COT Procedures 2024

In this guide

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Benchmark dose modelling in a UK chemical risk assessment framework

1.65 In 2021, as part of a horizon scanning exercise, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) identified the UK in future may need benchmark dose (BMD) modelling guidance. As part of its ongoing evaluation of New Approach Methodologies (NAMs) in chemical risk assessment, the Food Standards Agency (FSA) and the COT were considering the use and practice of BMD modelling within a UK food safety context.

1.66 The discussion paper set out the theory and practice of BMD modelling. The paper drew on previous evaluations by regulatory bodies and authorities. It also included a discussion of the areas of consensus and divergence between organisations and expert groups. The paper included a case study from the FSA

Computational Fellow.

1.67 BMD modelling represents a useful tool in toxicology, but the No-observed-adverse-effect level (NOAEL) approach remains valid and, in many cases, is the only option (e.g. where effects are observed only at the highest dose). The requirement for deeper knowledge of the statistical and computational basis of the BMD approach may represent a barrier for further adoption in traditional toxicology. Applying the BMD approach to toxicology data is a more complex undertaking than the traditional NOAEL approach. Some areas where BMD modelling may provide advantages over the traditional NOAEL approach include potency comparison, establishing toxicological equivalency factors (TEFs) and for situations where a reference point needs to be identified in the absence of a NOAEL.

1.68 With respect to the development of new BMD software these pieces of software have their own capabilities, which allow them to be tailored for specific scenarios and tasks. However, there is concern that this might lead to further divergence rather than convergence of BMD approaches. For example, the recent development of Bayesian BMD software as part of European Food Safety Authority (EFSA's) modelling suite there are concerns around how the Bayesian BMD modelling is used in practice, specifically with the selection of priors and whether this would introduce subjectivity into the analysis. Uncertainties have been expressed in the literature with respect to the Environmental Protection Agency (EPA) Bayesian modelling software.

1.69 There is debate about the role of benchmark dose modelling in other areas, such as genotoxicity testing, and the COT is aware of the views on BMD modelling by other UK Scientific Advisory Committees notably the COC and COM. BMD modelling is already being used by some expert groups, such as the UK Expert Committee on Pesticides and it would be useful to capture their experience.

1.70 The Committee acknowledged the rapidly developing nature of the BMD guidance, the development of new approaches, such as Bayesian approaches; and the recent proliferation of new BMD software but noted that it was still uncertain if, or what, important divergences existed between these developments.

1.71 BMD modelling should be viewed as a step towards a larger goal of more realistic, toxicodynamic systems approaches to risk assessment. This may become more feasible with the further development of models based on *in silico* and *in vitro* approaches.

1.72 The Committee noted that BMD modelling should be taken into consideration when updating COT guidelines.

COT ways of working

1.73 The workload of the Committee and in particular the Chair has increased over recent years, partly, though not solely, as a result of the UK's exit from the EU, including the additional activities associated with the authorisation of regulated products. It was therefore timely to review the current working practices of the Committee to ensure that it remains sustainable. In addition, due to the increase in hybrid and virtual meetings, it was important to ensure the Committee could work in an effective manner, with Members being able to fully contribute and be engaged. Committee Chairs are appointed through an open recruitment process so it would not be appropriate to train current Members for the role or to have a formal succession planning process. However, it was agreed that, in addition to chairing the meeting when the Chair was unavailable or had a conflict of interest, it could be useful for the Deputy Chair to lead in a particular topic area to reduce the workload of the Chair. It was subsequently agreed that the COT Deputy Chair, Professor Shirly Proce, would focus on regulated products to strengthen links between the COT and the Joint Expert Groups.

1.74 The process by which small groups of Members were attached to particular papers to lead the Committee discussion was discussed. It was agreed that the small group work should start at an earlier stage for more complex topics and could also follow the process through to the preparation of first draft statements. Lay members and/or associate members could also be included in the small groups where appropriate.

1.75 Since final statements and position papers were the final output of the Committee, later drafts needed to be considered and agreed by the full Committee since they represented a collective view.

1.76 Since over half of the Committee's meeting are fully online, Members discussed some potential changes to the current procedures; No changes were agreed but the topic remans under review.

1.77 The role of the lay Members was considered; while they may sometimes find it difficult to participate at meetings due to the very technical content, their contribution was much valued. It was agreed that lay Members from different Committees should meet to share their perspectives and consider best practice.