

COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT**MEETING TO DISCUSS DRAFTING OF COM GUIDANCE REVISION.****Present**

Dr G Clare (COM)
Mr J Battershill (COM Secretariat)
Dr D Mason (COM Secretariat)

1. The Secretariat welcomed Dr Clare to the meeting. Unfortunately Professor Farmer had been unable to attend at short notice.

Format of revised COM guidance.

2. A number of potential titles for the revised guidance were discussed. One suggestion put forward was '*A strategy for the assessment of the genotoxicity of chemicals*'. It was agreed that COM should consider, at the outset, what format and content would be required. It was agreed that the format of the revised guidance should be flexible and it was envisaged would cover publication as a stand alone document, a set of internet guidance documents (which could be updated) and form the basis of a publication in a peer review journal. A draft outline contents page was discussed (appended to this write up). It was noted the proposed contents had sections on assessment of potential thresholds, and potency evaluation. It was agreed the contents page of the COC guidance should be resubmitted for comparison.
3. A number of other topics would also be relevant, e.g. target organ mutagenicity. With regard to *in vitro* genotoxicity testing, it was agreed that evidence for mode of action for positive chemicals would be important for evaluating the significance of positive results and would be of particular importance in situations where no *in vivo* testing would be undertaken on a particular chemical.
4. The current recommended strategy where the most common second tissue study (rat liver UDS) was discussed. It was agreed a more compound specific strategy would be required. It was noted that one relevant paper had been identified during the horizon scanning exercise which provided evidence of the low accuracy of prediction of the rat liver UDS compared to transgenics or comet assay regarding rodent carcinogens. .
5. The approach to *in vivo* germ cell testing was briefly discussed. It was agreed the current strategy needed considerable revision.

Many of the tests were not currently used. One idea was to consider if genotoxicity tests could be appended to multigeneration studies. The secretariat would investigate if any groups had undertaken such an approach and whether appropriate publications could be identified.

6. With regard to evaluation of *in vivo* genotoxic potency, it was noted that a number of research groups were considering this aspect in detail and appropriate references had been cited in the horizon scanning paper (MUT/08/17). Proposals included consideration of tissue concentrations of mutagens in relation to mutagenic response for a range of chemicals. It was noted that obtaining relevant tissue concentration (exposure) data might be particularly difficult (e.g. mouse bone marrow), and was not routinely undertaken, but this aspect was a continuing problem in assessing *in vivo* genotoxicity test data. One proposal for expressing genotoxicity potency data would $\mu\text{M}/\text{h}$ for a specified response such as LED.
7. It was noted that many groups were making recommendations on genotoxicity test strategies. Whilst the COM guidance should consider all relevant aspects of testing, evaluation and risk assessment, it was agreed that it would be inappropriate to specifically compare guidance between groups. The COM guidance was principally meant to be the best scientific advice available.
8. The testing, evaluation and risk assessment of mixtures was also considered. It was noted the COM had provided guidance on some aspects of mixture genotoxicity testing and evaluation but it was possible that further consideration was needed on risk assessment. (One potentially relevant paper regarding mixtures of impurities in pharmaceuticals was noted in the horizon scanning paper, MUT/08/17).

Time line for revision of COM guidance

9. It was agreed that the revision of COM guidance should be given more prominence on COM agendas.

Further consideration

10. It was agreed the COM should consider the write up of this meeting and proposed outline contents at the 23 October 2008 meeting, with some initial draft material (for one or more specified sections) provided for the February 2009 COM meeting.

Secretariat September 2008