



MUT/MIN/2022/03

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

Minutes of the meeting held at 10.30 on 13th October 2022 at UKHSA, Nobel House, 17 Smith Square, Westminster, London, SW1P 3JR and via MS Teams.

Present:

Chairman: Professor G Jenkins

Members: Mr A Bhagwat
Dr C Beevers
Dr A Doherty (Co-opted member)
Dr P Fowler
Dr N Goldsmith (Associate member)
Dr G Johnson
Professor D Harrison (Ex officio)
Professor S Doak
Ms J Kenny
Dr A Povey
Mr P Rawlinson
Mrs M Wang

Secretariat: Dr O Sepai (UKHSA Scientific Secretary)
Mr S Robjohns (UKHSA Secretariat)
Ms B Gadeberg (UKHSA Secretariat)
Dr D Gott (FSA Secretariat)
Dr B Doer (FSA Secretariat)

Secretariat Support: Dr R Bevan (IEH Consulting)

Assessors: Ms F Fernandez (VMD)
Ms F Hill (BEIS)
Ms Jo Little (HSE)
Dr Akosua Adjei (MHRA)
Dr I Martin (EA)

Observers:

Professor A Boobis (COT)
Mr J O'Brien (Food Observatory)
Paula Braun (PETA)

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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. Apologies were received from Ms Liz Lawton (Defra).

ITEM 2: ANNOUNCEMENTS

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

3. The Chair informed the COM that a new member had been appointed, namely, Paul Rawlinson. Paul had previously worked for Unilever and Syngenta, had experience in cosmetics safety, pharmaceuticals, research and development toxicology and genetic toxicology. He had spent the last four years as the lead toxicologist at Gentronix, specialising in genetic toxicology. Dr Ann Doherty was introduced as a co-opted member for this meeting to provide additional expertise, while awaiting current vacancies in the COM to be advertised and filled. Ann Doherty had previous experience at Astra Zeneca and had vast experience in genetic toxicology. Additionally, the Chair welcomed a new and the first associate member, Dr Nathan Goldsmith. This two-year associate membership would enable Nathan to gain experience of attending COM meetings, which would then help with any future application to becoming a full COM member. Nathan had previously completed a PhD at Public Health England on nicotine delivery devices, such as electronic cigarettes and has had three years of experience as a toxicology consultant at Exponent with experience in plant protection products and biocides.

4. The COM was informed that there were currently two vacancies for COM members and that recruitment for these positions would start soon.

5. The Chair announced the sad news of the death of Dr Mike O'Donovan who had previously resigned from the COM due to ill health and had been a valuable member of the committee for a number of years. The COM would send its condolences to his family.

ITEM 3: MINUTES OF THE MEETING HELD ON 9th JUNE 2022 (MUT/MIN/2022/02)

6. The minutes of the COM meeting held on the 9th of June 2022 were agreed subject to minor typographical amendments.

ITEM 4: MATTERS ARISING

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

RESERVED ITEM

ITEM 5: DISCUSSION PAPER ON A CAN COATING (MUT/2022/09 MUT/2022/10)

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

OPEN MEETING

ITEM 6: REVIEW OF TITANIUM DIOXIDE GENOTOXICITY

9. Following the publication of the European Food Safety Authority (EFSA) opinion on titanium dioxide in 2021, which concluded that titanium dioxide could no longer be considered to be 'safe' for use in food, the Food Standards Agency (FSA) initiated a review of the EFSA opinion.

10. The EFSA opinion was presented to the COM in June 2021 (MUT/2021/03) and to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) in July 2021 (TOX/2021/36). The COM had a number of concerns over the EFSA opinion on the genotoxicity of titanium dioxide. Due to this and following the advice of the COT the FSA initiated an independent evaluation of the safety of the use of titanium dioxide as a food additive.

11. In October 2021, paper MUT/2021/08 was presented to the COM, which summarised the available genotoxicity on titanium dioxide. Members considered that it was not possible to evaluate the genotoxicity of titanium dioxide at that stage. The COM suggested a sifting approach to the available genotoxicity should be adopted as a first step before evaluation. The Chair of the COM, a subgroup of the COM and the secretariat subsequently attended meetings to discuss and agree the criteria and methodology for sifting to identify suitable papers for the evaluation of titanium dioxide.

12. At the COM June 2022 meeting, paper MUT/2022/05 provided information and papers on approaches relating to the sifting and evaluation of the quality genotoxicity studies and evaluating data on nanomaterials. As an update since that meeting, members were informed that a sub-group of the COM had met to discuss the process to select relevant and appropriate studies to be reviewed by the committee. A proforma had been produced, which would be shared with members. This considered two levels, namely, whether the characteristics of the test material had been sufficiently described (e.g., micro or nano sized particles) and the quality and reliability of how the genotoxicity studies had been conducted. Members were requested to send any comments on refining the suggested sifting approach via email.

ITEM 7: FIRST DRAFT OF COM GUIDANCE STATEMENT – THE USE OF BIOMARKERS IN GENOTOXICITY RISK ASSESSMENT (MUT/2022/11)

13. At the March 2022 meeting, COM considered the revised COC Guidance Statement G04 'The Use of Biomarkers in Carcinogenic Risk

assessment', with a particular focus on the DNA adducts and genotoxicity biomarkers sections, both of which have been shortened in the current version. It was considered that it would be helpful for COM to produce its own, more comprehensive and in-depth guidance on biomarkers relevant to its area of expertise. A COM document on this topic, could then be referred to by other expert Committees when needed and as appropriate.

14. A draft scoping document was presented and discussed by members at the COM meeting in June 2022 (MUT/22/06). Following comments and suggestions from the June 2022 meeting a first draft document had been produced for this meeting (MUT/2022/11).

15. During discussions COM members considered that the document should have a greater distinction from the COC Guidance Statement and focus on *in vivo* biomarkers of DNA damage only. For members who had not yet provided feedback, any additional comments were requested to be sent via track changes by the end of October 2022. The plan was to modify the document and agree changes by email correspondence and Chair's action.

ITEM 8: HORIZON SCANNING: MEETINGS AND WORKSHOPS (MUT/2022/12)

16. A summary paper was presented outlining some of the current issues being discussed at a recent meeting and workshop covering issues that may be of interest to COM for future horizon scanning. The first summary gave a brief overview of topics discussed at the UKEMS Next Generation Sequencing Workshop, held in May 2022 in London. The second provided a summary of some sessions of the UK Environmental Mutagen Society (UKEMS) Annual Meeting, held in July 2022 in Harrogate.

17. A number of suggestions were made by members during discussion of the paper. These included consideration of: iPS organoids as model systems (COM and COC); the use of genomics in toxicity testing strategies; and whether epigenetics should/can be incorporated into standard toxicity testing.

ITEM 9: NON-EXPERT SUMMARIES FOR COM WEBSITE (MUT/2022/13)

18. The During discussions at the COM meeting in June 2022, it was agreed that the general public could benefit from the addition of non-expert summaries to the start of each COM guideline document.

19. The paper presented at this meeting for discussion was a draft non-expert summary for the overarching COM guideline, 'Guidance on a strategy for genotoxicity testing of chemicals.

20. Members considered that some text could be removed, as this was available on the COM website, and a link provided to that website. In addition, it was recommended that links to the glossary should be utilised fully as this

provided an immediate and understandable definition for readers. Specific comments on the paper were requested to be sent directly to the Secretariat so that the paper could be updated.

ITEM 10: OECD UPDATES

21. Members were informed of a proposal from Norway to update OECD Test Guideline 489 on the *in vivo* alkaline comet assay to include the investigation of germ cells. Currently any modifications have not been sufficiently validated, but it was early stages for the OECD.

22. The COM also heard that the OECD Test Guideline 488 Transgenic rodent somatic and gene mutation assays had been updated and published.

ITEM 11: AOB

23. The COM were informed of a presentation at the NGS (subgroup of UKEMS) meeting in May 2022 on statistical interpretation of how to interpret biological responses and how to analyse for variance in historical controls. The need for a gastrointestinal micronucleus test was also highlighted, which could be relevant for aneugens and substances that do not reach the bone marrow. There were also discussions at the meeting about the interpretation of the *in vivo* micronucleus test in terms of sufficient and low bone marrow exposure; genotoxicity risk assessment in term of BMD modelling, severity of effects, duration of exposure and uncertainty factors; and on the genotoxicity gene therapy.

ITEM 12: DATE OF NEXT MEETING

24. Date of the first meeting in 2023 is to be confirmed.