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

Minutes of the meeting held on Tuesday 28th March 2017 in Aviation House, London.

Present

Chairman:	Professor A Boobis
Members:	Prof D Harrison
	Mr D Bodey
	Prof J Cade
	Dr R Crevel
	Dr M Graham
	Dr A Hansell
	Dr J Thompson
	Prof B Lake
	Prof I Morris
	Prof R Smith
	Prof F Williams
Food Standards Agency (FSA) Secretariat:	Dr D Gott
	Ms C Mulholland
	Mr B Maycock
	Ms H Gbormittah
	Ms F Hill
	Ms R Acheampong
	Dr D Hedley
	Dr J Shavila
	Ms K Sturgeon
	Ms C Potter
Public Health England (PHE) Secretariat:	Ms B Gadeberg
	Dr O Sepai

Invited Experts and Contractors:	Prof P Aggett	SMCN	
	Halina Garavini	Imperial College London	
	Nicole Robbins	Sabre	Item 9
	David Nance	Sabre	Item 9
	Robert Nance (All Sabre experts via TC from USA)	Sabre	Item 9
Observers	Prof John Foster	New COT member	
	Prof Matthew Wright	New COT member	
	Dr Phil Botham	New COT member	
	Dr Sarah Judge	New COT member	
	Ms Juliet Rix	New COT member	
	Ms Jane Case	New COT member	
Officials	Alastair McArthur	PHE	
	Rachel Elsom	PHE	
	Ian Smith	FSA Contaminants Branch	
Assessors:	Michaela Benton	HSE	

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Announcements

1. The Chair welcomed Members and other attendees to the meeting, including the new members attending as observers.

2. The new members present were Professor John Foster, Professor Matthew Wright, Dr Phil Botham, Dr Sarah Judge, Ms Juliet Rix and Ms Jane Case. This was the last meeting for Dr Nick Plant, Mr Derek Bodey, Professor Rob Smith, Dr Anna Hansell, Professor David Harrison, Professor Brian Houston and Professor Ian Morris. Professor Janet Cade had agreed to serve one further year until another epidemiologist is appointed to the Committee.

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 Prof B Houston, Prof Roy Harrison, Dr James Coulson, Dr Nick Plant and Dr Caroline Harris of the Committee, Dr Ovnair Sepai from PHE and PHE assessor Prof Tim Gant.

Item 2: Draft minutes of the meeting held on 7th February 2017.

5. The minutes were agreed with minor amendments.

Item 3: Matters arising from the meeting held on 7th February 2017

Item 3: Matters arising from previous meetings:

6. The SACN/COT sub-group on the timing of introduction of allergenic foods into the infant diet

The subgroup met on 17th March and finalised its conclusions. The COT was updated on the conclusions reached, which will be published in due course.

7. Para 7: COT recruitment. The secretariat had been authorised to recruit new members and had been asked to look at new ways of targeting specialities that are required but had been hard to fill.

8. Para 9: PBDE statement. The draft statement on PBDEs had been finalised and was ready to be cleared by Chairman's action.

9. Para 11: The draft Statement on evidence regarding maternal and infant dietary exposures and risk of atopic outcomes and autoimmune disease was still in the process of being finalised ahead of clearance by Chairman's action. Dr Robert Boyle was carrying out an updated literature review to revise the systemic review for publication. This would put it out of alignment with the COT statement. However it is unlikely that the conclusions would change.

Item 4: Potential future discussion items

10. Para 14: The joint COT/COC/COM meeting will take place on Monday 9th October at PHE in Chilton. The meeting will focus on whether and how epigenetics could be taken into account in risk assessment but will also provide opportunities for horizon scanning.

Item 6 First draft addendum to the 2013 COT statement on potential risks from vitamin A in the infant diet.

11. Para 26: The addendum would be finalised shortly.

Item 8: Potassium based replacements for sodium chloride and sodium based additives

12. Para 37: The draft final report of the joint COT/Scientific Advisory Committee on Nutrition (SACN) working group on potassium based replacements was discussed at the SACN meeting on the 16th March. SACN were broadly content with the report but had several questions and suggestions. These would be addressed by the Secretariat and it was hoped that the report can be cleared by Chairman's action and published shortly along with the accompanying statements from COT and SACN.

Item 12: Toxicological evaluation of novel tobacco products

13. Para 1 (reserved business): The May COT meeting has been set aside to allow the manufacturers of novel tobacco products to make presentations to the three expert committees (COT, COC and COM) and to allow the expert committees the opportunity to question the different manufacturers and discuss the topic.

Item 10: Draft guidance on submission of papers to COT regarding irritant sprays and information required (reserved business)

14. Para 11 (reserved business): CAST have provided some input on the draft list of requirements for irritant sprays. PHE may therefore bring this back to the Committee for further discussion later in the year

Item 11: Draft statement on a new formulation of PAVA irritant spray (reserved business)

15. Para 17 (reserved business): The draft statement on TW1000 irritant spray has been finalised and will be sent for clearance by Chairman's action shortly.

Item 4: Reports of the COT-COC Synthesising Epidemiological Evidence Subgroup (SEES) TOX/2017/13

16. At the meeting in October 2014 the Committee discussed a proposal to produce guidance on the COT's approach to assessing the quality of epidemiological research and synthesising the evidence that it generated since there was currently no written documentation that could potentially be made available on the website to aid the transparency of the risk assessment process. Development of such guidance would provide a timely review on current practice and support for members and secretariat. It was noted that various expert bodies were working on similar initiatives; these included a working group of the Food Standards Agency (FSA)'s General Advisory Committee on Science (GACS), which was looking at the use of scientific evidence more generally and the European Food Safety Authority (EFSA), which was developing guidance on the weight of evidence (see Item 13 below). An expert workshop on "Implementing systematic review techniques in chemical risk assessments: challenges and opportunities" was held in November 2014 at the Royal Society of Chemistry. A follow-up workshop on "Implementing systematic review methods in chemical risk assessment: addressing the challenges of problem formulation and quality assurance" was held in December 2016 and subsequent activity has been aimed at finalising a code of practice for publication. The Department for the environment, food and rural affairs (DEFRA)'s Hazardous Substances Advisory Committee had produced a document on evaluation of risks from chemicals. In addition, the Chartered Institute of Environmental Health, the United States Environmental Protection Agency, and the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) were pursuing initiatives in this area.

17. At the COT meetings in October and December 2014, Members agreed that it would be useful and timely to set out how the COT looked at evidence, in the light of guidance from other groups, since although the COT process was considered to be robust, it was not explicitly documented. This was also discussed by COC at its

meeting in November 2014, which welcomed the initiative and agreed that a small working group lead by a COT Member and including epidemiologists from the COC, should undertake this task. The objective would be to produce an overview document explaining the approach of the COT and COC, which would also draw on what other groups were doing, including the Committee on the Medical Effects of Air Pollutants (COMEAP). It was agreed that initially the guidance would focus on epidemiology, and a decision could then be made on whether to extend it to include the assessment of toxicological evidence from studies in experimental animals and other model systems (e.g. *in vitro,* computational) .

18. The subgroup met on four occasions between July 2015 and February 2017. During this time the scope of review was refined and the approaches to epidemiological evidence used by the COT and COC were reviewed. Scoring systems and methods for systematic reviews of epidemiological evidence were discussed in depth.

19. The subgroup produced a report entitled “Report of the Synthesising Epidemiological Evidence Subgroup (SEES) of the Committee on Toxicity and Committee on Carcinogenicity”, intended to form the basis of a guidance document (referred to below as the Report). The subgroup also produced a document entitled “Report on SEES subgroup methods of working and recommendations”, which served as a record of the subgroup’s activities. The Report had been discussed at the meeting of the COC on 23rd March 2017 and received favourable review. The Report would provide useful guidance for new Members and for the secretariat.

20. The Chair thanked Dr Hansell for leading the subgroup and preparing and presenting the documents.

21. The Committee discussed the documents. It was highlighted that the Report would reinforce what is already done and formalise the process. It would also help increase transparency. The main guidance would comprise section 6 and the checklist.

22. A Member commented that there was already a lot of comparable information and questioned the likelihood that this guidance would be used in practice. However, it was considered the guidance would help Members to understand what they should be expecting from the consideration of such evidence. The Secretariat suggested that the guidance be trialled by them and Members could review its application and usefulness after a period of time (2 years).

23. It was agreed that a guidance document for toxicity testing and chemical risk assessment would also be useful for new Members of the Committee and could be prepared using top level information from other review documents (e.g. EFSA, WHO EHC 240 (“Principles and methods for the risk assessment of chemicals in food”),

the Joint FAO/WHO Expert Committee on Food Additives (JECFA)). However this was unlikely to be a priority given the current resource constraints.

24. A number of minor changes to the report were requested and the addition of more information on EFSA's Prometheus project and the weight of evidence document produced by EFSA (see item 13 of this meeting).

25. The layout of the report was compared to a similar document by EFSA where consideration of quantitative synthesis had been addressed in different places. Members agreed that the ordering of the SEES document made more sense as it was important that the papers were read prior to quantitative synthesis being considered or carried out. Quantitative synthesis might be the best approach, but it was not necessarily the default and it should only be used after due consideration, due to the resources required.

26. The Committee discussed the recommendations with some minor changes being requested. Members agreed that the one of the recommendations "A designated individual representing government advisory committees should have continued contact with international methodological initiatives (e.g. the Cochrane collaboration policy group, RISK21 group) and that resources are made available for this, including attendance at key meetings" should be brought to the attention of the Food Standards Agency's Chief Scientific Advisor.

27. The Committee agreed that, ideally, Committee reviews using this approach should be published in a journal to aid transparency in future.

28. The training section of the recommendations highlighted that there was a shortage of epidemiology training available which would cover the needs of the secretariat and (new) Committee Members. It was noted that a course most suitable to these needs was originally designed by IEH Consulting (the integrated environment and health consultancy) and had subsequently been taken over by the Interdepartmental Group on Health Risks from Chemicals (IGHRC). However there were currently no plans to repeat this course in the future due to funding constraints. The secretariat would bring this to the attention of the IGHRC Secretariat and also look into other options.

29. The further work section of the recommendations was also discussed and a decision would be made in future on the best approach to address "further work on combining epidemiological and toxicological evidence and understanding of cross-design synthesis studies". Since the recommendations would need to be considered by the FSA, the Chairs of the COC and the COT would write and bring the recommendations to the attention of the FSA's Chief Scientific Advisor.

30. The document would be finalised with input from the COC and COT and then circulated to other committees and the IGHRC. The Committee agreed that this Report would be of benefit to a wider range of people and organisations. The Committee recommended that the Report should also be published in the scientific literature. It was agreed that the subgroup should aim for submission in the summer.

Item 5: Discussion paper on the potential risks from cadmium in the diets of infants aged 0 – 12 months and children aged 1 to 5 years – TOX/2017/14

31. The Chair declared that he had been a member of the EFSA CONTAM panel and the working group that had compared the EFSA and JECFA health-based guidance values for cadmium (Cd) in 2011.

32. The COT had been asked to consider the toxicity of metals in the diets of infants (0 to 12 months) and young children (1 to 5 years), in support of a review by the SACN of Government recommendations on complementary and young child feeding. This discussion paper addressed the risks of dietary cadmium in these age groups.

33. Members had no general comments on the paper, but it was noted that the values in Table 1 for the SUREMilk survey needed correction.

34. A number of changes were suggested to the content of the paper, notably the foods with the highest levels of Cd should be identified in the main body of the paper, not just in the Appendices. Also Table 22 and related discussion needed to be clarified since it appeared to show the levels of Cd in tap water, whereas it actually showed that tap water levels of Cd had no effect on the total amount of Cd in food to which infants were exposed, as estimated by the Total Diet Study.

35. Members noted that the Kovar study[1] used to estimate UK breast milk levels was very old (1984) but also agreed that the only other UK study, the 2006 SUREMilk study, was inadequate. It was suggested that the similarity of the Cd levels in milk in the Kovar study to more recent studies from other parts of the world may indicate that more Cd was in the environment in the UK in 1984 than at present and that other countries may be lagging behind in their Cd remediation. Thus the current level of Cd in UK breast milk may be lower than indicated by the Kovar study. An indication of the change in UK Cd emissions with time should be included to illustrate this possibility.

36. It was agreed that the EFSA statement on comparing the EFSA and JECFA HBGVs should be noted in the COT statement. The calculations used by EFSA were complex and Members could not see a reason for rejecting the EFSA value in favour of the JECFA one.

[1] Kovar *et al* (1984). Arch. Dis. Child. 59, 36-39.

37. Members pointed out that infants of less than 1 year of age produce less metallothionein than adults so this difference in biology may influence the toxicity of Cd in different age groups.

38. Although the EFSA Provisional Tolerable Weekly Intake of Cd was exceeded by infants in some cases, this exceedance was not great (260% maximum) and applied to only a short period of life, not over the 50 years of bioaccumulative exposure considered by EFSA in setting the HBGV. The Committee decided that this was therefore not a major cause for concern, although it was agreed that efforts should be made to reduce dietary cadmium intakes as far as possible.

Item 6: Second draft addendum to the potential risks from iodine in the diets of infants aged 0 – 12 months and children aged 1 to 5 years – TOX/2017/15

39. No interests were declared.

40. The COT had been asked to consider the toxicity of chemicals in the diets of infants (0 to 12 months) and young children (1 to 5 years), in support of a review by the SACN of Government recommendations on complementary and young child feeding. A scoping paper (TOX/2015/32), highlighting some of the chemicals for possible consideration was discussed by the COT in October 2015. Members had concluded that a full review of the exposures from iodine should be completed.

41. A discussion paper on iodine (TOX/2016/38) was presented to the COT in December 2016. Members' comments were noted and a first draft statement was discussed at the meeting in February 2017 where several suggestions were made on the structure of the statement.

42. Members made a small number of comments on the wording, especially the conclusions. Members were content that the statement could be cleared by Chairman's action once these changes had been made. The COT agreed that due to the proximity of the health-based guidance values to the dietary reference values, collaboration with the Scientific Advisory Committee on Nutrition (SACN) would be necessary to prepare integrated advice on the overall health impacts of iodine.

Item 7: Second draft addendum to the potential risks from nickel in the diets of infants aged 0 – 12 months and children aged 1 to 5 years – TOX/2017/16

43. No interests were declared.

44. The COT had been asked to consider the toxicity of chemicals in the diets of infants (0 to 12 months) and young children (1 to 5 years), in support of a review by the SACN of Government recommendations on complementary and young child

feeding. A scoping paper (TOX/2015/32), highlighting some of the chemicals for possible consideration was discussed by the COT in October 2015. Members concluded that a full review of the exposures from nickel should be completed. A discussion paper on nickel (TOX/2016/41) and a first draft statement (TOX/2017/02) were presented to the COT in December 2016 and February 2017 respectively.

45. Since the COT meeting in February, the Nickel Producers Environmental Research Association (NiPERA) had shared a manuscript by Haber *et al*., (in press) with the Food Standards Agency. Toxicity reference values had been derived for adults, toddlers and sensitised individuals. Annex A to this paper (TOX/2017/16) included a summary of the derivations for toddlers and sensitised individuals given in the manuscript and also included details of the tolerable daily intake (TDI) and the reference point used for a margin of exposure (MOE) approach for sensitised individuals established by EFSA. A second draft statement was also included incorporating the changes requested at the February meeting including the addition of preliminary risk characterisation and conclusions.

46. Members agreed that the value of 20 µg/kg bw/day established by Haber *et al*., using an endpoint relevant to the general infant and young child populations, should be used as the TDI for comparison with chronic dietary nickel exposures in these populations.

47. The Committee were not able to reach a conclusion at this time, on a health based guidance value for sensitised individuals.

48. A third draft of the statement would be considered by the Committee at a future meeting and would include a revised risk characterisation and conclusions as well as the minor changes requested by the Committee.

Item 8: Updated discussion paper on the result of the 2014 survey of metals and other elements in infant foods – TOX2017/18

49. No interests were declared.

50. The FSA has 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). The results of the survey provide 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).

51. Details of the concentration data derived from this survey, and the subsequent exposure assessments, were presented to the Committee in a discussion paper (TOX/2016/29) at the July 2016 meeting. To aid the discussions, brief toxicology summaries for each of the elements surveyed had been included in the discussion paper. The discussion paper had provided updated toxicological summaries and conclusions and included minor revisions suggested by the Committee.

52. The Committee discussed the paper and requested minor revisions to the document and alterations to the conclusions for arsenic and lead. A first draft statement would be presented at a future meeting.

Item 9: Further submission for the reformulation of 2-chlorobenzylidene malononitrile (CS) as an irritant spray – Reserved business - TOX/2017/23.

53. No interests were declared.

54. This item is reserved business as it is commercially confidential, so the minutes for it are recorded separately and will not be published at this time.

Item 10: EFSA consultation on draft guidance on the risk assessment of substances present in food intended for infant below 16 weeks of age – TOX/2017/17

55. No interests were declared.

56. Health based guidance values do not apply to infants below 16 weeks of age (or below 12 weeks for JECFA evaluations). However, risk assessment may still be necessary for chemicals in food to which young infants may be exposed. Such chemicals could be either contaminants or a limited number of approved additives.

57. Following a request from the European Commission, the EFSA Scientific Committee (SC) had prepared guidance for the risk assessment of such chemicals which had been published for consultation. In developing the guidance, the Scientific Committee considered a number of areas including exposure assessment, knowledge of organ development in human infants, and the overall toxicological profile of substances obtained by standard testing strategies, before considering the risk assessment process as a whole.

58. The Committee were asked to consider the guidance document and to provide any comments for submission to EFSA.

59. Members agreed that the guidance document was a useful compilation of information.

60. Concerns were expressed that the decision tree could be interpreted as suggesting that an extended one generation reproductive toxicity study would be necessary for a substance to be assessed, when it would be more appropriate to use alternative methods to obtain information in the first instance. In fact, the decision tree was referring to the small number of chemicals deliberately added to food, for which such a study would be required before they could be approved e.g. the additives used in infant formula. The use of the mini-pig was discussed, but it was unclear whether this was being recommended as the species of choice.

61. It was considered that the guidance should apply to term infants only, since the physiology of pre-term infants could be very different, particularly with regard to phase 1 metabolic enzymes and gastrointestinal absorption.

62. The document noted that an additional uncertainty factor of 3 should be considered in certain situations to allow for extra toxicokinetic differences. This is presumably because this would apply to an age group which would normally be excluded from the ADI so that the conventional uncertainty factors of 10 x 10 would not apply; however it might be useful to clarify this.

63. Members were thanked for their comments which would be submitted to EFSA.

Item 11: Draft EFSA protocol for a systematic review on health outcomes related to the age of introduction of complementary food for the scientific assessment of complementary feeding in an infant's diet – an update – TOX/2017/19

64. No interests were declared.

65. This paper was emailed to members prior to the meeting for comments as the closing date for the consultation was before the COT meeting. Only one comment was received from members and this agreed with the comments already submitted by Dr Robert Boyle from Imperial College London. Therefore no submission from the COT was made to this consultation.

Item 12: EFSA consultation on draft guidance on biological relevance– TOX/2017/20

66. Professor Smith declared a non-personal non-specific interest as he was a member of the EFSA Panel on Plant Protection Products and their Residues (PPR Panel). No other interests were declared

67. The Committee was invited to provide any comments it wished to be submitted to EFSA on this draft guidance which had been produced by the EFSA Scientific Committee and released for public consultation.

68. Members noted that the draft guidance appeared to apply primarily to experimental data rather than observational epidemiological data. The examples in the draft guidance and the use of tables were valuable.

69. A Member observed that homeostasis per se should probably not be considered as an example of an adaptive response. Adaptation might be one type of homeostatic response, but not vice versa. The text completely separates MoA and adverse outcome pathways (AOPs). However, these are functional almost the same and there are important learnings to be acquired from respective practitioners. Separate conceptualisation will act as a barrier to this.

70. The document described “disease signature” and “network perturbations” as terms used in epidemiology but Members were not familiar with such uses.

71. Members noted that the Bradford-Hill considerations were not criteria and suggested that it would be helpful for the document to list the modified Bradford-Hill considerations to which it referred. Confounding was not one of the Bradford-Hill considerations.

72. Members disagreed with a statement in the document that a threshold could never be proven experimentally “as a matter of principle.” This is a very strong statement and perhaps it relates to empirical observation rather than experiment per se. The document should make clear what type of threshold it was referring to in this statement and what is meant by “experimentally”.

73. Members questioned what was meant by the statement that chemical risk assessment usually addresses risks at the population level. Risk assessments are intended to cover the majority of individuals within a population. Members suggested that the text be amended to avoid confusion with ecotoxicological risk assessments of effects on population size.

74. The document stated that lack of statistical significance should not be the sole rationale for concluding a lack of a treatment- or exposure- related effect. Of course,

in practice there is always uncertainty about this possibility, as it would require acceptance of the null hypothesis. But there is a difference between uncertainty about whether there could be an effect and concluding that there is one. The document should indicate what information would allow such a conclusion in the absence of statistical significance.

75. Where the document discusses “background variability for the control group, this appears to be related to historical control data. If so, it might be helpful to reference published work on the use and misuse of such data. If the discussion of how a treatment-related effect which falls within the background variability could be considered irrelevant for risk assessment was intended to apply to epidemiological data, then it should be noted that a small shift in a distribution whilst a small change on average could result in a substantial effect in some individuals at an end of the distribution. Alternative, if this text was intended to apply only to experimental data that should be made clear.

76. The document referred to “positive” effects where “beneficial” or “desirable” would be clearer. The discussion of effects that were not in themselves adverse or beneficial but are linked directly or indirectly to an adverse or beneficial outcome would benefit from linking it to emerging concepts on the use of key events in MOAs and AOPs. Hence, it is suggested there should be suitable cross-referencing, for example to work by IPCS on MOAs and OECD on AOPs

77. A figure in the document was observed to be somewhat simplistic, with yes or no arrows for an effect being adverse or beneficial, whereas this might depend on other factors, such as the population under consideration and could critically depend on exposure. Again, it may well be that the interpretation of the figure depends very much on the purpose for which the document is designed. However, the present text is not entirely clear on this.

78. The Committee wished to congratulate the EFSA Scientific Committee for tackling the topic and producing the draft guidance. With input from stakeholders during the consultation it could become a very valuable document. Members did consider the document to be very long which might limit its usability.

Item 13: EFSA consultation on draft guidance on the use of the weight of evidence approach in scientific assessments – TOX/2017/21

79. Professor Smith declared a non-personal non-specific interest as he was a member of the EFSA Panel on Plant Protection Products and their Residues (PPR Panel). No other interests were declared.

80. The Committee was invited to provide any comments it wished to be submitted to EFSA on this draft guidance which had been produced by the EFSA Scientific Committee and released for public consultation.

81. As the Committee commented for the last item, this draft guidance document was very long and could be shorter, with the salient points distilled, which would increase its usability.

82. It was observed that the conceptual framework differed from that discussed in the draft SEES report.

83. Every evaluation involves weight of evidence assessments. For example, in most standardised procedures there will still need to be weight of evidence considerations for a number of effects (e.g. genotoxicity, carcinogenicity, reproductive toxicity, systemic toxicity) and even for individual effects for a given endpoint (e.g. liver toxicity, renal toxicity, cardiotoxicity). It would be helpful if the document could be more explicit about the type of problems it was aiming to address.

84. The document used “reliability” throughout where this could be called “validity” in other contexts. It would be useful if the document could point out to the reader that reliability can also be referred to as validity.

85. The document discussed variability in data due to measurement error, but this would be considered by many as uncertainty. Indeed, the use of the term in this way is at odds with EFSA (2016). Elsewhere in the document, the terms uncertainty and variability are used more conventionally.

86. The document incorrectly described the Bradford-Hill considerations as criteria and stated that they are frequently used as a checklist in risk assessments, which is not how they were intended to be used.

87. Members observed that evidence rating systems had been grouped together. Whilst these had some superficial similarity, they were very different, and questioned whether such overall grouping was appropriate. For example, GRADE (Grading of Recommendations, Assessment, Development and Evaluation) was formulated for a clinical setting and rates the strength of evidence, downgrading evidence based on observational epidemiological evidence, whereas the IARC classifications synthesise the totality of different pieces of evidence in a different way.

88. Members saw quantification as a tool, rather than an end in itself as appeared to be the case in the draft guidance. The draft guidance mentioned standard statistical methods used in meta-analysis, but not other aspects such as pooling.

89. The Committee considered the categories for weight of evidence methods given in the draft guidance, “Listing evidence,” “Best professional judgment,” “Causal criteria,” “Rating” and “Quantification” as opaque, thus the approach taken to an assessment would need to be forced to fit into one of the groups.

90. Members disagreed that quantitative analysis was necessarily more rigorous than other methods. A quantitative analysis might be possible but inappropriate, depending on the context.

Item 14: Horizon scanning follow-up – TOX/2017/22

91. The Committee considered a list of items resulting from the horizon scanning discussion at the last meeting, along with an action plan.

92. A Member noted that the draft EFSA / European Chemicals Agency (ECHA) guidance on endocrine disruptors was due to be released for consultation in the summer and wondered if this timing would make it difficult for the COT to consider it ahead of the deadline for submitting responses.

93. Most of the papers from the RISK21 work had been published, so the Committee agreed to receive a presentation on the RISK21 approach in September or October.

94. Members agreed that it would be useful to explore the issues around adverse outcome pathways (AOPs) and how they could be used in chemical risk assessment.

95. Deferred from the last meeting, Members considered the balance of expertise of the Committee. It would be useful to recruit one Member with expertise in computational biology, including modelling and systems biology.

Item 15: Paper for information: FSA Scientific Advisory Committees (SACs) update – TOX/2017/24

96. This paper was provided for information.

Item 16: Any other business

97. No other business was raised.

Date of next meeting

98. Tuesday 16th May 2017 in Conference Rooms 4&5, Aviation House, 125 Kingsway, London, WC2B 6NH.