BFGoodrich

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Mr. Art Gellner
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P.O. Box 253
Sulphur, Louisiana 70664

Dear Art:

I am enclosing my comments on the draft VCM Toxicological Profile. I will forward any additional comments from my colleagues on the Medical Subcommittee as soon as they are available. Please let me know when you will have a copy of the final draft ready for internal VI review.

Best regards,

Bob Hinderer

Robert K. Hinderer, Ph.D.
Manager, Toxicology

jp 80311-1

cc: Dr. Roy Gottesman*
Dr. M. M. O'Mara*
G. F. Lefebvre/W. C. Holbrook/J. W. Lewis
Dr. Paul Gurba
Dr. J. R. Drumwright
Dr. W. Hartgrove

* Comments only; without supporting documents

Comments on EPA Toxicological Profile on VCM

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 VCM (1988) is intended to meet this requirement, it falls far short of both the letter and spirit of the Act in many ways.

1) This document fails to incorporate key data.

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

3) Because there is no identification of toxicological testing needs, we assume that all the data is considered adequate. The graphs appear to indicate the data is adequate. However, there is no clear statement in the text to this point and the detail of discussion of this subject is not adequate to draw any conclusions.

4) Referencing of data in tables and texts is inadequate.

5) There are some instances where reference books and computerized databases are utilized instead of the original references. The problem with this procedure is

that it does not allow critical review and it presents the opportunity for perpetuating errors and misstatements. We know for a fact that this has been a frequent problem or real concern for at least one of the reference books used.

6) The detail of information provided generally 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 authors' use of a number of terms is questionable. The term FEL is misused on p.42, paragraph 1. Increase in DNA synthesis is not a frank effect. Also the descriptor "minimal" (p.44 General Discussion) is a poor choice. 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

Consumer Exposure in Cars (Section 1.2, page 1, paragraph 1; Section 7.2.4, page 71, paragraph 3)

At the February, 1988 VI Technical Committee meeting Roy Gottesman mentioned that GM had conducted a study of VCM levels in new cars. We should make sure that this information is provided to EPA.

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, paragraphs 2; Section 7.2.4, page 71, paragraph 2)

The VI has generated considerable data on the leaching from PVC pipe. I have asked Alan Olson (BFG) to prepare comments and provide the data.

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 VCM is very misleading. The document states that "lower concentrations cause "vinyl chloride disease" but fail to note

that these effects are not of concern at present workplace and ambient concentrations. Furthermore, this section suggests that VCM can cause cancer of the "liver, brain, lung and possibly other organs." IARC Supplement 4 (1982) clearly states that "Vinyl chloride causes angiosarcoma of the liver" and distinguishes other tumor with lesser weight of evidence being "associated with."

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 VCM causes liver cancer, specifically angiosarcoma, is strong. However, the combined data on respiratory cancer fail to support an association of VCM and lung cancer. In the case of brain and lymphatic and hemopoietic 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/Developmental (Section 1.4, page 2, paragraph 1; Section 2.2.11, pages 13-14; Section 4.3.3.1; Section 4.4)

The profile on VCM fails to note that there is no evidence that VCM causes birth defects or reproductive effects but that it's only a concern from the point of view of potential

transplacental carcinogenicity. The lack of focus on this conclusion or any conclusion may be due to the lack of consideration of key documents which are described in "Potential Effects of Vinyl Chloride on Human Offspring" (1987). Also, the absence of critical review has contributed to a misleading presentation.

It is also interesting to note that the discussion of developmental toxicity on p. 13 appears to avoid the fact that "VCM 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 rationale is a common deficiency in this document.

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 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).

Genotoxicity (Section 2.2.1.1)

Because Paul Gurba had prepared some comments on this area earlier, I requested that he address this category.

FDA Regulations (Section 1.7, p. 6; Section 2.2.3.1, page 18)

Statement on FDA regulation of food packaging is inaccurate. The FDA has recently proposed to amend the prior sanctions and regulations regarding vinyl food packaging to limit VCM to 5 to 50 ppb not ppm. Also, there is no current official "action level" or "regulatory level" for VCM but there are manufacturer's voluntary guidelines.

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 is Bi et al (1985). The authors fail either here or on p. 50 to ask whether these observations

are consistent with observations in other long-term studies. In fact, a review of the data indicates it is not (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 would 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 VCM, the data indicates that VCM 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 VCM-related liver disease and suggest it might be useful in population monitoring. What is not pointed out, however, is that while it is indicative of liver disease, it is not specific to VCM or chemical induced liver disease.

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 to in item 4 are unclear.

Interactions (Section 4.4)

The document fails to discuss the interaction of VCM and alcohol (i.e. metabolism and cancer in workers).

Drinking Water and Health, Vol. 4, National Academy Press, Washington, D.C., p.153.

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