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The attached chronology concerns attention to occupational health aspects of vinyl chloride, particularly that in which the Manufacturing Chemists Association (MCA) has had a part on behalf of U. S. producers of vinyl chloride monomer (VCM) and polyvinyl chloride (PVC).

This material is provided as background and for use as you wish.

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FOR RELEASE

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For Immediate Release

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VINYL CHLORIDE CHRONOLOGY

While it had been recognized for decades that exposure to high concentrations of vinyl chloride monomer (VCM) might cause liver and kidney injuries, the U. S. chemical industry was not aware of any cancer-related potential of VCM until May 1970.

From the time polyvinyl chloride (PVC) -- the principal product of VCM -- was first produced in this country in the 1930s, the major worker hazard concern with VCM was believed to be flammability and explosions. Controls were designed to cover these.

The Manufacturing Chemists Association's (MCA) Chemical Safety Data Sheet on vinyl chloride, published in 1954, stated, "Aside from the risk of fire or explosion, vinyl chloride presents no other very serious problem in general handling. The presently accepted maximum allowable concentration is 500 parts per million (recommended by the American Conference of Governmental Industrial Hygienists -- ACGIH -- later in 1962) . . . In concentrations well above 500 ppm, vinyl chloride acts as a mild general anesthetic."

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In 1961, The Dow Chemical Company reported that long-term (4½ to 6 months at what would correspond to normal working hours) VCM exposures of animals to down to 100 ppm VCM resulted in slight liver injuries, and recommended working exposure levels b reduced to 50 ppm.

This recommendation for worker exposure was not accepted by ACGIH. In 1962, on the basis of work done at Yale University, from which the authors concluded that 500 ppm offered an adequat saf ty margin for human exposure to VCM, ACGIH published 500 ppm as the recommended standard.

In 1971, the Occupational Safety and Health Administration (OSHA) established 500 ppm VCM as a national standard. This changed in April 1974 when OSHA, following voluntary disclosur by The B. F. Goodrich Company of liver cancer deaths possibly related to vinyl chloride exposure, set a temporary emergency standard at 50 ppm. Then, on May 10, citing the findings of an MCA-administered study that showed liver cancer in mice at 50 ppm, OSHA proposed a "no detectable" standard, as previously recommend d by the National Institute of Occupational Safety and Health (NIOSH).

The following is a brief chronology of vinyl chloride activiti s, r lating to worker health. It is based on MCA records and input from U. S. producers of VCM and/or PVC.

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January 1967

Because of reports of finger abnormalities in the early 1960s, MCA arranged for a study at the University of Michigan on acroosteolysis -- softening of finger tip bones -- among VCM/PVC workers, particularly those who cleaned polymerization kettles. Study cover d clinical, epidemiological and industrial hygiene aspects.

August 1968

Research by The Dow Chemical Company showed slight alteration in liver function in workers industrially exposed to concentrations of up to 300 ppm VCM.

F bruary 1970

Findings of the MCA acroosteolysis study were submitted for scientific publication. They appeared in the "Archives of Environmental Health," published by th American Medical Association in January 1971. The authors were unable to pinpoint the cause of this disease and recomm nded animal studies be undertaken to develop an experimental model. They also recomm nded a worker exposure limit of 50 ppm VCM.

May 1970

At the 10th International Cancer Congr ss, Houston, Texas, Dr. P. L. Viola, of th Regina Elena Institute for Cancer Research, Rome, Italy, reported 30,000 ppm VCM exposures at four-hours-a-day, five-days-a-week for a year, caused canc rs of the skin, lung and bones of rats. He concluded that "no implications to human pathology can be extrapolated from the experimental model reported in this paper." He exposed these animals in an attempt to develop an experimental mod l for acroosteolysis.

August 1970

ACGIH considered a reduction of the work r exposure limit to 200 ppm VCM, but did not publish it as a recommendation until August 1972.

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Sept mber 11, 1970	In spite of Dr. Viola's study and his conclusions of no human implications, MCA's long-standing Occupational Health Committee (OHC) considered the need for additional VCM research.
Octob r 27, 1970	At the suggestion of the OHC, MCA wrote to a number of laboratories regarding the conducting of toxicological studies on laboratory animals with VCM.
April 12, 1971	MCA invited Dr. Viola to visit with th OHC and discuss his findings.
May 5-6, 1971	Dr. Viola came and discussed his work to date and referred to other European studies in progress. He stated the vinyl chloride used in his tests was impure. He reported tentative observation of tumors in the ears of rats exposed to 5000 ppm VCM, but gave his opinion that 2500 ppm would not produce this effect. He stat d that he would not be concerned about workers exposed to less than 500 ppm VCM.
May 6, 1971	MCA's OHC recommended U. S. VCM/PVC producers sponsor animal exposure and epidemiological research on VCM carcinogenicity (cancer-causing) to be administered by MCA.
May 1971	MCA acted on Dr. Viola's statement that other studies were being conducted in Europe and attempted, unsuccessfully, by correspondence and direct visits of a U. S. company representative, to learn of them.
July 7, 1971	MCA corresponded with medical contacts of member companies, alerting them to potential occupational health problems with VCM and asked them about interest in supporting related research.

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Nov mber 5, 1971

MCA received a letter from Dr. Viola confirming observation of tumors in rats at 5000 ppm VCM (and perhaps less) and made some suggestions for further animal studies.

Nov mber 16, 1971

At a vinyl chloride meeting arranged by MCA in Washington for interested U. S. company representatives, a Europ an representative of Solvay et Cie. report d that he was aware of further studies just beginning in Europe. He said it was too soon to expect any data, and that he was not free to describe the source of his information nor the location of the studies. He said the exposure concentrations rang d from 20,000 ppm to 50 ppm and that groups of 25 male and 25 female rats were being exposed. He expressed concern about th purity of the vinyl chloride used in Dr. Viola's original study, since it was reported to contain one to three percent of impurities. The representative stated that Dr. Viola had observed a 10 to 15 percent incidence of ear tumors in rats exposed to 5000 ppm of vinyl chloride. Suggestions for epidemiological and animal exposure studies to be administered by MCA, on behalf of interested companies, were discussed at this meeting.

March 30, 1972

Seventeen U. S. companies had agreed to financially support VCM studies.

April 1972

MCA's Chemical Safety Data Sheet on vinyl chloride was revised to state: "Recent research studies reported from Italy indicate that repeated, long-term high level exposures of rats to vinyl chloride, monomer vapor can result in the development of malignant tumors. However, many y ars of industrial experience with human exposures to concentrations frequently far above current standards have not demonstrated any carcinogenicity to humans."

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April-June 1972

To enable the MCA program to be designed so as to yield data of optimum significanc , overtures were made by MCA to establish technical liaison with the new European research mentioned at the November 16, 1971, meeting in Washington.

August 16, 1972

A letter to MCA bearing this date, sent on behalf of the European sponsors, offered technical cooperation under the condition that "no disclosure of information arising from the European investigation should be made outside the individuals comprising the technical coordinating task group without the specific consent of the Europ an group." The purposes of such restriction were (1) that preliminary indications not be released until they had been validat d, thereby to minimize unwarranted speculation, and (2) that releases remain subject to the control of the project's proprietors.

Nov mber 14, 1972

At an MCA meeting of company technical officials, an MCA representative who visit d Europe October 19-20 reported he had obtained a copy of the testing protocol of Dr. Cesare Maltoni, director of the Institute of Oncology, Bologna, Italy, the principal investigator of the European sponsors, and was told only that results were surprising. The European group declined to release European data because agreement had not yet been reached to comply with the European group's stipulation of confidentiality.

December 1972

After much deliberation and with great reluctance to pledging confidentiality, the participating U. S. companies and MCA did so in an MCA communication to a representative of the European group. This was done becaus of the vital importance of learning of any indications from the European research, and thus having a base to proceed on further studies, if needed, without the delays which could have resulted from duplications of effort.

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January 17, 1973 — The U. S. VCM/PVC industry technical delegation visited the European sponsors and Dr. Maltoni's facilities to learn in more detail about his experimental procedures and results.

January 30, 1973 — At an MCA meeting of participating company technical representatives, a brief oral progress report on Dr. Maltoni's work was presented by those who had visited him. It was reported that, in experim nts with rats, in addition to tumors of th ear canal, tumors of the kidney and liver were observed at concentrations as low as 500 and 250 ppm VCM, but not at 50 ppm nor in the controls. The European work was observed to be of high quality, similar to that which would be done in U. S. laboratories. At this meeting, it was decided by the U. S. group of participating companies to initiate an epidemiological study of VCM/PVC workers, recognized earlier as an important compl m nt to animal testing, but most usefully carried out with the benefit of the animal research background.

January 31, 1973 — MCA wrote to prospective contractors regarding an epidemiological survey.

February 1, 1973 — Having benefited from the European study indications in setting the protocol for the MCA research program, MCA signed a contract with Industrial BIO-TEST Laboratories, Inc., to conduct animal exposure studies. Subsequently, a press release was issued announcing, on behalf of participating companies, animal inhalation studies with VCM that would expose rats, mice and hamst rs to VCM concentrations of 2500, 200 and 50 ppm for one year, with the animals to be kept on observation for an additional year. By contractual stipulation, the study results would be made public.

February 20, 1973 — Four prospective contractors met with MCA to discuss the epidemiological study.

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March 1973 — MCA and participating compani s initiat d steps to present the details of VCM-r lat d research to the appropriate U. S. governm nt agency.

April 17, 1973 — MCA proposed to meet with executives of sponsoring companies of the European project concerning the desire to make a presentation to the U. S. government, with inclusion of European research observations, the latter preferably presented by a representative of the European group. A date of May 9 was suggested for this visit, but it proved impossible to arrange until mid-June.

Jun 15, 1973 — Following up on the proposal, four MCA representatives visited European group executives in Brussels. They were given assurance of the European companies' willingness to release their data -- although still incomplete — to the U. S. government, and agreement to participat in its presentation. The European compani s requested time to prepare the information for prior release to their respective governments, also. A presentation to the National Institute of Occupational Safety and Health (NIOSH) was planned for the week of July 16.

Jun 27, 1973 — An MCA press release announced an epidemiological survey, to be conducted by Tabershaw-Cooper Associates, Inc., to document the health experience of pres nt and former employees who worked with VCM. Again, by contractual stipulation, the results would be made public.

June 28, 1973 — MCA requested a meeting with NIOSH to brief the agency on the status and background of VCM research.

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July 11, 1973

Three U. S. industry representatives reported to the MCA group the results of the Brussels visit on June 15. Th European information then discussed includ d epidemiological data which indicated no increase in gross mortality from canc r and no increase in cancer morbidity or incidence of cancer among workers expos d to VCM.

July 17, 1973

A presentation was made to NIOSH. A summary of the published toxicity data on vinyl chloride, along with a description of the industry and full details of the studies contracted under MCA administration were presented by MCA representatives, with expressed interest in taking advantage of any suggestions NIOSH might offer. A representative of the European group (a physician), reporting on the Europ an studies, said that tumors had been obs rv d in rats down to 250 ppm, but that an epidemiological survey had indicated no increase in gross mortality from cancer and no increase in cancer morbidity or incidence of cancer among workers exposed to VCM.

Summer-Fall 1973

Companies involved in the Tabershaw-Coop r survey assembled their personnel records and death certificates of employees having had vinyl chloride exposure.

November 28, 1973

A further progress report of Dr. Maltoni's studies was given to MCA by a European group representative. Results confirmed earlier observation of malignant tumors in rats at 10,000, 6000, 2500, 500 and 250 ppm VCM, <u>but not at 50 ppm.</u>

January 23, 1974

The B. F. Goodrich Company announced that Kentucky health officials and NIOSH had been notified of the company's investigation of whether cancer deaths of three workers in PVC operations in its Louisville, Ky. plant were related to occupational causes.

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January 29, 1974	Goodrich reported, in a press releas , that the death of another former employ had been tentatively identified as du to angiosarcoma of the liver.
February 1, 1974	MCA proposed to the European group that they make arrangements for Dr. Maltoni to come to the OSHA hearings on vinyl chloride, February 15.
February 6, 1974	MCA issued a press release announcing that it had stopped circulation of its Chemical Safety Data Sheet on vinyl chloride, because of the Goodrich reports -- now questioning the validity of the Data Sheet statement noting that carcinogenicity to humans had not been observed.
February 15, 1974	Goodrich reported the death of a fifth employee due to liver angiosarcoma.
February 15, 1974	MCA and Dr. Maltoni presented separate statements at OSHA hearings on vinyl chloride, giving background on work done to date.
February 21, 1974	Union Carbide Corporation notified NIOSH of the death of a PVC worker from liv r angiosarcoma.
March 1, 1974	The Goodyear Tire & Rubber Company, in a press release, announced a vinyl chloride worker fatality resulting from angiosarcoma of the liver.
March 6, 1974	Goodrich reported cases of liver angiosarcoma in two living employees.

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March 22, 1974 — Goodyear, in another press release, announced two more worker fatalities from liver angiosarcoma.

April 9, 1974 — Industrial BIO-TEST Laboratories phon d MCA and reported that preliminary findings in the animal exposure study showed angiosarcoma was produced in mice at 50 ppm VCM.

April 10, 1974 — MCA reported these preliminary findings to OSHA, NIOSH and the Environmental Protection Agency (EPA) by phone.

April 15, 1974 — MCA representatives and officials from OSHA, NIOSH and EPA met at Industrial BIO-TEST Laboratories, Inc., Northbrook, Ill., to be briefed on the findings.

April 16, 1974 — MCA issued a press release announcing preliminary indications that VCM exposure produced liver cancer in mice at s v ral exposure levels, down to 50 ppm.

April 16, 1974 — Firestone Plastics Company, Division of The Firestone Tire & Rubber Company, in a press release, announced an angiosarcoma death of a PVC plant employee.

May 7, 1974 — In another press release, the results of the Tabershaw-Cooper survey were given. The survey showed that workers exposed to VCM have experienced overall death rates from cancer that are comparable to those experienced by other U. S. industrial populations, but less than in the general public. This is in spite of the now w ll-recognized risk of higher incidence of angiosarcoma of the liver among such work rs Also, there did appear to be suggestive dose-related increases in cancer incidenc in respiratory tracts and the brain in longer-exposed workers.

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May 10, 1974

It was reported at the New York Academy of Sciences' meeting that The National Cancer Institute had diagnosed a liver angiosarcoma in a living Union Carbide employee. The company reported this case to NIOSH in March 1974 as a liver ailment.

Four supplementary research projects on VCM proposed for MCA administration are now in near prospect:

- Rat metabolism study
- Rat fetus study
- Animal chronic exposure study at levels below 50 ppm VCM
- Animal acute exposure study to test potential effects from a possible single massive release causing extremely high VCM atmospheric concentrations.

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