MUT/2023/01

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

Scoping document for COM Guidance Statement (G0X): The Use of In Vitro Biomarkers in Genotoxicity Risk Assessment

1. At the February 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.

2. Following discussions, it was considered that it would be helpful for COM to produce its own, more comprehensive, guidance statement on in vivo biomarkers relevant to its area of expertise. This document could then be referred to by the other Committees when needed and as appropriate.

3. The guidance statement on in vivo biomarkers is in the final stages of drafting. However, it was considered that a complementary guidance statement detailing the use of in vitro biomarkers may also be useful.

4. The purpose of this scoping document is to provide a brief overview of the proposed content of a COM guidance statement on in vitro biomarkers of genotoxicity, for discussion and agreement by members. This is given at Annex A.

Questions for the Committee

1. Members are asked to consider the proposed guidance document outline, and, in particular, to:

   i. Comment on the suggested sections and whether additional themes need to be included.

   ii. Comment on the key themes that need to be covered under each section.

   iii. Consider next steps in progressing the document

IEH Consulting under contract supporting the UK HSA COC and COM Secretariat

February 2023

MUT/2023/01 – Annex A

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COM Guidance Statement (G0X): The Use of In Vitro Biomarkers in Genotoxicity Risk Assessment

Draft scoping document

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Proposed guidance statement outline

- To increase the specificity and sensitivity of detecting DNA damage, a combination of in silico, in vitro and in vivo genotoxicity assays is used, commonly referred to as the "battery approach," for predicting the carcinogenicity potential of a chemical in humans.

- The focus of the guidance statement is the use of biomarker data determined using in vitro assays for the assessment of genotoxicity risk.

- This complements the COM guidance statement on the use of biomarker data from in vivo assays for genotoxicity risk assessment (in progress) and the COC Guidance Statement G04 'The Use of Biomarkers in Carcinogenic Risk assessment'.

- How are in vitro assays included in COM and other guidance on genotoxicity testing.

- Explain three types of genetic damage commonly measured: mutagenicity; clastogenicity; and aneugenicity.

- In vitro assays with OECD TGs: Ames (TG 471); micronucleus (TG 487); chromosomal aberration (TG 473). Include limitations - generation of misleading positives.

- Other approaches/under development: transcriptomics; γH2AX formation???