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TO: Has Shah**FAX NO.:** 703-741-6091**FROM:** Tom Downs**DATE:** March 5, 1996**TOTAL NUMBER OF PAGES (including cover page):** 6

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COMMENTS: Please call me to confirm the changes we discussed. I will have the final version couriered to your office. Thank you.

CMA 113538

March 6, 1996

Ms. Jennifer Heise
Peer Review Coordinator
ERG
110 Hartwell Avenue
Lexington, MA 02173

Re: ATSDR Medical Management Guidelines for Vinyl Chloride

Dear Ms. Heise:

This letter transmits the Chemical Manufacturers Association (CMA) Vinyl Chloride Panel's comments on the Medical Management Guidelines for Vinyl Chloride under development by the Agency for Toxic Substances and Disease Registry (ATSDR). At the request of Scott Wright of ATSDR, CMA is submitting these comments directly to you.

Please call me at (703) 741-5637 if you have questions or need additional information on the enclosed comments.

Very truly yours,

Hasmukh C. Shah, Ph.D.
Manager
Vinyl Chloride Panel

Enclosure

cc: Scott Wright

CMA 113539

**Comments of the
Chemical Manufacturers Association
Vinyl Chloride Panel Health Committee
on the Agency for Toxic Substances and Disease Registry's
Proposed Medical Guidelines for Vinyl Chloride**

March 6, 1996

Introduction

The Agency for Toxic Substances and Disease Registry (ATSDR) recently requested review and comment on proposed Medical Management Guidelines for Vinyl Chloride. The Chemical Manufacturers Association (CMA) Vinyl Chloride Panel, which represents producers of vinyl chloride, is pleased to provide these comments.

CMA applauds ATSDR's efforts to produce medical management guidelines for vinyl chloride that are scientifically accurate. In order to achieve that goal, CMA's specific suggestions are presented below.

Page 1, Route of Exposure, Inhalation

The fifth sentence (beginning "Occupational exposures have resulted") should be revised to read as follows: "Occupational exposures well above the current threshold limit value (TLV®) have resulted in the occurrence of a syndrome consisting of acroosteolysis, scleroderma-like skin changes, and Raynaud's phenomenon."

The last sentence (beginning "Chronic exposures have led to cancer") should be revised to read as follows: "Chronic exposures (well above the current TLV®) have led to increased risk of cancer, particularly of angiosarcoma of the liver. Increased risks of cancer of the lung and brain have been reported but not substantiated."

Page 3, Health Effects, boxed text

The third sentence (beginning "Vinyl chloride has been shown") should be revised to read as follows: "Vinyl chloride has been shown to induce angiosarcoma of the liver in humans and in laboratory animals with chronic exposure."

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The fourth sentence (beginning "Immunological effects") should be revised to read as follows: "Immunological effects and effects on reproduction have not been conclusively demonstrated in humans or animals."

Page 3, Acute Exposure, Cardiovascular

The last sentence (beginning "Chronic exposure to vinyl chloride") should be removed from the Acute Exposure section and placed under Chronic Exposure, on page 4. The sentence also should be revised to read as follows: "Chronic exposure to vinyl chloride (well above the current TLV®) can cause a syndrome consisting of acroosteolysis (dissolution of the bones of the terminal phalanges of the fingers, toes, and sacroiliac joints), Raynaud's phenomenon, and scleroderma-like skin changes."

Page 4, Chronic Exposure, Carcinogenicity

This paragraph should be revised to read as follows:

"The Environmental Protection Agency has classified vinyl chloride as a known human carcinogen. Vinyl chloride has been shown to induce cancer of the liver (angiosarcoma) in humans and laboratory animals when they are exposed for long durations above the current TLV®. There is inconsistent and inconclusive evidence suggesting that vinyl chloride exposure also may be associated with cancer of the lung, brain, and central nervous system."

Page 5, Reproductive and Developmental Effects

The first paragraph should be revised to read as follows:

"Occupational vinyl chloride exposure has been reported to result in decreased sexual performance both in men and women, although this theory has not been substantiated in controlled epidemiologic studies. In men, occupational exposure has been reported to be associated with decreased libido, impotence, and decreased testosterone production. In women, vinyl chloride exposure has been reported to result in decreased sexual function and elevated blood pressure and edema during pregnancy (i.e., pre-eclampsia). The reports of these findings largely have been based on individual random cases, and are not considered strongly suggestive of vinyl chloride's health effects. Animal studies have not conclusively demonstrated the presence or absence of vinyl chloride reproductive toxicity, but additional studies currently under way should clarify these issues."

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Supplementary material

The information that follows should be added to the Chronic Exposure section or possibly to a new section entitled "Occupational Exposure":

- ◆ **ANGIONEUROTIC DISORDERS IN THE HANDS AND FEET (RAYNAUD'S PHENOMENON)**
exposure criteria:
minimum intensity of exposure:
confirmed occupational exposure, assessed if possible by:
 - anamnesis and study of exposure conditions
 - and, if appropriate, atmospheric sampling
- ◆ **ACRO-OSTEOLYSIS IN THE UNGUAL PHALANGES OF THE HANDS AND FEET**
May accompany angioneurotic disorders confirmed by X-ray (loss of substance from bones)
exposure criteria:
minimum intensity of exposure:
confirmed occupational exposure, assessed if possible by:
 - anamnesis and study of exposure conditions
 - and, if appropriate, atmospheric sampling
- ◆ **DISTAL SKIN DISORDERS**
Pseudoscleroderma syndrome with penetration of the skin, possibly accompanied by general symptoms (arthralgia, myalgia); follows on from angioneurotic disorders.

exposure criteria:
minimum intensity of exposure:
confirmed occupational exposure, assessed if possible by:
 - anamnesis and study of exposure conditions
 - and, if appropriate, atmospheric sampling
- ◆ **LIVER FIBROSIS WITH PORTAL HYPERTENSION**
Portal Hypertension syndrome fibrosis confirmed by endoscopy or histology or indirectly by echography.
exposure criteria:
minimum intensity of exposure:

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confirmed occupational exposure, assessed if possible by:

- anamnesis and study of exposure conditions
- and, if appropriate, atmospheric sampling

◆ **ANGIOSARCOMA**

angiosarcoma, usually hepatic

exposure criteria:

minimum intensity of exposure:

confirmed occupational exposure, assessed if possible by:

- anamnesis and study of exposure conditions
- and, if appropriate, atmospheric sampling

CMA 113543