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CC/08/12

**COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD,
CONSUMER PRODUCTS AND THE ENVIRONMENT**

REVISION OF 1981 OECD TEST GUIDELINES TG 451, (CHRONIC CARCINOGENICITY STUDY IN RODENTS), TG 452 (LONG-TERM CHRONIC TOXICITY STUDY IN RODENTS BY ORAL ADMINISTRATION) AND TG 453 (COMBINED CHRONIC TOXICITY/CARCINOGENICITY STUDIES)

Background

1. The OECD Test Guidelines are being revised to bring them into line with current scientific knowledge and good practice.
2. The OECD consultant, Iona Pratt, has drafted revised OECD Test Guidelines for chronic toxicity and carcinogenicity (TG 451, 452 and 453), based on the discussions at a workshop held in Washington in February 2008 and the meeting of National Coordinators (WNT) held in April 2008. Iona has tried to produce 3 texts that are pretty well consistent with each other (i.e. similar wording in all 3, when dealing with the same issues), and to address comments and suggestions raised, as far as possible.
3. The COC is asked to focus on the Chronic Carcinogenicity Test Guideline, TG 451. These comments will also be relevant for the carcinogenicity part of TG 453. The latter is included in the papers but separate comments are not required.
4. The issue of the duration of the studies, in particular dealing with mortality before the scheduled termination was discussed in agenda item 4.1 and will be applied to TG 451 as appropriate.
5. The COC is asked to bear mind the general agreements already reached at the WNT (see Appendix 2). You will note that there was no agreement on the scope for changes in the number of animals per dose group, particularly in relation to a BMD approach, which may benefit from testing at more dose levels. The WNT agreed to await a report from a statistics expert prior to discussion of this aspect. Concern was also raised about the need for validation of any changes to the Test Guidelines. National Coordinators were also invited to seek information and identify in their country any research ongoing on prenatal/perinatal exposure in carcinogenicity and chronic toxicity testing.
6. The draft revisions of TG 451, TG 452 and TG 453 were circulated to the OECD Shadow group and the comments received relevant to TG 451 will be presented orally at the COC meeting.

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7. A Guidance Document is being produced alongside these revised Test Guidelines and the COC considered the Chapter on dose selection for chronic animal bioassays at its meeting on 10 April 2008. The COC also agreed to contribute to a Chapter on Histopathology for this Guidance document and will be kept informed of progress on the various Chapters for this Guidance.

Attached Papers

8. The following papers are attached:

Appendix 1 Draft revised Test Guidelines TG 451 and 453

Appendix 2 Extract of the Draft Minutes of the meeting of OECD National Coordinators April 2008

Appendix 3 Current (1981) OECD TG 451 and 453

Advice sought

9. The COC is asked to:

- i. comment on the draft revised version of TG 451
- ii. provide a general steer on the issue of numbers of animals required per dose group and/or indicate whether they wish to wait until a statistical report is available.
- iii. indicate whether any of the changes to the Test Guideline require validation
- iv. provide information on any research of which they are aware of that relates to prenatal/perinatal exposure to chemicals and carcinogenicity.