**MUT/MIN/2025/03**

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

Minutes of the meeting held at 10:30 am on 16th October 2025 via MS Teams.

**Present:**

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| **Chairman:** | Professor G Jenkins |
| **Members:** | Dr A Doherty<br>Dr P Fowler<br>Dr N Goldsmith (Associate member)<br>Dr G Johnson<br>Ms J Kenny<br>Dr A Povey<br>Dr R Searle Foster<br>Dr R Smith<br>Mrs M Wang<br>Dr C Beevers |
| **Secretariat:** | Dr O Sepai (UKHSA Secretariat)<br>Mr S Robjohns (UKHSA Secretariat)<br>Ms N Stratford Devalba (UKHSA Secretariat)<br>Ms C Potter (FSA Secretariat)<br>Ms B O'Connell (Bibra Toxicology Advice & Consulting Ltd) |
| **Assessors:** | Ms A Baker (VMD)<br>Dr P Paramasivan (HSE)<br>Ms K Boss (FSS)<br>Ms K Webster (HSE)<br>Dr J Clements (MHRA) |
| **Observers:** | Professor D Harrison (COC)<br>Ms G Chettuvatty (UKHSA)<br>Ms M Chatterjee (UKHSA) |

## ITEM 1: WELCOME AND APOLOGIES FOR ABSENCE

1. The Chair welcomed the COM members, assessors, secretariat and observers. Apologies were received from Ms Cath Mulholland (FSA secretariat), the COM member Mr Paul Rawlinson, and the assessors Ms Liz Lawton (Defra), Ms Frances Hill (OPSS) and Ms Claire Moni (FSS).

## ITEM 2: ANNOUNCEMENTS

2. This was the last meeting of the COM member Dr Andrew Povey. The Chair thanked him for his work over the years.

3. The Chair had a meeting with the Department of Health and Social Care (DHSC) and was informed that COM has been changed from a non-departmental advisory public body to an expert advisory committee. This was confirmed on the 15th of October 2025. This will have no effect on how COM operates but members will be receiving new contracts. Recruitment will also no longer require ministerial sign off.

4. Tom Fraser has a new role within UKHSA and therefore there is a vacancy for committee administrator. Currently, these responsibilities are being covered by Natalie Blowfield of UKHSA.

## ITEM 3: MINUTES OF THE MEETING HELD ON 19TH JUNE 2025 (MUT/MIN/2025/02)

5. The minutes for the closed item are to be received from FSA.

6. Otherwise, the minutes of the COM meeting held on the 19th June 2025 were agreed subject to minor typographical amendments.

## ITEM 4: MATTERS ARISING

7. There were no matters arising not already on the agenda.

## ITEM 5: "THE END OF THE GENETIC PARADIGM OF CANCER" – DISCUSSION PAPER (MUT/2025/05)

8. A discussion paper (MUT/2025/05) drafted by Bibra UKHSA COM secretariat support on the Huang et al. (2025) publication "The end of the genetic paradigm of cancer" (PLoS Biology Mar 18;23(3):e3003052) was presented. The discussion document noted the main arguments presented by Huang et al. (2025) relating to their view that the somatic mutation theory (SMT) is insufficient to explain the complexity of cancer. The Huang et al. (2025) paper was summarised (Annex A) in MUT/2025/05, and brief results of related literature searches were given (Annex B). Several questions in MUT/2025/05 were put forward to COM members, which were discussed.

9. The COM members stated that the idea that the SMT is not sufficient to cover the complexity of cancer is not new; many tumours are formed by mechanisms for which the SMT is not relevant. However, the Huang et al. (2025) paper did not account for these modes of action. In addition, the Huang et al. (2025) paper was not written with chemical toxicology or risk assessment in mind. It did not mention regulatory testing or safety assessment. Instead, it focused on the categorisation of individual tumours, with some reference to treatment options.

10. It was also noted that Huang et al. (2025) had possibly misinterpreted some of the evidence presented, for example that almost every gene in the genome has been associated with cancer; the work referenced was clear that the associations were not causal for every gene.

11. The Huang et al. (2025) paper highlighted some areas in which current thinking could be extended in future, such as the regulation of gene expression for example, epigenetics. While there are currently challenges in testing for epigenetic effects leading to cancer, a previous joint COC and COM workshop on epigenetics concluded that the current safety assessment methods used with genotoxicity data are sufficient.

12. Cancer is viewed as a disease of the tissues, including interactions between cancer and stromal tissues, an idea already accepted by COM members. The Huang et al. (2025) paper supported the COM view that in cancer hazard and risk assessment it is appropriate to consider supplementary processes alongside DNA damage or mutagenicity, such as epigenetics, the tissue microenvironment, and inflammatory processes. Another point raised by Huang et al. (2025) was that some non-cancerous

tissues may have several oncogenic ‘driver mutations’, and some cancer tissues may have none. COM members supported the idea that methods such as error-corrected DNA sequencing should therefore not be solely relied upon for cancer assessment.

13. The COM noted that a good correlation between mutagenicity and carcinogenicity has been seen for nitrosamines, and there is ongoing work by Health Canada and RIVM in extending this to other mutagens.

14. Huang et al. (2025) described how treatment with a chemotherapeutic drug might cause a tumour to diminish, but that another genetically different tumour could return. However, COM members acknowledged that chemotherapeutic agents themselves can cause mutations leading to secondary tumours. On the other hand, the example of acute myeloid leukaemia was put forward, pre-existing clones of which may come back after the initial cancer has been treated. Secondary tumours may be new, or pre-existing clones.

15. After considering the Huang et al. (2025) paper, COM members were satisfied that current practices for carcinogenicity evaluations are appropriate and sufficiently health protective. They also emphasised the importance of communication to inform, rather than scare the public, but not to tell too simple a story. Rephrasing of question (vii) in the discussion paper (MUT/2025/05) was proposed so as not to suggest that interspecies or interindividual variation are not currently accounted for in cancer risk assessment; if a statement is published, this should be edited.

16. At this stage, it was agreed that a more detailed review is probably not needed, and that the views and opinions of the COM on this item could be useful for the COC to consider in November 2025. If useful, the COM and COC could make a joint statement on the Huang et al. (2025) paper.

## ITEM 6: “WEIGHT OF EVIDENCE ASSESSMENT OF GENOTOXICITY DATA: DISCUSSION” – PRESENTATION AND DISCUSSION

17. Dr Carol Beevers and Dr Paul Fowler (presenting the opinion of Professor David Kirkland) gave two presentations regarding weight of evidence (WoE) assessments for genotoxicity.

18. Dr Carol Beevers discussed the challenges that were faced by the Joint Expert Group on Additives, Enzymes and other Regulated Products (AEJEG) when evaluating genotoxicity WoE for smoke flavourings. Most applicants appeared to use the European Food Standards Authority (EFSA) WoE approach, while the AEJEG evaluation followed the Synthesis and Integration of Epidemiological and Toxicological Evidence (SETE) approach published by the COT and COC to evaluate each study for adequacy, reliability and relevance. However, the SETE guidance does not focus on genotoxicity, so

challenges were faced during the initial assessment due to the lack of clarity on the definition of adequacy, reliability and relevance, and the consistency of how these terms were used.

19. There are differences in the definition of terms between SETE, EFSA and the AEJEG assessment – for example, SETE and AEJEG had an unclear distinction between adequacy and reliability, while adequacy is not used by EFSA. There are differences between international regulatory and expert groups with respect to genotoxicity testing, and between Food standards Agency (FSA) group themselves (for example, the WoE approach used by AEJEG when evaluating smoke flavourings differed from that adopted by COM when evaluating titanium dioxide).

20. Additional guidance on the relevance and reliability of studies for a genotoxicity WoE approach would improve consistency between various committees and expert groups.

21. The presentation from Dr Paul Fowler highlighted the differences in weighting applied to the relevance of different tests between the EFSA WoE approach and the Brusick et al. (2016) approach. Brusick et al. (2016) has five default weight categories which can be adjusted according to the reliability of the study and quality of the data. The categories are high, moderate-to-high, moderate, low-to-moderate, and low. High, moderate-to-high and moderate are considered acceptable for further evaluation, while low-to-moderate and low are not. In this approach, more weight is given to in vivo tests compared to in vitro tests.

22. The EFSA approach gives high relevance to the relevant endpoint but allocates the same weight to in vitro and in vivo studies for the same endpoint. It has three weighting categories: high, limited and low, with high and limited weightings considered acceptable for further evaluation.

23. Brusick et al. (2016) and EFSA categorise comet assays differently: the in vivo comet assay is given a weighting of moderate by Brusick et al. (2016), while EFSA categorise it as high weighting. The in vitro comet assay is given a low weighting by Brusick et al. (2016) for all test materials, while nanoparticles are given a weighting of limited in the EFSA approach (all other materials are given a low weighting).

24. The EFSA approach affects the interpretation of certain scenarios. For example, a positive in vitro micronucleus test and a negative in vivo micronucleus test would result in the overall WoE being negative using the Brusick et al. (2016) approach. However, the EFSA approach would apply the same weighting for both these tests, therefore the outcome of the WoE assessment is harder to interpret.

25. Discussion and agreement are required to help determine the relevance criteria for different endpoints and test systems, how relevance can me modified in light of robustness of study design and quality of data, and how conflicting data from different

endpoints should be weighted in overall WoE assessments. It was emphasised that a framework is required to help determine the reliability of a set of data.

26. The Committee agreed that this is an important issue and a framework to aid consistency in genotoxicity WoE assessment would be beneficial. Including “what not to do” to highlight worst practices as well as best practices and including publication bias would be useful.

27. It was noted that EFSA are currently reviewing and rewriting their genotoxicity guidelines. The publication date for this is unknown, however it is expected to be the second half of 2026. EFSA are holding a stakeholder workshop for their genotoxicity guidelines on the 3rd and 4th of November 2025 – registration for interest in attending closes on the 20th of October 2025.

28. COM will create a subgroup to put together this guidance. An email will be sent to members, but any interested parties should also contact Ovnair Sepai. The opinion of the COC, COT and relevant regulatory bodies in the UK will be sought. This guidance will build on the SETE guidance but will be tailored for genotoxicity testing.

**ITEM 7: OECD UPDATES**

29. The COM was informed that a detailed review paper (DRP) for Gamma H2AX/pH3 assay for DNA damage had been submitted to the Working Group of National Co-ordinators of the Test Guidelines programme (WNT). The document was circulated only to the OECD genotoxicity working group for review, and the OECD co-ordinator is currently collating comments for the DRP drafting group to review and address. The intention was to move forward with developing OECD guidelines next year.

30. The OECD test guidelines for ToxTracker have been made available for public comment. There will be an OECD expert group meeting for Toxys and member countries to make comments on the guidelines.

**ITEM 8: AOB**

31. There was no other business.

**ITEM 9: DATE OF NEXT MEETING**

32. Date of next meeting: 19th February 2026.