

06-K-004

Shell Development Company

A Division of Shell Oil Company



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May 8, 1980

Mr. Joseph E. Hadley, Jr.
Keller & Heckman
Suite 1000
1150 17th Street, N.W.
Washington, D.C. 20036

Dear Joe:

A few last minute changes in the OSHA VCM response.

1. Draft page 5, line 3: Insert a period after "defects" and delete the remainder of the sentence.
2. Draft page 81, mid-page, immediately below the small table thru page 83: Revise to read as follows:

"A review of historical control data for this strain should reveal if the above incidences are greater than normally expected. If so, it would suggest some extraneous factor had impacted on the experimental animals, control and treated. If, on the other hand, the incidence of pulmonary tumors in the control mice in this study is within the expected range of normal, the strain was probably a poor choice for evaluating lung tumorigenesis. In general, strains/species with a high incidence of spontaneous tumors should be avoided in carcinogenesis bioassays^{3/}. It would also have been useful had the experimental design included control groups equal in numbers to the treatment groups. Such design is dictated by good toxicological practice^{4/}.

"Another facet of Hehir's experimental design which is not apparent is whether or not the control animals were handled in the same manner as the exposed animals, especially whether or not they were sham exposed. In view of the number of extraneous factors which are known to affect spontaneous tumor incidence in experimental animals^{5/}, control and treatment groups should be as nearly equivalent as possible in all regards except exposure to the test agent.

^{3/}"The Testing of Chemicals for Carcinogenicity, Mutagenicity, and Teratogenicity," Minister of Health and Welfare, Canada, 1973.

^{4/}"Principles and Procedures for Evaluating the Toxicity of Household Substances," Washington, D. C., National Academy of Sciences, 1977.

^{5/}Bickerton, R. K.

Spontaneous Tumors and Related Changes. In "Carcinogenesis Testing of Chemicals," L. Golberg, Ed., Cleveland, CRC Press, 1974.

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"Behr et al do not refer to the statistical methods used in analyzing the data when they discuss significance and such a description is necessary to determine if their conclusions are indeed appropriate.

"C. General Comments

"There are other aspects of this study as a whole which are troublesome. Firstly, the only tissue in these mice responding to the supposed carcinogenic doses of VCM was the lung. Secondly, if the mouse is susceptible to the doses employed in the study, at least some microscopically detectable changes in the rat would be expected, the reported eosinophilic foci in the liver notwithstanding. In our view, these two facts make the findings in the mouse lung even more suspect.

"In summarizing, it should be pointed out that the CPSC study as it is now reported contributes little to the understanding of VCM carcinogenesis. This is truly unfortunate in view of the fact that over 3000 animals were employed and considerable resource expended. However, we do not suggest that nothing can be concluded from the study but, rather, that any conclusions must await a comprehensive evaluation of the data developed. We would hope the authors would undertake such an evaluation before final publication of the work.

"As a final note, we would like to point out to OSHA that information and data relevant to the CPSC study has been requested from both the Commission and the performing laboratory^{6/ 7/}; the requests have fallen on deaf ears. We find this an unfortunate situation. In addition, consideration must be given to requesting a full audit of the study."

Fifty-plus copies of Figure 1 have been sent to you today via Federal Express. The figure should appear following the equivalent of page 15 of the draft.

If you have any questions, please call.

Regards,

V. L. Kirkland, Ph.D.
Senior Research Toxicologist

6/Letter dated August 20, 1979 from ICI, Ltd., to Dr. J. McLaughlin, Jr. of CPSC and Dr. B. McNamara of Edgewood Arsenal.

7/Letter dated _____ from Dow Chemical, U.S.A. to _____

cc: C. D. Kary
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