welcomed Members and Assessors to the meeting.

2. The acting Deputy 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 Brian Houston and Roy Harrison, and Dr James Coulson. Apologies were also received from the Chairman, Professor Alan Boobis, and the Vice Chair of the Scientific Advisory Committee on Nutrition (SACN), Professor Peter Aggett. Professor Harrison, the Deputy Chairman was unexpectedly delayed but chaired the meeting from item 5 onwards. Written comments had been submitted by the Chair and one Member.

Item 2: Draft minutes of the meeting held on 27th October 2015 – TOX/MIN/2015/05

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

Item 3: Matters arising

Item 3: Matters arising from previous meetings

5. Para 6: The COT-Committee on Carcinogenicity (COC) Synthesising Epidemiological Evidence Subgroup had held its second meeting on Thursday 29th October, and had reviewed the approaches to epidemiological evidence used by the COT and COC. Members were informed that the high level guidance document, due to be completed by the end of the third meeting, had been discussed, along with scoring systems and systematic reviews of epidemiological evidence. A date had still to be set for the third meeting.

6. Para 9: The statement on the effects of soya consumption on thyroid status would be finalised in the near future as the research had now been published.

7. Para 10: Members of the Secretariat had met informally with representatives from the Specialist Cheesemakers' Association and the Provision Trade Federation who had previously supplied data on histamine in cheese based on a survey of their members. The Secretariat had been able to discuss a number of points that had

arisen from the survey as well as more general topics such as market share and supply chains. Some information from other industry sources was still outstanding, and it was hoped that this information would be brought to a future COT meeting.

8. Para 12: A meeting of the SACN Working Group (WG) on vitamin D had been held in November. The WG had considered the comments that they had received following public consultation on the draft report on vitamin D. A number of comments had been received but none of these were relevant to the COT. A revised report would be considered in December and publication of the final report was expected in March 2016.

Item 5: Review of risks arising from the infant diet and the development of atopic and autoimmune disease

9. A second draft Statement had been prepared for consideration under item 5 of the agenda.

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

10. This topic was considered under item 6 of the agenda.

11. Members were informed that the Department for Transport Minister had sent a letter to everyone who had submitted queries or parliamentary questions about the COT's position on cabin air, giving the COT's conclusions in full. A copy of the letter was tabled for information.

12. No other matters were raised.

Item 4: Review of potential risks from polybrominated biphenyls (PBBs) in the diet of infants and 1 to 5 year old children – TOX/2015/34

13. The Chair, Professor Boobis, had previously declared a non-personal, non-specific interest in this item as he had been a member of the European Food Safety Authority's (EFSA) Working Group on Brominated Flame Retardants (BFRs) in Food which had drafted the scientific opinion on polybrominated biphenyls (PBBs); he had provided written comments on this item in his absence. Both the Chair and the FSA Scientific Secretary, Dr Benford, had been on the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) that had adopted the scientific opinion on PBBs.

14. PBBs were a class of additive BFRs that had been used in the production of synthetic fibres and polymers. Over the previous four decades the production and use of PBBs had been restricted progressively across the world, and there were no longer any permitted uses in the UK. Despite the restrictions on their production and

use, as PBBs were chemically stable, persistent, and bio-accumulative in the environment, human exposures were considered likely to continue for some time.

15. There are 209 different PBB congeners; the position of the bromine atoms around the biphenyl structure determines whether a congener is non-planar or able to adopt a planar configuration. In the planar configuration congeners have structures similar to 2,3,7,8-tetrachloro-p-dibenzodioxin (TCDD), and are likely to cause toxicity through activation of the aryl hydrocarbon receptor (AhR). Non-planar congeners are more likely to cause toxicity though activation of nuclear receptors such as the constitutive androstane receptor (CAR) and the pregnane-X receptor (PXR).

16. Different approaches would be taken when assessing the potential risks from planar or non-planar PBBs. The toxic equivalency factors (TEFs) that had previously been assigned to dioxin-like polychlorinated biphenyls (PCBs)[1] would be applied to the estimated exposures from the corresponding planar PBB congeners to determine toxic equivalences (TEQs). The contribution of these TEQs to the tolerable daily intake (TDI) of 2 pg WHO-TEQ/kg bodyweight (bw) would then be assessed. For non-planar PBBs, margins of exposure (MOEs) would be calculated by dividing a no observed adverse effect level (NOAEL) of 0.15 mg/kg bw/day, from a National Toxicology Program (NTP) carcinogenicity study[2] where the key toxicological endpoint was hepatocarcinogenicity by a non-genotoxic mode of action, by the estimated exposures and then assessing the magnitude of the MOE.

17. The profiles of PBB congeners present in the environment differed from those present in the technical mixtures that were previously commercially-produced and tested for toxicity. This variation, and the observation that different studies had often focused on measuring different congeners in food and the environment, had been noted previously (COT Statement 2015/03[3]).

18. Paper TOX/2015/34 was presented to the Committee as part of a series related to the toxicity of chemicals in the infant and young child diet, in support of a review by the SACN of Government recommendations on complementary and young child feeding. The SACN's review was being conducted in two stages; focussing first on advice for the feeding of infants aged 0 to 12 months, and then on advice for young children aged 1 to 5 years. The COT had considered the potential risks from PBBs in the infant diet (0 to 12 months) in COT Statement 2015/03, and had stated

[1] Van den Berg, M. *et al*. (2006) 'The 2005 World Health Organization re-evaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds' *Toxicological Sciences* 93(2) pp.223-241

[2] NTP (1993) NTP technical report on the perinatal toxicology and carcinogenesis studies of polybrominated biphenyls (Firemaster FF-1) (CAS no. 67774-32-7) in F344/N rats and B6C3F1 mice (feed studies). Research Triangle Park, NC, US Department of Health and Human Services, NTP (NTP TR 398 NIH publication No. 92-2853)

[3] Available with a lay summary at: http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cot-statement-2015/cot-statement-on-polybrominated-biphenyls-pbbs-in-the-infant-diet

that no meaningful risk assessment could be performed as a reliable estimation of infants' exposure to PBBs was not possible.

19. At the October COT meeting, the Members had discussed a scoping paper for the proposed work on the second stage of the SACN's review (TOX/2015/22). Members had requested that PBB exposure assessments be performed for 1 to 5 year olds, and that a literature review be undertaken to capture any new UK occurrence data for PBBs that had become available since the statement on the potential risks from PBBs in the infant diet was completed.

20. Paper TOX/2015/34, provided the COT with upper bound exposure estimates[4] based on exposures to PBBs in infants (0 to 12 months) and young children (1 to 5 years) from the diet and the environment. As the Committee had previously stated that planar and non-planar PBBs would need separate consideration, the exposure estimates to the planar and non-planar PBBs had been calculated separately, and the risks to each had been assessed according to the two approaches described above.

21. The dietary exposures presented in TOX/2015/34 had been calculated using consumption data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC), for infants aged 4 to 18 months, and the National Diet and Nutrition Survey (NDNS), for children aged 18 months to 5 years. When assessing exposures in exclusively breastfed infants (0 to 6 months old), the default consumption values estimated by the EFSA[5] had been used; as some breast milk consumption data had been available in the DNSIYC, this had been used to estimate exposures via breast milk in 4 to 18 month olds. No new UK occurrence data had been published since COT Statement 2015/03, and, as no relevant data had been available for PBB concentrations in air, soil or water, the environmental exposures in TOX/2015/34 focussed solely on those via the ingestion of dust. The exposures to dust had been calculated for infants aged 9 to 12 months, and for children aged 1 to 5 years, using an ingestion figure calculated by the United States Environmental Protection Agency (US EPA). For all sources of exposure, a significant proportion of the available occurrence data were below the limit of detection (LOD).

22. The only relevant occurrence data available for planar PBBs related to their presence in food (excluding breast milk or formula). The 97.5th percentile upper bound exposures to planar PBBs were up to 0.21 pg WHO-TEQ/kg bw/day in the diet of 4 to 12 month olds, and up to 0.13 pg WHO-TEQ/kg bw/day in the diet of 1 to 5 year olds. These upper bound exposures made contributions to the TDI of less than 10.5% in 4 to 12 month olds, and less than 6.5% in 1 to 5 year olds. Because of the

[4] Where a concentration was below the limit of detection (LOD), it had been assumed that it was equal to the LOD. A lower bound approach would usually assume that a concentration below the LOD was equal to zero.

[5] EFSA (2010) 'Scientific opinion on polybrominated biphenyls (PBBs) in food' *EFSA Journal* 8(10) pp.1789

large number of data below the LOD, the upper bound approach overestimates actual exposure, and because extrapolating the TEFs assigned to PCB congeners to the corresponding PBB is conservative, actual contributions to the TDI could be very much lower.

23. As occurrence data were available for non-planar PBBs in both food and breast milk, the two sources had been assessed separately and are presented below as diet (excluding breast milk), and breast milk. No relevant occurrence data were available for formula. The 97.5th percentile upper bound exposures to non-planar PBBs were up to 1620 pg/kg bw/day in the diet of 4 to 12 month olds, and up to 1544 pg/kg bw/day in the diet of 1 to 5 year olds. Overall, 97.5th percentile upper bound exposures to non-planar PBBs from the diet (excluding breast milk) resulted in MOEs greater than 92,600 for 4 to 12 month olds, and MOEs greater than 97,200 for 1 to 5 year olds.

24. Exposures via breast milk had been assessed as exposures in exclusively breastfed 0 to 6 month olds, and exposures in 'non-exclusively' breastfed 4 to 18 month olds, based on the highest reported concentration of PBBs in breast milk sampled in the UK. In exclusively breastfed 0 to 6 month olds, high level exposures to non-planar PBBs were up to 4391 pg/kg bw/day. In 'non-exclusively' breastfed infants, 97.5th percentile exposures were up to 3440 pg/kg bw/day in 4 to 12 month olds, and up to 1620 pg/kg bw/day in 12 to 18 month olds. Overall, the high level exposures to non-planar PBBs in exclusively breastfed 0 to 6 month olds resulted in MOEs greater than 43,600, and the 97.5th percentile exposures in 'non-exclusively' breastfed 4 to 12 month olds and 12 to 18 month olds resulted in MOEs that were greater than 43,600 and 93,000 respectively.

25. The occurrence data for non-planar PBBs in dust (obtained from a study in South Africa) resulted in 95th percentile exposure estimates of up to 159 pg/kg bw/day in 9 to 12 month olds, and up to 144 pg/kg bw/day in 1 to 5 year olds. These exposures resulted in an MOE of 943,000 for infants aged 9 to 12 months and of MOEs greater than 1,040,000 for 1 to 5 year olds. Relevant occurrence data were not available for other non-dietary sources of exposure (i.e. air or soil).

26. Members confirmed that extrapolating the TEFs assigned to PCB congeners to the corresponding PBB congeners was a conservative approach. In addition, Members noted that the use of the NOAEL derived from the NTP carcinogenicity study to calculate the MOEs for non-planar PBBs was not inappropriate as the critical endpoint for the study was considered to have a threshold as it had occurred by a non-genotoxic mode of action (calculation of a benchmark dose would be the more usual approach to carcinogens with a genotoxic mode of action).

27. Regarding the lack of occurrence data for PBBs in water, Members stated that PBBs would not be expected to be present at significant levels, as based on the behaviour of similar compounds it was likely that they would bind to sediment.

28. Members agreed that the approach taken in the provisional risk assessment was conservative, due in part to the upper bound approach that was taken with the large number of data that were below the LOD.

29. In Statement 2015/03, the Committee had concluded that the available carcinogenicity data for non-planar PBBs was of questionable relevance to humans, and that the technical mixture that was tested in the NTP carcinogenicity study, was not representative of the profiles of PBBs to which people are exposed in the environment and foodstuffs, and that this introduced further uncertainty. At the current meeting, the Committee confirmed that this conclusion was still appropriate.

30. Overall Members agreed that, taking into account all of the uncertainties surrounding the exposure estimates, the contributions made by planar PBBs to the TDI for dioxin-like compounds were minor, and the large margins of exposure in the assessment of non-planar PBBs did not indicate a cause for concern. Members confirmed that there were still insufficient occurrence data to be able to complete a meaningful risk assessment, and that, as there were no new data available, it would not be worthwhile preparing a new statement. The minutes of the meeting would therefore provide the record of the COT views and conclusions.

Item 5: Review of risks arising from the infant diet and the development of atopic and autoimmune disease: Second draft statement on the role of hydrolysed cows' milk formulae in influencing the development of atopic and autoimmune disease – TOX/2015/35

31. No interests were declared at the meeting. The Chair, Professor Boobis, had previously declared a non-personal, specific interest in this item as he also worked for Imperial College London; he had provided written comments on this item in his absence. Dr Hansell similarly declared a non-personal, specific interest for the same reason.

32. Professor Ian Kimber was present to provide the Committee with additional expertise on allergic and atopic disease. The lead contractor who prepared the review, Dr Robert Boyle from Imperial College London, was also present.

33. Imperial Consultants had been commissioned by the FSA to conduct a systematic review of the published scientific literature on infant formulae containing hydrolysed cows' milk protein, and their ability to influence the risk of infants and young children developing atopic and autoimmune disease. This review had been

commissioned in support of the SACN's Subgroup on Maternal and Child Nutrition's (SMCN) review of UK government recommendations on breastfeeding and the introduction of solid foods in the diet.

34. The Committee had considered this review at their meetings in September 2015 and a Statement had been drafted for consideration at the October meeting. Significant amendments were discussed and Members had asked to see the statement again at the December meeting. Members made a number of requests for changes to the structure and text of the second draft Statement and asked to see the revised draft at the next meeting in February.

Item 6: Potassium replacements for sodium chloride and sodium-based additives – TOX/2015/36

35. Dr Crevel declared a non-specific, personal interest and did not take part in the discussion of this item.

36. The COT statement on potassium replacements for sodium chloride and sodium-based additives, and its accompanying lay summary, had been finalised in the summer. The review of the potential benefits of potassium replacement had also recently been updated and finalised by the SACN. The COT Chair recently met with the Chair and Deputy Chair of SACN as well as members of the two Secretariats to discuss how to take this work forward. It had been agreed that a joint subgroup would be set up to take a risk–benefit approach to the two strands of work so that a joint outcome could be agreed and presented to risk managers. The subgroup would be co-chaired by the COT and SACN Chairs. It was hoped that the first meeting would take place in early 2016.

37. Members were asked to consider the draft terms of reference (TORs) for the subgroup and were asked for any suggestions they may have with regard to membership, topics to be considered or approaches that might be taken.

38. It was agreed that the TORs should refer to vulnerable groups since this was where there were concerns regarding the potential adverse effects of increased potassium intake.

39. Dr Thompson agreed to take part in the subgroup and several suggestions were made with regard to possible external members.

40. It was suggested that modelling should be conducted to assess the effects of potassium replacement on the diets of vulnerable groups. However, modelling had been attempted previously but the data available from industry were limited to a few food categories which made it difficult to do reliable modelling, but it was possible that it could be revisited if more data became available.

41. In written comments, the Chair had suggested that frameworks developed for risk-benefit assessment by the EFSA and the Benefit Risk Assessment for Food (BRAFO), a European Commission funded project, would be useful.

Item 7: Review of potential risks from lead in the diet of 1 to 5 year old children and updated exposures for infants aged 0 to 12 months – TOX/2015/37

42. Dr Diane Benford declared that she had been on the EFSA CONTAM panel that had adopted the scientific opinion on lead in 2010. The Chair had also been a member of the EFSA CONTAM panel at that time. In addition, he had chaired the working group that prepared the opinion on lead.

43. The SACN had been undertaking a review of scientific evidence that would influence the Government's dietary recommendations for infants and young children. The 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, most of which had been completed, and young children aged 1 to 5 years. The reviews would identify new evidence that had emerged since the Government's recommendations had been formulated, and would appraise that evidence to determine whether the advice should be revised.

44. This discussion paper 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 because new data had become available since the 2013 COT statement on potential risks from lead in the infant diet (Statement 2013/02[6]).

45. Members requested that in order to better take account of lead exposure from water, a number of scenarios should be developed to obtain a reasonable estimate of the possible range of exposures.

46. The Committee discussed the use of probabilistic modelling and whether this approach should be used. This approach had been used in the past for acute exposure scenarios, but not chronic. However there was a concern that there would be some individuals with very high exposures and it would be good to know how many would be in this situation. Probabilistic modelling could put the exposures into context.

47. The levels of lead in soil were discussed and it was agreed that it was unlikely that levels in soil now would be higher than in the soil samples taken 30 years ago, which could be used as a worst case scenario. However the Committee requested

[6] Available with a lay summary at:
http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2013/lead

that a comment be added to the effect that most people live in urban areas, especially as more houses were being built on brownfield sites.

48. It was agreed that the evaluation of lead exposures would be written in the form of an addendum to the Statement 2013/02. This would need to highlight what the new data were and where the potential data gaps were. Members requested that exposure estimates for air, soil and water use median and 97.5th percentile occurrence data. The addendum should also include information as to whether levels of lead in food have changed, provide any information on the sources of lead, and compare the new exposure estimates to those calculated previously in the infant statement.

49. The Committee was content with the approach to the risk characterisation and agreed with the conclusions made and the approach to the exposure assessment. It was decided that the probabilistic modelling approach would be interesting to see, but that in this instance the water could be dealt with in the text.

Item 8: Review of potential risks from aluminium in the diet of 1 to 5 year old children and updated exposures for infants aged 0 to 12 months – TOX/2015/38

50. Dr Crevel declared that he was employed by Unilever who have previously used aluminium in some of their healthcare products. This was not considered a conflict and Members were happy for him to take part in discussions. Dr Diane Benford declared that she had been involved in the EFSA and Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) evaluations of aluminium.

51. The SACN had been undertaking a review of scientific evidence that would influence the Government's dietary recommendations for infants and young children. The 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, most of which had been completed, and now on young children aged 1 to 5 years. The reviews would identify new evidence that had emerged since the Government's recommendations were formulated, and would appraise that evidence to determine whether the advice should be revised.

52. This discussion paper provided estimates of aluminium exposures for children in the UK aged 1 to 5 years, and also an updated exposure assessment for infants

aged 0 to 12 months because new data had become available since the 2013 COT statement on potential risks from aluminium in the infant diet (Statement 2013/01[7]).

53. Members were content with the approach undertaken for the exposure assessment, including the age ranges used. It was decided that the evaluation of aluminium exposures would be written in the form of an addendum to Statement 2013/01.

54. Members requested that information be provided on the uptake of aluminium by soya plants and whether there were other species of plant that showed similar behaviour towards aluminium.

55. It was noted that there was no comment on the dermal absorption of aluminium, but Members agreed that this probably was not necessary in relation to young children. The Committee requested that a comment be included regarding aluminium nano-particles especially with regards to inhalation and any associated risks.

56. It was requested that further comments be made regarding aluminium in soil, especially with regard to aluminosilicates and their bioavailability. Members also requested that bioavailability of soluble/insoluble aluminium species be looked at in more detail and to comment on whether the diet or soil is the major route of aluminium exposure.

57. When looking at exposures from drinking water the Committee requested that median and 97.5th percentile levels of aluminium be used.

58. The Committee also requested that a standardised format be adopted for the tables.

Item 9: Paper for information: FSA Scientific Advisory Committees (SACs) update – TOX/2015/39

59. This paper was provided for information only.

Item 10: Any other business

60. The Secretariat wished Members a very happy Christmas and a successful New Year.

[7] Available with a lay summary at:
http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2013/aluminium

61. No other business was raised.

Item 11: Date of next meeting

62. Date of next meeting – Tuesday 2nd February 2016, Conference Rooms 4&5, Aviation House, 125 Kingsway, London, WC2B 6NH.