OCT 1 4 1975

Air Products and Chemicals INC.

ALLENTOWN, PENNSYLVANIA 18105

13 October 1975

Dr. T. R. Torkelson
Dow Chemical Company
Health & Envir. Research
[illegible] Building
Midland, Michigan 48640

Dear Tod:

You will recall that when Dr. Tamburro made his presentation to the Research Coordinators at the MCA on 8 September 1975 under his Medical Surveillance Program he listed the following:

1. Biochemical
2. Radiology
3. Pulmonary
4. Cardiac
5. History and Physical

It is my opinion that most companies are not making a cardiac examination under their current medical surveillance of those people exposed to vinyl chloride. I think it pertinent that you or perhaps better Milton Freifeld ask each of the member companies in the MCA program whether cardiac examinations and specifically, EKG's are done.

Sincerely yours,

Mayo

W. Mayo Smith

WMS:chw

cc: Milton Freifeld, MCA

UCC
002149

Air Products and Chemicals INC.

ALLENTOWN, PENNSYLVANIA 18105

OCT 20 1975

14 October 1975

Dr. T. R. Torkelson
Dow Chemical Company
Health & Envir. Research
9008 Building
Midland, Michigan 48640

Dear Ted:

Subject Vinyl Chloride and Circulatory Aspects

This is further to my note to you and Milt Freifeld of 13 October. Attached is an article relating to Kema Nord, the only PVC producer in Sweden and one of excellence.

You will recall that Dick Wheeler at our September meeting mentioned the ORC showed among fabricators according to my notes diseases of circulatory system to be higher than expected as 1,576 observed with expected 1,444. You may also remember that Maury Johnson thought these differences were significant.

The Kema Nord report lends further evidence that we should immediately contact all member companies of the VCA Vinyl Chloride Program. My question of yesterday was whether any cardiac examinations are made and my question of today is what have been the findings, if so done.

With best regards.

Sincerely yours,

Mayo

W. Mayo Smith

WMS:c'M

Attachment - Chemical Engineering, September 29, 1975

cc: Milton Freifeld, VCA

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002150

VINYL CHLORIDE RESEARCH PROGRAM

Financial Statement - August 28, 1975

Revised as of October 1, 1975

	Invoiced (Committed)	Received	Research Contract	Disbursements: Administrative Time	Administrative Travel	Administrative Misc.	Research Contracts	Total	Unpaid Balance On Contract	Balance on Hand
1. Epidemiology Study Tabershaw/Cooper Assoc.	$ 91,940	$ 91,940								
(a) Health Study of VC Workers (6/13/73)			$ 71,345							
(b) Adjustment/- Travel (8/16/73)			$ 3,950			$ 45	$ 91,895	$ 91,940	-0-	-0-
(c) Adjustment/- Extension (3/12/74)			$ 5,250							
(d) Retabulation of Data (7/13/74)			$ 1,000							
(e) Study of Workers/ 4 plants (11/5/74)			$ 10,350							
(f) Extended Epidemiology Study (4/22/75	$ 52,597	$ 51,913	$ 32,000	$ 646	-0-	-0-	$ 18,625	$ 19,271	$13,375	$ 32,642
Sub-Total	$144,537	$143,853	$123,895	$ 646	-0-	$ 45	$110,520	$111,211	$13,375	$ 32,642
2. Chronic Inhalation Studies Industrial BIO-TEST Labs	$190,281	$190,281			$2,665/1	$279/2		$143,319		$ 46,962
(a) Original-Protocol (2/1/73)			$149,000				$130,375		$18,625/3	
(b) Additional Animals- 100 rats (5/22/73) (Restart-Agreement (8/31/73)			$ 15,000				$ 10,000		$ 5,000/3	
(c) I B-T L Contract Adjustments	$ 50,000	$ 49,405		$1,498				$ 1,498		$ 47,907
Sub-Total	$240,281	$239,686	$164,000	$1,498	$2,665	$279	$140,375	$144,817	$23,625	$ 94,869
3. Dow Studies	$101,250	$101,250						$ 70,000		$ 31,250
(a) Metabolic			$ 50,000				$ 50,000			
(b) Teratology			$ 20,000				$ 20,000			
(c) Extension of Studies	$149,990	$148,205		$1,031	-0-	-0-		$ 1,031	-0-	$147,174
Sub-Total	$251,240	$249,455	$ 70,000	$1,031	-0-	-0-	$ 70,000	$ 71,031	-0-	$178,424
GRAND TOTAL	$636,058	$632,994	$357,895	$3,175	$2,665	$324	$320,895	$327,059	$37,000	$305,935

Note:
1. Gasque, Kociba & Torkelson to Italy
2. Cylinders for Vinyl Chloride
3. Due I B-T L - Receipt of Final Report

UCC
002151

SEP 24 1975

THE DOW CHEMICAL COMPANY

BENNETT BUILDING
2030 DOW CENTER
MIDLAND, MICHIGAN 48640

September 22, 1975

Mr. Milton Freifeld
Manufacturing Chemists' Association
1825 Connecticut Avenue, NW
Washington, D.C. 20009

One of the companies sponsoring the studies on vinyl chloride received the following information in response to an inquiry "on the various studies of vinyl chloride (VCM) being conducted as recommended by the Vinyl Chloride Task Force."

The Office of Toxic Substances has completed the preliminary investigation for EPA's ~~epidemiology~~ study, which will be started soon. In EPA, the Office of Research and Development's Health Research Laboratory in Cincinnati, Ohio, 45268, is sponsoring a study: "Toxicological Investigation of Vinyl Chloride with Relevance to Non-Worker Populations, with Emphasis on Transplacental Carcinogenesis and Cofactors" (Contract #68-03-2148, Project Officer, Dr. Jerry Stara). No data have yet been derived. Another study, "Sampling of Automobile Interiors for Vinyl Chloride" (Contract #68-02-1404, Task 1, Project Officer, Dave Benny), is now underway, being sponsored by the Control Systems Laboratory, ORD, EPA, Research Triangle Park, N.C., 27711.

Several studies are being sponsored by other agencies. You should contact them for specifics: Consumer Product Safety Commission, 7315 Wisconsin Avenue, Washington, DC, 20014 (Contract #72-2084, Project Officer, Dr. Robert Hehir).

National Institute of Environmental Health Sciences, Research Triangle Park, NC, 27711 (Contract #210-75-0051, Project Officer, Dr. James J. Woods).

The Center for Disease Control, Atlanta, Georgia, 30333, is analyzing 300 reported cases of hepatic angiosarcoma, to determine all possible correlations. Dr. Henry Falk is managing this study.

Please attach a copy of this letter with your next mailing to the sponsoring companies.

Sincerely,

Theodore R. Torkelson
Corporate Medical Department

164

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

TO : Mr. Edward Klein
Office of the Solicitor
Department of Labor

DATE: August 22, 1974

FROM : Director

SUBJECT: OSHA Public Hearing on Vinyl Chloride

Enclosed is a review of the Connecticut cases by Dr. Louis B. Thomas, Chief, Laboratory of Pathology, National Cancer Institute, which should be included in the record of the OSHA Public Hearing on Vinyl Chloride.

In accordance with Public Health Service policy, I have blacked out the names of the patients. However, for your purpose it should be sufficient to note that case #5 in Dr. Thomas' memorandum was the accountant at the vinyl cloth plant, and case #6 worked in an electric company applying PVC insulation.

Marcus M. Key, M.D.
Assistant Surgeon General

Enclosure

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

31 July 1974

NATIONAL CANCER INSTITUTE

Dr. Philip Landrigan
Communicable Disease Center
1600 Clifton Road, N.E.
Atlanta, Georgia 30322

Dear Dr. Landrigan:

On July 19th we sent you pathology reports for six of the eight Connecticut cases. Enclosed are reports for the other two patients; [redacted]

After completing the individual reports, Dr. Popper, Dr. Lingeman and I reviewed the eight cases once more in order to make some evaluation about their possible similarity or dissimilarity to lesions seen in VC-PVC workers. Our comments about this are listed below:

(1) [redacted] We believe the angiosarcoma of the liver of this patient is different from most of the angiosarcomas seen in VC-PVC workers. Sinusoidal dilatation and/or megalocytosis of hepatocytes were not seen. Also there was no hepatic fibrosis similar to that seen in the VC-PVC workers.

(2) [redacted] Carcinoma involving pancreas and liver, possibly primary in the pancreas. We do not have a carcinoma of this type among the known VC-PVC workers whose lesions we have reviewed.

(3) [redacted] The carcinoid type bronchial adenoma seen in the lung of this patient almost surely has no relationship to the hepatic lesions (? hemangiomas) in the liver. We have not seen any bronchial adenomas in the VC-PVC worker sections we have examined.

(4) [redacted] The angiosarcoma in this patient forms capillary, slit-like spaces and replaces hepatic tissues. We only occasionally found this type of histological pattern in the angiosarcomas of the VC-PVC workers and, in those patients, always also found multicentric areas of angiosarcoma with a sinusoidal and/or papillary pattern. We did not see these types of pattern in Mr. Mulloy's section. Thus we do not think his hepatic angiosarcoma is characteristic of the angiosarcomas seen in the VC-PVC workers. Also [redacted]

liver is definitely cirrhotic with large deposits of iron. These features also were not seen in the VC-PVC workers with hepatic fibrosis and with or without hepatic angiosarcomas.

(5) [redacted] We cannot be certain, one way or another, about this case. One histologic feature, i.e. the cells of the angiosarcoma are somewhat "fibroblastic," is dissimilar to angiosarcomas seen in most of the VC-PVC workers. However several other histological features are similar to the VC-PVC workers hepatic lesions; namely, sinusoidal dilatation, tectorial and enveloping features of the sinusoidal lining cells, portal tract fibrosis, and variability in size of hepatocytes. In summary, there are sufficient histological similarities that we cannot exclude this as a so-called "VC-PVC type case."

(6) [redacted] Please refer to the note on our surgical pathology report S74-1506. In brief, we are not completely certain that this is an angiosarcoma of the liver or even a primary sarcoma of the liver. It is not like any of the other tumors we've seen in the livers of VC-PVC workers.

(7) [redacted] The histological features of the hepatic angiosarcoma and portal tract fibrosis seen in this case are similar in nearly all respects to the lesions we have seen in most of the VC-PVC workers' livers.

(8) [redacted] We have reviewed needle biopsies only from this patient's angiosarcoma. The amount of material is insufficient for a definite comparative statement, but we do not see the histologic features which we believe are most characteristic of the angiosarcomas in VC-PVC workers.

In conclusion we interpret five of these cases as having definite hepatic angiosarcomas and an additional case [redacted] as possibly having a hepatic angiosarcoma. In one patient [redacted] the overall histologic features are the same as or very similar to the hepatic lesions seen in most of the VC-PVC workers. In another case [redacted] there are several similar features and one or two dissimilar features.

We want to emphasize that we do not think there is any single, histological feature either of the angiosarcomas or of the hepatic fibrosis which is pathognomonic of vinyl chloride exposure. For example, all the changes we've seen in the livers of the VC-PVC workers can apparently be produced by exposure to arsenicals. However, certain types of hepatic fibrosis,

sinusoidal dilatation, multicentric angiosarcomas with sinusoidal, papillary and cavernous patterns together with megalocytosis of hepatocytes collectively form a spectrum of hepatic lesions which are "characteristic" of the VC-PVC workers' lesions. It is with these facts in mind that we have attempted to evaluate the Connecticut cases and compare their similarities and dissimilarities with the VC-PVC workers.

Thank you for getting this material for our review. We would like to keep the submitted sections awhile longer in order to take photomicrographs of the various lesions. Also our conclusions about some of these cases might be more definite if we examined additional sections or prepared additional sections and special stains. We will write you later about individual cases which might be studied further.

Sincerely,

Louis B. Thomas, M.D.
Chief, Laboratory of Pathology

June 25, 1974

TABLE 1

CONFIRMED CASES OF LIVER ANGIOSARCOMA AMONG WORKERS EXPOSED TO VINYL CHLORIDE OR POLYVINYL CHLORIDE

COUNTRY	CASE #	BIRTH DATE	1st VC or PVC EXPOSURE	DX ANGIO-SARCOMA	AGE AT DX	YRS 1st EXP TO DX	TOT YRS EXP	DATE OF DEATH
			VC MONOMER PRODUCTION WORKERS					
Sweden	02	11-27-11	00-00-45	05-15-72	61	27	23	08-16-72
			POLYMERIZATION WORKERS					
United States	01	00-00-22	12-09-48	03-00-71	49	22	16	03-03-73
United States	02	00-00-34	11-15-55	05-00-70	36	14	13	09-28-71
United States	03	00-00-15	11-28-45	12-00-73	58	28	28	12-19-73
United States	04	00-00-24	07-06-52	08-00-67	43	15	15	01-07-68
United States	05	00-00-12	06-19-44	04-00-64	52	20	18	04-06-64
United States	06	00-00-29	01-17-62	02-00-74	45	12	12	ALIVE
United States	07	05-03-22	08-00-44	00-00-68	45	24	18	03-23-68
United States	08	05-06-20	10-07-46	08-00-61	41	15	15	08-29-61
United States	09	00-00-31	05-28-45	03-01-74	43	29	17	ALIVE
United States	10	08-16-13	06-00-51	05-00-68	55	17	17	05-10-68
United States	11	05-27-09	10-14-46	03-00-70	61	23	23	03-16-70
United States	12	11-17-18	09-13-49	05-00-69	50	20	15	05-02-69
United States	13	12-01-21	08-19-44	05-00-74	53	30	30	ALIVE
W. Germany	01	07-26-31	10-14-57	00-00-71	40	14	14	12-14-71
W. Germany	02	06-04-30	10-01-57	00-00-69	39	11	11	01-25-69
Great Britain	01	00-00-01	00-00-46	12-00-72	71	26	20	12-00-72
Norway	01	12-23-15	03-00-50	12-20-71	56	22	21	01-04-72
Sweden	01	06-23-27	08-14-51	02-00-70	43	19	18	10-20-70
			[illegible] SECONDARY MANUFACTURING					
United States	14	00-00-13	08-18-38	06-00-73	60	36	00	07-03-73
United States	15	00-00-25	00-00-00	07-00-72	47	00	00	02-15-73

Note: '00' indicates unknown date

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OCT 8 1975

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

October 3, 1975

NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES
P.O. BOX 12233
RESEARCH TRIANGLE PARK, N.C. 27709

Mr. Milton Freifeld
Project Manager
Vinylidine Chloride Research
Manufacturing Chemists Association
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Mr. Freifeld:

In keeping with our agreement to send you information regarding our research activities on vinyl chloride and related substances, I am enclosing for your information a copy of our contact proposal entitled "Evaluation of the Environmental Toxicant, Vinyl Chloride Monomer (VCM). Included is an addendum describing additional studies we are conducting on vinylidine chloride, as well as some extra VCM tests which were added after the proposal was written.

The work on this contract has begun this September, and we will be happy to send you copies of the progress reports as they become available. Please continue to send us whatever information you derive from your studies in this area.

Yours truly,

James S. Woods, Ph.D.
Head, Biochemical Toxicology Section
Environmental Toxicology Branch

Enclosures

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES
P.O. BOX 12233
RESEARCH TRIANGLE PARK, N.C. 27709

OCT 2 0 1975

October 15, 1975

Dr. Milton Freifeld
Assistant Technical Director
Occupational Health
Manufacturing Chemists Association
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Dr. Freifeld:

This letter is in response to your inquiry of October 2, 1975. Information on vinyl chloride is enclosed, and information only on extramural projects dealing with vinylidene chloride and polyvinyl chloride is enclosed. Inquiry to NIEHS staff about the other compounds is in process; the resultant information will be forwarded to you when received by this office.

Sincerely,

John L. Braun, Ph.D.
Office of Program Development

Enclosures

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002159

October 8, 1975

OCT 2 0 1975

VINYL CHLORIDE RESEARCH
NIEHS

Intramural

In cooperation with Dr. Robert T. Drew and Mr. Mike Riley, a mutagenesis prescreen using Salmonella typhimurium with vinyl chloride is being conducted to test a system for handling gases in tier-one testing.

Contract

Ongoing vinyl chloride (VCM) studies (MRI Contract No. NIH-NIEHS-72-2084) seek to determine the biochemical and pathological alterations in specific organ functions of rats and mice chronically exposed to low and mid-level doses of VCM or vinylidene chloride (VDM). Dr. James Woods is the project officer for this contract and should be contacted directly if more information is needed.

LIST OF PROJECTS

1. 5 ROl ES 01027-02
SOBELS, Frederick H.
Department of Rad., Gen., Chem.
Mutagenesis
University of Leiden
Leiden, Netherlands

Induction of Genetic Damage by Chemical Mutagens.

Studies include preliminary screening, with Drosophila as the test system, of a number of suspected mutagens, including vinyl chloride, to be followed with investigation of effects on male germ cell stages and determination of mutagenic mechanisms.

2. 1 ROl ES 01150-01
VAN DUUREN, Benjamin L.
New York University Medical
Center
New York, New York

Carcinogenic Intermediates and Metabolism of Vinyl Chloride and Analogs.

Study based on the premise that an epoxide not vinyl chloride per se is the proximate carcinogen. Will attempt to determine the transformation and action mechanisms of vinyl chloride and/or its metabolites in liver.

3. 1 ROl ES 01287-01 (Energy Award)
SICILIANO, Michael J.
University of Texas System Cancer
Center
Houston, Texas

Multiple Loci Screen for Mutations in Mammalian Cells.

Study of the detection of mutations in cultured mammalian cells (mainly Chinese hamster ovary cells) by simultaneously screening cloned isolates for electrophoretic variants at 50 or more loci, using a number of known or suspected mutagenic agents, including vinyl chloride.

4. 5 P10 ES 00002-13
WHITTENBERGER, James L.
Harvard University School of Public Health
Boston, Massachusetts

Occupational and Environmental Health.

Studies in the Environmental Toxicology Group include the determination of binding sites in relation to toxicity and mode of action of vinyl and vinylidene chlorides.

Dr. Richard Monson, Department of Epidemiology, and others are engaged in mortality studies involving identification of cases in different locations for diseases (cancer, leukemia or congenital anomalies) caused by various factors, including vinyl and vinylidene chlorides.

5. 5 P10 ES 00159-10
SUSKIND, Raymond R.
University of Cincinnati
Cincinnati, Ohio

Center for the Study of the Human Environment Methods are being developed for analysis of low ambient levels of vinyl chloride and for evaluating permeation tubes for preparing accurate gaseous vinyl chloride standards.

6. 5 P10 ES 00928-02
SELIKOFF, Irving J.
Mount Sinai School of Medicine
City University of New York
New York, New York

Center for the Study of Biological Effects of Environmental Agents.

This laboratory has a number of studies underway dealing with medical surveillance of workers exposed to asbestos and vinyl chloride in the manufacture of vinyl floor tiles, mortality experience of a cohort of vinyl chloride-polyvinyl chloride workers, prevalence of vinyl chloride-associated disease among exposed workers, and chromosome damage induced in exposed workers by vinyl and polyvinyl chlorides.

MAY 14 1975

U.S. CONSUMER PRODUCT SAFETY COMMISSION

WASHINGTON, D.C. 20207

May 6, 1975

Dr. Theodore R. Torkelson
Corporate Medical Department
The Dow Chemical Company
Bennett Building
2030 Dow Center
Midland, Michigan 48640

Dear Dr. Torkelson:

Thank you for your letter dated April 23, 1975, regarding CPSC's proposed protocol for inhalation studies on vinyl chloride.

As I remember, you have a copy of the original protocol scheduled to be performed at Edgewood Arsenal.

Attached is a copy of the proposed changes. In regard to the schedule, the acute study of 1 hour only with rats and mice and holding for 24 months is now in its second month.

The three generation reproductive studies are now in the 60 day exposure stage.

The sub-acute inhalation stage is entirely new and is just beginning.

If I can be of any further help, do not hesitate to call or write.

Sincerely,

Robert M. Hehir, Ph.D.
Director
Bureau of Biomedical Science

Attachment

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002163

CONSUMER PRODUCT SAFETY COMMISSION

During a visit to Biomedical Laboratory by Drs. McLaughlin and Wyer on 27 March 1975, it was mutually agreed by the contract project officer, Dr. McLaughlin and Dr. McNamara, Edgewood Arsenal Contract Administrator, that the following technical changes would be made in the toxicological testing of Vinyl Chloride monomer:

1. No biochemical or enzymatic work would be performed in the vinyl chloride studies.

2. The three generation reproductive studies will be changed as follows:

a. The number of animals per dose will be increased from 10 to 25.

b. The exposure concentration and time of exposure will be 50 and 500 ppm, 5 days week/10 weeks.

c. The parent generation will be held and observed for 2 years.

d. No teratology studies will be performed.

3. A sub-acute inhalation study will be added to the acute work. The exposure schedule is as follows:

Sub-Acute Vinyl Chloride Inhalation Study
(Exposure Schedule)

Dose Level	Species (Strain)	Number Exposed	Frequency of Exposure
50	Rat (Fisher)	180	5 dy/wk - 20 wks
	Mouse (A/J)	180	" "
500	Rat (Fisher)	180	5 dy/wk - 2 wks
	Mouse (A/J)	180	" "
Control	Rat 50 ppm	100	- -
	500 ppm	100	- -
	Mouse 50 ppm	100	- -
	500 ppm	100	- -

The observation and sacrifice schedule is as follows:

Sub-Acute Vinyl Chloride Inhalation Study
(Observation and Sacrifice Schedule)

Dose Level (ppm)	Time of Observation & Sacrifice (Months)					
	8		16		24	
	Rat	Mouse	Rat	Mouse	Rat	Mouse
50	20 20	20 20	20 20	20 20	50 50	50 50
500	20 20	20 20	20 20	20 20	50 50	50 50
Controls 50 ppm level	10 10	10 10	10 10	10 10	30 30	30 30
500 ppm level	10 10	10 10	10 10	10 10	30 30	30 30
Totals	120	120	120	120	320	320

Total Animals: Rats - 560
Mice - 560

CEP
CHEMICAL ENGINEERING PROGRESS

September 1975 CODEN CEPRA 9 Volume 71, No. 9

Vinyl Chloride Emission Control

Reprinted from the Archives of Environmental Health
July 1975, Volume 31

Vinyl Chloride Exposure in a Controlled Industrial Environment

A Long-Term Mortality Experience in 594 Employees

Marvin Gerald Ott, MS; Ralph R. Langner, PhD; Benjamin B. Holder, MD

Vinyl chloride has been associated recently with findings of angiosarcoma in animals and man. The present study examines the mortality experience of individuals occupationally exposed to vinyl chloride and lesser amounts of vinylidene chloride and other compounds.

Employees were grouped into four exposure categories according to the highest levels of vinyl chloride exposure experienced for at least one month. Although no angiosarcomas were found and there were no deaths due to any liver malignancy, the observed malignancy deaths exceeded the expected among workers in the high-exposure category. Fewer than expected malignancy deaths were observed in the remaining exposure categories.

Vinyl chloride has a 30- to 40-year history of industrial use. Until recently, it was thought to be a relatively benign material and, in fact, was once considered for use as a surgical anesthetic. Reports documenting anesthetic effects in animals and humans and liver injury in animals from chronic exposure were published in 1960 thru 1963 by Mastromatteo et al,[1] Torkelson et al,[2] and Lester et al.[3]

Submitted for publication Aug 26, 1974; accepted Feb 25, 1975.

From the Dow Chemical Company, Midland, Mich.

Reprint requests to the Dow Chemical Company, Corporate Medical Department, 2030 Dow Center, Midland, MI 48640 (Mr. Ott).

A new clinical entity associated with vinyl chloride exposure, acroosteolysis, was reported in the United States by Wilson et al in 1967.[4] This was elaborated by Cook et al,[5] Dodson et al,[6] and Dinman et al.[7]

In 1972, an environmental study of vinyl chloride workers by Kramer and Mutchler[8] revealed laboratory indications of liver disease in workers exposed to a time-weighted average concentration for an eight-hour day (TWA) of 300 ppm or above. Reports of other effects associated with exposure to high levels of vinyl chloride were summarized by Marstellar and Juhe[9] in the European literature.

Neoplasia was first associated with vinyl chloride in 1971 by Viola et al.[10] Maltoni[11] later reported malignant changes in animals, including angiosarcoma of the liver. Creech and Johnson[12] supported this observation by their report of angiosarcoma of the liver in vinyl chloride workers. In May 1974, Tabershaw and Gaffey[13] released their industry-wide epidemiological study of vinyl chloride workers that suggested increased numbers of malignant neoplasms at other body sites.

This report summarizes the mortality experience of an industrial population exposed to vinyl chloride in an environment for which many years of monitoring data are available. Many of the employees were also included in the Tabershaw and Gaffey report; however, in the present study the mortality experience was combined with more clearly defined levels of exposure and follow-up of former company employees.

HISTORY

Research involving vinyl chloride started at this company location in the mid-1930s. In 1941, a small copolymer plant was constructed that employed four operators, two miller-packagers, one foreman, and one superintendent. In the late 1940s, the plant capacity was enlarged and two assistant operators joined the work force. The copolymer plant continued to grow and other types of copolymer were developed, which resulted in a larger department with a new group of operating, clerical, and supervisory personnel. A small production unit to produce vinyl chloride monomer and a copolymer semiplant also were operated during this period.

Continued research resulted in a new outdoor homopolymer (PVC) and copolymer unit being constructed in 1952. The rapid development of the market for PVC resin in the 1950s outstripped the new plant capacity. In response, PVC production was begun in a portion of a third copolymer unit that had previously used only limited quantities of vinyl chloride. Thus, besides the research efforts and monomer production, three polymer units were in operation. The PVC was produced until 1969, when the decision was made to discontinue production of homopolymer and use the facilities to modernize copolymer production. The modernization allowed the closing of the plant built in 1941.

CC: Mellon Institute (MCA)

GJS

W. M. Smith

Ann. occup. Hyg. Vol. 16, pp. 241–250. Pergamon Press 1973. Printed in Great Britain

COMPARISON BETWEEN *IN VITRO* TOXICITY OF POLYMER AND MINERAL DUSTS AND THEIR FIBROGENICITY

J. A. Styles and J. Wilson

Imperial Chemical Industries Limited, Industrial Hygiene Research Laboratories, Alderley Park, near Macclesfield, Cheshire

Abstract—The cytotoxicity of a variety of polymer dusts to suspensions of rat alveolar and peritoneal macrophages in culture was measured using trypan blue as an indicator of cell death. Suspensions of the same dusts were administered to rats by intraperitoneal injection and the tissue reaction examined at 1 month and 3 months. A good correlation was found between the cytotoxicity of the dusts to macrophages in culture and the degree of fibrosis caused by them in the animals.

INTRODUCTION

The relationship between cytotoxicity of mineral dusts to macrophages *in vitro* and their fibrogenic activity *in vivo* was examined by Marks *et al.* (1956) using a quantitative *in vitro* technique (Marks and Mason, 1956). Further work was carried out by Conning *et al.* (1971) who compared the ability of several mineral and polymer dusts to produce progressive or persistent fibrosis after intraperitoneal or intratracheal injection in rats, and their cytotoxic activity in rat alveolar and peritoneal macrophages in culture. They were able to distinguish three distinct levels of cytotoxicity *in vitro* which related directly to the degree of fibrogenicity of the dusts *in vivo*. The dusts of low cytotoxicity did not cause persistent fibrosis; those of intermediate cytotoxicity were comparable to silica in their ability to cause progressive fibrosis. Only asbestos was placed in the third category of cytotoxicity and this produced the most fibrosis.

The results of these investigations suggest that there is a direct relationship between cytotoxicity of a dust to macrophages in culture and fibrogenicity in the living animal. With the limited material available they were unable to elucidate the effects of changes in particle size and configuration. Marks *et al.* (1956) examined only mineral dusts, and Conning *et al.* (1971) examined two mineral and two polymer dusts. The present study examines the relation between cytotoxicity to macrophages in culture and the fibrogenic activity *in vivo* of a much wider range of polymer and mineral dusts allowing more general conclusions to be drawn.

MATERIALS AND METHODS

Animals

Specific pathogen free albino Wistar rats (Alderley Park strain) of both sexes and of a weight range 200–250 g were used.