Meeting

Friday 17th of April 2020: SETE meeting

Third meeting of the COT and COC SETE subgroup

COT/COC subgroup on the synthesis and integration of epidemiological and toxicological evidence in risk assessments

Agenda

TC/Skype/Teams Meeting 10:00 am - 13:00 pm on Friday 17th of April 2020

1. Welcome and goals of meeting
2. Discussion of the Cefic documents provided by Lesley and Alan prior to the meeting
3. Discussion of the outline of the guidance document provided prior to the meeting

   Do Members agree with the outline and sections included
   Additional sections Members wish to add

   For the SEES WG, two documents were produced. One was a report on the activity of the group, and the other was a stand-alone guidance document.

   Should this also be applied to SETE.

4. Agreement on forward plan and assignments
5. Administrative

- Could Members please confirm they are happy for their emails to be shared so it can be minute
- Agreement of the minutes from the 1st and 2nd Meeting, so the SETE website can be finalised and the minutes can be made available on the website.
- Plan next meeting(s)

Minutes

Present:

Chair: Alan Boobis

Committee Members:

- Gill Clare
- Phil Botham
- Gunter Kuhnle
- David Lovell
- Neil Pearce
- Lesley Rushton
- Mireille Toledano
- Heather Wallace
- Valentina Guercio, PHE

Secretariat:

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

Apologies were received from George Loizou and Alison Gowers (PHE).

The Chair welcomed Members and other attendees.

Dr Lesley Rushton provided a brief summary of the work package reports of the Cefic-LRI project on comparing NOAELs from animal data with those from human data, which were circulated to Members in advance of the meeting. The (unpublished) documents described the approach taken on comparing and quantitatively integrating dose-response data from human and animal studies. Due to time restrictions during the project, no statistical methodology was developed, but a more general approach for comparing no observed adverse effect levels (NOAELs) and dose-response slopes was used. Members noted that currently there is no one method that fits all, hence a case by case approach is needed. Members did however agree, that the work included important information and that it would be beneficial to the WG and the intended guidance document to be able to refer to the work done by the Cefic-LRI project.

As it was unlikely for the material to be published in the scientific literature at this late stage, Dr Rushton offered to contact Cefic to discuss whether it would be possible to make the work packages available in the public domain (potentially on the Imperial College London website).

Members were in favour of basing the guidance document on the general structure and approach of the Epid-Tox Framework, were applicable, and discussed the separate parts of the proposed guidance document.

Members agreed that the introduction and problem formulation should be focused and would need to consider the urgency/level of concern in which an answer might be sought. Therefore, Members further agreed, that it was not practical to suggest a formal systematic review for all cases, yet the document needed to cover separate (search) strategies to consider the relevance of studies. It was suggested that reference be made to the SEES framework as these aspects have been covered there previously.

Members discussed the quality assessment of studies and the potential criteria to apply. All types of studies were considered useful and applying a tick box approach, as regularly done by some other Committees/bodies, would exclude potentially relevant studies, especially epidemiology/observational studies. Often, studies deemed to be less reliable could be useful in combination with other evidence or if there was bias towards the null and an effect was still apparent. Members concluded that it would be useful and practical to include guidance on criteria indicating study quality and relevance, such as the endpoint being addressed and whether or how deficiencies in studies could be counteracted by other studies.

Members agreed that the Bradford-Hill considerations are a useful foundation for assessing the weight of evidence and that most of the considerations would be applicable within the context of the guidance document. The Epid-Tox framework focuses strongly on the mode of action (MoA) for weighing evidence and Members agreed that the approach developed would have to be more flexible than this. Members agreed that absence of knowledge of the MoA would not necessarily exclude a conclusion of a causal relationship. However, knowledge of the MoA (or any mechanistic data) would strengthen any conclusion of causality derived from other studies.

Members agreed that scaling the strength of evidence for the conclusions and visualising these graphically, as in the Epid-Tox Framework would be a useful means of communicating the process and conclusions. Members did, however,

stress that this step requires expert judgement and that therefore there was a risk of bias, which needed to be addressed in the process. Members acknowledged the difficulties of explaining transparently conclusions based on expert judgment in which many years of accumulated knowledge and experience, some of which was axiomatic to the expert, were integrated. However, such expert judgment would need to be reflected as explicitly and transparently as possible. In this respect, it is important that, where possible conclusions and their justification are challenged by colleagues, comprehensible (written) explanations of how a conclusion was reached and what factors influenced this, including discussions about data/studies that may have been excluded and why.

Following the discussions minuted above, the key elements for the guidance document were agreed and Members formed sub-groups to start drafting considerations on methods to assess epidemiological studies, toxicological and non-animal studies, and how to scale the lines of evidence.

Members further agreed that the guidance document should be short and practical and hence adopted the same approach as the SEES Working Group. There will be two outputs after the WG has concluded its work, a guidance document, focusing on the practical application and a report which will include information on the discussions of the working group and supplementary information such as future recommendations.

Several papers were provided by Members of the Working Group to the Secretariat prior and during the meeting and will be circulated to the group.

All Members and other attendees present at the meeting agreed for their email addresses to be shared among the WG. The agreement of Members and external experts not in attendance would be obtained via email. (Note: The agreement of all Members has been received)

Members were asked to send any comments on the minutes from the first (3/12/2019) and second (10/02/2020) meetings to the Secretariat within the next seven days, at which point the minutes would be considered agreed and would be finalised for web publication.

The next meeting will be held on 22nd June 2020, via TC.