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September 9, 1991

Chuck Bush

SUBJECT: VI UPDATE

The Medical Committee presently has two outstanding activities. We are giving top priority to the completion of the remaining three papers on the primate/rodent studies with PVC/HCl which were conducted at SWRI. We plan to submit these to the VI for approval by the end of September and, subsequently, to Fundamental and Applied Toxicology for publication.

Because of the importance of publishing this work and the pressing matters, we will not devote any time to the monograph project until the primate studies have been submitted for publication. Practically, we would not be in a position to complete the monograph until these studies are published anyway. Once we resume this process, I will ask Drs. Hirschler and Kaplan to take prime responsibility for the combustion and toxicity areas, respectively. I will provide editorial/technical oversight.

One other item which I should mention is Roy Gottesman's request for comments on the mouse as a model for indoor air pollution. Clearly the mouse is a poor model for primates (i.e., man) with respect to the prediction of HCl lethality and the potential to cause pulmonary damage. However, from a purely theoretical point of view, the mouse "model" should be able to predict the relative irritancy of HCl. While Alarie et al. have published some information in this area, I am not certain that they have convincingly shown this to be the case. Therefore, it would be reasonable to ask Anderson Laboratories, Inc. to present their best case (supporting data).

A final item of interest, although it does not fall under the Technical Committee's activities, is the development of Emergency Exposure Guidelines for VCM. Jim Knaak (Occidental) reports that he will have a draft document to me by the end of September. The ultimate goal is to submit this to AIHA for adoption.

Bob

Bob Hinderer

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September 13, 1991

Mike Marshall

SUBJECT: CRITIQUE OF "PCB" FETAL TOXICITY STUDIES

In response to your request, I am enclosing some comments on the following papers that you provided:

1. Fein et al. (1984) Prenatal Exposure to Polychlorinated Biphenyls: Effects on Birth Size and Gestational Age. J. Pediatrics 105(2): 315-320.

   This paper is neither well conducted, or well reported. The areas of this study which appear to merit a greater degree of confidence is the analyses of PCBs in cord and maternal serum and the variables measured to assess infant health and viability. Generally, these are less subjective in nature.

   The biggest area of concern with this study is the information which was gathered (or not gathered) and how that information was obtained. In any study like this extreme care must be taken in designing the questionnaire and interviewing the participants. The authors appear to have increased the potential for bias by only asking whether or not fish was part of their diet. This not only highlighted or signaled "concern" to the volunteer, but they ignored other potential dietary variables which also could be contributing factors. There is also no mention of how the authors confirmed that the fish came from Lake Michigan. Considering that the authors noted that this was an upper socioeconomic group, it is quite likely their fish was obtained from restaurants (i.e., flown in). In fact, much "fish" is flown into groceries/fish markets.

   It is also equally unfortunate that the authors limited their analyses to just one chemical. Numerous chemicals which are also reasonably expected to be possible contaminants in fish are not considered. An even stronger association might have been missed.

   Still, the most important finding seems to have been quickly dismissed. Table I shows that in the exposed (fish eating) group, twice as many people consumed alcohol before pregnancy and three times as many consumed alcohol during pregnancy. This observation is very important because alcohol is a known fetal toxin. Although the authors state (Table II) that they adjusted for the effects of alcohol, I'm not convinced. I would like to know how they did it.

Furthermore, it would have been nice to know how many drinks a day were consumed by each participant (a simple question) and whether they were smokers.

I am also concerned about the potential effect of different sample sizes: 71 vs. 242 (Table II). However, I'll leave this to a biostatistician.

In conclusion, good epidemiology studies are hard to design and hard to conduct. This isn't one of them. Alcohol and/or smoking are better bets as causal agents.

2. Jacobson et al. (1990). Effects of in Utero Exposure to Polychlorinated Biphenyls and Related Contaminates on Cognitive Functioning in Young Children. J. Pediatrics 116(1): 38-45.

This is the new and improved version of Fein et al. (1984). They probably have learned from peer review and possibly earlier manuscript rejection in other journals. They look at lead and DDT, as well as PCB's. They include smoking. They also record the number of cigarettes smoked and drinks (alcohol) consumed. Unfortunately, this paper suffers from many of the same problems. They do not tell, or perhaps do not test, whether there are correlations with these or other variables.

In summary, these studies do not/cannot show that PCB's are associated with fetal toxicity. There are a number of technical issues such as the appropriateness/implication of log transformation of the data (Jacobson et al. (1990), which warrant further in-depth assessment.

If the Chlorine Institute sponsors a more in-depth analysis, I would appreciate receiving a copy.

Bob Hinderer

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cc: C. Bush
R. Gomez
C. Mattia