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 2017

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

- The COT-COC synthesising epidemiological evidence subgroup (SEES)

- Potassium replacements for sodium chloride and sodium-based additives

- Results of FSA-funded research on toxicokinetics of persistent organic pollutants in obese individuals.

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 2017.

Items carried forward from the 2016 horizon scanning

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

10. 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

11. 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 2016. PHE have also noted interest from COM and COC in the issue and are proposing that a joint symposium of all three Committees should be held in place of the autumn COM meeting. The date will be confirmed soon.

Role of chemicals altering the microbiome and potential human health effects

12. 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 due to other Committee priorities. There will be a symposium at the 2017 British Toxicology Society Annual Congress on “Toxicology and the Human Microbiome”. The session is outlined in Table 1. A short write up of this session could be presented at a subsequent Committee meeting after which Members could discuss the priority of this topic and approaches to taking it forward.

Table 1: Outline of BTS Symposium on Toxicology and the Human Microbiome

Chair: Professor Tim Gant (PHE)	
Dr Alan Walker (University of Aberdeen)	The gut microbiome in health and disease
Professor Elaine Holmes (Imperial College London)	Microbiome and the metabonome
Professor Tom Van de Wiele (Ghent University)	Environmental exposures, toxicology and the microbiome
Dr Andrew Patterson (Pennsylvania State University)	Microbiome and xenobiotic metabolism

New suggestions for topics

Risk Assessment in the 21st Century (RISK21)

13. 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.

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

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

Modelling kinetics

16. 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.

17. 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.

18. As noted at paragraph 4 above, the results of the FSA-funded research on toxicokinetics of persistent organic pollutants in obese individuals will be presented to the COT at a meeting during 2017.

19. Members are invited to comment on whether they are aware of further developments in this area that should be followed up during 2017?

Balance of expertise on the Committee

20. 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	

21. 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.

22. Members are invited to comment on whether this list is still appropriate and if there are important gaps amongst the current membership,.

Questions on which the views of the Committee are sought

23. Members are invited to comment on each of the above areas and the questions in paragraphs 15 and 19 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.

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

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

Secretariat
January 2017

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A 21st century roadmap for human health risk assessment
Timothy P. Pastoor, Ammie N. Bachman, David R. Bell, Samuel M. Cohen, Michael Dellarco, Ian C. Dewhurst, John E. Doe, Nancy G. Doerrer, Michelle R. Embry, Ronald N. Hines, Angelo Moretto, Richard D. Phillips, J. Craig Rowlands, Jennifer Y. Tanir, Douglas C. Wolf, and Alan R. Boobis
Crit Rev Toxicol, 2014; 44(S3): 1–5

Available online at
http://www.tandfonline.com/doi/pdf/10.3109/10408444.2014.931923

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Potential future discussion items – horizon scanning

Risk assessment in the 21st century: Roadmap and matrix
Michelle R. Embry, Ammie N. Bachman, David R. Bell, Alan R. Boobis, Samuel M. Cohen, Michael Dellarco, Ian C. Dewhurst, Nancy G. Doerrer, Ronald N. Hines, Angelo Moretto, Timothy P. Pastoor, Richard D. Phillips, J. Craig Rowlands, Jennifer Y. Tanir, Douglas C. Wolf, and John E. Doe
Crit Rev Toxicol, 2014; 44(S3): 6–16

Available online at
http://www.tandfonline.com/doi/pdf/10.3109/10408444.2014.931924?needAccess=true