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CC/08/14

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

Proposed strategy for reviewing carcinogen-carcinogen mixtures

1. At the last meeting, the committee considered a preliminary review of the literature on the assessment of chemical mixtures for carcinogenicity (CC/08/06). The paper noted that a number of designs are available to study the carcinogenicity of simple mixtures, as are a number of methods to analyze the data. However, the assessment of potential interactions in the context of carcinogenicity is complex, due to the multi-stage nature of the process and the high cost of carcinogenicity studies. During the discussion of CC/08/06, the committee commented that its initial discussion of mixtures could be confined to mixtures of carcinogens alone, in line with the COM, which had considered mixtures of mutagens alone. This would have the advantage of focussing the initial work. Members also asked for further consideration of the mode of interaction in initiation-promotion studies. A number of examples were presented in the paper of studies which had aimed to explore interactions. The committee noted that, not surprisingly, few studies exploring effects of mixtures with respect to carcinogenesis had used cancer as an endpoint.

2. This paper proposes a strategy to examine this topic further and this is outlined below:

- a) The initial stage will be to identify points in the carcinogenic process where it is possible for carcinogens to interact. This includes, for example, ADME, DNA adduction, mutagenicity, early preneoplastic changes and formation of neoplasia. The COM considered mutagenicity and reached some conclusions on the types of compounds and mechanisms which might be further examined.
- b) The next stage will be to search the literature for examples of these potential interactions. This be carried out initially in limited groups of chemicals: heterocyclic amines, PAHs, and oestrogens where initial searches indicate there may be data to cover one or more of the end points listed in a).
- c) We will also take forward the proposal made at the last COC meeting ie to examine some initiation-promotion papers to study the endpoints separately, e.g. number of tumours or preneoplastic foci produced or time to tumour, with a view to defining the mechanisms which might be operating.
- d) From the results of this work, the implications for testing of carcinogens will be considered.
- e) The implications will also be considered for the risk assessment of environmental carcinogens.

3. A set of criteria will be drawn up to aid in the evaluation of interaction studies in terms of the quality of design, data and interpretations. The COM adapted a set of criteria described in a paper by Bogert et al (2001) and these will be explored in relation to assessing studies on interactions between carcinogens.

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4. Members are asked for their views on the proposed strategy.

Secretariat
June 2008

Reference

Bogert CJ, Price B, Wells CS and Simon GS (2001). Evaluating chemical interaction studies for mixture risk assessment. *Human and Ecol Risk Assessment* 7(2), 259-306.