Minutes

Final minutes of the 10th May 2022 meeting

Meeting of the Committee at 10:00 on 10th May 2022 at Mary Ward House, London and on Microsoft Teams

Present

Chair:	Prof Alan Boobis

COT Members:	Dr Phil Botham
	Ms Jane Case
	Dr Stella Cochrane
	Dr James Coulson
	Professor Gary Hutchison
	Professor Thorhallur Ingi Halldórsson
	Dr Sarah Judge
	Dr David Lovell
	Professor Shirley Price
	Dr Mac Provan
	Ms Juliet Rix
	Dr Michael Routledge
	Dr Cheryl Scudamore
	Dr Natalie Thatcher
	Professor Matthew Wright
	Professor Maged Younes

Professor Paul Haggarty	SACN Liaison
Professor John O’Brien	Science Council Liaison

	Ms Cath Mulholland	
	Ms Claire Potter	
	Dr Alex Cooper	FSA Scientific Secretary
Food Standards Agency (FSA)	Dr Olivia Osborne	
Secretariat:	Mr Michael Dickinson	
	Ms Emma French	
	Ms Rhoda Aminu	
	Ms Sabrina Thomas	
	Dr Gail Drummond	
	Ms Cleanncy Hoppie	
	Ms Sophy Wells	
	Dr Gaetana Spedalieri	
	Mr Thomas Hornsby	
	Mr Lawrence Finn	
	Dr David Gott	
	Mr Shaddad Saleh	
	Dr Emily Hudson	
	Dr David Kovacic	
	Mr Alexander Smith	

UK Health Security Agency (HSA) Secretariat:	Ms Britta Gadeberg	UK HSA Scientific Secretary
Invited Experts and Contractors:	Dr Sarah Bull	Institute of Environment and Health (IEH) Consulting
	Dr Ruth Bevan	IEH Consulting
	Dr Kate Vassaux	IEH Consulting
Assessors:	Ms Valerie Swaine	Health and Safety Executive (HSE)
	Prof Tim Gant	UKHSA
	Dr Sam Fletcher	Veterinary Medicines Direct orate (VMD)
	Mr Ian Martin	Environment Agency
	Ms Frances Hill	Department of Business, Enterprise and Industrial Strategy (BEIS)
	Ms Susannah Brown	Office of Health Improvement and Disparity (OHID)
Observers	Dr Emma Bradley	FERA
	Mr Alexander Kalian	Kings College London

	Mr Adib Khondkar	
	Dr Amie Adkin	
	Prof Rick Mumford	
	Mr Vincent Greenwood	
	Mr Tim Chandler	
	Ms Nuala Meehan	
	Ms Tasila Mwale	
	Mr Miguel Guijarro	
FSA and other Officials:	Ms Eli Amanatidou	FSA
	Mr Mark Willis	
	Ms Frederique Uy	
	Ms Ben Haynes	
	Ms Ayah Wafi	
	Ms Katie Mears	
	Ms Emily Pycroft	
	Ms Annalisa Leone	
	Ms Afielia Choudhry	
	Ms Adekunle Adeoye	

Ms Sharon Gilmore	FSA NI
Ms Catherine Cleland	
Dr Marianne James	
Mr Will Munro	Food Standards Scotland (FSS)
Ms Krystle Boss	
Ms Lucy Smythe	
Dr Alison Gowers	UKHSA/ Committee on the Medical Aspects of Air Pollution (COMEAP) Secretariat (Item 4)
Mr Nigel Dowdall	Civil Aviation Authority CAA (Item 7)
Ms Rachel Elsom	OHID
Mr James Issac	
Ms Helen Nakeeb	UKHSA
Dr Ovnair Sepai	
Dr Helen McGarry	HSE (Item 4 and 5)
Ms Ruth Coward	DEFRA (Item 4 and 5)
Mr Edward Latter	DEFRA (Item 4 and 5)

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Date of the next meeting	12th July 2022

Announcements

1. The Chair welcomed Members and other attendees.

Interests

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

Item 1: Apologies for absence

3. Apologies were received from COT Members Prof. Mireille Toledano, Dr Simon Wilkinson and Professor Philippe Wilson. Apologies were also received from Mr Barry Maycock, Dr Barbara Doerr, Dr Joseph Shavila, Ms Chara Tsoulli, Ms Jocelyn Frimpong-Manso and Ms Chloe Thomas of the Secretariat.

Item 2: Draft Minutes from the meeting held on 29th of March 2022 (TOX/MIN/2022/03)

4. There were no comments and the minutes and reserved minutes were accepted as an accurate record.

Item 3: Matters arising from the meeting held on 29th March 2022

Matters arising: First draft statement on vitamin D exposure levels in formula fed infants and children (TOX/2022/27*)*

5. In 2006, the European Commission established a minimum vitamin D content for infant- and follow-on formulae of 1 µg per 100 kcal (Directive 2006/141/EC). Subsequently in 2016, in Commission Delegated Regulation 2016/127, this was doubled to 2 µg per 100 kcal. This new regulation became applicable in Great Britain from the 1st of January 2021. EU legislation on

nutrition continues to be directly applicable in Northern Ireland.

6. In order to inform discussion across the four nations on whether existing advice around vitamin D supplements remains appropriate or needed updating in light of the increase in the minimum vitamin D content of infant- and follow-on formulae, the FSA has conducted an exposure assessment to determine whether this increase could result in infants (0 – 12 month-olds) and young children (1-4 year-olds) exceeding their tolerable upper levels (TULs).

7. This first draft statement presented in paper TOX/2022/27 provided an exposure assessment for infants and young children, regarding their vitamin D intake from infant formulae products, vitamin D supplements, and other dietary sources (including breast milk) compared to the relevant EFSA TULs, one of which had been recently revised: Members had previously requested additional information setting out the rationale for the revision of the TUL for 6 - 12 month-olds from 25 to 35 µg/person/day. The Committee agreed with the revised TUL for this age group of 35 µg/person/day.

8. The Committee concluded that the new minimum vitamin D content in infant formulae did not lead to excessive vitamin D exposure in infants or young children, as minor exceedances of their respective TULs occurred only when, in combination with other sources such as the recommended supplements, the quantities of infant formula consumed reached 1000 ml. Current NHS guidance is that supplementation is not needed if more than 500 ml infant formula is being consumed.

9. The Committee concluded that UK government guidance on vitamin D supplementation should include consideration of the nutritional recommendations of the Scientific Advisory Committee on Nutrition (SACN). It would therefore not be appropriate for the COT to make any specific recommendation for a change in the UK guidance, based purely on consideration of the possibility of adverse effects from high intakes. However, the Committee agreed that the outcome of the exposure assessment indicated that the current guidance did not give rise to any toxicological concerns.

10. It was agreed that the Statement could be finalised by Chair’s action.

Chemical strategy

11. The Committee were informed about the developing UK chemical strategy being produced by the UK Government and the devolved administrations. This

was a component of the 25 year Environmental Plan which was published in 2018. The plan provides a framework for future policy decisions and enables, for example, UK REACH to reflect decisions on how to manage chemicals and enable external stakeholders to review the decisions as part of a wider strategic approach.

12. The Committee were informed that the plan was intended to be a UK cross government strategy. Member of the working groups responsible for developing the strategy include representatives from Defra, UKHSA, HSE, EA, Department for International Trade (DIT) and the devolved administrations.

13. Members were informed that the external stakeholder engagement phase of the chemical strategy had now begun and was started by a Ministerial round table meeting on the 27th of April. A series of stakeholder workshops will be held over spring/summer 2022 addressing some policy themes including actions to address priority chemical issues, managing of chemicals throughout their life cycle and sustainable chemistry. COT, COC, COM and the Hazardous Substances Advisory Committee (HSAC) will be invited to participate in the workshops along with UK-wide external associations including industries, Non Governmental Organisations (NGOs) and academia.

14. The workshops are due to begin at the end of May and Members could indicate their interest in attending.

Item 4: First draft sub-statement on the effects of microplastics – inhalation route (TOX/2022/28)

15. Professor Boobis declared a non-personal specific interest as he was a member of a WHO expert group undertaking an assessment of the human health risks to micro- and nano-plastic particles (MPs and NMPs), as a follow-up to their drinking water assessment. He was also involved in an ILSI Europe-convened multi-stakeholder round table discussion to identify data gaps in the assessment of the risk to human health of microplastics. No other interests were declared.

16. In 2019, as part of horizon scanning, the COT identified the potential risks from microplastics as a topic it should consider, to inform FSA discussions on this area (TOX/2019/08). Since then, several discussion papers have been presented to the Committee (Annex A1 of paper TOX/2022/28) and in 2021, the COT published an overarching statement on the potential risks from exposure to

microplastics (COT Statement 2021/02). This provided a high-level overview of the current state of knowledge, data gaps and research requirements with regards to this topic. This was followed by a more detailed sub-statement covering oral exposure.

17. As there is evidence for the presence of plastic particles in indoor and outdoor air, inhalation is a possible route of exposure.

18. The purpose of the sub-statement was to provide supplementary material to the overarching statement and to consider in detail the potential toxicological risks of exposure from microplastics via the inhalation route. It is based on currently available literature and data from internal tools at the UK FSA (these internal tools include: a literature search application and signal prioritising dashboards). Members were invited to comment on the draft sub-statement.

19. The Committee agreed that a definition of MPs/NMPs was required as it was unclear whether some studies were referring to microplastic particles or particles in general, with extra details also being needed on exposure and an environmental description. Members suggested that this terminology should be introduced at an early stage in the document. It was also noted that the terminology used referred to primary and secondary particles but this was not relatable to plastics, instead the terms fresh and aged should be used.

20. Members commented that different metrics were used in different studies, or no metrics used, making comparisons difficult, highlighting the need for standardization in experiments. Members agreed that clarification was needed for historic papers since there was limited information on the characterization of microplastics and on the units of measurement used in these studies.

21. Members recommended a search be carried out to find reviews and to cross reference with studies of synthetic fibres, particularly the importance of aspect ratio and rigidity in their toxicological effects, including information on confounders and duration of exposure.

22. The Committee were informed that the 2015 COMEAP statement mentioned in the draft sub statement referred to secondary particles in general and a more recent 2020 statement from COMEAP referred to non-exhaust emissions, including tyre-wear particles, and this should be added to the statement.

23. Members suggested removing reference to impact on human lung health for experiments that used cell lines only. Members raised the issue that 3D

models were now being used and the statement should discuss the available models. Members agreed that more information was needed in relation to NAMs, with a suggestion to move the section to either the conclusion or the background.

24. On the issue of observed alterations, the Committee considered that there was little or no histological evidence and therefore caution needed to be given to the weighting of the Lim et al. 2021 *in vivo* study (Chemosphere 262: 128330).

25. The Committee discussed the possible presence of pre-formed Reactive Oxygen Species (ROS) in microplastics, given the very short half-life of most ROS. As the topic was speculative it was suggested to add this information as a diagram. In addition, more information needed to be included on the different pathways involved e.g. macrophage and neutrophil influx.

26. Members agreed that transport modelling of microplastics and how they interact with other chemicals/substances in the environment looks at specific components instead of the overall picture, and it would be expected that different particle compositions would have different toxicities. It was also noted that particle reference standards were needed.

27. The list of data gaps was discussed by the Committee who agreed that methods for the detection of microplastics in tissues and their systemic effects should be included.

28. Members discussed the research priorities and suggested that they should be prioritised and a call put out to researchers; a workshop to discuss this might be useful.

Item 5: Evaluation of the potential approaches to mixture risk assessment for future UK REACH assessments - update (TOX/2022/29)

29. Professor Alan Boobis stated that, as declared previously, he had participated in the European Horizon 2020 project EuroMix on mixture toxicology. It was agreed that this interest did not prohibit him from taking part in the discussion. No other interests were declared.

30. In March 2022, a report was presented to the Committee, authored by the UK Health Security Agency (UKHSA) and the Environment Agency (EA) (supported by IEH Consulting). The report evaluated potential approaches for risk assessment

of unintentional mixtures under UK REACH. It had been produced at the request of the UK Chemicals Delivery Board, as the EU are considering the use of a Mixture Assessment Factor (MAF) for addressing the risks from unintentional mixtures under EU REACH. Following Members' comments in the March meeting, the report was updated, in particular to strengthen the conclusions in Section 6 - recommendations on how to assess mixture risks. The COT's views were sought on the science supporting the conclusions in the updated report.

31. It was noted that the FSA and US Environmental Protection Agency (EPA) had both previously carried out an appreciable amount of work on chemical mixtures. This work was not included in the report because it had focused more on the methodology of mixture risk assessment, as opposed to the need for a MAF, and so was beyond its scope. It was noted that these workstreams did not change the conclusions of the report.

32. Members recognised that while there were publications hypothesising that environmental mixtures of chemicals might have an additive effect, the evidence available suggested that any potential effects were almost always driven by exposure to a small number of chemicals, even when there were a large number of substances in the mixtures considered. It was noted that, in addition, similar findings had been reported in three European Food Safety Authority (EFSA) retrospective cumulative risk assessments of dietary exposure to mixtures of pesticide residues, which could be cited in the report. The Committee also noted the lack of research available to address the question of whether there was dose addition for chemicals present in a mixture at concentrations below their health-based guidance values (HBGVs). In many studies, whilst findings at effect levels were consistent with dose addition, they were also consistent with response addition (independent action). Hence, whilst dose addition might be a reasonable default at exposure levels above health-based guidance values, it was highly questionable whether this was the case at lower levels and consequently whether a MAF was needed.

33. Overall, Members agreed with the revised report. The Committee concluded that the recommendations made by the COT in the March meeting had been satisfactorily addressed and agreed with the conclusions drawn in Section 6. In particular, the Committee agreed that there was strong scientific evidence within the report to support not adopting the use of a MAF in human health risk assessments.

34. It was agreed that the minutes from the COT's discussion would be presented to the Chemicals Delivery Board, along with the updated report. These

would be used to inform policy decision making over the adoption of a MAF in risk assessments involving unintentional mixtures under UK REACH.

Item 6: UK legislation on Food Contact Materials – an overview – Presentation by FSA FCM policy team

35. The Committee have been discussing a number of food contact materials (FCM) items over the past year and were given a presentation providing an overview of the current UK legislation on FCMs.

36. The categorisation of advanced materials was discussed by the Committee. It was highlighted that advanced materials may be categorised as active and intelligent materials, but it was necessary to look at the individual components of the final article. If it fails to meet these criteria, then it would fall under the framework requirements. However, the Plastics Regulation does include multi-component materials.

37. The Committee discussed the practical implications of regulations for testing that needs to be carried out for a new bio-based material. It was noted that a number of steps would need to be adhered to by the Food Business Operator (FBO).

38. Members were informed that the policy team were looking to reform the legislation on FCMs, in line with the proposals by the EU, in order to make things more practical for operators, but ultimately to ensure that products placed on the market would be safe for consumers.

39. The Committee were made aware that in the case of materials with multiple uses, it was hoped that the FBOs were using due diligence. However, in some situations the regulations may not be applicable for the product produced and therefore, a cross-cutting approach might be needed.

40. There was close collaboration between FCM policy at the FSA and other Government Departments, allowing the FBOs to be signposted to the relevant Department.

41. Members were informed that environmental considerations were being taken into account, but the main focus of legislation would be on the human health implications.

Item 7: Introductory paper to an update of the COT position on aircraft cabin air (TOX/2022/30)

42. The paper was prepared by IEH consulting on behalf of UK HSA. An interest was declared since Professor Paul Harrison of IEH Consulting is an author on some of the papers identified in the search; the work was undertaken while he was at Cranfield University. This was not considered to be a conflict for the COT.

43. The COT have previously reviewed aircraft cabin air, publishing a statement on aircraft cabin air in 2007 and a position statement in 2013. The COT have been asked by the Department for Transport (DfT) to review any new data that have been published and to re-evaluate their previous views set out in the original statement and the position statement. Paper TOX/2022/30 outlined the literature searches undertaken to update the evidence base and set out an outline of proposed topics for consideration.

44. Members noted that data from 2002 onwards was deemed more relevant when pilots started to be locked in the cockpit and smoking had been banned in the cabin. It was mentioned that there was limited data on which to undertake a risk assessment, as well as limited information on how aircraft cabins differ from other work environments. For the majority of aircraft, the source of air for the cabin was bleed air from the engines, but there were some for which this was not the case. Major fume events were rare, making sampling of fume events challenging.

45. Recently, research on concentrations of ultra-fine particles under different flight conditions had been published, with minimal amounts of particles being measured during cruising but with potentially increased exposures during take-off and landing. It was suggested that organic compounds may be adsorbed on to particles.

46. The total chemical environment of the cockpit and cabin was not clearly understood and it was agreed that it was difficult to define a hazard. The Committee agreed that exposure levels should be put into the wider context of other environments. It was noted that advice could be sought from aircraft engineers on aircraft environmental control systems.

47. There were some discussion on what a fume event was and whether there was any follow up, including biomonitoring. It was noted that in COT’s previous statements, the potential for a nocebo effect had been discussed. A number of

factors, in addition to potential chemical exposures, have potential to impact on health in the cabin air environment especially from an occupational perspective, including time zone shifts, altitude and work practices.

48. The European Aviation Safety Agency (EASA) had continued to commission research after the DfT commissioned work COT had previously considered, and the Committee requested sight of this research. It was agreed that clarity should be sought on the problem formulation for this piece of work from DfT and CAA to ensure that the advice provided by the Committee best meets their needs, particularly on whether the focus should be on fume events with short-term high exposures, or on the chemical environment of the cockpit and cabin more generally.

Item 8: Lead in the maternal diet statement (TOX/2022/32)

49. No interests were declared.

50. This item is part of the ongoing work programme of work on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth, and up to 24 months after delivery being conducted by the Scientific Advisory Committee on Nutrition (SACN), with the COT advising on the effects of chemical contaminants and excess nutrients in the diet.

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

52. The Committee considered a discussion paper on lead at the March 2022 meeting and a number of recommendations were made by Members, which were incorporated into this first draft statement. These included; an additional exposure assessment of lead from soil and dust, further information on lead exposure from the air and clarification of lead resorption from bone during pregnancy. This first draft statement sought to address the points raised following the discussion paper.

53. The Committee requested that it should be clarified in paragraph 3 that the January 2020 meeting noted was a COT meeting.

54 Members discussed the occurrence of pica in the population and suggested that up to 20% of women experience pica and therefore it may not be

‘uncommon’ as suggested. The Committee suggested that an additional review of the literature should be performed to determine whether more specific information could be identified and included in this section.

55. The Committee requested that an additional aggregate exposure assessment should be included, in order to understand combined risk from all sources. It was stated that this should not just be a summation of worst-case scenarios.

56. Members suggested that a review of the wording in paragraph 51 should be considered in relation to the use of the phrase ‘clinically significant’. Members suggested that the phrase ‘unlikely to be a health concern at this level of exposure’ would be more suitable.

57. A second draft of the statement will be presented to Members in due course

Item 9: Review of the potential risks of Ochratoxin A in spices at the new proposed Codex MRLs (Reserved) (TOX/2022/31)

58. No interests were declared.

59. The COT were asked by policy colleagues in the FSA to review the toxicity of OTA in spices, at current UK/EU maximum levels (MLs) and at the recently proposed MLs by the Codex Alimentarius Commission (Codex). This item may inform FSA policy and is currently reserved.

Item 10: Paper for information: Update on the work of other scientific advisory committees (TOX/2022/33)

60. This paper was circulated for information. Members were asked to send in any questions or comments on the document to the Secretariat.

Item 11: Any other business

61. There was no other business.

Date of next meeting

62. The next meeting of the Committee Meeting will be at 10:00 on the 12th of July 2022 in person and via Skype or Teams, at Broadway House, Tothill Street, Westminster, SW1H9NQ.