MUT/MIN/2022/01

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

Minutes of the meeting held at 10.30 on 1st March 2022 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 Ms J Kenny Dr A Povey Mrs M Wang
Secretariat:	Dr O Sepai (UKHSA Scientific Secretary) Mr S Robjohns (UKHSA Secretariat) Ms B Gadeberg (UKHSA Secretariat) Ms C Mulholland (FSA Secretariat) Dr D Gott (FSA Secretariat) Ms C Potter (FSA Secretariat) Ms C Tsoulli (FSA) Dr A Cooper (FSA)
Secretariat Support:	Dr R Bevan (IEH Consulting)
Assessors:	Ms F Fernandez (VMD) Ms F Hill (BEIS) Ms Jo Little (HSE) Dr A Axon (HSE) Dr W Munro (FSS) Mr H Penrose (DHSC)

In attendance	Dr J O'Brien (Food Observatory)
	Mr M Symington (UKHSA)

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ITEM 1: WELCOME AND APOLOGIES FOR ABSENCE

1. 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 the member Dr Paul Fowler.

ITEM 2: ANNOUNCEMENTS

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

3. Members were informed that an advert for five COM vacancies had closed. A small number of applications had been received. Interviews would take place in March 2022. Professor Shareen Doak had come to the end of her term on the COM, but due to a number of current member vacancies had been co-opted onto the committee until the end of 2022. Dr Carol Beevers had come to the end of two terms on the COM and an application had been made for Dr Beevers to be retained for a third term.

ITEM 3: MINUTES OF THE MEETING HELD ON 12 OCTOBER 2021 (MUT/MIN/2021/03)

4. The minutes of the COM meeting held on the 12th October 2021 were agreed subject to minor typographical amendments.

ITEM 4: MATTERS ARISING

5. The COM were informed that a decision had been made to postpone a report on Quantitative Structure-Activity Relationship (QSAR) models. A draft document had previously been brought to the committee on a number of occasions. Members had advised that the document should focus on providing advice on the appropriate use of QSARs in evaluating potential mutagenicity rather than providing detailed descriptions of each model. It had also been suggested that such a document could be combined with advice on the assessment of the mutagenicity of mixtures and the impurities they may contain.

RESERVED ITEM

ITEM 5: FIRST DRAFT STATEMENT ON THE GENOTOXICITY OF HYDROXYANTHRACENE DERIVATIVES IN FOOD (MUT/2022/01)

RESERVED ITEM

ITEM 6: UPDATE ON THE REVIEW OF THE GENOTOXICITY OF TITANIUM DIOXIDE

OPEN MEETING

ITEM 7: UPDATE ON THE COM REVIEW OF SMOKE FLAVOURINGS

12. Smoke flavourings are added to food, such as meat or cheese, to give them a 'smoked' flavour, as an alternative to traditional smoking. Smoke flavourings can also be added to foods which are not traditionally smoked, such as soups or sauces. Smoke flavourings need to be authorised before they can be placed on the market in Great Britain. Current authorisations will expire on 1st January 2024. Renewal applications must be submitted 18 months before the authorisation expires. This means that application dossiers for renewal need to be submitted before the end of June 2022 and this must include genotoxicity data.

13. This means that the FSA and the relevant FSA Joint Expert Groups may need to consult with the COM soon regarding the genotoxicity data submitted with applications for renewal of approvals for smoke flavourings.

ITEM 8: UPDATE ON THE COM REVIEW OF THE EFSA EVALUATION OF BISPHENOL-A

14. The FSA provided an update on EFSA consultation on its draft opinion proposing a lowering of the Tolerable Daily Intake (TDI) for bisphenol A. EFSA published a consultation on its draft opinion, which closed on the 22nd February 2022. In response to this consultation the FSA requested that the Committee on toxicity of chemicals in food consumer products and the environment (COT) provide a view to EFSA. The COT had a number of concerns over the approach used by EFSA in its evaluation, which the COT considered made it difficult to assess the toxicity database as a whole and had a number of concerns relating to the studies used to derive the new EFSA proposed TDI. The COT had requested the opinion of COM members on the EFSA evaluation of the genotoxicity data on bisphenol A and thanked the COM for its contribution. COM members were generally content with the EFSA review of the genotoxicity data and agreed with the overall EFSA conclusion that DNA strand breaks, clastogenic and aneugenic effects seen in mammalian cells *in vitro* following exposure to bisphenol A were very likely due to oxidative stress related mode of genotoxicity and that bisphenol A was not mutagenic *in vivo*. The combined COT and COM comments had been submitted to EFSA.

15. Following the publication of the finalised EFSA opinion the FSA would need to consider whether it needs to be referred to the UK expert advisory committees again. It was considered unlikely that there would be a need to consult the COM further on the genotoxicity aspect and would more likely be referred to one of the other expert committees, such as the Committee on the carcinogenicity of chemicals in food consumer products and the environment (COC).

ITEM 9: DRAFT COC GUIDANCE STATEMENT "THE USE OF BIOMARKERS IN CARCINOGENIC RISK ASSESSMENT" (MUT/2022/03)

16. No interests were declared for this item.

17. The COC has periodically published guidance for the evaluation of chemicals for carcinogenicity which was separated into individual documents to allow faster revisions to be made in the case of rapidly developing areas. This included a separate document addressing the use of biomarkers in carcinogenic risk assessment (G04).

18. As part of ongoing updates of G04 the COC considered it would be helpful to have COM comment on the DNA adducts and genotoxicity biomarkers sections, which have been shortened in the current version (presented as MUT/2022/03 at Annex A). In addition, COC have requested that COM consider whether they wish to produce guidance on biomarkers relevant to its area of expertise, which could then be referred to by the COC in its guidance documents.

19. A number of points of clarification were suggested by COM members to provide consistency in presenting the information within the DNA adducts and genotoxicity biomarkers sections. Inclusion of references to show monitoring of biomarkers in, for example, cancer patients was requested. It was also considered important to include discussion of endogenous levels of DNA adducts to give perspective to the reader. Members advised that the discussion of chromosomal aberration/micronucleus formation should be balanced with discussion on mutation and how both sets of data can be combined. Extracellular vesicles and exosomal biomarkers and aneuploidy had not been included in the draft and it was suggested that these should be added for completeness.

20. COM members were advised that, as COC were not experts in the field being discussed, any of the changes made to the paper at Annex B would be at a higher level. It was agreed that these changes would be added to the revised G04 document and assessed by COC members at the meeting in July 2022. The development of a separate COM guidance document on biomarkers relevant to the assessment of genotoxicity was discussed by members. It was agreed to take this forward with a scoping paper to be presented at the COM meeting in June 2022.

ITEM 10: DRAFT COC, COM, COT DOCUMENT "HOW DO THE COMMITTEES EVALUATE THE RELEVANCE AND RELIABILITY OF DATA WHEN ASSESSING A CHEMICAL OF CONCERN (MUT/2022/04)

21. No interests were declared for this item.

22. The topic of 'biological relevance and statistical significance' has been raised as an area of interest during Committee horizon scanning activities for a number of years. A scoping paper was presented at the

Joint COC/COM meeting in November 2020 (CC/MUT/2020/03 – presented at Annex A) also attended by some COT members, which outlined some of the more relevant and significant work that has been published on this issue in recent years. Following discussion of the scoping paper, it was agreed that the general public would benefit from guidance that provided clarity on how the expert Committees evaluate data with respect to consideration of biological relevance and statistical significance

23. The paper (MUT/2022/04 - Annex B) provided a brief outline of the Committee evaluation process focussing on the relevance and reliability of data and was written specifically to inform the lay person. It was reviewed by lay members of the three Committees and was discussed by COC (CC/2021/06) and COT (TOX/2021/18) in March 2021. During discussions, members of COC and COT proposed that two documents be developed from the paper, one aimed at the lay audience about the process used by the Committees to evaluate evidence and reach conclusions and the second aimed at a more informed audience on statistical significance testing and consideration of biological relevance, using the current document as the basis.

24. During discussion COM members highlighted the need for guidance on how to assess the impact of study limitations on the data and any statistical findings, and the value of including or omitting such studies in an overall evaluation of evidence. Inclusion of examples to illustrate this was suggested to help the reader. The current version of the paper was considered to be a good guide for educating the public and complicating it with a significant amount of new data may detract from that. In addition, the paper was considered a useful addition to other on-going initiatives (for example at OECD) which are debating the same issues.

25. COM members considered that the link between statistical significance and reliability may need to be highlighted more within the paper. The link between choice of test and the p values should also be discussed as they are not absolute values and can change according to the types of tests used. The paper and summary should define and discuss transparency and objectivity, including the source of data and robustness of that due to possible publication bias. Going forwards, it was confirmed that the amended version of the paper at Annex B would be a standalone piece across the three Committees.

ITEM 11: ANY OTHER BUSINESS

26. Members were informed that draft OECD Test Guidelines on the mini-Ames and the *in vivo* PIG A assay may be sent to COM members for comment soon.

27. The FSA informed the COM that EFSA was updating its opinion on Benchmark dose modelling and that this may also be sent to COM member for comment when the EFSA draft opinion is published for public consultation.

ITEM 12: DATE OF NEXT MEETING

28. 9TH June 2022.