

May 21, 1973

INFORMATION ON VINYL CHLORIDE TO BE PRESENTED ORALLY TO NIOSH

I. Description of the Vinyl Chloride and Polyvinyl Chloride Industry

Vinyl chloride is a commodity used in very large quantities to make polyvinyl chloride resins (polymer and copolymer). The following estimated figures for 1972 illustrate the tremendous importance of this industry which has operated for 35 years in the United States and 40 years in Europe.

	<u>Vinyl Chloride</u>	<u>Polyvinyl Chloride</u>
U.S. Production	5.2 billion lbs (0.65 exported)	4.4 billion lbs
U.S. Capacity	5.9 billion lbs	
World Production	22 billion lbs	
Annual growth last 5 years	14%	
Projected annual growth, U.S.	11%	
U.S. Plants	14	37 (23 companies)
U.S. Workers	1500	5000
World Workers	10,000	

Virtually all (>99%) vinyl chloride is used in production of polyvinyl chloride and other polymers. It is difficult to estimate the number of workers employed in converting, molding, and fabricating these polymers but it is of the order of 10's of thousands, working in thousands of plants. It has been estimated that the wholesale value of fabricated products is over \$3 billion.

Almost all of the vinyl chloride and polyvinyl chloride producers in the U.S. are participants in the MCA Technical Task Group on Vinyl Chloride Research. Over 95% of the

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repeatedly exposed day after day, without adverse effect." In 1963 the ACGIH modified their recommendation so that 500 ppm was to be a maximum concentration (or ceiling) rather than a time-weighted average. This change was in part due to the publication by Torkelson, Oyen, and Rowe (American Industrial Hygiene Association Journal Vol. 22, p 354, 1961) of the results of six-months repeated inhalation studies on laboratory animals. These authors reported slight reversible liver injury in rats exposed 7-hours per day to 100 ppm and recommended that the time-weighted average exposure of workers not exceed 50 ppm. However, this recommendation was not considered appropriate by Lester, Greenberg, and Adams (ibid. Vol. 24, p 265, 1963) who did not consider significant injury to have resulted in rats which they had repeatedly exposed to 500 ppm v/v.

About 1963-1964 reports appeared in the European literature describing pain and tenderness in the fingers of polyvinyl chloride workers. X-ray examination showed that the bones of the hand were dissolving. This condition known as acroosteolysis was also investigated by American vinyl and polyvinyl chloride companies and similar disease was found in workers who cleaned polymerization vessels. The epidemiological data from this investigation was published in January 1971. (Archives of Environmental Health, Vol. 22, pp 61-91, 1971). This epidemiological study was directed at workers currently employed by the companies. In May 1970, Dr. P. Luigi Viola, an Italian physician, reported in Houston that he had attempted to create a bone condition in rats similar to human acroosteolysis. (Tenth Intl. Cancer Congress, Houston, Texas, May 22-29, 1970). Dr. Viola observed tumors in the ear canals of rats exposed to 30,000 ppm (3%) vinyl chloride vapor 4 hours per day for 12 months. Viola also reported tumors in the lungs and bones of these rats but these later tumors are of questionable significance.

These data were subsequently published (Viola, P. L., Bigotti, A., and Caputo, A., Cancer Research 31, 516-522, May 1971).

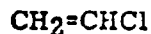
In 1970 the ACGIH proposed reduction of their recommended TLV to a time-weighted average of 200 ppm primarily on the basis of work reported by Kramer and Mutchler at a 1968 Gordon Research Conference on Toxicology and subsequently published in January 1972 (American Industrial Hygiene Association Journal, Vol. 33, p 20, 1972). The authors reported evidence of clinical findings in workers exposed to a time-weighted average concentration of 300 ppm VCM for many years.

In 1972 the ACGIH took vinyl chloride from the list of Intended Changes and changed the value in their regular list to 200 ppm. This value remains the recommended value in the 1973 list. A copy of the Documentation for the ACGIH TLV for vinyl chloride as published in 1971 is attached.

In order to get more details of Dr. Viola's experiments, including additional unpublished studies and observations that he might have compiled, he was invited by the Manufacturing Chemists Association to visit Washington and discuss his findings with MCA's Occupational Health Committee. On May 5 and 6, 1971, he discussed data published in 1971 and referred to other studies completed and underway. Dr. Viola was extremely vague and evasive in giving details. He did report that his vinyl chloride was quite impure and claimed to have seen tumors in rats exposed to 5000 ppm. He thought 2500 ppm would be without such an effect. He produced no data and refused to give details. He claimed he would not be concerned about workers exposed to less than 500 ppm. We are not aware of any further publications by Dr. Viola on this subject.

DOCUMENTATION OF THE THRESHOLD LIMIT VALUES FOR
SUBSTANCES IN WORKROOM AIR - Third Edition 1971

VINYL CHLORIDE



200 ppm (Approximately 770 mg/m³)

Vinyl chloride is a flammable gas with anesthetic properties at high concentrations. At anesthetic concentrations (8 to 12%) it has serious effects on cardiac muscle resulting in arrhythmias and sensitization in dogs(1,2). There is a wide margin between anesthetic and lethal concentrations (30-40%)(3). Torkelson, Oyen and Rowe(4) reported that repeated seven-hour exposures for six months at 200 ppm resulted in histologic changes in the central lobular region of the livers of rabbits, but not in rats, guinea pigs and dogs. At 100 ppm there was only slight liver enlargement. A subsequent report by Lester, Greenberg and Adams(5) on the effects of repeated exposure of rats to vinyl chloride assaying 99 + percent purity at 2 and 5% concentration stated that, although liver changes were noted, they were not considered to be of pathological significance. In their opinion, a recommended TLV of 500 ppm was satisfactory for worker exposure.

An interim report was made by Mutchler and Kramer(6) of long industrial health experience with vinyl chloride workers. Beginning in 1950, continuous monitoring was begun at five or six stations and the results compared with breath analyses(7) for vinyl chloride for 50 workers. Between 1950 and 1967 the mean air concentration was 160 ppm, with one maximal peak at 600 ppm of vinyl chloride and with great daily variation from 30 to 170 ppm, on the average. During part of this time vinylidene chloride* was an associated air contaminant estimated at around 5 ppm. Twenty-one clinical parameters were measured for comparison with the environmental data, and relationships were obtained by stepwise multiple linear regression analysis. Of medical examinations numbering 404 on 97 workers, 66 were used for comparison with 650 controls. These examinations with final diagnoses made according to the international classification of diseases, failed to reveal any overt condition attributable to vinyl chloride (or vinylidene chloride) exposure. No differences of physiologic significance were found in blood pressure, hemoglobin, electrocardiograms, and no body abnormalities (acro-osteolysis) appeared. No one was clinically ill. Six clinical parameters appeared to be altered, however. Among these, beta lipoprotein, icterus index, and bromosulfalein retention time may have some physiologic significance. The investigators felt, from a review of the interim findings, that a time-weighted average exposure concentration at 300 ppm (combined vinyl chloride and 5 ppm vinylidene chloride) could result in some degree of liver dysfunction. The multiphasic screening tests are continuing on all exposed workers, and analysis of the findings is being made on an individual worker basis. In the meantime, a time-weighted average threshold limit value of 200 ppm vinyl chloride (with a few ppm vinylidene chloride) seems appropriate to prevent adverse systemic effects from long-continued daily exposure.

(* A 90-day animal inhalation exposure to vinylidene chloride at 5 ppm was without observable effect.)

References:

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6. Mutchler, J.E., Kramer, C.G.: Report on Relation of Exposure to State of Health of Dow Chemical Workers, Gordon Conf., Tilton, N.H. (August, 1968).
7. Baretta, E.D., Stewart, R.D., Mutchler, J.E.: *Am. Ind. Hyg. Assn. J.* 30, 537 (1969).

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III. Toxicity Studies in Progress

1. MCA-Sponsored Inhalation Studies.

As announced in March of 1973, the Manufacturing Chemists Association has contracted with Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois, to conduct two-year studies on rats, mice and hamsters. Groups of 100 male and 100 female of each species (600 total) will be exposed to either 0 (control), 5000 ppm, 500 ppm, or 50 ppm of vinyl chloride monomer, 7 hours per day, 5 days per week for 12 months. They will then be observed for an additional 12 months (6 months for mice). These animals will not have food and water during exposure.

This "lifetime" study is designed primarily as a cancer study and will include only a limited amount of other observations. Because Viola's studies involved simultaneous exposure of food, water, and bedding, a separate group of 100 rats of one sex will receive exposures to 5000 ppm along with their food, water, and bedding. This group is included to determine the possibility that a reaction of the vinyl chloride monomer with either the food, water, or bedding results in a toxic reaction product.

Exposure of these animals started in May 1973. A complete copy of the protocol is attached.

2. MCA-Sponsored Epidemiological Studies

The Manufacturing Chemists Association has contracted with Tabershaw-Cooper Associates, Berkeley, Calif., to conduct a study of the cause of death in vinyl chloride and polyvinyl chloride workers. The objectives are:

- (a) to compare the mortality of individuals who have worked in vinyl chloride plants with that of the general population, corrected for area, age, and sex;
- (b) to compare mortality patterns within the population of vinyl chloride workers, based upon estimated occupational exposure; and
- (c) to compare mortality among vinyl chloride workers with the mortality of other occupational groups which TCA, Inc., has studied.

This study is expected to require at least 8 months for completion and reporting. A copy of the protocol is attached.