MUT/MIN/2026/01

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

Minutes of the meeting held at 10:30 am on 19th February 2026 via MS Teams.

Present:

Chairman:	Prof Gareth Jenkins
Members:	Dr Ann Doherty Dr Paul Fowler Dr George Johnson Ms Julia Kenny Dr Andrew Povey Mr Paul Rawlinson Dr Robert Searle-Foster Dr Robert Smith Dr Carol Beevers Ms Madeleine Wang
Secretariat:	Dr Ovnair Sepai (UKHSA Scientific Secretariat) Mr Steve Robjohns (UKHSA Scientific Secretariat Ms Natalie Stratford Devalba (UKHSA Scientific Secretariat) Ms Cath Mulholland (FSA Scientific Secretariat)
Secretariat Support:	Dr Beth O'Connell (Bibra Toxicology Advice & Consulting Ltd) Dr Chris Waine (Bibra Toxicology Advice & Consulting Ltd)
Assessors:	Ms Poornima Paramasivan (HSE) Ms Frances Hill (BEIS) Ms Kerrie Webster (HSE) Mr Ross Hawkes (MHRA) Ms Cass Boccia (DHSC)
Observers:	Prof David Harrison (COC) Prof Tim Gant (UKHSA) Dr Anthony Lynch (GSK)

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ITEM 1: WELCOME AND APOLOGIES FOR ABSENCE

1. The Chair welcomed the COM members, assessors, secretariat and observers. Apologies were received from Mr Ian Martin (EA), Ms Liz Lawton (DEFRA) and Ms Claire Potter (FSA Scientific Secretariat).

ITEM 2: ANNOUNCEMENTS

2. This was the last COM meeting of Professor David Harrison as he had come to the end of his term as Chair of COC. The Chair thanked him for his contributions to COM and work with COC over the years.

3. Associate member Dr Nathan Goldsmith had come to the end of his term of office with COM. The Chair thanked for his role and asked those present to consider whether they knew anyone who would be interested in this position and if so to send their interest to the Chair and Dr Ovnair Sepai (UKHSA Scientific Secretariat).

4. Dr Andrew Povey would be remaining as a COM member for 2026.

5. There will be recruitment for three expert members and one lay member for COM. It is expected that these roles will be advertised in February 2026. Members were asked to share these adverts with anyone who may be interested in joining COM.

6. Dr John Clements (MHRA) has stepped down as an assessor. He is replaced by Mr Ross Hawkes (MHRA).

7. The Chair reminded members to update membership details and declarations of interest as soon as possible and to send them to Natalie Blowfield (UKHSA).

ITEM 3: MINUTES OF THE MEETING HELD ON 16th OCTOBER 2025 (MUT/MIN/2025/03)

8. The minutes of the COM meeting held on the 16th of October 2025 were agreed subject to minor typographical amendments.

ITEM 4: MATTERS ARISING

9. It was agreed at the previous meeting that a sub-group would be formed to put together guidance on a genotoxicity weight of evidence approach. Members who have expressed an interest in joining this sub-group will be contacted by Dr Ovnair Sepai (UKHSA Scientific Secretariat) and an initial online meeting will be organised, possibly for March 2026.

ITEM 5: HORIZON SCANNING PRESENTED BY DR CHRIS WAINE – BIBRA TOXICOLOGY ADVICE & CONSULTING LTD

10. There were no interests to declare.

11. Bibra have been asked to look at ways of standardising the process of horizon scanning to put a more robust process in place. Dr Chris Waine from Bibra gave a presentation on this standardised approach. Feedback and input from COM members were welcomed.

12. Horizon scanning is complex because topics of interest to the committees need to be identified early, and there are many possible sources. Balanced scanning requires all sources from a given category to be included, and inclusion of non-UK sources increases complexity.

13. Sources for horizon scanning will include worldwide regulatory agencies, not just UK and Europe. Bibra already have an in-house scanning process to look at sources to continually update the TRACE database and databank and to find contributions to *Toxicology and Regulatory News* which Bibra publish monthly. An abridged list of sources for both TRACE and *Toxicology and Regulatory News* was presented to COM.

14. Other sources for horizon scanning include news and media outlets. These will also be sourced globally though it is limited to publications in the English language for practical reasons. Sources would include a mixture of print, broadcast and different

news agencies. Looking at all these sources would take a large amount of time and resource, so an aggregator (Feedly) will be used. This allows searching and filtering of relevant sources to easily highlight relevant articles and topics. There is also the possibility of including AI-powered searches (built into the Feedly tool).

15. There will be a spreadsheet for internal use by Bibra and UKHSA that will capture the key information for each item that may be relevant to the committees. The spreadsheet will indicate whether the topic might be of interest to one or more of the Committees. Bibra and UKHSA can discuss these items and decide which may be suitable for a more detailed discussion by committees. Scans for new information will be conducted monthly.

16. There will be a dedicated email inbox to send items to if they are identified by colleagues at Bibra, UKHSA or Committee members in the course of their work.

17. The use of AI to aid with horizon scanning was encouraged. Bibra already look at some sources which include food, such as the European Food Safety Authority (EFSA), but any additional sources will be fed in from the Food Standards Agency (FSA). Social media trends change rapidly, and algorithms are different for different people, so topics on social media are difficult to capture. There is also the issue of possible misinformation. If there is a topic that is heavily discussed on social media, this is usually captured in traditional news outlets which are included in the horizon scanning process. In addition, UKHSA may receive enquiries regarding issues that are on social media, and, if deemed necessary for COM to comment on, these can be added to the horizon scanning list of topics. Horizon scanning can be multi-directional – with input not just from Bibra but also from colleagues within UKHSA, colleagues on other governmental departments, and from members should they come across a topic that they think the Committees should discuss. If such topics are identified these can be sent to the Secretariat to be added to the horizon scanning output.

18. Going forward, the topics that may be of interest to COM will be circulated prior to every COM meeting. If there is an item a member wishes to raise with COM from that list, they have an opportunity to at every COM meeting through the AOB item. When it is appropriate, the COM can focus on one item in more detail to allow for a more detailed review paper to be produced by Bibra. The timing of this can be kept flexible to be able to discuss relevant topics within an appropriate time frame.

ITEM 6: “THE OECD PROCESS” PRESENTED BY DR OVNAIR SEPAI – UKHSA

19. There were no interests to declare.

20. Dr Ovnair Sepai (UKHSA Scientific Secretariat) gave a presentation on what the Organisation for Economic Co-operation and Development (OECD) is and COM’s involvement in the OECD process. It is important for COM to be aware of work being proposed and developed before test guidelines are agreed so members can give their input.

21. There is an annual OECD Working Group National Coordinators (WNT) meeting where agreements on new test methods and guidelines are made. COM members would need to formulate opinions and pass these onto the human health national coordinator for the UK to the OECD test guideline programme who attends these meetings. If these opinions are not passed on in time, they would have to wait until the meeting the following year. To note – there is also a Department for Environment Food and Rural Affairs (DEFRA) representative at these meetings to cover environmental aspects.

22. The OECD WNT process is a collaborative effort among member countries and international organisations to ensure safety and sound management of chemicals in relation to human health and the environment. Once the Standard Project Submission Form (SPSF) is formally accepted by the WNT (though not all SPSFs are accepted by the WNT) and integrated into the OECD Test Guidelines Programme work plan, the developmental phase of the of developing a test guideline can begin. This includes discussions with experts, validation of test methods and drafting of OECD Test Guidelines and validation reports. If the SPSF is submitted as a UK lead, this will go via the human health national coordinator for the UK. The methods undergo validation and standardisation to ensure they are reliable and reproducible. There should also be UK input at this stage of development. Detailed Review Papers (DRPs) are produced plus there are two commenting rounds on the draft Test Guidelines. This is another opportunity for COM input. Approved Test Guidelines are forwarded to the Joint Meeting for review and endorsement.

23. The OECD Mutual Acceptance of Data (MAD) system ensures quality data for regulatory decision making. Those who follow a published OECD test guideline correctly will not need to repeat their experiment, therefore saving costs and reducing animal testing.

24. The importance of commenting at the SPFS stage was emphasised, with the examples of the *In Vivo* Mammalian Comet Assay (OECD TG 489) and Gamma H2AX/pH3 assay receiving comments on suggested changes after the SPSF had been agreed, therefore no further changes could be made to the scope of these assays.

25. Requests for comments from OECD is often out of sync with COM meetings, so it can be difficult for members to find the time to comment. It was agreed that COM could schedule one-off meetings when required to discuss any SPSF or equivalent documents that have been distributed for comment. This would encourage members to read and put forward opinions on the document, and then a collective COM opinion could be returned to the human health national coordinator for the UK for the OECD. COC could also be included in these meetings.

26. It was commented that some members give feedback in a professional capacity outside of COM, and currently members are requested to give comments as an individual who is a member of COM, but there is no current collective COM position

which is sent back to the OECD. These meetings would allow for a collective COM response to be put forward. Members showed support for this approach and commented that it could add weight to the response as it is from the COM as a whole.

ITEM 7: OECD ERROR CORRECTED SEQUENCING PRESENTED BY DR ANTHONY LYNCH – GSK

27. Dr Robert Smith declared that Labcorp intend to offer Error Corrected Sequencing as a service. This was noted but did not exclude him from being present for the item.

28. Dr Anthony Lynch gave an update on project 4.175: DRP on the application of error-corrected next generation DNA sequencing (ecNGS) for gene mutation evaluation. The project is being co-sponsored by the US and the UK.

29. The SPSF for ecNGS was submitted in 2024. Also in 2024, alongside the DRP, the goal was to draft a Retrospective Performance Assessment (RPA) on the use of error-corrected sequencing (ECS) methods for gene mutation evaluation starting with *in vivo* assays followed by *in vitro* assays. The goal of this was to demonstrate the applicability of ECS for improving chemical testing, providing mechanistic insights, and alignment with the 3R principles ((Replacement, Reduction and Refinement in animal testing). In 2026 it was decided that the RPA will focus only on *in vivo* assays and i*n vitro* assays will be looked at separately due to the complexities of *in vitro* assays. The WNT will be updated of this change and will also be notified of the intent for a new SPSF to amend TG488 (Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays) based on the DRP.

30. Next generation sequencing (NGS) has been around for a number of years and detects clonal mutations. NGS assays have an inherent error rate on the order of 1/100 to 1/1000 base pairs sequenced so rare mutations may not be detected. ecNGS uses specially designed sequencing strategies and bioinformatics to identify and remove spurious errors to overcome the high error rate of NGS. ecNGS allows detection of mutations at a frequency of $1x10^{-7}$ to $1x10^{-8}$, on par with background levels of somatic cell mutagenesis. By directly sequencing DNA, mutation frequency and spectra can be obtained from any tissue or organism, therefore ecNGS can be applied to *in vivo* mutagenicity assessments, allowing for the transition away from phenotypic analysis of mutagenesis to sequencing approaches that support the 3Rs.

31. ecNGS assays can improve upon traditional mutagenesis assays by extending testing beyond the Transgenic Rodent mutation assay (TGR) and single gene selection assays, identifying mutation types, and improving sensitivity to detect weak mutagens. This means there are several applications for ecNGS, including mutagenesis, off-target effects in cell and gene therapy, and investigating cancer driver mutations in carcinogenesis via sequencing clonal expansions.

32. A number of ecNGS platforms have been developed using different strategies to identify rare mutations. The methods have been published in peer-reviewed

journals, and a comparison of these different platforms was presented to the Committee.

33. The International Working Group on Genotoxicity Testing (IWGT), of which Dr Anthony Lynch is a member, published an ecNGS position paper with the aim of promoting the acceptance of the platforms for regulatory mutagenicity testing. The IWGT found that ecNGS and OECD tests showed 100% concordance in mutagenicity hazard calls with strong dose-response agreement; there was correlation between TGR and ecNGS platforms; ecNGS showed sensitivity at low doses (lower than TGR assays); and there was cross-laboratory reproducibility, with consistent results for mutation frequency and spectra. ecNGS tests have been conducted in a broad chemical space and ecNGS was found to meet regulatory expectations for robust, reproducible and transparent assays.

34. Multiple components in ecNGS are already validated, such as the DNA extraction methods commonly used in ecNGS, quality of DNA, sequencing parameters for quality data, and provenance of ecNGS platforms in other application domains such as oncology and disease biology. Library preparations are ecNGS platform specific but are increasingly being commercialised and automated. Many tools are publicly available for bioinformatic processing.

35. Typically, two further aspects of validation would typically be required: regulatory need for *in vivo* mutagenicity testing and relationship of the endpoint determined by the test method to the *in vivo* biological effect and toxicity of interest. However, these aspects of OECD GD 34 have already been established by the adoption of OECD TG 488 “Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays”.

36. A group has been set up to draft the DRP which will meet weekly. Currently an outline has been drafted, and the aim is for a first draft to be complete by May ready for submission in June.

37. Some potential gaps and consideration regarding ecNGS have been identified. Most ecNGS work targets DNA-reactive mutagens and fewer data exist for non-DNA reactive carcinogens, aneugens, or complex mixtures. This is important for clarifying when ecNGS is expected to be negative and how to interpret the broader weight of evidence. Liver and bone marrow dominate the current data, so data on other tissues such as brain and heart are limited. There is variability on the primary endpoints reported in literature and harmonised primary endpoints and statistical approaches will be needed. Platform harmonisation and cross-calibration is required, and systemic cross-platform comparisons on the same *in vivo* material remain sparse. There needs to be regulatory guidance on acceptable performance and reporting as formal criteria (for example minimal coverage, allowable variance, QC thresholds) have yet to be codified.

38. Spread and variability across ecNGS platforms is expected to be minimal and trends in mutation frequency and overall spectra will be highly correlated. It is expected that whole genome sequencing will have less variability, but it depends on depth of sequencing applied to whole genome. This is not expected to affect overall assay interpretation.

39. The future of this assay is expected to be in wild-type animals where it could be integrated with other genotoxicity studies in, for example, a 28-day repeat-dose toxicity study, therefore reducing the number of animals required for genotoxicity testing and supporting the 3Rs.

40. This approach is already being used, for example with nitrosamines, and is being seen by regulators pre-guideline. The way this data is seen and used by regulators is thought to depend on the industry domain in question.

41. Some regulatory agencies are looking at whether ecNGS can be used over a TGR result where variability has been seen with the idea that the lower variability of ecNGS could give a more definitive response. Ranges in chemical potencies within chemical classes is reflected in ecNGS data. In all assays there is a limit of detection which is also true for ecNGS so some compounds will be difficult to interpret. However, the ability to define mutation frequency and changes in mutational spectra will aid analysis of datasets and recognising true chemical effect on DNA. Interpretation is required to determine what a small change in mutation frequency means in terms of risk, and this is currently not known.

42. Currently, ecNGS is not being used in many regulatory industries besides pharmaceuticals, and there is concern that there will be a high bar of acceptance in other industries. Other genotoxicity tests will still be required even with use of ecNGS to cover areas that ecNGS does not, for example aneuploidy and cytogenetic damage.

43. There is not a lot of data on nanomaterials for ecNGS so this is an area which may need to be addressed.

44. The Committee showed support for this project. It is hoped that COM will be able to provide some input during the commenting round.

ITEM 8: OECD DETAILED REVIEW PAPER ON THE GAMMA H2AX/PH3 ASSAY
PRESENTED BY DR CAROL BEEVERS – CORTEVA

45. No interests were declared.

46. Dr Carol Beevers presented on the development of a DRP and RPA for the *in vitro* Gamma H2AX/pH3 method for OECD project 4.168. This project is jointly led by France and Germany, and the aim is to evaluate the performance of the *in vitro* Gamma H2AX/pH3 method relative to the OECD-recognised genotoxicity assays.

47. The reasoning for the development of the Gamma H2AX/pH3 assay is to expand the current battery of *in vitro* genotoxicity tests as they suffer from low

specificity due to a high incidence of misleading positive results compared to the *in vivo* study outcome. These assays also do not provide quick mode of action information (additional work required) and are not high throughput.

48. Gamma H2AX and pH3 are proteins which form part of the histone core in the chromosome. When there is a DNA break under the presence of a clastogenic chemical, Gamma H2AX becomes phosphorylated. pH3 becomes phosphorylated during mitosis; in the presence of an aneugen there is a pause in mitosis causing an accumulation of phosphorylated pH3. In principle, multiplexing these two biomarkers together in the same treatment allows for the detection of clastogens and aneugens at the same time, thereby determining mode of action as well as determining whether something is genotoxic. DNA strand breaks can become a gene mutation depending on how they are fixed, therefore this is reflected in the DRP.

49. The *in vitro* Gamma H2ax/pH3 assay has a number of advantages. It has been reported to be more predictive of genotoxic potential (higher specificity and sensitivity) than commonly used assays like the *in vitro* micronucleus assay or the Ames test and can provide quantitative dose-response data. It is considered an easy and reliable method for determining mode of action and is less influenced by classical “false-positive” genotoxic chemicals that act as apoptosis or p53 inducers. The assay can be applied to different cell types (different species or cell lines from different organs) and a separate assay with metabolic activation is not required as it can be conducted in cell lines or primary cells with different metabolic capacities. It is amenable to high throughput and can be performed with suspension or monolayer cell cultures. Commercialisation of the assay is supported by Gamma H2AX and pH3 antibodies and kits being commercially available from suppliers.

50. In the DRP and RPA, only studies with a cytotoxicity measurement were included, and only compounds with at least one existing genotoxicity result were included to allow for comparison to the Gamma H2AX/pH3 assay. A curated genotoxicity database based on several reference papers, online databases, and PubMed research was used for this comparison. If a genotoxic mode of action was indicated, then this was also recorded. In total, data from 300 publications on 815 chemicals using over 170 different cell lines was included for the DRP and RPA. Chemical space analysis showed good correlation with databases like Drug Bank and OECD toolbox.

51. The overall call (OC) of Gamma H2AX/pH3 was compared to OC for the standard assays (grouped and individually). Some chemicals are known for false positives in genotoxicity testing, and for some chemicals the only *in vitro* data available was an Ames test. These chemicals were grouped to allow for comparisons to be made both with and without them. Retrospective analysis showed that the Gamma H2Ax/pH3 assay OC performed well in all performance metrics (accuracy, sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate) when compared to the OC from traditional genotoxicity assays,

both with and without the groups described above. Strength of agreement was also high as demonstrated by the Kappa coefficient. It was noted that Gamma H2AX/pH3 assay cannot detect the aneugenic Aurora kinase inhibitor class of compound.

52. The DRP has been through one review from the OECD genotoxicity Expert Group, and second review will take place in March 2026. The aim is for the DRP and RPA to go to the WNT in April 2026.

53. The Gamma H2AX/pH3 is not intended to replace the existing battery of *in vitro* tests, and while the remit of the assay could have been widened at the SPSF stage to include additional biomarkers, it is still valuable as it allows for a multiplex approach to get more information from the same experiment.

54. There was some concern expressed about whether there will be a number of screening assays with Test Guidelines in the future, and how these would be viewed by regulators. The presence of an OECD Test Guideline should mean that the assay methodology is done in a robust and standardised manner across the board. If new Test Guidelines are produced, these will be for COM to discuss as part of the COM's overarching guidance statements.

55. In traditional *in vitro* assays, false positives were considered to be cell line dependent, but this has not been observed in the Gamma H2AX/pH3 assay and good concordance has been shown across cell lines.

ITEM 9: ANY OTHER OECD UPDATES

56. ToxTracker has gone through the second round of comments on the Test Guideline and will be presented to the OECD Genotoxicity Expert Group. It is expected that it will then go to the WNT in April 2026.

ITEM 10: DRAFT ANNUAL REPORT 2025 (MUT/2026/01)

57. Members were asked to update their declarations of interest and send them to Natalie Blowfield (UKHSA).

58. The members did not have any comments on the content of the draft Annual Report for 2025.

ITEM 11: AOB

59. A request was made for any members who would be willing to be a deputy Chair should the Chair not be able to attend a future meeting last minute or is unable to chair a certain item due to conflict of interest.