MUT/MIN/2021/03

COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Minutes of the meeting held at 10.30 on 12th October 2021 via MS Teams.

Present:

Chairman:	Professor G Jenkins
Members:	Mr A Bhagwat Dr C Beevers Dr G Johnson Professor D Harrison (Ex officio) Professor S Doak Dr S Dean Professor P Fowler Ms J Kenny Dr A Povey Mrs M Wang
Secretariat:	Dr O Sepai (UKHSA Scientific Secretary) Ms C Mulholland (FSA Secretariat) Dr D Gott (FSA Secretariat) Ms C Tsoulli (FSA) Dr A Cooper (FSA)
Secretariat Support:	Dr R Bevan (IEH Consulting)
Assessors:	Dr F Fernandez (VMD) Dr H Stempleski (MHRA) Ms F Hill (BEIS) Dr L Koshy (HSE) Dr A Axon (HSE) Dr W Munro (FSS)
In attendance	Dr M Jacobs (PHE)

Dr J O’Brien (Food Observatory)
Dr K Broom (UKHSA)
Miss H Banks (HSE)
Miss K Lochrie (HSE)
Paula Braun (PETA)
Dr S Bull (IEH Consulting)

ITEM 1: ANNOUNCEMENTS/APOLOGIES FOR ABSENCE

1. This was the second meeting for Professor Gareth Jenkins as the new chair of the COM. The Chair welcomed the COM members, assessors and secretariat. The Chair also welcomed Dr Ruth Bevan from IEH Consulting providing support to the COM secretariat. An apology had been received from Liz Lawton (Defra).

2. The June 2021 meeting of COM was the last for Dr Ruth Morse who had come to the end of her term on the COM. The Chair thanked Dr Morse for all her contributions over the years. In addition, the Chair informed members that this was Steve Dean's last meeting, after 10 years on COM, and thanked him for his contributions.

3. Members were requested to declare any interests before the discussion of any items.

ITEM 2: MINUTES OF MEETING ON 10th June 2021 (MUT/MIN/2021/02)

4. Members agreed the minutes of the COM meeting held on the 10th June 2021 (MUT/MIN/2021/02), subject to minor typographical amendments.

ITEM 3: MATTERS ARISING

5. Frances Hill from BEIS provided some background information on how the newly formed Office for Product Safety and Standards (OPSS) was likely to interact closely with COM and the other expert Committees going forward. OPSS primarily looks at the safety of cosmetics and toys and is currently a temporary group, due to finish in February 2022. The needs and requirements for OPSS after that time are being evaluated to provide a more permanent solution. Terms of reference and the membership of OPSS is available on the website.

ITEM 4: Draft Annual Report for 2020 (MUT/2021/10)

6. Members were informed that this was a draft report which collated previous activities undertaken by COM during 2020 and asked to comment on whether it was a fair representation. It was suggested that due to the technical content of the report, a lay person's introduction was needed at the start of the report to say what the COM does, similar to that in the combined COT/COM/COC 2019 annual report. It was confirmed that this would happen when the three committee reports were collated.

ITEM 5: Discussion – QSAR and Genotoxicity

7. A range of Quantitative Structure-Activity Relationship (QSAR) models have been developed to predict genotoxicity. The COM has previously agreed that where no genotoxicity data are available, the intrinsic chemical and toxicological properties of a chemical must be considered prior to developing a genotoxicity testing programme, as reported in "*Guidance On A Strategy For Genotoxicity Testing Of Chemical Substances*" (COM, 2011) and as updated in 2021 (to be published). This guidance describes a staged

approach to testing consisting of stages 0 (preliminary considerations including physico-chemical properties), 1 (*in vitro* genotoxicity tests) and 2 (*in vivo* genotoxicity tests). QSARs are incorporated into Stage 0 of the COM guidance.

8. Alternatives to animal testing and the usefulness of computational methods in the prediction of genotoxicity are areas of increasing research. QSAR models and their predictions currently cannot replace the need to undertake the *in vitro* and *in vivo* genotoxicity tests required to derive conclusions on mutagenic hazard except in specific regulatory settings. As the development and use of QSAR is a rapidly developing field, it was agreed that the current text in the COM overarching guidance document should be reduced and a larger 'stand-alone' guidance statement be prepared which could be updated as needed.

9. A draft document - 'Guidance Statement on the use of QSAR models to predict genotoxicity' was prepared and discussed by COM in February 2019 (MUT/2019/03). Following amendments, a revised paper was discussed in February 2020 (MUT/2020/02) and November 2020 (MUT/2020/20). No agreement was reached as to whether the draft guidance statement was 'fit-for-purpose' and it was also suggested that QSARs could be incorporated into the COM guidance on impurities, as this is where it is likely to be used.

10. A sub-group discussion with some COM members was held in September 2021 to plan a way forward. It was suggested that, based on current acceptance and use of QSARs, incorporation of examples of use and reporting of data should be included in the updated impurities guidance document, with a link to the OECD portal provided to give the most current perspective/tools etc. A more general description (taken from the current draft document) would then be re-introduced into the COM overarching guidance document to support the Stage 0 testing text.

11. Members agreed that it was important for any COM guidance to highlight applications of QSAR, as for the assessment of impurities, rather than proving a list of QSAR models and approaches. As such the proposed approach was accepted with a draft statement to be considered at the COM meeting in June 2022.

12. It was also agreed that a sub-group of interested members would be convened to facilitate updating of the impurities guidance statement. A timeline for this was not discussed.

ITEM 6: Discussion – OECD Draft Detailed Review Paper on the Miniaturised Versions of the Bacterial Reverse Gene Mutation Test.

13. Members have been previously sent the OECD Draft Detailed Review Paper (DRP) on the miniaturised Ames test (bacterial reverse gene mutation test) for review. The COM were asked to provide comments on the DRP by the 15th October in the OECD template, with justifications as necessary, for collation by the National Coordinator at UK HSA. Assessors were requested to also send any comments which would be submitted separately.

14. It was noted that the DRP will not lead to a revision of the TG (TG471), but the aim of the review was to provide recommendations on the use of each of the mini-Ames tests proposed. From a UK perspective it was considered important to highlight and record any controversial points that were not in line with UK practice.

15. There was general agreement with the recommendations of the DRP. It was felt that until a robust validation process of the mini-Ames assays had been carried out, no further progress could be made in implementing the assays for regulatory testing. Further justification was asked for including better definition of what the assay is for, e.g. increasing output and reducing costs, incorporation of information relating to how laboratories were chosen to take part and whether there is a clear benefit of using mini-Ames assays above TG471. A short written summary of the text submitted to OECD would be provided to COM members at the meeting in March 2022.

RESERVED ITEM

ITEM 7: REVIEW OF THE GENOTOXICITY OF TITANIUM DIOXIDE (MUT/2021/11)

16. This item was classified as reserved business. The minutes will be published at a later date.

RESERVED ITEM

ITEM 8: HYDROXYANTHRACENE DERIVATIVES (MUT/2021/12)

17. This item was classified as reserved business. The minutes will be published at a later date.

OPEN SESSION

ITEM 9: Any other business

18. There was no additional business.

ITEM 10: Date and venue of next meeting

19. 1st March 2022, venue to be confirmed.