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June 10, 1983

Susan G. Austin, Sc.D.
Corporate Director of Epidemiology
Union Carbide Corporation
Old Ridgebury Road
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Dear Dr. Austin,

I have reviewed the manuscript describing the NIOSH case-control study of brain tumor cases in the Union Carbide Texas City plant.

The study seems to have been undertaken with great care and attention to detail and one gets the impression that the investigators are competent and thorough. With respect to the study and analysis itself, I have only one point to make. This is that in limiting analysis to those chemicals to which four or more cases were exposed the investigators are, in a sense, stacking the cards. They have selected those chemical associations which by chance alone are likely to have proportionally more exposed cases than controls. This is a legitimate thing to do, since the objective is to explain an observed excess of tumors. However, it should be discussed as another reason (in addition to the multiple test issue) why some things might be found to be "significantly" associated when they are in fact not. It might have been instructive to identify one control in each matched set, select those chemicals to which at least one of the identified controls were exposed and see whether there were as many exposures that appeared to be protective as there are that appear to be positively associated in the present analysis. This would have given a more balanced view than the present one which is geared solely to detecting positive associations. Since, in my view, the question of whether there is a real increase in risk of CNS tumors in this plant is still open, I think the balanced approach would be more appropriate.

Apart from the analysis itself, I have a few problems with the manuscript. Specifically:

(1) The summary. Insofar as occupational chemical exposures are concerned I interpret the findings as essentially negative, and the authors' own Discussion also leaves that impression. This is not, however, the impression

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that is left by the Summary. The reader who reads only the Summary - and they are probably in the majority - will get the impression that all the chemicals listed there were found to be associated with risk. The Summary does not state that only for carbon dioxide is the association statistically significant by both methods of analysis (including and excluding maintenance workers) and even there the results are inconsistent with respect to time of exposure. The last sentence of the Summary is particularly misleading because, although it is true, it implies that the associations referred to earlier were statistically significant.

(2) On page 5, the first sentence of the third paragraph is not true. In fact, duration of exposure is assessed in Table V for all the chemicals listed in Tables III and IV - regardless of whether they were "significantly associated with brain tumors" in the analyses of frequency of exposure.

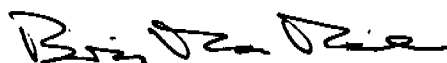
(3) On page 11, it hardly seems appropriate to refer to the chemical exposures as "risk factors" (line 2) when they have not been shown to be associated with increased risk.

(4) On page 13, line 6, this sentence should end after the word "chemical". The rest is gratuitous; it is always true and it suggests that the authors do not believe their own findings.

(5) On the same page, paragraph 2, the first sentence is a very strange summarization of the findings. Far from being conclusive, the evidence for carcinogenicity is not even suggestive.

I hope these comments will be useful to you.

Sincerely,



BM:dc

Brian MacMahon, M.D.
Professor

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