

ECETOC Document

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ECETOC Statement on Formaldehyde

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ECETOC STATEMENT ON FORMALDEHYDYDE

In Sept. 1982 ECETOC issued Technical Report no. 6 "Formaldehyde Toxicology: An up-dating of the ECETOC Technical Reports 1 and 2". Further work reported since is worthy of comment.

1. Epidemiology. A UK study (Acheson, E.D. et al., Formaldehyde in the British chemical industry. The Lancet, March 17, 1984, pages 611-616; Acheson, E.D. et al., The Lancet, May 12, 1984, pages 1066-1067) led the authors to conclude that "The findings of this study do not support the hypothesis that formaldehyde is a human carcinogen. The strength of the negative evidence is, however, limited by the small number of men (605) exposed to "high" levels for more than 5 years and followed by more than 20 years after first exposure. Further studies of groups exposed to formaldehyde are needed". Although this qualification must be recognised, these results give general support to the conclusion reached on page 8 of ECETOC's report no. 6 that "The new epidemiological data confirm that there is no relationship between formaldehyde exposure and cancer in humans".
2. Mechanism of action. Swenberg, J.A. et al. (Non-linear biological responses to formaldehyde and their implications for carcinogenic risk assessment. Carcinogenesis, 4(8), 1983, pages 945-952) have examined the reasons why exposure to formaldehyde is associated with cancer of the respiratory tract in experimental animals, but not in humans. Experimental observations on the physiology of breathing, and phenomena in the respiratory tract, indicate that in assessing the risk to humans, by extrapolating data from animals exposed to high concentrations (14ppm) of vapour to humans exposed to low concentrations (of around 1-2 ppm), it is essential to consider the dose delivered to the target tissue rather than the dose administered (atmospheric concentration). The delivered dose does not vary linearly with the administered dose, and at low atmospheric concentrations the delivered dose falls significantly below that expected.

At levels to which humans are normally exposed in practice it seems that the delivered dose is insufficient to induce cancer of the respiratory tract.

3. Classification. ECETOC (Monograph No. 2, "A Contribution to the Strategy for Identification and Control of Occupational Carcinogens", Sept. 1980) has recommended the classification of carcinogens into 3 categories (see footnote), depending on the nature of the scientific evidence available. Insofar as classification might be used in legislative decisions, ECETOC is of the opinion that formaldehyde

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should be classified as a "Questionable Human Chemical Carcinogen" because it clearly conforms to the qualifications b) and c) in the definition. It is not a "Putative Human Chemical Carcinogen" because the concentrations producing tumours in long-term animal bioassays were at levels beyond human endurance. These concentrations were also cytotoxic to the mucous membranes of the test animals. Thus the relevance of these studies to man is questionable since the exposure conditions do not correspond to those for humans.

ECETOC agrees with Squire et al. of the (US) John Hopkins University (Squire, R.A. and Cameron, L.L.; An analysis of potential carcinogenic risk from formaldehyde. Regul. Toxicol. and Pharmacol., 4, 107, 1984) in their conclusion that "humans are likely to be less sensitive than test rodents to potential carcinogenic effects and that the risk at low-level exposure would not be linearly-related to that observed at the higher levels which were found to be carcinogenic in animals. Risk assessment and risk management decisions should incorporate all of the relevant biological information, such as that discussed, rather than rely solely on a mathematical approach which is likely to yield inaccurate and misleading conclusions".

Footnote :

1.2 Proven human chemical carcinogen :

-A proven human chemical carcinogen is a substance for which a causal relationship has been established between previous exposure and the occurrence of malignant neoplasms in man-

1.3. Putative human chemical carcinogen :

-A putative human chemical carcinogen is a clearly-defined chemical substance which causes malignant neoplasms in adequate animal experimentation, under exposure conditions which correspond to those in man, or where the relevance of the exposure conditions can be deduced-

1.4 Questionable human chemical carcinogen :

-A questionable human chemical carcinogen is a clearly-defined chemical substance for which there is incomplete evidence of carcinogenicity, which is based either on (a) observations in man which are suggestive, but do not allow a firm conclusion of a causal relationship between previous exposure and the occurrence of malignant neoplasms; or (b) findings obtained in animal experiments in which the experimental model is not appropriate to conditions in man and therefore the result cannot be regarded as relevant; or (c) positive findings in at least two standardised short-term tests, with unrelated end-points, which have been verified as useful for screening for carcinogenic potential-

1.5. Human chemical non-carcinogen

-An ultimate proof of non-carcinogenicity is impossible. However, a clearly-defined chemical substance which has consistently shown negative results in adequate studies in man or adequate animal experimentation should be considered a "Human chemical non-carcinogen" for practical purposes-