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

Minutes of the meeting held on Tuesday 5th September 2017 in Aviation House, London.

Present

Chairman:	Professor Alan Boobis	
COT Members:	Dr Phil Botham	
	Ms Jane Case	
	Dr Rene Crevel	
	Professor John Foster	
	Dr C Harris	
	Professor Roy Harrison	
	Dr Sarah Judge	
	Professor Brian Lake	
	Ms Juliet Rix	
	Professor Faith Williams	
	Professor M Wright	
Food Standards Agency (FSA) Secretariat:	Ms C Mulholland	FSA Scientific Secretary
	Mr B Maycock	
	Dr D Gott	
	Ms F Hill	
	Dr J Shavila	
	Ms R Acheampong	
	Dr D Hedley	
	Ms C Potter	
	Dr B Dörr	
Public Health England (PHE) Secretariat:	Britta Gadeberg	PHE Scientific Secretary
Assessors:	Prof Tim Gant	PHE
Officials:	Dr C Baskaran	FSA
	Mr M Willis	FSA
	Mr I Smith	FSA
Other Invited Experts and Contractors:	Prof P Aggett	SMCN
	Dr Sarah Bull	WRc

Dr Ruth Bevan
Dr Kate Vassaux
Ms Elena Ollett Home Office

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Announcements

1. The Chair welcomed Members and other attendees to the meeting.

2. The Chair welcomed Dr Barbara Dörr as a new member of the Secretariat

3. 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

4. Apologies were received from Members Prof J Cade, Dr M Graham, Dr J Thompson and Dr J Coulson (from whom tabled comments were received) and from Ms Michaela Benton, HSE.

Item 2: Minutes from the meeting held on 16th May 2017 - TOX/MIN/2017/03

5. The minutes were agreed subject to minor amendments and the addition of the following text to Item 8:

6. "The Committee discussed the storage of food products in the home during which mycotoxin levels may increase. Members were concerned that, as a result, exposures calculated just from concentrations measured in products in the TDS might not be representative."

Item 3: Matters arising from the meeting held on 4th July 2017

Item 3: Matters arising from previous meetings

7. PBDE statement. The draft statement on PBDEs had been revised. It would be sent shortly to the Chairman for clearance by Chairman's action.

8. Para 7: The draft final report of the joint COT/Scientific Advisory Committee on Nutrition (SACN) working group on potassium-based replacements was almost complete. It was expected to be published shortly along with the accompanying statements from the COT and SACN. The Secretariat was in discussion with the SACN secretariat to try and establish a firm date for publication. Given the delay to date, members requested that this be expedited to the extent possible.

9. Para 8: The finalised statement on iodine would be published once final comments had been received from SACN.

Item 7: Third draft statement on potential risks from nickel in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

10. Para 26: Statement on nickel. This was being finalised and would be shortly sent to the Chairman for clearance by Chairman's action.

Item 10: Second draft addendum to the 2013 COT statement on potential risks from vitamin A in the infant diet - TOX/2017/33

11. Para 44: Second draft addendum to the 2013 COT statement on potential risks from vitamin A in the infant diet. This would be published once final comments had been received by SACN.

Item 4: Joint Statement from the Scientific Advisory Committee on Nutrition and the Committee on Toxicity of Chemicals in food, Consumer products and the Environment: Assessing the health benefits and risks of the introduction of peanut and egg into the infant diet before six months of age in the UK

12. Para 5 of reserved minutes: Joint SACN/COT statement on assessing the health benefits and risks of the introduction of peanut and egg into the infant diet before six months of age in the UK. This statement had been published and was available at: https://cot.food.gov.uk/cotwg/joint-sacn/cot-working-group-on-the-timing-of-introduction-of-allergenic-foods-into-the-infant-diet/sacn/cot-working-group-report

Item 4: Second draft guidance for submission of papers to COT regarding irritant sprays and information required – TOX/2017/35

13. No interests were declared.

14. The Home Office Centre for Applied Science and Technology, CAST, regularly sought expert advice from the COT on the safety-in-use of formulations of irritant sprays for use by the police. To date, this has been on an ad hoc basis. Following the most recent discussions, it was agreed that the COT should provide specific guidance to applicants on the type of information that should be supplied to enable the Committee to develop an opinion about the safety of the formulation.

15. A first draft of this document was considered in February 2017. The updated version addressed the comments raised by COT at that time and had also been reviewed by CAST. It was requested that the Committee prioritise the information required for any evaluation, and also indicate what data were considered essential and what would be considered supplementary and suggest the types of test which

could be undertaken to address the list. Any guidance was likely to cover applications for new active substances or formulations.

16. Information had previously been requested on droplet size, but CAST noted that all operational sprays were delivered as a stream of liquid (as per the Home Office Standard). Members noted that information on distribution of particle size may help ascertain if any compound was respirable. Members queried whether it was possible to estimate the dose reaching the target person or the operators. The guidelines stipulated that the formulation should be sprayed from a pre-determined distance for maximal effects in the intended area. It was likely that the manufacturers would have information on the dose to the target person.

17. Members could not stipulate the specific methods to be used for providing toxicity information, but agreed that they needed to be in line with agreed international standards such as OECD. The guidelines should also note that alternative methods to testing in animals should be used where possible. Reference to some recommended toxicity testing strategies for chemicals should be provided.

18. The COT reiterated the need for manufacturers to make relevant information readily available for the evaluation of these compounds. It was agreed that the revised version of the guidance should include a reorganisation of the categories of the essential and supplementary information, and should highlight the value of active surveillance in target individuals as well as operators.

Item 5: Draft statement on reformulation of 2-chlorobenzylidine malonate (CS) as an irritant spray – TOX/2017/36 – Reserved Business

19. No interests were declared.

20. This item is reserved business as it is commercially confidential. The minutes are recorded separately and will not be published at this time.

Item 6: Review of the potential risks from T2 toxin, HT2 toxin and neosolaniol in the diet of infants aged 0 to 12 months and children aged 1 to 5 years – TOX/2017/41

21. Interests were declared by Professor Alan Boobis (Chair) who was a Member of the EFSA CONTAM panel that agreed the EFSA 2011 Opinion.

22. The Food Standards Agency (FSA) had completed a survey of 36 mycotoxins in the 2014 TDS – mycotoxins analysis (FSA, to be published). The results of the

survey included information on the concentrations of HT2 toxin, neosolaniol and T2 toxin in relevant foods. Estimates of dietary exposures had been calculated for each toxin for UK infants and young children aged 4 to 60 months using food consumption data taken from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) and the national diet and nutrition survey (NDNS).

23. Details of the concentration data derived from this survey, and the subsequent exposure assessments, had been presented to the Committee in a scoping paper (TOX/2017/30) at the July 2017 meeting. The Committee had requested that more information be provided around the derivation of the group TDI for T2, HT2 and neosolaniol. To aid the discussions, summaries of *in vivo* toxicological studies carried out since 2011 were provided. The derivation of all of the health based guidance values established by EFSA, JECFA and the SCF were detailed. A more in-depth exposure assessment had also been carried out on the TDS data.

24. The Committee discussed the use of the mink as an appropriate model for emesis in humans and considered whether it was relevant. It was noted that EFSA had used inter-individual but not interspecies uncertainty factors and this may have been suitable for establishment of the Acute Reference Dose (ARfD). More information on this was requested including any comparative data that were available.

25. There was also some concern that the BMDL range of the Benchmark Dose (BMD) analysis carried out by EFSA for the ARfD was too wide. The Committee thought that this indicated an unstable estimate as the upper and lower bound (BMDL-BMDU) varied by more than 10-fold and so seemed to conflict with current EFSA guidance. As the Committee had some concerns about an ARfD based on this POD, it was suggested that the Secretariat should model the data (using the PROAST software) and use model averaging to allow comparison of the estimates. The Committee also noted that when deriving the TDI the current EFSA guidance for BMD analysis had been used and that there was a need to be consistent.

26. Members discussed the use of the potency factors for the toxins and felt that the proportion of metabolite in relation to the parent compound was unclear and this made it uncertain whether the same potency should be assumed. It was unclear whether there were sufficient data available to resolve this and it was noted that a a large number of assumptions were being made. Any information on co-exposure was requested.

27. The Committee discussed the use of the TDS for exposure estimates of these mycotoxins and concluded that the data were unsuitable for this purpose, due to the extensive degree of mixing of different food items to form a given group. Thus, for non-ubiquitous contaminants the compositing of multiple food items into a group prior to analysis could result in significant dilution of levels that represent each TDS

food group. The Committee agreed that EFSA data and data from an FSA survey of oats in 2014 should be used to calculate exposures. It was requested that a comment also be included regarding possible exposures, or lack of exposures, in infants aged 0 to 4 months.

Item 7: Second draft statement on potential risks from cadmium in the diet of infants ages 0 to 12 months and children aged 1 to 5 years – TOX/2017/37

28. The Chair declared that he had been on the EFSA CONTAM panel involved in their 2009 Scientific Opinion on cadmium in food. No other interests were declared.

29. The Scientific Advisory Committee on Nutrition (SACN) was undertaking a review of scientific evidence that would inform the Government's dietary recommendations for infants and young children. The review of cadmium was part of a sequence of papers supporting this work. Public Health England (PHE) had produced information for the general public on the risks of exposure to cadmium but there were currently no Government dietary recommendations for infants and young children which relate to this metal.

30. A first draft statement (TOX/2017/28) was prepared and presented to the Committee on 4 July 2017. Members requested a number of amendments and typographical corrections be made. Of particular note were the Committee's views on the SUREmilk study, the section on the influence of industrial emissions and Cd in the food chain and breast milk and the wording or the overall conclusion to the paper.

31. Members were generally content with the changes made since the last meeting but made some further suggestions to clarify the meaning of various parts of the text.

32. Members agreed that the final draft statement could be finalised by Chair's action.

Item 8: Proposal for a breast milk analysis study using pre-existing samples held by Imperial College London – TOX/2017/38

33. The Chairman declared a personal non-specific interest as he was affiliated to the Centre at Imperial College London responsible for the study in question; it was agreed that he would chair discussion on the item but would not be involved in the formulation of the conclusions or recommendations on this item. Professor Harrison

declared a personal, non-specific interest as his colleagues at Birmingham University were involved in the ongoing study. He participated in the discussion, but was not involved in the formulation of the conclusions or recommendations on this item

34. Members had questions on the design of the study and how representative of contaminants in breastmilk for the general population the samples would be, since they were originally taken to investigate the impact of municipal waste incinerators (MWI). The Committee was informed that the samples could be considered as representative because, although a significant proportion of the population lived within 20 km of an MWI, emission control from such sites was currently very efficient and a large number of the samples were also taken from people who lived further than 20 km away from an MWI. The COT were also made aware of the large amount of demographic and dietary survey data collected from each participant, which would be available to the FSA and the Committee if funding were available to participate in this project. Members were also informed that analysis was being carried out in contract laboratories with accredited methods to maximise the analyses that could be carried out on each sample.

35. It was noted that designing and commissioning a new study of breastmilk that would fill the data gaps identified by the Committee would be prohibitively expensive and given the difficulties in collecting samples, would still not result in a perfect dataset. Therefore, collaboration in this pre-existing study would be a value for money alternative that would give the FSA and COT the opportunity to recommend future analyses as well as gain access to useful data from analyses that have already been funded. Members were clear that prioritisation of chemicals needed to take into account the amount of toxicological data: exposure data with little or no toxicological background data would not be useful. Overall, given the lack of robust breastmilk data available at the time, the committee considered that this would be a valuable addition to the current dataset.

36. The Committee asked the Secretariat to liaise with the study co-ordinators to produce a list of priority chemicals to fill the data gaps for chemicals for which exposure reduction may be a possibility, for discussion at a future COT meeting.

Item 9: Discussion paper on the potential risks from chromium in the diet of infants ages 0 to 12 months and children aged 1 to 5 years – TOX/2017/39

37. No interests were declared.

38. The review of chromium was one of the series of topics considered as part of the COT contribution to the SACN review of scientific evidence that would inform the Government's dietary recommendations for infants and young children. There were

currently no Government dietary recommendations for infants and young children which relate to chromium.

39. Members concluded that the evidence chromium was an essential trace element in humans was doubtful at best.

40. It was agreed that information was necessary to explain why chromium appeared to be an intestinal carcinogen in rats and mice but not in humans after ingestion: the papers on which EFSA based this assertion should be considered by the committee. The statistical association between Cr(VI) inhalation and lung and paranasal cancer should also be reviewed.

41. Members suggested that more emphasis should be placed on chromium sensitisation since this metal was regarded as almost as potent as nickel in this respect.

42. The Committee concluded that aggregate exposures were unnecessary, given the minor contribution of sources other than the diet. It was also agreed that, in view of the large margins of exposure, chromium could be included in the overarching statement on metals in the infant diet, when this was written, rather than as a statement on its own, with a table summarising the intakes from different food types.

Item 10: Second draft statement on the results of the 2014 survey of metals and other elements in infant foods – TOX/2017/40

43. Interests were declared by Professor Alan Boobis (Chair) who was a Member of the EFSA CONTAM panel when the Scientific Opinions on cadmium, arsenic and lead were prepared.

44. The Food Standards Agency (FSA) had completed a survey of 15 elements in the 2014 survey of metals and other elements in infant formula, commercial infant foods, and other foods (non-infant specific foods) (FSA, to be published). The results of the survey provided information on the concentrations of aluminium, antimony, arsenic (including inorganic arsenic), cadmium, chromium, copper, iodine, iron, lead, manganese, mercury, nickel, selenium, tin and zinc in these foods. Estimates of dietary exposures had been calculated for each element for UK infants and young children aged 4 to 18 months using food consumption data taken from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013).

45. Details of the concentration data derived from this survey, and the subsequent exposure assessments, were presented to the Committee in discussion papers (TOX/2016/29) and (TOX/2017/18) and a first draft statement at the July 2016 March and July 2017 meetings, respectively. To aid the discussions, brief toxicology summaries for each of the elements surveyed were included. The Committee commented on the concentration data and the results of the exposure assessments, and suggested some revisions to the wording of the toxicological summaries. This second draft statement (Annex A) contained updated toxicological summaries and conclusions.

46. One of the Members had investigated the speciation of metals and their analysis and updated the Committee. It was noted that some metals occurred in different forms e.g. organic or inorganic, or in different valency states and it would help to refine exposure assessments if specific analysis could be achieved. Information received from the different commercial laboratories that had been contacted indicated that it was difficult to analyse the different forms of some metals and that, in general, they tended to analyse only total metal concentrations. However, arsenic and inorganic arsenic could be analysed separately and some laboratories would soon be able to analyse methylmercury separately from inorganic mercury.

47. Following a question at a previous meeting, the Committee decided that a discussion of food grown on allotments should not be included in this statement, as this was outside the intended scope of the survey. However, consideration should be given as to whether home grown produce should be reviewed in more detail as a separate issue.

48. It was agreed that this statement could be finalised by Chair's action; it would then be published later this year.

Item 11: Toxicological evaluation of novel heat-not-burn tobacco products: preliminary review of literature from sources not associated with product manufacturers and developers

49. Professor Boobis declared that he was a member of the World Health Organization Study Group on Tobacco Product Regulation (WHO TobReg) and Chairman of the International Organization for Standardization (ISO) Technical Committee (TC) 126 Working Group 10 on "Intense smoking regime". Professor Williams declared a personal non-specific interest in that her brother-in-law was a retired senior manager from British American Tobacco and in receipt of a pension. It was agreed that, while Professor Williams could contribute to the discussion, she should not contribute to the conclusions.

50. The COT, with support from the Committees on Mutagenicity (COM) and Carcinogenicity (COC), had been asked to assess the toxicological risks from novel heat-not-burn tobacco products, and to compare these risks with those from conventional cigarettes. The Committees had considered scoping papers on the topic at previous meetings and, at the COT meeting in May 2017, in which members of COC and COM participated, presentations of data by manufacturers of two heat-not-burn products that had been notified to PHE in accordance with the Tobacco and Related Products Regulations 2016. The Committees had requested a review of the literature on heat-not-burn tobacco products published by sources that were independent of the developers/manufacturers of these products. Literature searches had been performed and the results were reported to this meeting.

51. The aim of the review was to consider to what extent the results of independent studies were consistent with or contradicted the results reported by the heat-not-burn product companies. A total of nine independent papers on heat-not-burn tobacco products had been identified. These included one that examined components of mainstream emissions and two that examined side-stream emissions; one that studied immunotoxicity *in vitro*; one that evaluated acute subjective and physiological measures in human volunteers; one clinical case report that associated the use of a heat-not-burn tobacco product with acute eosinophilic pneumonia; and three reviews and commentaries on heat-not-burn and other products, their marketing and use.

52. A study of chemicals in the mainstream aerosol of one heat-not-burn product reported results similar to those of the companies. In contrast, an *in vitro* immunotoxicity study appeared to indicate similar or worse results than conventional cigarettes. However, this study was difficult to interpret due to it having examined effects on dendritic cells. It was also observed that the heat-not-burn product tested was not one of those notified to PHE and was not on the UK market.

53. A Member noted that a review had reported studies suggesting that “less harmful cigarettes” may be more harmful than conventional cigarettes due to variations in puffing or post-puffing behaviour of users, differences in physical and chemical characteristics of the inhaled aerosols and longer exposure conditions. It was noted this appeared to be the interpretation of the authors, while the Committee’s aim was to identify any new primary data; however, the Committee highlighted the lack of knowledge on the nature and pattern of use and on the demographics of the users of these products.

54. Overall the Committee concluded that very little information was available from the independent literature. It had sought to determine the extent to which data from the independent literature verified or not the research by manufacturers of heat-

not-burn products it had already seen. The limited data available did not appear to contradict the data already reviewed by the Committee.

Item 12: Heat-not-burn tobacco products – second draft statement

55. Professor Boobis declared that he was a member of the World Health Organization Study Group on Tobacco Product Regulation (WHO TobReg) and Chairman of the International Organization for Standardization (ISO) Technical Committee (TC) 126 Working Group 10 on "Intense smoking regime". Professor Williams declared a personal non-specific interest in that her brother-in-law was a retired senior manager from British American Tobacco and in receipt of a pension. It was agreed that while Professor Williams could contribute to the discussions, she should not contribute to the conclusions.

56. The first draft statement had been considered by the COT and Committee on Carcinogenicity (COC) at their July 2017 meetings and also by correspondence, after the COC meeting, by Members of the COC and Committee on Mutagenicity (COM). The COT was asked to consider a revised draft statement.

57. This item was taken as reserved business as it would potentially include discussion of commercially sensitive information. The minutes have been recorded separately and will not be published at this time.

Item 13: Paper for information: FSA Scientific Advisory Committees (SACs) update – TOX/2017/34

58. This paper was provided for information.

Item 14: Any other business

59. The Committee was asked to suggest speakers for the proposed microbiome meeting to be held in the 6th February 2018. The venue had yet to be finalised but would probably be outside London.

60. The risk assessment on the recent incident on fipronil in eggs was tabled for comment. The Chair pointed out that a standard 100-fold uncertainty factor had been used to derive the ADI and ARfD for fipronil and that individuals who had ingested doses of fipronil at the level found in these eggs would be unlikely to suffer irreversible effects.

61. The Committee was informed that they were free to comment on the FSA Social Science review.

62. The Committee was asked to begin considering the regulatory toxicological requirements and any necessary changes to the existing Scientific Advisory Committees post-EU exit, including the decisions that may be delegated to the Secretariat.

63. A poster on the feeding of infants and young children had been accepted by Eurotox and would be presented at the 2017 meeting.

Date of next meeting

64. There will be a Joint COT/COC/COM meeting on Monday 9th October at PHE Chilton.

65. The next COT meeting will be on 13th December 2017. The location for this meeting will be confirmed neater the date