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 https://cot.food.gov.uk/cot-meetings/forthcoming-cot-meetings

Agenda items for 2020

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. There are a couple of outstanding items which will hopefully be finalised by mid-2020.
- Electronic nicotine (and non-nicotine) delivery systems (E(N)NDS) – e-cigarettes
- Developing Methods for Potency Estimation research workshop and project
- PBPK modelling project for PFOA
- Microplastics
- Microbiome

- Dioxins
- Maternal diet
- Plant-based drinks
- SETE subgroup

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 https://www.food.gov.uk/research/research-projects.

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. phthalates, dioxins and dioxin-like PCBs in feed and food, aflatoxins, chlorinated paraffins in 2019). Similarly, EFSA documents on toxicological risk assessment approaches with potential relevance to the working practice of the COT may also be discussed. It is anticipated that further relevant EFSA documents will be presented to COT during 2020.

Items carried forward from the 2019 horizon scanning

9. 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. These were detailed in the 2018 Horizon Scanning paper (TOX/2018/11)[1]. The key topics to be focussed on are outlined below:

10. 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. The COT may wish to be aware of an ECHA workshop in 2016 on new approach methodologies and use in regulatory science[2]. 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.

New suggestions for topics

Further work on e-cigarettes and vaping products

11. The Secretariat are currently looking at the data from the US on e-cigarette, or vaping product, use associated lung injury (EVALI) and are planning to bring a short paper on this to the Committee in 2020

Derivation of human biomonitoring guidelines

12. The Secretariat will be bringing papers to COT and COC this year (likely in the summer) on the derivation of human biomonitoring guideline values and assessment of examples produced in the HBM4EU project.

Approaches to the risk assessment of residues of human pharmaceuticals in food

13. Residues of human pharmaceuticals are sometimes reported in foods, mostly at very low levels. For example, there are occasional findings of ibuprofen in cattle and pig kidney in the UK's national surveillance scheme for veterinary medicine residues (VMD, 2013, 2014, 2015, 2017, 2018). In some cases, contamination during sampling has been suspected, in others the cause has been unknown.

14. Low concentrations of human pharmaceuticals are also expected to occur in the food chain because they occur in surface waters via sewage water treatment works effluent. Because of the occurrence in surface waters there have been various considerations of potential risks from exposure via drinking water. However, the treatment of drinking water reduces concentrations of pharmaceuticals to varying degrees (WHO, 2011), and freshwater fish and shellfish would also be expected to be a source of exposure. For example, taking ethinyloestradiol as an example, the fish bioconcentration factor (BCF)[3] has been reported to be around 600 (European Commission, 2011).

15. In 2011, researchers from Spain and Morocco published a paper in which they had developed a sensitive method for the simultaneous analysis of 20 pharmaceuticals in food using a combination of continuous solid-phase extraction and gas chromatography–mass spectrometry, and tested the method using samples of cow's and goat's milk purchased in Spain and Morocco (Azzouz et al., 2011). Limits of detection ranged 0.2-1.2 ng/kg. Some of the pharmaceuticals that were measured, at low concentrations, are used in human medicine and not authorised for use as veterinary medicines, including pyrimethamine, niflumic acid, mefenamic acid and ethinyloestradiol.

[3] The bioconcentration factor (BCF) is the ratio of the concentration of a substance in an aquatic water-respir- ing organism and the concentration in water at steady state.

16. As noted above, there have been a few assessments of possible risks from pharmaceuticals in drinking water, considering modelled or measured concentrations (DWI, 2007; Snyder et al., 2008; NRMMC, EPHC and NHMRC, 2008; WHO, 2011). The approaches taken to the hazard characterisation have been to establish ADIs based on toxicological NOAELs or LOAELs, to establish "surrogate ADIs" based on the use of the minimum therapeutic dose used in humans and applying uncertainty factors, or to calculate margins of exposure (MOEs) based on the minimum therapeutic dose.

17. The use of the minimum therapeutic dose, either to establish surrogate ADIs or to calculate MOEs, has been commonly used due to the lack of readily available toxicological data in the public domain (WHO, 2011). When using the minimum therapeutic dose an uncertainty factor of 1000 has most commonly been applied, or an MOE of at least 1000 considered to be of low concern. This was to allow for the point of departure not being a NOEL (factor of 10), inter-individual variation (factor of 10) and an additional factor of 10 applied to ensure protection of infants and children. For cytotoxic drugs and steroid hormones, a larger uncertainty factor of 10,000 was applied by NRMMC, EPHC and NHMRC (2008). In contrast, Bull et al. (2011) suggested that an overall uncertainty factor or MOE of 100 applied to the minimum effective daily dose should be sufficient for most pharmaceuticals (Bull et al., 2011). However, they considered that additional uncertainty factors / margins should be considered for pharmaceuticals that produce serious adverse health effects at therapeutic doses, for pharmaceuticals that are only intended for short term use and for carcinogens, and that the occurrence of mixtures should be taken into account (Bull et al., 2011).

18. It would be useful to receive the COT's views on the approaches that should be taken to the risk assessment of human pharmaceuticals in the food chain.

19. Members are invited to provide any comments and to advise whether this would be a suitable topic for further consideration by the Committee.

Maternal Diet

20. In 2018, SACN and SMCN agreed that nutrition and maternal health should remain a priority for a future SACN risk assessment focussing on diet and nutrition during preconception, pregnancy and up to 24 months after delivery. It is envisaged that the report will predominantly focus on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery. In this context, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) would be asked to review the risk of toxicity of a number of chemicals in the diets of pregnant and lactating women.

21. Following the discussion at the first SACN working group meeting in December 2019, the advice of the COT is sought on whether exposure to the following chemicals would pose a risk to maternal health:

• excess intake of micronutrients (through diet and/or micronutrient supplements): vitamin A/retinol, vitamin C, vitamin D, vitamin E, iodine and selenium

• intake of toxins formed in food during storage or processing such as mycotoxin, acrylamide and heterocyclic amines (HCAs)

• intake of environmental toxins or pollutants, including polychlorinated biphenyl (PCB), bisphenol A (BPA), dioxins, pesticides and heavy metals (such as leads, mercury and arsenic)

• toxicological issues associated with oily fish consumption

• intake of caffeine

• intake of phytoestrogens

22. Resveratrol and heterocyclic amines were mentioned by a Member of the SACN subgroup as being of potential interest and the COTs advice is sought whether these should be considered.

23. SACN support COTs upcoming cumulative assessment of mycotoxins and the inclusion of pregnant and breastfeeding women as a vulnerable group. While, BPA is of interest, it is not considered high priority and SACN is content with waiting until the new assessment by EFSA has been published.

24. The COTs advice is sought on the necessity of a full assessment of these chemicals in the diets of pregnant and lactating women, including excess intake of micronutrients and intake of environmental toxins or pollutants, or if other sources, such as EFSA or EVM could be utilised, and whether the Committee has any other chemicals they would find appropriate to be added to the list.

Alternatives to plastic packaging

25. At present there is lot on interest in alternatives to plastic packaging. This is a very fast moving area, but examples of these types of materials and articles which include:

- alternatives to single use plastic and/or paper cups -
    - wheat-based cups
- multiple use cups -
    - bamboo & rice husk cups
- alternatives to plastic straws -
    - wheat straws
- alternatives to plastic tableware -
    - wood / plant-based knives & forks
- alternatives to traditional plastic water bottles -
    - seaweed-based pouches

- alternative plastic films -
    - chitin bio-based film
    - coffee grounds bio-based film
    - bees wax wraps.

26. Such products intended to be brought into contact with food are covered by legislation on Food Contact Materials. Some novel materials may not have had their risks completely assessed before placing onto the market. There will also be many materials still in the developmental stage that need to have the appropriate tests carried out. The Chemicals team have been asked to review this area by policy colleagues and a scoping paper will be presented in the Spring. Topics that will be considered include – breakdown to allergenic components, chemicals that could leach out from the material or the matrix it is in, plant treatment products, and heavy metals from local geology or contamination.

27. Members may wish to make some general comments or suggest other topics that should be considered.

Joint Committee Horizon Scanning

28. It may be of use to consider a Joint Committee Horizon Scanning towards the end of 2019 to monitor any changes brought about by the EU Exit. This could also include members from the Joint Expert Groups. Members may consider it more pertinent to have a joint training/awareness day.

29. ***At this time the Secretariat do not have any further items for 2020. Do Members have any ideas/suggestions that they would like discussed at the meeting?***

Balance of expertise on the Committee

30. 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	

31. 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.

32. **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

33. Members are invited to comment on each of the above areas and 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.

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

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

Secretariat

January 2020

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