This is a paper for discussion. It does not represent the views of the Committee and must not be quoted, cited or reproduced.

MUT/2023/05

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

Draft non expert summaries for COM statements

1. It was agreed at the COM meeting in June 2022 that the general public could benefit from the addition of non-expert summaries at the start of each COM guideline statement.

2. The paper provided at Annex A is a third draft non-expert summary for the overarching COM guideline entitled 'Guidance on a strategy for genotoxicity testing of chemicals'. This has been amended following comments from Members at the COM meeting in October 2022 (MUT/2022/13) and in February 2023 (MUT/2023/03), and by a lay member of COM following the meeting in February 2023.

Questions for the Committee

3. Members are asked to consider the third draft non-expert summary presented in Annex A, and, in particular, to:

i. Comment on whether the language used is consistent with that for a lay person (considered to be 'A-level' standard).

ii. Consider whether the draft non-expert summary provides an accurate overview of the respective COM statement.

IEH Consulting under contract supporting the UK HSA COC and COM Secretariat
June 2023

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MUT/2023/05 – Annex A

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

Third draft non-expert summary for COM document: Guidance on a strategy for genotoxicity testing of chemicals

Third draft non-expert summary for COM overarching guidance document.

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

June 2023

Committee on Mutagenicity

This is a paper for discussion. It does not represent the views of the Committee and must not be quoted, cited or reproduced.

The Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) is an independent expert advisory committee with specific interest in the inherent genotoxic properties of chemicals. More detailed information on the COM can be accessed via the website.

This document outlines the strategy that the COM considers to be the most scientifically appropriate for the genotoxicity testing of chemicals. It takes into account currently available methods and the need to avoid the use of live animals (in vivo studies) where practical and validated alternative methods (for example, in vitro studies) exist.

A staged testing approach is recommended by COM, as follows.

Stage 0 considers any available information regarding the physical and chemical properties of the chemical under investigation, the identification of any relationship between chemical structure and biological activity (structure activity relationships (SAR)) and the data from scaled-down in vitro genotoxicity assays used for screening large numbers of test chemicals.

Stage 1 consists of in vitro genotoxicity assays that allow the identification of three types of genetic damage to: genes, chromosome structure (clastogenicity), and/or the number of chromosomes (aneuploidy). Core tests comprising the 'Ames test' and the 'in vitro micronucleus test' are advised by COM to be sufficient to detect genotoxic chemicals.

Stage 2 consists of three core in vivo genotoxicity assays that allow the identification of two types of genetic damage. Tests include: the 'rodent micronucleus/ chromosome aberration assay' (that detects aneuploidy and clastogenicity), the 'transgenic rodent gene mutation assay' and the 'rodent alkaline comet assay' (that detects DNA damage).

For most chemicals, the core in vivo tests are sufficient to evaluate whether a chemical can cause genotoxicity in the human body, which is a primary concern in the development of some cancers. However, in some cases further in vivo studies may be needed to provide more detailed information on the genotoxic response or to determine the mechanism by which the chemical causes genotoxicity (genotoxic mode of action).