COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Potential future discussion items – horizon scanning

Background

1. The Committee Terms of Reference specify *"To advise at the request of" (……government departments)*. Therefore, the work of the Committee is primarily reactive and the agendas are set by the Secretariat based upon the need for advice from government departments and agencies particularly, but not exclusively, the Food Standards Agency (FSA) and Public Health England (PHE).

2. The Code of Practice for Scientific Advisory Committees (Office of Science and Technology, December 2001), specifies that "*committees should ensure that they have mechanisms in place that allow them to consider on a regular basis whether new issues in their particular areas of responsibility are likely to emerge for which scientific advice or research might be needed*".

3. Members have agreed that it would be useful to have an annual agenda item to discuss potential future topics. The list of topics is displayed on the Committee's website at http://cot.food.gov.uk/cotmtgs/futurecotmeetings/

Agenda items for 2018

4. There are a number of ongoing items, either on the current agenda or scheduled for further discussion at a future meeting:

- COT input into the Scientific Advisory Committee on Nutrition (SACN) review of complementary and young child feeding focussing on children age 1 to 5.
- Advice to Department of Health on novel tobacco products
- e cigarettes
- Review of Risk Assessment Unit and approaches
- Developing Methods for Potency Estimation research project

5. Requests for COT advice are frequently received at short notice.

6. The FSA has a substantial programme of surveys to monitor the safety and quality of food. Details of these are available on the FSA website at http://food.gov.uk/science/surveillance/foodsurvprog.

7. Where appropriate, the Committee's advice will be sought on the health implications of the results.

Potential discussion topics

Consultations of the European Food Safety Authority (EFSA)

8. EFSA frequently consults on draft documents on issues of generic relevance across its remit, or that are particularly high profile. When these have been of particular importance to the Food Standards Agency, the COT has been invited to respond to the consultation (e.g. aspartame, bisphenol A, acrylamide and caffeine). Similarly, EFSA documents on toxicological risk assessment approaches with potential relevance to the working practice of the COT have also been discussed (e.g. default values to be used in risk assessment in the absence of actual measured data, and draft guidance on uncertainty). It is anticipated that further relevant EFSA documents will be presented to COT during 2018.

Items carried forward from the 2017 horizon scanning

Analysis of the evidence gap for postulated human health effects of Endocrine Disrupting Chemicals

9. Members agreed that a systematic review of the health effects of Endocrine Disrupting Chemicals (EDCs) would be useful but recognised that this would be a major task. A similar task had been conducted by the WHO but more focussed questions would have been helpful. Without a coordinated systematic review to understand the evidence base (possibly an "umbrella" review of reviews to obviate author selection bias) the impact of EDCs was uncertain. In the first instance, a paper on the evidence gaps should be prepared by PHE but other priorities have meant that this item has not been progressed. This is likely to continue to be the case in 2017.

Update on the COT 2008 Trans and multigenerational toxicity statement

10. Members noted that the knowledge base on this topic had moved on since the last COT statement was published in 2008. The Committee agreed that the statement should be updated, however resource constraints have not permitted progress during 2017. Due to the interest from COM and COC in PHE held a joint symposium of all three Committees in 2017.

Role of chemicals altering the microbiome and potential human health effects

11. The Committee agreed that since the importance of the microbiome in many areas of health and disease was becoming increasingly apparent, the effects of xenobiotics on the microbiota and of the microbiota on xenobiotics should be considered in a short discussion paper. Both the makeup of the microbiological population, i.e. the species of bacteria and other microorganisms present, and its functional makeup, i.e. the biochemical pathways contributed by the total mass of microorganisms, would be taken into account, along with other potential interactions, for example between air pollution, microorganisms in the respiratory tract and the development of asthma. Progress has not been possible during 2016 and 2017 due to other Committee priorities.

Risk Assessment in the 21st Century (RISK21)

12. The International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) created the Risk Assessment in the 21st Century (RISK21) Project. This multi-sector, international initiative began in 2009 and has involved the active participation of over 120 individuals from 12 countries, 15 government institutions, 20 universities, 2 nongovernmental organizations, and 12 corporations. RISK21 has developed a conceptual framework called the roadmap and a simple exposure-toxicity comparison matrix. The matrix enables exposure and hazard to be evaluated and compared effectively and transparently using all relevant sources of information sufficient for decision-making to address the specific problem formulated. The overarching principles of the RISK21 approach and an introduction to the roadmap and visualization matrix are described by Pastoor et al. (2014) and application of the RISK21 roadmap in risk assessment is described in detail by Embry et al. (2014) Annexes 1 & 2 respectively.

13. The Chair has suggested that the Committee have a presentation on the RISK21 approach.

14. **Do Members have any comments on RISK21 and would they like a presentation in the coming year?**

Modelling kinetics

15. The Committee agreed that it would be useful to keep abreast of developments in the area of physiologically-based toxicokinetic (PBTK) modelling, particularly as it might be asked in the future to advise on risk assessments using such models. This issue was also discussed in the context of the COT symposium on the implications of obesity on the kinetics of persistent organic pollutants held in March 2015.

16. Insufficient data had been presented at the COT symposium to consider building PBTK models. It was considered that compared to pharmaceutical drugs, for environmental chemicals there was usually a lack of good PBTK data which can be used in modelling. The US had made a heavy investment into the replacement, reduction and refinement of animals in research (the 3Rs) and had started to take a bottom-up in vitro and in silico approach, in which toxicokinetic extrapolation plays a key role. It was noted that the COT should keep a watching brief on this topic.

17. **Members are invited to comment on whether they are aware of further developments in this area that should be followed up during 2018?**

Items discussed at the 2017 Joint COC, COM and COT Horizon Scanning meeting in October 2017

18. A Joint Committee Horizon Scanning took place in October 2017 and a number of items were discussed which could be discussed at future COT meetings. Minutes from the meeting, along with the Horizon Scanning papers from each of the Committees are included in Annex A.

19. Briefly, the following topics could be of interest to the COT: uncertainty in risk assessment (including modelling approaches and toxico-kinetics); extrapolation from lifetime animal studies to early human less than lifetime exposure; balance between environmental exposure and food exposure; by-products of various drinking water disinfection treatments.

20. It was suggested that data presented to the COT during consideration of the heat-not-burn tobacco products could be used in a case study of the RISK21 framework.

21. A potential concern over natural products and “new” natural products had been raised. There is no overall framework or systematic approach to natural food products in general. It was suggested that it would be useful to know if there is a potential health risk from taking these products before taking this further, and a brief survey using the National Poisons Information Service could be undertaken in the first instance.

22. The use of epidemiological evidence in a health risk assessment was discussed. It was noted that a sub group of the COT and COC was finalising a document on synthesising epidemiological evidence and how this could be used by Committees. The question of how to deal with poor published studies was raised. Members noted that such studies could cause difficulties for various expert Committees, where poor studies were used to question Committee opinions in some cases. It was noted that EFSA currently required scoring of individual papers and used a weight of evidence approach in its evaluations using its PROMETHEUS approach.

23. In terms of priorities for joint Committee consideration, it was suggested one important area was how to evaluate the biological or toxicological relevance of

a reported response or perturbation, especially where this may be an atypical endpoint and how statistics can, and should, be used to help determine this. This should encompass how the Committees could judge whether the statistics used were appropriate. Consideration of sufficient levels of health protection and dealing with uncertainty could also be useful, for example, the degree of confidence over a non-significant result in relation to health protection. Another area of importance was how to deal with different sources of evidence considered by the Committees (e.g. predatory journals and poor quality non-standard tests), which could be a follow up to the SEES group work. In addition, a watching brief should be maintained on nanomaterials, especially as size distribution is of relevance for e-cigarettes and also heat-not-burn tobacco products.

New suggestions for topics

24. The Secretariat would welcome members views on whether the current structure of three separate Committees remains appropriate and sustainable in light of future challenges or whether they should explore other possibilities in consultation with the Secretariats of COC and COM and departmental sponsors.

25. ***At this time the Secretariat do not have any additional items for 2018. Do Members have any ideas/suggestions that they would like discussed at the meeting?***

Balance of expertise on the Committee

26. It has previously been agreed that the following types of specialist expertise are required by the Committee for some or all of its evaluations:

Analytical techniques	Biochemistry
Bioinformatics	Cell biology
Clinical practice	Dietary exposure assessment
Endocrinology	Environmental exposure assessment
Epidemiology	Human toxicology
Immunology	Mathematical Modelling
Mechanistic toxicology	Molecular biology
Neurotoxicology	Nutrition
Paediatrics	Pharmacokinetics
Pharmacology	Probabilistic modelling
Reproductive toxicology	Respiratory toxicology
Risk assessment	Statistical aspects of experimental design
Statistics	Systems biology
Toxicogenomics	Toxicological pathology
Xenobiotic metabolism	

27. It would not be necessary to have an individual member for each listed expertise as some people would have a combination of the required skills. Additional key experts are also invited to attend meetings for specific topics to supplement missing knowledge.

28. **Members are invited to comment on whether this list is still appropriate and if there are important gaps amongst the current membership or in light of possible future developments.**

Questions on which the views of the Committee are sought

29. Members are invited to comment on each of the above areas and the questions in paragraphs 17, 25 and 28 also to consider the following questions:

    a. Do Members have additional suggestions for future topics for:

        - Specific issues to be included as routine agenda items
        - Focussed topics for one-day open meetings
        - Generic issues requiring establishment of a Working Group.

30. Do Members have proposals for research that FSA should fund in order to improve future COT risk assessments?

31. Members are reminded that they may draw particular issues to the attention of the Secretariat at any time.

Secretariat
January 2018