The Vinyl Institute

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

April 21, 1988

552-36-224

TO: Larry Thomas
Lew Freeman
Bob Sherman
~~Pat~~ Toner
Margaret Rogers

RE: VI Comments To ATSDR: Toxicological Profile on Vinyl Chloride

Enclosed are comments submitted to the Agency for Toxic Substances and Disease Registry on the draft Toxicological Profile for Vinyl Chloride required by Section 110 of SARA. These comments were developed jointly by the Vinyl Institute Technical and Health, Safety and Environment Committees and have been approved by counsel.

By way of background, these comments were originally to be submitted to ATSDR through the CMA Program Panel process. Due to the long delay in distribution of the profiles and the large number of peer reviewers (including individuals, companies and trade associations) involved in the process, it was decided that comments on the chemical-specific toxicological profiles would be submitted directly by the affected interests. CMA has served as the facilitator-coordinator of this effort. CMA is developing comments (some of which have already been submitted) on the issues that cut across chemical-specific lines.

If you have any questions on the comments, please let me know. To save you file space, I have chose not to send you the voluminous appendices.

Meredith

Meredith N. Scheck
Assistant Director

MNS/pmb
enclosure
cc: P. de la Cruz

SPI-02375

BEFORE THE
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, DEPARTMENT OF HEALTH AND HUMAN SERVICES, AND ENVIRONMENTAL PROTECTION AGENCY

COMMENTS OF
THE VINYL INSTITUTE
ON ATSDR'S TOXICOLOGICAL PROFILE FOR VINYL CHLORIDE

Vinyl Chloride Toxicological Profile;	)	
	)	
Request For Comment:	)	Docket No. ATSDR-2
	)	
52 Fed. Reg. 38340 (October 15, 1987)	)	

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April 18, 1988

COMMENTS ON
EPA TOXICOLOGICAL PROFILE ON VINYL CHLORIDE

General Comments

As described in Section 2.3.1., SARA directs EPA to prepare toxicology profiles that will include an examination of the data, a determination of adequacy, and, where appropriate, an identification of needed toxicology testing. Although the draft Toxicological Profile for vinyl chloride (January 1988) is intended to meet this requirement, it falls far short of both the letter and spirit of the Act in many ways for the following reasons:

1. This document fails to incorporate key data.

2. It fails to provide the critical review necessary to draw a conclusion.

3. There is no identification of toxicological testing and the detail of discussion of this subject is not adequate to draw any conclusions.

4. Referencing the data in tables and texts is inadequate.

5. There are some instances where reference books and computerized data bases are utilized instead of the original references. This procedure does not allow critical review and it presents the opportunity for perpetuating errors and misstatements. This has been a frequent problem or real concern for at least one of the reference books used.

6. The detail of information provided is insufficient to provide any confidence in the NOAEL, LOAEL, Minimal Risk levels or conclusions or a clear understanding of how they arrived at these. To this end, we would recommend the use of NAS guidelines for use of safety factors (NAS,1982).

7. The use of a number of terms is questionable. The term FEL is misused on page 42, paragraph 1. Increase in DNA synthesis is not a frank effect. Also, the descriptor "minimal" (page 44, General Discussion) lacks specificity. Standardized terms such as "Adequate" (or "Clear"), "Some" (or "Limited"), "Equivocal"), "No Evidence" and "Inadequate" should be used because their meanings transcend the subject of carcinogenicity and are broadly applicable. Furthermore, it would be better if adequacy was assessed in these terms.

Specific Comments on Section 1 - Public Health Statement

CONSUMER EXPOSURE IN CARS (Section 1.2, page 1, paragraph 1; Section 7.2.4, page 71, paragraph 3)

The Toxicological Profile states "air inside new cars may contain levels of vinyl chloride higher than expected background levels, because vinyl chloride may seep into the air from the new plastic parts". Support for this sweeping statement is an EPA report referenced as (EPA 1985b) (Health and Environment Effects Profile for Chloroethene. Cincinnati, Ohio; Environmental Criteria and Assessment Office. ECAO-CIN-P155). The data on page 71 of the Toxicological Profile "gives the analysis of interior air for two new cars (underline added for emphasis) and shows ranges of 0.3 to 1.2 ppm of vinyl chloride. There is no information on background levels, nor is there information concerning the accuracy of the analytical method employed.

Since the OSHA standard has a permissible exposure limit (for employees in an occupational setting) of not greater than 1 ppm averaged over any 8-hour period, the significance of the levels of vinyl chloride found in these two cars is clearly questionable. Further, it would be important to have additional data and particularly analysis made after the car has been in use for a period of time. Vinyl chloride emissions would be expected to be considerably reduced from the initial emissions in a "new" car and therefore would not represent a continuing exposure source.

PLASTIC PIPE LEACHING DRINKING WATER EXPOSURE (Section 1.2, page 1, paragraph 2; Section 1.3, page 2; Section 2.2.3.2, page 18, paragraph 2; Section 2.3.3.3, page 24, paragraph 2; Section 7.2.4, page 71.

Currently, PVC pipe (per the National Sanitation Foundation standards) must be $\leq$ 2 ppm in the bulk wall so that vinyl chloride in the extraction test is $\leq$ 1 ppb. The U.S. Environmental Protection Agency limit is 2 ppb. Therefore, the leaching of vinyl chloride into drinking water from PVC pipe is inaccurate.

Behrens and Daniels have determined that the principal factors controlling vinyl chloride migration from polyvinyl chloride pipe are the initial vinyl chloride monomer content, thickness of the PVC section, temperature and age of the pipe. Their experimental data indicates that PVC pipe containing $\leq$ 1 ppm residual vinyl chloride will result in vinyl chloride concentrations of less than 0.002 mg/kg (0.2 ppb) under any expected service conditions. The Behrens and Daniels paper is provided as Appendix A.

Further, a study conducted at McKesson Environmental Sciences Inc., on Effects on Water Quality By Leachable Substances From Copper Tubing, CPVC Piping and Galvanized Pipe Fittings is provided as Appendix B. The study used chlorinated polyvinyl chloride pipe (CPVC) as a worst-case since CPVC could be expected to have more potentially leachable impurities.

The McKesson study had as its objective quantifying the rate of leaching of organic contaminants into water as a result of passage through chlorinated polyvinyl chloride (CPVC). Full data can be found in the McKesson Report (Part Three, pg. III-1 ff). The significant finding is that "no vinyl chloride" was detected (see pg. III-2) in these studies.

CARCINOGENICITY AND OTHER DISEASE (Section 1.4, page 2, paragraph 1; Section 2.2.1.1, page 14, paragraph 1; Section 4.3.6.4.).

The discussion of the types of disease and cancer caused by vinyl chloride is very misleading. The document states that "lower concentrations" cause "vinyl chloride disease" but fails to note that these effects are not of concern at present in the workplace and under ambient concentrations due to the OSHA standard which strictly regulates occupational exposure (see Section 1910.1017 at 40 FR 23072, May 28, 1975). Furthermore, this section suggests that vinyl chloride can cause cancer of the "liver, brain, lung and possible other organs." IARC Supplement 4 (1982) clearly states that "Vinyl chloride causes angiosarcoma of the liver". It distinguishes other tumor having a lesser weight of evidence as being "associated with" other cancers.

A recent assessment of the data by the world-renowned epidemiologist Sir Richard Doll (1987) further supports this distinction. He notes that the evidence that vinyl chloride causes liver cancer, specifically angiosarcoma is strong. However, the combined data on respiratory cancer fail to support an association of vinyl chloride and lung cancer. In the case of brain and lymphatic and meopoietic cancers, he indicates that the excesses are not statistically significant and that there is nothing to suggest that they are occupationally related.

EFFECTS ON OFFSPRING/DEVELOPMENT (Section 1.4, page 2, paragraph 1; Section 2.2.11, pages 13-14; Section 4.3.3.1; Section 4.4).

The Toxicological Profile on vinyl chloride fails to note that there is no evidence that vinyl chloride causes birth defects or reproductive effects. It is only a concern because of potential transplacental carcinogenicity. The absence of a critical review has contributed to a misleading presentation. Such a review should include consideration of

key documents which are described in "Potential Effects of Vinyl Chloride on Human Offspring" (1987). This document is included in its entirety as an appendix to these comments. It is also interesting to note that the discussion of developmental toxicity on page 13 appears to avoid the fact that "vinyl chloride did not cause significant embryonal or fetal toxicity and was not teratogenic in any of the species at the concentrations tested". (John et.al., 1977) Based on these results it is incongruous that the document would espouse any NOAEL, not to mention one at 50 ppm. Unfortunately, there is no information provided to support the 0.7 ppm minimal risk level or the 50 ppm NOAEL. Such absence of detail and supporting rationals is a common deficiency in this document.

A report reviewing "Potential Effects of Vinyl Chloride on Human Offspring" prepared by The Vinyl Institute Medical Subcommittee and issued December 1987 is provided as Appendix C.

CANCER RISK ESTIMATES (Section 1.6.2, page 4; Section 2.2.1.1, pages 14-15).

Estimates of cancer risk are limited to those derived by EPA in 1985. Since risk estimates have been derived by others, these should be identified and discussed. This is particularly important since some of these estimates (NHCH, 1987) differ by more than 2 orders or magnitude from that presented by EPA. Furthermore, EPA has recently revealed the fact that it is now using new risk assessment procedures which have dramatically lessened risk estimates for many chemicals (Chemical Regulation Reporter, 1988). An updated risk assessment based on the newly-developed procedures being used by EPA is thus warranted.

Specific Comments on Section 2

GENOTOXICITY (Section 2.2.1.1; 4.3.5.1; 4.3.5.2)

Numerous studies have evaluated the genotoxicity of vinyl chloride. Although vinyl chloride has been found to cause mutations in some non-reproductive cells, particularly *in vitro*, the *in vivo* evidence for sommatic and germinal mutations is far less convincing.

The ability of vinyl chloride to induce sommatic mutations *in vivo* in human cells was examined in three separate, independent studies conducted by Funes-Craviato et.al. (1975), Ducatman et.al. (1975), and Purchase et.al. (1975). All of the studies examined workplace exposure to vinyl chloride, but all suffer from a number of flaws including lack of exposure data, inappropriate statistics, and no descriptions of how control groups were selected. The studies show a slight association between potential vinyl chloride exposure and chromosomal

breaks in lymphocytes. Two of the studies, Funes-Craviato et.al. (1975), Ducatman et.al. (1975), actually found that the number of chromosomal aberrations were often lower among workers as their length of employment increased. This last observation indicates that there is no evidence of a dose or compound-related response. Because of all of the information that is missing from these studies, it is hard to draw any conclusions on the relationship between vinyl chloride exposure and chromosomal aberrations. Workplace exposure and chromosomal aberrations among lymphocytes of male workers was also examined by Leonard et.al. (1977). The workers studied were employed in a vinyl chloride facility in Belgium where there was no record of exposure levels. The authors assumed that employment during early exposure years was initially 500 ppm which was eventually reduced to 10 ppm. Controls who were employed in the laboratory of the same facility and were assumed to be exposed to less than 1 ppm. An additional 10 controls were obtained from outside the factory and were assumed to never have been exposed. The average of the number of aberrations per 100 cells was approximately the same for each group. Even though some specific chromosomal aberrations were found in the exposed group, the significance of the finding is questionable since each of those workers received regular radiologic examinations which could produce the same observations. Consequently, the Leonard study does not support the premise that vinyl chloride causes mutations in human subjects.

Fleig and Thiess (1978) studied aberrations of lymphocyte chromosomes among workers at a BASF plant in Germany. The actual plant exposures have not been documented in this study, but they were reported to be comparable to the German workplace standard which was around 1,000 ppm in 1945 and decreased to 150 ppm in 1973. The subjects chosen in this study had overt signs of vinyl chloride toxicity which included angiosarcoma of the liver, and the controls were carefully matched and took into account smoking, alcohol, vaccinations and other medical problems or treatment. Fleig and Thiess reported that they could find no difference between the exposed workers and controls with the exception of one exposed worker who was receiving chemotherapy for cancer. The Fleig and Thiess study was not able to demonstrate an increase in chromosome aberrations as a result of high level vinyl chloride exposure in the workplace.

The ability of vinyl chloride to produce germinal mutations was examined by Anderson et.al. (1976) using the dominant lethal assay. Male mice were exposed to vinyl chloride for 6 hours per day for 5 days to concentrations of 3,000, 10,000, and 30,000 ppm. This study employed two known mutagens as positive controls (cyclophosphamide and ethyl methane sulphonate). No mutagenic effects were noted at any of the

stages of spermatogenesis in the vinyl chloride-exposed animals. However, evidence of mutagenicity was observed in the positive controls. The dominant lethal mutations study was later repeated by Himeno et.al. 1983) in CD-1 mice under two different exposure conditions. One group of mice was exposed for four hours per day during five consecutive days to 10,000 ppm of vinyl chloride and the second group of mice was exposed for four hours per day, five days per week over a 10-week period to 5,000 ppm vinyl chloride. This study, like the earlier study of Anderson et.al. (1976) discussed above, was not able to demonstrate any dominant lethal type of mutations as a result of vinyl chloride exposure, and this independently supports the observation that vinyl chloride is non-mutagenic.

INHALATION EXPOSURE (Section 2.2.1.1, page 8, paragraph 1)

Human deaths from high level occupational exposure should be put in proper perspective. Most if not all of those fatalities were the result of workers performing in a confined atmosphere with poor or little ventilation and vinyl chloride concentrations in the range of tens of thousands of ppm. There is a long history of workplace fatalities from confined workspace environments for many other agents than vinyl chloride, and all have been controlled by either using supplied airline respirators or proper ventilation. As in Section 4.3.1.1, it should be pointed out that the most likely cause of death in the circumstances is due to narcosis.

FDA REGULATIONS (Section 1.7, page 6; Section 2.2.3.1, page 18)

The statement regarding Food and Drug Administration regulations is not accurate and as written, suggests that ingestion of vinyl chloride is a public health problem when in fact, FDA has concluded otherwise.

On February 3, 1986, FDA proposed a new regulation (51 FR 4, 177) to "provide for the safe use of certain vinyl chloride polymers by establishing limits on the amount of residual vinyl chloride monomer (RVCM) they may contain". Specifically, FDA proposed:

1. A 5 part per billion (ppb) limit on RVCM for plasticized films, coatings, and plasticized applications.

2. A 10 ppb limit on RVCM for rigid and semi-rigid food containers.

3. A 50 ppb limit on RVCM for pipe used to carry water inside a food processing plant.

4. A 50 ppb limit on RVCM in vinyl chloride - vinylidene chloride copolymer films and coatings.

5. A recognition of prior sanctioned status of both homopolymer and copolymer PVC resins used as films, coatings, water pipe, flexible tubing, gaskets, bottle or jar liners and rigid sheet.

The proposal contained FDA's analysis of migration from bottles used for food contact use and estimated that individual exposure to vinyl chloride from PVC packaging would not exceed 25 nanograms per day. FDA calculated an individual lifetime risk of less than 1 in 10 million.

Based on these considerations, FDA tentatively concluded that the use of PVC as food-contact materials, with the RVCM limits as established, was safe.

The Public Health Statement section should be revised to reflect this.

EFFECTS ON OFFSPRING/REPRODUCTIVE (Section 2.2.1.1, page 14)

No reference is provided to indicate what animal data is being discussed. We assume this refers to the work of Bi et.al. (1985). The authors of the Toxicological Profile fail either here or on page 50 to question whether these observations are consistent with observations in other long-term studies. In fact, a review of the data indicates the results of this study are not consistent with those observed in other long-term studies. (Maltoni and Mehlman, 1984).

More importantly, it should be noted that histopathologic organ changes are evidence of systemic changes even if they are found in reproductive tissues. Although observations of toxic effects in reproductive tissues could lead one to question whether the reproductive capacity of an animal might be compromised, it does not provide any evidence that a chemical is a reproductive toxin. In the case of vinyl chloride, the data indicates that vinyl chloride does not affect reproduction.

BIOLOGICAL MONITORING (Section 2.2.2, page 16, paragraph 3)

The authors note observations of elevated urinary coproporphyrin as a common finding associated with vinyl chloride-related liver disease and suggest it might be useful in population monitoring. What is not pointed out, however, is that while this finding is indicative of liver disease, it is not specific to vinyl chloride or chemical-induced liver disease..

LEVELS FOUND IN THE ENVIRONMENT (Section 2.2.3.1, page 18, paragraph 1)

The discussion of vinyl chloride associated with landfills suggests that all the vinyl chloride is the result of disposal of vinyl chloride-containing materials. Information is available which shows that vinyl chloride can also result from the biodegradation of 1,1,1-trichloroethane which is found in many household products commonly deposited at waste sites and landfills.

Thus, the finding of vinyl chloride over landfills may not at all be related to disposal of vinyl chloride or polyvinyl chloride.

ADEQUACY OF DATA (Section 2.3.2.1, page 20)

Item 2 should note that while a potency factor or potency factors can be derived, the precision of those estimates is unknown.

The health effect and exposure route referred in Item 4 are unclear.

Specific Comments on Section 4 - Toxicological Data

INTERACTIONS WITH OTHER CHEMICALS (Section 4.4, page 60)

The document fails to discuss the interaction of vinyl chloride and alcohol (i.e., metabolism and cancer in workers). John et.al. (1977) in a study on tetratogenicity in mice, rabbits and rats found that co-administration of ethyl alcohol with vinyl chloride exaggerated all aspects of maternal toxicity.

References

References cited in this submission that do not appear on the list of references in the Toxicological Profile on Vinyl Chloride (January 1988) are the following:

- Drinking Water and Health, Volume 4, National Academy Press,
  Washington, D.C., page 153.

- Fleig, I., and Thiess, A.M., 1978. "Mutagenicity of Vinyl Chloride", J. Occupat Med, 20 (8), 557-561

- "Prediction of Vinyl Chloride Monomer Migration From Rigid PVC Pipe", A.R. Berens and C.A. Daniels, Polymer Engineering and Science, Volume 16, 8, August 1976.

- Leonard, A., Decat, G., and Leonard, E.D., 1977. "Cytogenetic Investigations on Lymphocytes From Workers Exposed to Vinyl Chloride", J. Tox. Env. Health, 2, 1135-1141.

- Himeno, S., Okuda, H., and Suzuki, T., 1983 "Lack of Dominant Lethal Effects in Male CD-1 Mice After Short-Term and Long-Term Exposures to Vinyl Chloride Monomer", Tox Letter, 16 (1-2), 47-53.

- Maltoni, C., and Mehlman, M.A. Experimental Research on Vinyl Chloride Carcinogenesis, Volume II, Princeton Scientific Publishers, Inc., Princeton, New Jersey 1984.

- "Effects of Exposure To Vinyl Chloride: An Assessment of the Evidence", Doll, Sir Richard, FRS (Consultant To Imperial Cancer Research Fund, Cancer Epidemiology and Clinical Trials Unit, Radcliffe Infirmary, Oxford, April 1987 (UNPUBLISHED).