Meeting

Wednesday 13th of January 2021

Seventh 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 seventh Meeting, Wednesday 13 January 2021, 14:00 am to 17:00 pm, via teleconference

1. Welcome and goals of meeting

2. Discussion of the section on data integration (section 5)

- Exposure
- Text on PBPK modelling (GL)
- Examples for data integration

3. Next steps

- COT Meeting March 2021
- Drafting of text for guidance document and finalising report

4. AOB

- Interim papers by the Science Council on Quality of Third-Party Evidence
- IHE document
- Plan next meeting(s)

Minutes

Present

Chair: Alan Boobis

Committee Members:

- Phil Botham
- Gill Clare
- Alison Gowers
- Valentina Guercio
- Gunter Kuhnle (until 3.30 pm)
- George Loizou
- David Lovell
- Neil Pearce
- Lesley Rushton
- Mireille Toledano (from 2 pm)
- Heather Wallace

Secretariat:

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

Officials:

- Ruth Bevan, IHE
- Catriona McCallion, FSA
- Paul Harrison, IHE
- Kate Vassaux, IHE

The Chair welcomed Members and other attendees.

Discussing the current draft, Members noted that the sections on quality assessment provided different approaches, with the epidemiological draft text focusing on how all evidence is assessed and the toxicological section focussing more generally on existing guidance. Members agreed that the report would benefit from some additional introductory text recognising the differences in the two approaches and highlighting that, despite the differences, both epidemiology and toxicology apply a weight of evidence approach in their assessment of evidence.

Dr George Loizou provided an overview of the draft text on PBPK modelling in the section on data integration, focusing on what PBPK modelling is and how it can be used as a platform for the integration of data. Members noted that the OECD is

currently in the process of publishing a guidance on PBPK modelling. It would therefore be useful for the SETE document(s) to refer to the OECD guidance, where applicable, and identify and include the key points that assessors should consider for data integration. Members acknowledged that PBPK modelling requires expertise and can be time consuming. However, even the application of a basic model is still favoured over no kinetic predictions. Hence, this section would benefit from some introductory text on kinetics, leading into the more sophisticated approach that is PBPK modelling.

Members confirmed their view that providing practical examples of the integrated approach would be beneficial to the report and discussed the previous information on tropane alkaloids and caffeine as well as the new information provided by the Secretariat on cadmium and aspartame. Caffeine continued to be considered a good example as the information is dominated by human data, while cadmium shows similar and consistent toxicological effects in humans and animals. Contrary to initial discussions, tropane alkaloids were also considered a useful example, due to the large data base (animal, human) and clear mechanism of action. In addition, the WHO assessment has recently been published and can be utilised here. Aspartame was not deemed a suitable example for the report, as the data in both animals and humans were generally negative, other than at very high doses. Members agreed that it would be beneficial to apply the framework to any future assessment of aspartame.

Going forward, a subgroup was formed to consider the section on evidence integration and the initial lines of evidence for caffeine, cadmium and tropane alkaloids provided by the Secretariat, before discussion of this section, including the visualisation of causality, at the next SETE meeting.

Members agreed to take the SETE report and guidance to the next COC and COT meetings on March 11th and March 23rd, 2021, respectively. In the interest of time the working group will not only discuss a full draft of the report but also a first draft of the guidance document at the next SETE meeting. Members also considered it appropriate to start thinking about presenting the work of the SETE working group at scientific conferences. EUROTOX and SOT were suggested as possible options.

Catriona McCallion from the FSA and Ruth Bevan, Paul Harrison and Kate Vassaux from IHE attended the meeting to take comments and answer questions regarding the development of a document on third party evidence and a non-

technical document explaining biological relevance and statistical significance by the FSA and COC, respectively. Members discussed the relevance and crossover to the current work undertaken by SETE. As these documents are ongoing work, the discussions were held as reserved business. However, additional information on the COC's work can be found on the COC website; the FSA's work on third part evidence will be published later this year.

The next meeting will be held on 11th February 2021, via TC.