

BIO-MEDICAL RESEARCH
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Brief Summary

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basis for many years after the publication of the six-month test results. In effect, the toxicological reviewers of this paper (if there were toxicological reviewers) allowed a great deal more to be said about the applicability of the results to chloroform TLV levels than is warranted and in this respect the publication is also misleading.

Kingsley Kay, Ph.D.

Mount Sinai School of Medicine
City University of New York
New York, NY 10029

Editor's note: Two of the leading toxicologists in the field were the reviewers.

Dear Sir:

We appreciate very much the opportunity to respond to the criticism leveled by Dr. Kingsley Kay at us and at the AIHA Journal for publishing the results of some toxicological studies we did quite a number of years ago (AIHA Journal 37, 706, 1976). This work was not published earlier because it was not completed to our satisfaction; that is, a no-adverse-effect dose was not determined. However, at the time NIOSH was preparing their Criteria Document on Chloroform, they were aware of this work and they requested that since there were no other similar data available, that we make our results available to all through publication. This we have done.

Dr. Kay seems to feel that the results of toxicological studies of less than some period greater than six months should not be accepted for publication. Frankly we vigorously object to this. Unfortunately, in today's political climate, it appears to be difficult for some toxicologists to remember that there are other toxic effects, many of which are as important, or more important than cancer. We would not be surprised if for chloroform, liver injury other than cancer will be the limiting toxicological effect at low levels of exposure. We are anxiously awaiting studies which can evaluate this.

Dr. Kay states that our conclusions are misleading with respect to carcinogenicity even though he acknowledges that we specifically address this point. We said, "None of the studies were of sufficient duration to assess carcinogenicity". We wonder what more we could have said? Our paper states exactly what had been done, and we think

properly concluded that on the basis of the experimental data, workers' exposures should be controlled below 25 ppm with a time weighted average below 10 ppm. We did not state how much below 10 ppm the TWA should be because the data to do so were not available.

Dr. Kay's comments about our laboratory's publication in 1961 on vinyl chloride appear to reflect his lack of understanding of the whole of the vinyl chloride problem. Had our recommendations based upon relatively simple toxicology been followed then, the difficulties of today may never have occurred.

V. K. Rowe
Toxicological Affairs
T. R. Torkelson
Corporate Medical
Dow Chemical U.S.A.
Midland, Michigan 48640

Dear Sir:

The December 1976 issue of the AMERICAN INDUSTRIAL HYGIENE ASSOCIATION JOURNAL contained a rather disappointing article entitled "Report on Carcinogenesis Bioassay of Technical Grade Chloroform (Kepone)." The (anonymous) author has attempted to paraphrase the official report, but failed to mention many of the original report's caveats nor any of the apparent failing in the underlying study.

Insofar as the finding of animal carcinogenicity is concerned, the reported "hepatocellular carcinomas" refer to cellular morphology of liver nodules which are common in mice and rats and have no necessary connection with cancer as normally defined. The original report tacitly recognized the questions raised by such diagnostic terminology when it conceded that no evidence of invasion or metastasis was observed. Similarly, there are no indications that the liver lesions *per se* were the cause of death in any of the test animals. Indeed, most of the lesions were discovered only on terminal sacrifice, and the animals with lesions in general survived those who succumbed from the direct toxic effects.

The conclusions drawn from the tests are particularly suspect in light of the weaknesses in the test itself; e.g.: the unusually small number of matched controls (5-10) when compared to approximately 50 dose

volatile and, usually need constant improvement.

We at OSHA feel we are a part of such a mix, and certainly are aware of a need for improvement. OSHA and I, as an individual, would be pleased and happy to discuss any specific suggestions along this line with Mr. Hertlein and the readers of the JOURNAL.

Joe Mancias, Jr.
Director
Office of Public and Consumer Affairs
USDOL/OSHA
Washington, DC 20210

Dear Sir:

I would like to point out a redundancy in the title of the paper of Pelfrene in American Ind. Hyg. Assoc. J. 37 (December), p. 706, 1976. Benzo(a)pyrene is what used to be termed 3,4-benzopyrene. If one uses the IUPAC nomenclature—benzo(a)pyrene, the 3,4 is a redundancy. I note that the mistake was not repeated in the text.

There was a paper by Torkelson et al in the same issue as referred to above. That covered tests of chloroform toxicity over six months. It is of interest that the investigating laboratory did a six-month test on vinyl chloride in 1961 and missed its carcinogenicity (Amer. Ind. Hyg. Assoc. J. 22, 354-361, 1961). While the Journal cannot restrict authors to report on specified test periods, it can control through reviewers the interpretation placed on results for whatever period. In the six-month chloroform experiment as might be expected from what is known about chemical carcinogenesis, cancers did not develop. The report as it stands is really misleading to many concerned professionals because the question as to whether cancers might have developed over the longer exposure period used in the National Cancer Institute chloroform tests was not answered (notwithstanding that p. 698 contains a brief reference to the test duration as being inadequate to disclose carcinogenicity).

The non-carcinogenic toxicity of chloroform in a six-month test may indeed be inconsequential in comparison with its carcinogenicity—as was virtually the case with vinyl chloride which continued to be used in the trade on the wrong safety

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