

Comments by the Advisory Committee on Hazardous Substances¹ on the COM draft document Guidance on a strategy for Genotoxicity testing and mutagenic hazard assessment of chemical substances²

General comments

The guidance is comprehensive and represents a good summary of the current status of the various testing methods.

A list of the specific questions addressed in Stages 0, 1 and 2 - perhaps presented in the form of a text box - may make the strategy easier to follow, and the questions easier to refer back to as necessary.

A flow chart illustrating the three stages, including the recommended core tests to be conducted at each stage would be helpful. Figures 1, 2 and 3 do, to some extent, address this. Figures 1 and 2 are helpful and clear. Perhaps figure 3 could be simplified by removing the discussion of points for consideration to the main text.

A few more page breaks may make the text easier to read, and summaries for each section would also help (with the "key questions" outlined).

Depending on the target audience for the guidelines (practitioners, intelligent readers, or lay audience), it may be possible to compress the brief history/overview of QSAR and other techniques into a table listing approaches and possible techniques (pages 11-14). Is this a "how to" guide or an "information about" guide? Some of the information presented here perhaps could go in an annex.

The information presented from Section VI onwards is important, but may be overshadowed by the amount that is contained therein. Two separate sections may be required to firstly describe the approach (as briefly outlined in Section V but in more detail) and then the tests.

It would be helpful if the document closed with a brief paragraph summarising the recommendations. This could, perhaps, also be used as an Executive Summary at the beginning. The addition of a short summary paragraph (restating the key points from the document) along with the "possible future developments" highlighting the issues that still need to be addressed, would help to identify and clarify the uncertainties remaining within the science.

¹ The Advisory Committee on Hazardous Substances (ACHS) is an UK Government advisory Committee that provides expert advice on the science behind hazardous chemicals. Further details on the Committee are at: <http://www.defra.gov.uk/environment/quality/chemicals/achs/index.htm>

² The ACHS would like to acknowledge and express its gratitude to Dr Lesley Stanley and Dr Sophie Rocks as the primary authors of this ACHS response to the COM consultation.

Specific comments

Para 43 discusses the selection of test item concentrations for *in vitro* testing, but does not mention issues of solubility, which may be significant at the high concentrations cited. This should be rectified and the possible consequences of test item precipitation should be mentioned. It may also be useful to comment, at least briefly, on vehicle selection.

Para 49, on the Ames test, does not mention approaches for compounds requiring metabolic activation (e.g. the use of hepatic microsomes, S9 mixes or recombinant CYPs), although this is mentioned in passing in para 69. Metabolic activation systems should at least be mentioned in para 49 although the discussion does not need to be exhaustive.

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