

Parma, 24 January 2010

EFSA WG on Genotoxicity Testing Strategies:

Comments on the UK COM Guidance on a strategy for genotoxicity testing and mutagenic hazard assessment of chemical substances.

The guidance has been prepared by the UK Committee on mutagenicity of chemicals in food, consumer products and the environment.

The EFSA Scientific Committee Working Group on genotoxicity testing strategies and the EFSA PRAPeR Unit have been given the opportunity to provide comments.

General comments:

- The EFSA WG welcomed the opportunity to comment on the COM guidance and noted that many of the topics addressed in the draft guidance were also being addressed in the EFSA WG.
- The figures at the end of the document were found very helpful and important for understanding of the approach suggested in the main body of the text, but it was not easy to locate the relevant part of the text describing the outline of the strategy.
There has been much discussion and several papers in the scientific literature on the possible use of the TTC concept for low dose exposures. There is no explicit consideration in the COM guidance on how it might impact on any genotoxicity testing strategy.

Specific comments:

- Page 5, paragraph 7 and 8: the definition of mutation in paragraph 7 appears to include gene (point) mutation, chromosome aberration (“blocks of genes”, “...larger changes, including deletions and rearrangements of DNA”) and aneuploidy (“alteration may involve ... whole chromosomes”) whereas in paragraph 8 (definition of genotoxicity) the use of the term “mutation” seems to exclude structural and numerical chromosomal damage (“It is a broad term, that, as well as mutation, includes ... chromosomal damage...”). It should be clarified whether COM is considering structural and numerical chromosome damage as mutations or not.
- Page 9, step 2, line 21: it is not clear how SAR approaches may help in identifying misleading genotoxicity results. The text in Step 2, page 9, lines 19-20, also seems to contradict what is said on page 15, paragraph 29, lines 7-10.
- Page 10, paragraph 20, line 12: “low exposure level of 1.5 µg/kg bw/day” should be corrected to “low exposure level of 0.15 µg/person/day”.
- Page 10, line 14: implies above TTC value of 0.15 µg/person /day should be considered but the guidance is not clear on that.
- Page 12, paragraph 24, line 24 onwards: a number of SARs are mentioned but there are no comments on their performance. It would be helpful to have at least few words on their different performances.
- Page 16, paragraph 31, line 1: Do you mean “differential survival” rather than “differential growth”?

- Page 22, paragraph 44, lines 8-10: we suggest removing the last bullet point “the result...” as it does not make sense, given the preceding text.
- Fig 2, last box on the bottom left: the text should read “**if high, moderate AND (not “OR”) prolonged exposure**”. This would then reflect what is in the main text.
- Fig 2, in the box under the green box “**NEGATIVE** results..”: Should there be a third bullet “ADME” after “Results of other tests” as is stated in the main body of the text.
- Fig 2, orange box “**EQUIVOCAL**”: There is no definition of equivocal result in the main text.
- Fig 2, in the box under the orange box “**EQUIVOCAL** result”, reproducibility and historical control data are mentioned, but is it not also normal practice to consider reproducibility and historical control data when assessing positive and negative results?