Meeting

Monday 16th of November 2020

Sixth meeting of the COT and COC SETE subgroup

COT and COC subgroup on the synthesis and integration of epidemiological and toxicological evidence (SETE) in risk assessments

Agenda

Agenda of the sixth Meeting, Monday 16th of November 2020, 10:00 am to 1:00 pm, via teleconference.

1. Welcome and goals of meeting
2. Brief update on the work of the epidemiological subgroup and the work of the toxicological subgroup. The sections on Mode of Action, Problem formulation, literature retrieval.
3. Discussion of the section on data integration (section 5): Scaling, Tropane alkaloid as an example and discussion of exposure
4. Next steps: general outline of the guidance and drafting of text for guidance document and report.
5. Administrative; TEAMs and Plan next meeting(s) – with a view of potentially bringing the first draft of the SETE report (and guidance) to the February/March 2021 COT meeting

Minutes

Present

Chair: Alan Boobis

Committee Members:

- Phil Botham
- Gill Clare
- Alison Gowers
- Valentina Guercio

- Gunter Kuhnle
- George Loizou
- David Lovell
- Neil Pearce
- Lesley Rushton
- Mireille Toledano
- Heather Wallace

Secretariat:

- Barbara Doerr, FSA
- David Gott, FSA
- Cath Mulholland, FSA
- Britta Gadeberg, PHE

The Chair welcomed Members and other attendees.

Members agreed with the modifications/additional text in the sections on mode of action, problem formulation and literature retrieval. However, Members noted some repetition/overlap in a number of sections on the text on literature retrieval and asked the Secretariat to rationalise the text for the next meeting.

Prof Gunter Kuhnle provided an update on the work of the epidemiology subgroup. The subgroup favoured a flexible approach to combine all studies and considered triangulation to be the most suitable approach and to avoid a check list approach. However, Members acknowledged that not every Committee shared this approach but may place most weight on randomised control studies, with less weight given to observational studies; hence it would be beneficial to expand the section and include the advantages of observational studies, such as the longer study/observational time and number of individuals. Members asked to also include some explanatory text on the uncertainties, considerations and concerns surrounding the potential quality of epidemiological studies. Members agreed that the SEES report is still a valid and comprehensive piece of work on which this section builds; the current work takes certain aspects such as triangulation a step further. Members therefore asked for inclusion of a paragraph at the start of the section stressing that the information provided in the SETE report should be read in conjunction with the SEES report.

Dr Phil Botham provided an update on the work of the toxicology subgroup. Following the discussion at the last meeting the information on in vitro studies, extrapolation from in vitro to in vivo and dose-response have been expanded.

Members however agreed that some additional text on internal dose would be beneficial to the section.

Members noted that both sections discuss check list approaches and agreed that the section on quality assessment in the Report would benefit from either introductory or summarising text stressing that check list approaches have been looked at and included for completeness. However, neither section, epidemiology nor toxicology, are developing/favouring a check list approach but are aiming to provide guidance for experts and Committees to assess all information and apply good judgement transparently in a weight of evidence approach.

Following the updates by the subgroups, Members discussed the section on data integration in more detail. Members agreed that the first step in the integration process is the question of whether exposure to a substance causes an effect in humans and the subgroup on exposure will provide draft text for the next meeting. Members noted that the terminology “scaling” implied quantitative assessment. While the Working Group recognises quantitative assessment as the next step and future work, the current guidance document focuses on the qualitative assessment of causation. Members suggested determining what terminology other authorities apply and whether any is applicable to the work conducted here.

Members were still in agreement that providing (a) practical example(s) of the integrated approach would be beneficial to the report and discussed the information on tropane alkaloids provided by the Secretariat following discussions at the last meeting. Members noted that contrary to initially thought, the data presented on tropane alkaloids did not include epidemiological data per se but predominantly clinical trials and human poison cases at very high doses. While Members did not disregard tropane alkaloids as a useful example, Members felt there might be other more appropriate examples available. The Secretariat will therefore provide information on cadmium, aspartame and further detail on caffeine, for discussion at the next meeting. Having different data sets available with varying information on toxicological (animal) data, epidemiological data and/or mode of action/mechanistic data may present the opportunity to apply the guidance differently and stress test the guidance.

The next meeting will be held on in mid-January 2021, via TC.