



MUT/MIN/2025/01

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

Minutes of the meeting held at 09:30 am on 13th March 2025 at UKHSA, UKHSA Chilton.

Present:

Chairman: Professor G Jenkins

Members:

Dr A Doherty
Dr P Fowler
Dr N Goldsmith (Associate member)
Dr G Johnson

Dr A Povey
Mrs M Wang
Mr P Rawlinson
Dr Rob Smith
Dr Robert Searle Foster

Secretariat:

Dr O Sepai (UKHSA Scientific Secretary)
Mr S Robjohns (UKHSA Secretariat)
Dr N Raja (UKHSA Secretariat)
Dr C Mulholland (FSA Secretariat)
Dr C Potter (FSA Secretariat)
Mr T Fraser (UKHSA)
Ms Chara Tsoulli (FSA Secretariat)

Assessors:

Kerry Webster (HSE)
Ms Ann Baker (VMD)
Mr Ian Martin (EA)
Mr Will Munro (DHSC)

Observers:

Ms Natalie Stratford Devalba (UKHSA)

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ITEM 1: WELCOME AND APOLOGIES FOR ABSENCE

1. The Chair welcomed the COM members, assessors, and secretariat. An apology for absence had been received from Ms J Kenny.

ITEM 2: REVIEW MINUTES FROM COM MEETING IN JUNE 2024 (MUT/MIN/2024/02).

2. The minutes of the COM meeting held on the 20th of June 2024 were agreed with minor amendments.

ITEM 3: DECLARATION OF INTERESTS

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

4. Dr Nathan Goldsmith noted that he has received funding for his European research project on smoke flavourings; however, this was not considered a declaration of interest. Paul Fowler has conducted QSAR analysis for a smoke flavouring and, as a result, would not participate in discussions related to this topic. This was not considered a conflict for this meeting as no data were discussed.

5. Dr Robert Searle-Foster (Lhasa) declared an interest because he works for an organization that develops QSAR models. This declaration does not represent a conflict of interest, as his expertise is necessary for developing the guidance document on the use of QSAR.

6. Dr George Johnson has worked with Firmenich and the International Organisation of the Flavours Industry (IOFI), specifically on smoke flavourings but not on mixtures. Dr Robert Smith declared that he has authored a paper on smoke flavourings. These were not considered a conflict for this meeting as no data were discussed.

7. Additionally, there was a general discussion of Non-Disclosure Agreements (NDA). It was agreed that any members who had signed an NDA would withdraw from discussions of relevant agenda items if they believed there may be a conflict of interest. Meeting minutes would be carefully reviewed, adjusted and shared as needed to ensure confidentiality is maintained.

ITEM 4: MATTERS ARISING

8. The Chair invited members to express their interest in any topics for Horizon Scanning, noting that the contract with IEH has now come to an end and the process to let a new contract to supporting the secretariat has started. Members asked whether the COM primarily operates reactively or proactively in introducing new ideas. The Chair acknowledged that while COM has traditionally taken a reactive role, it may be beneficial to adopt a more forward-thinking and proactive approach in the future by introducing new ideas and publishing papers. In addition, to note the review and update of the guidance documents is a proactive activity.

9. A question was raised on how the committee addresses updates to guidance such as that published by EFSA. The FSA noted that it often relies on older EFSA Guidance. It was suggested that a COM discussion on a new approach to the Weight of Evidence (WoE) methodology and guidance on mixtures would be valuable. A COM consideration of artificial intelligence specifically in relation to genotoxicity was also suggested. This would build on the presentations in June 2024.

10. There was also some concern expressed over a lack of awareness of the committee's work. Increasing visibility of the work of the COM was suggested by engaging with groups such as UKEMS, potentially holding sessions to raise awareness about COM's role and its outputs.

11. The increasing availability of mutation data was highlighted and its potential significance and suggested as a priority area for future focus. An item on non-genotoxic carcinogens was proposed for horizon scanning. A speaker could be invited with expertise on non-genotoxic mechanisms of cancer. There was interest in having a representative from the Sanger Institute give a presentation on clonal expansion.

12. Additionally, the committee discussed how to make COM opinions more accessible. One suggestion was to publish occasional papers or use social media for better outreach. The Chair proposed using LinkedIn or other social media platforms to share COM's guidance more widely and extend invitations for broader participation.

13. Active promotion of COM's work within clinical, academic, and scientific communities was also suggested. The Chair further emphasized that the committee should also remain reactive considering emerging issues that require timely responses.

14. Finally, the committee explored ways to improve information flow, such as conducting joint meetings with other organizations like COC and COT. The Chair also noted the importance of cross-committee movement to foster collaboration and knowledge-sharing to include topics for horizon scanning.

ITEM 5: GUIDANCE ON THE USE OF QSARS GENETOX (MUT/2025/02)

15. Paper MUT/2025/02 was presented by Dr Paul Fowler (Sub-group Chair).

16. (Q)SAR is recommended in the overarching COM 'Strategy for testing of chemicals for genotoxicity' within stage 0 and for the assessment of impurities. However, COM guidance outlining best practice in the use of (Q)SAR is lacking. This paper was intended to provide information to support the production of COM recommendations for an evaluation of genotoxicity using (Q)SAR model(s), including the prioritization of compounds, selection of the (Q)SAR model, reporting of (Q)SAR predictions, considerations of expert knowledge, read-across approaches, and integration of findings into a weight-of-evidence evaluation.

17. . The objective of this guidance was to outline COM recommended approaches and considerations for selecting (Q)SAR models and reporting

(Q)SAR predictions for genotoxicity that meet regulatory standards, when necessary. The Committee agreed that the objectives of the guidance have been achieved.

18. Upon reviewing the guidance, the Committee agreed that the OECD principles as discussed in the draft COM Guidance were valid. These principles include: use of a (Q)SAR model where the scientific validity has been established; the substance should fall within the applicability domain of the (Q)SAR model; the prediction should be fit for regulatory purpose; and the information should be well documented. These principles can also be generally applied for most objectives using (Q)SAR for hazard identification.

19. Members noted that QSAR generated data had a limited lifespan in regulatory settings due to the fast-paced changing nature of the field. Regulatory agencies like the FDA often prefer recent QSAR data (e.g., QSAR generated within the last 12 months) and may question the validity of submitted QSAR data that is older than 4 to 5 years. To align with these expectations, updates to QSAR models and documentation are generally made on an annual basis or as significant changes occur.

20. The (Q)SAR guidance provided does not prescribe specific tools or approaches but rather acknowledges the availability of various tools and software allows users to make informed decisions based on their needs. It was the responsibility of the user to justify the use of the data that it submits. The focus should be on using the most up-to-date data whenever practically possible, as that ensures the reliability of conclusions.

The COM agreed that the guidance was clear. Members were requested to provide any further amendments or comments to the secretariat. It was agreed that this could then be signed off by Chair's action and published.

ITEM 6: HSE discussion paper – United Nations (UN) Globally Harmonised System (GHS): Revision of germ cell mutagenicity classification criteria (MUT/2025/03)

21. HSE is the UK representative in the international discussions relating to the development of the GHS. As part of the Working Group on germ cell mutagenicity hazard classification criteria (Chapter 3.5, UN GHS), HSE presented a paper to COM covering the proposed revisions. The paper provided background on the Working Group plans, the key issues identified by the Working Group, and an outline of the proposed changes to the criteria. Other updates on the text were also included with a draft copy of the chapter for review by the Committee.

22. The aim for the paper was to invite the Committee to review the changes to the draft chapter, with consideration being given to two key themes:

1. A view on merging Category 1B (c) into Category 1A, to make identification of established germ cell mutagens easier
2. An initial view on the issue of somatic cell mutagenicity as a hazard in its own right, with potential to merit an independent classification from the current germ cell mutagenicity framework.

23. HSE requested a range of opinions from members, rather than a full Committee position. Proposed changes to the chapter text were generally viewed positively by the members.

24. A comment was given on the wording around 'germ cells of exposed humans' under the proposed Category 1A (b) (Annex I of discussion paper), namely what would constitute evidence of exposure. HSE will work on providing guidance in the chapter as part of the Working Group for improved clarity on this point.

25. A concern was raised by one member regarding the current classification hazard categories and how tests are weighted. It was suggested that currently, in vivo indicator assays (e.g. comet assay) are given a similar weight to mutation assays (e.g. transgenic rodent assay), which can lead to issues with assessment. HSE will provide this feedback to the UN GHS.

26. General support was given on recognising somatic cell mutagenicity as an independent hazard to germ cell mutagenicity. It was noted by HSE that these discussions are on pause within the UN GHS Working Group, and that HSE may need to seek further input from the COM on this issue in the future.

27. HSE thanked the Committee for their initial thoughts on the proposed revisions. The current plans within the Working Group are to continue with the current work programme, as laid out in the current terms of reference¹. This includes making refinements to the guidance section of the chapter, whilst continuing discussions around the proposed classification criteria.

ITEM 7: Discussion of future review of Smoke flavourings (MUT/2025/04)

28. This Item was considered as reserved business.

ITEM 8: ANNUAL REPORT DRAFT FOR 2024

29. The draft COM Annual report for 2024 was agreed with minor amendments.

30. It was requested that declarations of interest be submitted to UKHSA (Tom Fraser) for inclusion in the annual report, prior to its publication.

ITEM 9: OECD UPDATES

31. The committee was informed that there were several ongoing OECD projects related to genotoxicity, including a new test guideline (TG) on the ToxTracker and proposed new TG for the 3D skin micronucleus assay and the comet assay. A proposed new OECD TG for the gamma H2AX assay for DNA

¹ [Terms of reference and work programme of the informal working group on the criteria for classification for germ cell mutagenicity | UNECE](#), (REF: ST/SG/AC.10/C.4/2021/3)

damage was at an early stage with a detailed review paper currently being drafted. The current status of OECD consideration of Error Corrected Next Generation Sequencing was uncertain.

32. One member involved with the OECD genotoxicity Test Guidelines process, was requested to provide a list of ongoing OECD genotoxicity projects and developments to the COM for awareness. The provided list of OECD projects presented to the OECD Genetox Expert Group that may be of interest to COM was as follows:

- New Test Guideline (TG) on the ToxTracker assay: a stem cell-based reporter assay for mechanistic carcinogenicity hazard assessment' – Lead by Netherlands. I believe the ToxTracker Test Guideline (TG) was approved by the WNT in April and should be available later in June 2025.
- 'In vitro genotoxicity testing for dermal exposure using 3D skin models: reconstructed skin micronucleus test and reconstructed skin Comet assay' – Lead by Germany/France. Aim to draft the TG following EURL ECVAM Scientific Advisory Committee (ESAC) peer review of the validation dataset.
- 'Update of TG 489 Comet Assay for gonadal cells to study germ cell specific genotoxic effects' – Lead by Norway/Denmark. Validation experiments being performed to support revision of TG 489.
- 'Support to UN GHS for modification of germ cell mutagenicity criteria in Chapter 3.5' – Lead by EC-JRC/OECD Secretariat.
- 'Detailed Review Paper (DRP) and a Retrospective Performance Analysis (RPA) for the in vitro gH2AX/pH3 method: a multiplexed biomarker approach that provides information on genotoxic mode of action' – Lead by France/Germany. Aiming to submit DRP to WNT by end of 2025.
- 'Validation of the In Vitro Micronucleus assay for Engineered Nanomaterials' – Lead by UK/DE/FR/NO and partners: US/LU. Planning inter-lab validation study.
- 'DRP on the application of error-corrected next generation DNA sequencing (ecNGS) for gene mutation evaluation' – Lead by US. Aiming for DRP and RPA submission to WNT by end of 2026. IWGT report is in preparation and expected to be published in 2025 prior to the IWGT in 2026.
- 'Revision of in vivo genotoxicity test guidelines' "Evaluation and Interpretation of Results" and "Test Report" language' – Lead by US/Canada. Updates approved by the WNT in April and should be available later in June 2025. Initial focus on TG 470 and 488 (in vivo Pig-a and in vivo TGR, respectively). Aiming to move to TG 474 and 489 (in vivo MN and Comet) once revisions agreed for TG 470 and 488.
- 'Adverse Outcome Pathway (AOP) network leading to genotoxicity' – Lead by Belgium/France. Aim to combine AOPs leading to permanent DNA damage into an AOP network to support the development of IATA for genotoxicity integrating in vitro NAMs.

It was suggested that it would be helpful that when there was a need or request for a COM view on the development or update of an OECD Test Guideline that the committee could be provided with advance warning and ahead of a COM meeting so that members were given sufficient time to consider and provide any comments.

ITEM 10: AOB

33. The Chair declared a new interest due to changes in staff at the University of Swansea: from May 2025 Professor Gareth Jenkins will be the principal investigator for a research grant from the Titanium Dioxide Manufacturers Association (TDMA). The COM had previously published an opinion on the genotoxicity of titanium dioxide. This future DOI has no impact on COM's prior conclusions.

ITEM 11: DATE OF NEXT MEETING

34. Date of next meeting – 19th June 2025. The meeting location is yet to be determined.