The Vinyl Institute

A Division of The Society of The Plastics Industry, Inc.

September 8, 1989

Mr. Robert Barham, Chief
Toxic Air Contaminant Identification Branch
Air Resources Board
Attn: Vinyl Chloride
1102 Q Street
Sacramento, California 95812

Re: Draft Report on Vinyl Chloride

Dear Mr. Barham

On August 29th, the Vinyl Institute* received the preliminary draft report on vinyl chloride dated July 1989 being prepared by the California Air Resources Board (CARB). There has been, therefore, a limited amount of time for our membership to thoroughly review the documents prior to the comment deadline.

Nevertheless, after reviewing the document, there are at least two areas of discussion that are inadequately treated in the California Air Resources Board (CARB) document. Therefore, most of the comments will be spent on those two areas. They are the pharmacokinetic knowledge of vinyl chloride in the risk assessment approach and a total inadequate treatment of the large number of epidemiology studies in the published literature. These are very concisely dismissed by the Department of Health Services (DHS) as being unacceptable to be used in the risk assessment process for regulatory purposes.

* The Vinyl Institute is an operating division of the Society of the Plastics Industry, Inc. Its members include Air Products and Chemicals, Borden Chemicals & Plastics, Certain-Teed Corporation, Dow Chemical USA, BFGoodrich Company, Georgia Gulf Corporation, Occidental Chemical Corporation, PPG Industries, Shintech Inc., and Vista Chemical Company. Together, these companies account for more than 80% of the domestic production of both vinyl chloride and polyvinyl chloride.

Point One: Pharmacokinetic Information. There are several publications in the literature not cited in the DHS document, that address the incorporation of pharmacokinetics in low dose risk estimation for chemical carcinogenesis. One such article was published as far back as 1980 in Toxicology and Applied Pharmacology, authored by Anderson, Hoel and Kaplan. That document demonstrates how to incorporate the pharmacokinetic information on vinyl chloride into a risk assessment approach for low dose risk estimation. There are numerous other publications on the pharmacokinetics of vinyl chloride as well. Another such document, published in 1981 in the Archives of Toxicology authored by Bolt, Filser and Buchter, demonstrates significant information that is relevant when extrapolating low level carcinogenic risk estimates from the existing data base. The DHS document fails to incorporate any of the established pharmacokinetic information in its treatment of theoretical risk for vinyl chloride.

A number of studies indicate that probably a reactive metabolite, not vinyl chloride per se is responsible for its toxicity. Although some inhaled vinyl chloride is excreted unchanged, depending on dose, a varying amount is metabolized. The metabolism of vinyl chloride has been the subject of numerous studies and it is currently thought that vinyl chloride is metabolized by epoxidation with subsequent production of chloroacetaldehyde. The further oxidation and conjugation with glutathione are responsible for the metabolites found in the urine. Gehring, et al. analyzed the metabolic and carcinogenic data from man and laboratory animals, and used several models to predict the incidence in man from the animal data. They found that all models over-predicted the risk to man unless corrections were made for the varying rates of metabolism and for the surface area differences of the different species.

Point Two: Epidemiology. There have been many published epidemiological investigations of occupational workers exposed to vinyl chloride at a variety of occupational exposure levels. Vinyl chloride may, in fact, be one of the most epidemiologically-studied industrial chemicals in the literature. To dismiss that data and relegate it only for comparative purposes to animal data is unacceptable. DHS demonstrates a bias towards the utilization of animal experiments as a priority over human evidence in their approach to risk assessment. This results in a dramatic overestimate of likely human risk at the low environmental levels being addressed by the document. The DHS goes on to state that risk extrapolations based on the human data yield results they judge to be comparable. The practical aspect of responding to an order of magnitude or two in risk assessment can often be dramatic, therefore risk estimates that yield order of magnitude different estimates of risk are extremely important. When adequate or substantial human evidence exists, that data should be given preferential treatment in the risk assessment process.

Many of the epidemiology studies that have been in the published literature have been updated in the past year or two. One example is the study Update of Vinyl Chloride Mortality authored by Dahar, et al. which was updated as recently as 1988 and further demonstrated a decreasing cancer incidence rate in workers as the latency period has been expanded substantially. The person years in this one particular study has been expanded from only approximately 4,000 person years to over 17,000 person years, thus a substantial increase in sensitivity of the study, as only one example. The Chemical Manufacturers Association (CMA) Vinyl Chloride Panel-sponsored epidemiology study was updated as recently as 1986. It is a very comprehensive epidemiology study consisting of a cohort of over 10,000 workers employed at 37 different plants belonging to 17 different companies. That study identified at that time, over 1,536 deaths. These are only several examples of many epidemiology studies published on vinyl chloride and DHS's approach to dismiss human epidemiology evidence in their risk assessment is inadequate.

Many of the human epidemiological studies point out a statistically-significant association between an increase in lung, liver and brain cancer and exposure to vinyl chloride. For brain cancer, three out of five studies demonstrate statistically-significant findings, although the results were somewhat variable. Positive findings occurred in studies with the greatest statistical power. Most reasonable interpretation of the data is consistent with the causal association of vinyl chloride exposure and an excess of brain cancer, however, the relative risk calculation for brain cancer is much lower than that for liver cancer. Only two out of eight studies on lung cancer yield statistically-significant results, and because studies with the higher power were negative, a causal association is unlikely. It is for these reasons, therefore, that the incidence rate on the angiosarcoma is the most suitable end-point for analysis of risk of exposure to vinyl chloride for a number of reasons:

1. Vinyl chloride angiosarcoma is a rare cancer in unexposed populations, thereby making the utilization of angiosarcoma as a demonstration of vinyl chloride exposure on the basis of work history truly a reasonable approach.

2. Angiosarcoma has been demonstrated to occur both in animals and humans when exposed to vinyl chloride.

3. It is therefore demonstrated unlikely that any other carcinogenic result from vinyl chloride would incur lower exposures than those lowest exposures that would induce angiosarcoma. Recent publications entitled Vinyl Chloride, An Assessment of the Risk of Occupational Exposure, was published in 1987 in the Fundamentals of Chemical Toxicology Journal, Volume 25, pages 187 to 202, 1987, authored by

Purchase, et al. A very extensive evaluation of the available information at that time is included in this article, and a very comprehensive examination of risk assessment approaches to vinyl chloride is examined. We believe that this document demonstrates a much more studied and scientifically defensible approach to assessing risk of exposure to vinyl chloride.

In summary, there are at least twenty epidemiological studies which involve over 45,000 workers who have occupationally been exposed to vinyl chloride. To dismiss this body of epidemiological study in favor of basing risk assessment on animal data is questionable at best. In the paper by Purchase, et al., information that is precisely the issue being addressed by DHS is present. In addition, an epidemiological study of populations living in the vicinity of VCM production facilities had been conducted previously. This study, Barr, et al. 1982, suggests that 100 ppb represented the estimated dose representing a 1x10-6 lifetime risk in man. That value is similar to the highest estimates derived from the animal data when taking biotransformation data into account. The studies discussed in the paragraphs above, will be forwarded under separate cover.

Finally, the Vinyl Institute is extremely interested in reviewing the revised draft document before it is forwarded to the Scientific Review Panel. Please add our organization to your distribution list. Materials should be forwarded to:

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Thank you for your attention to this matter.

Sincerely yours,

Meredith N. Scheck

Meredith N. Scheck
Assistant Director

MNS/pmb
cc: Mr. Richard Forey
Substance Evaluation Section
Air Resources Board
P.O. Box 2815
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