

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

### Overarching Guidance Statement (COC/G 01): Risk Assessment Paradigms

1. During discussion of this guidance statement at the last meeting, Members queried the risk assessment paradigm in Figure 1 (see Annex 1), which was stated to be the US National Research Council paradigm (NRC, 1983), and asked whether this appeared in the original COC guidance. The same paradigm appeared in the COC's last guidance document in 2004, although portrayed as a table rather than a diagram.

2. No diagram appeared in the original 1990 guidelines. The description of hazard and risk assessment was in the text, and is given in Annex 2. The 1983 NRC risk assessment paradigm is given in Annex 3 to this paper. It specifies Hazard Identification, Dose-Response Assessment, and Exposure Assessment as the stages leading to Risk Characterisation. A similar paradigm appeared in a 1994 NRC report (NRC, 1994) (Annex 4). However, the definition of hazard identification given in the latter report is wider than the description in the COC guidance statement and includes an element of hazard characterisation i.e. an evaluation of the conditions under which the form of toxicity might be expressed in exposed humans, as follows:

*Step 1: **Hazard identification** entails identification of the contaminants that are suspected to pose health hazards, quantification of the concentrations at which they are present in the environment, a description of the specific forms of toxicity (neurotoxicity, carcinogenicity, etc.) which can be caused by the contaminants of concern, and an evaluation of the conditions under which these forms of toxicity might be expressed in exposed humans. Information for this step is typically derived from environmental monitoring data and from epidemiologic and animal studies and other types of experimental work. This step is common to qualitative and quantitative risk assessment.*

The definition of dose-response assessment is as follows:

*Step 2: **Dose-Response Assessment** entails a further evaluation of the conditions under which the toxic properties of a chemical might be manifested in exposed people, with particular emphasis on the quantitative relation between the dose and the toxic response. The development of this relationship may involve the use of mathematical models. This step may include an assessment of variations in response, for example, differences in susceptibility between young and old people.*

3. The EPA has adopted the NRC paradigm although different parts of the EPA have presented it in different ways (see Annexes 5 and 6). The EPA's 2005 Guidelines for Cancer Risk Assessment used the NRC structure, but "adding the dimension of characterisation to the hazard identification step: an evaluation of the conditions under which its expression is anticipated". No diagram was included. The risk assessment questions addressed in the guidelines are stated to be:

- For hazard: Can the identified agent present a carcinogenic hazard to humans and, if so, under what circumstances?
- For dose-response: At what levels of exposure might the risk occur?
- For exposure: What are the conditions of human exposure?

- For risk: What is the character of the risk? How well do the data support conclusions about the nature and extent of the risk from various exposures?

4. Since there appear to be subtle differences in the way organisations view the components of the different stages of risk assessment, it is suggested that the COC guidelines include the current Figure 1 but that the legend is changed to read “Figure 1: Four stage approach to the risk assessment of chemical carcinogens, after the US National Academy of Sciences, 1983.” Alternatively, would Members want a different figure or narrative to describe the elements of risk assessment?

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