

Trichloroethylene (TCE):

Comments before the EPA Science Advisory Board TCE Panel

During the Conference Call, June 24, 2010

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Good afternoon. To date, chemicals in the “known human carcinogen” category, or “carcinogenic to humans” in EPA’s terminology, have strong evidence supporting the classification. Organizations such as IARC, NTP and EPA set the bar high for assigning this classification. I do not believe that TCE has the strength of evidence normally required to classify it as “known” or “carcinogenic to humans”.

In charge question 4., the SAB Panel was asked “Using the approach outlined in the U.S. EPA Cancer Guidelines (2005), does EPA’s hazard assessment of cancer logically, accurately, clearly and objectively represent and synthesize the available scientific evidence to support its conclusions that TCE is carcinogenic to humans by all routes of exposure?” So the Panel was directed to the Cancer Guidelines where specific criteria are laid down for the classes of carcinogen. Two sets of criteria, or conditions provide alternative routes to “carcinogenic to humans”, the first is clearly all, and only, epidemiology:

- This descriptor is appropriate when there is convincing epidemiologic evidence of a causal association between human exposure and cancer.

The second set of criteria includes evidence from animal studies – the emphases are in the Guidelines:

- Exceptionally, this descriptor may be equally appropriate with a lesser weight of epidemiologic evidence that is strengthened by other lines of evidence. It can be used when all of the following conditions are met: (a) there is strong evidence of an association between human exposure and either cancer or the key precursor events of the agent’s mode of action but not enough for a causal association, and (b) there is extensive evidence of carcinogenicity in animals, and (c) the mode(s) of carcinogenic action and associated key precursor events have been identified in animals, and (d) there is strong evidence that the key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information. In this case, the narrative includes a summary of both the experimental and epidemiologic information on mode of action and also an indication of the relative weight that each source of information carries, e.g. based on human information, based on limited human information and extensive animal experiments.

EPA considers that the evidence meets the conditions of the first, epidemiology only, basis for classification. This is founded in the use of the “modified Hill criteria” listed in the Cancer Guidelines. However, some of the criteria are not met and others barely met. A causal relationship based solely on epidemiological evidence cannot be supported. It is even

questionable whether a “strong evidence of an association” is met as required under (a) in the second set of criteria. Once past criterion (a), it is very doubtful whether the remaining criteria can be met in the unequivocal manner indicated by the wording.

Thus the highest classification that can be accorded TCE is “likely to be carcinogenic to humans”.

We respectfully request that the SAB Panel takes, one more time, a rigorous, step by step approach to addressing the conditions so carefully and clearly stated by EPA in the Cancer Guidelines.

[Subsequent speakers will address some of the aspects of epidemiological and toxicological information in the light of the classification criteria.]