

cc N. Lovejoy M.D.



MANUFACTURING CHEMISTS ASSOCIATION

1825 CONNECTICUT AVENUE, N.W. WASHINGTON, D.C. 20009 (202) 483-6126

October 21, 1975

To: Technical Panel on Vinyl Chloride Research

Subj: Action, Information, and Reference Items

ACTION:

1. Please note that confirming arrangements with Chairman Torkelson, the next Panel Meeting has been rescheduled for December 11 and the Research Coordinator's meeting for December 10 at MCA headquarters. Tentative agenda to follow. The Project Manager will be unavailable on dates previously chosen, December 8 and 9.

2. Industrial Biotest Laboratories (IBT) has requested permission to present the final Vinyl Chloride report at the annual meeting of the American Industrial Hygiene Association in May 1976. Please review the enclosed abstract on "Inhalation Studies with Vinyl Chloride" and be prepared to vote on it at the next meeting. In the interim, comments may be sent to me with copy to Dr. Torkelson.

IBT has already been informed of Dr. Torkelson's suggestion to add the phrase "...consistent with dose" to the last sentence and his questions about whether the animals are all expected to be dead and pathology completed by the deadline. IBT was also reminded that the full paper should be reviewed by the Panel before presentation.

INFORMATION:

3. A revised (October 1) Financial Statement is enclosed, correcting errors in the one distributed with the minutes of the last meeting. Also, subtotals have been added. The key change is in Grand Total Balance on Hand to \$305,935.

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RECEIVED
OCT 31 1975

4. A possible circulatory problem relating to Vinyl Chloride is brought up in Dr. Mayo Smith's enclosed letters of October 13 and 14. Answers to the questions posed should be suitable discussion items at the next meeting.

5. Updates on points raised in Dr. Torkelson's letter of September 22, enclosed, are in the following four items.

6. The subject of greatest interest, pathological backup for the National Institute for Occupational Safety and Health's (NIOSH) listing of angiosarcoma cases is still under investigation. The Project Manager received a copy of EPI-74-63-2, Angiosarcoma of the Liver Among Vinyl Chloride Workers, Louisville, Kentucky, May 13, 1974 from Dr. Henry Falk of the Center for Disease Control. Enclosed is a memorandum from Dr. Marcus Key with attachment which appears to cover case numbers 14, wire coating operator and case 15, accountant in NIOSH's Table 1 on VC/PVC workers of June 25, 1974. Further follow-up correspondence and telecons have not yet yielded all of the information desired.

7. A letter of October 3 from Dr. James Woods of National Institute for Environmental Health Sciences (NIEHS) is also enclosed. However, the December 31, 1974 proposal from Midwest Research Institute and modification of May 16, 1975 are too long to include herewith.

A listing of NIEHS extramural projects on Vinyl Chloride and cover letter of October 15, 1975 from Dr. Braun are enclosed.

8. The Consumer Product Safety Commission (CPSC) program is outlined in the Project Manager's communication to the Panel May 8, 1975 and in the enclosed letter of May 6, 1975 from Dr. R. M. Hehir to Dr. Torkelson. In a telecon October 1, 1975 CPSC's Dr. McLoughlin informed the Project Manager this study is going into it's seventh month and no patterns (e.g. in mortality) have yet emerged, nor have reports been written on it. The first sacrifice is scheduled for November 4, 1975.

9. In a telecon September 26 with Dr. Stara of EPA, the Project Manager learned the "Transplacental Carcinogenesis" work is to be done at Kettering Laboratory under the direction of Dr. Bingham. Chambers are being modified and it may be

months before start up. No new information has been received on EPA's "Automobile Interior" project.

REFERENCES:

10. The September 1975 issue of Chemical Engineering Progress, contents page enclosed, includes four papers on Vinyl Chloride Emission Control. Lead authors of two of these papers, Dr. Bell and Mr. Wheeler, are also members of our panel.

11. First page of article on Vinyl Chloride Exposure in a Controlled Industrial Environment from the July '75 issue of Archives of Environmental Health.

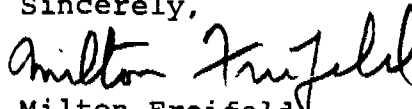
12. A booklet on Health and Safety Guide for Plastic Fabricators prepared by NIOSH is available from the Office of Technical Publications, National Institute for Occupational Safety and Health, Post Office Building, Cincinnati, Ohio 45202.

13. A 2nd edition, July 1975, of The Determination of Vinyl Chloride, A Plant Manual is available from Chemical Industries Association Ltd., Alembic House, 93 Albert Embankment, London, SE1 7TU.

14. Enclosed is the first page of an article on "Comparison Between In Vitro Toxicity of Polymer and Mineral Dusts and Their Fibrogenicity" from Annuals of Occupational Hygiene, Vol. 16.

15. The following reports and articles are brought to your attention: Measurements of Vinyl Chloride From Aerosol Sprays by Bruce W. Gay, Jr. et al.; EPA-650/4-75-020, May 1975 Environmental Monitoring Series report on Ambient Air Measurements of Vinyl Chloride in the Niagara Falls Area; Atmospheric Oxidation of Chlorinated Ethylenes report by B. W. Gay, et al., of EPA's Environmental Science Research Laboratory at Research Triangle Park, North Carolina 27711.

Sincerely,


Milton Freifeld
Project Manager

MF/mj
Enclosures

SL 068584

Inhalation Studies with Vinyl Chloride

M. L. Keplinger, J. W. Goode, D. E. Gordon, and J. C. Calandra
Industrial BIO-TEST Laboratories, Inc.
Northbrook, Illinois 60062

A study was conducted to determine the effects from inhalation of vinyl chloride monomer to rats, mice and hamsters. The study was designed as a life-span study in these species which is usually 1-1/2 to 2 years.

In this study, 200 rats, hamsters and mice (100 of each sex or 600 animals total per exposure group) were exposed to 50, 200 or 2,500 ppm vinyl chloride vapor 7 hours per day 5 days per week. Mice were exposed for 9 months while rats and hamsters were exposed for 12 months. The animals were then held for the rest of their natural lives.

The rats were COBS Charles River; mice were CDI Swiss Charles River; and the hamsters were Golden Syrian from the same source. Food was removed during exposure, water was present and no bedding was used at any time.

All 600 animals per level were exposed in a single chamber. The chambers were operated under dynamic conditions, sealed and under slight negative pressure. This was done so that in the case of an accidental leak, room air would flow into the chamber instead of contaminated air flowing out of the chamber.

SL 068585

The concentrations in the chamber were analyzed using gas-liquid chromatography. An automatic sampling device allowed samples to be drawn from 3 locations in each chamber. The concentrations at all locations in each chamber were monitored every day.

Moribund and dead animals received gross autopsies and gross lesions were photographed. The major organs of all animals were fixed, prepared and examined histologically.

Findings included angiosarcomas in the liver, alveologenic adenomas in the lung and adeno-squamous carcinomas in mammary glands.

OCT 14 1975



ALLENTOWN, PENNSYLVANIA 18105

13 October 1975

Dr. T. R. Torkelson
Dow Chemical Company
Health & Envir. Research
9000 Building
Midland, Michigan 48640

Dear Ted:

You will recall that when Dr. Tamburro made his presentation to the Research Coordinators at the HCA 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 HCA program whether cardiac examinations and specifically, EKG's are done. *

Sincerely yours,

Mayo
W. Mayo Smith

WMS:cm

cc: Milton Freifeld, HCA

SL 068587



Air Products and Chemicals
INC.

ALLENTOWN, PENNSYLVANIA 18105

OCT 20 1975

14 October 1975

Dr. T. A. Torkelson
Dow Chemical Company
Health & Envir. Research
9008 Building
Midland, Michigan 48667

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 ~~KemaNord~~ KemaNord, the only PVC producer
in Sweden and one of excellence.

You will recall that Nick 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 KemaNord report lends further evidence that we should immediately
contact all member companies of the MCA 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

H. Mayo Smith

MS:cm

Attachment - Chemical Engineering, September 29, 1975

cc: ~~Milton~~ Freifeld, MCA

SL 068588

VINYL CHLORIDE RESEARCH PROGRAM
Financial Statement - August 28, 1975

Revised as of October 1, 1975

	Invoiced (Committed)	Received	Research Contract	Disbursements			Research Contracts	Total	Unpaid Balance On Contract	Balance on Hand
				Time	Administrative Travel	Misc.				
1. <u>Epidemiology Study</u> 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 Epidem- iology 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. <u>Chronic Inhalation Studies</u> 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. <u>Dow Studies</u>	\$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	\$149,205		\$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

SL 068589

SEP 24 1975

THE DOW CHEMICAL COMPANY

September 22, 1975

BENNETT BUILDING
2030 DOW CENTER
MIDLAND, MICHIGAN 48640

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 Co-factors" (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.

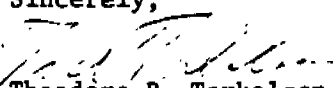
Several studies are being sponsored by other agencies. You should contact them for specifics: Consumer Product Safety Commission, 7315 Wisconsin Avenue, Washington, DC, 20014 (Contract #72-2084, Project Officer, Dr. Robert Hehir).

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

SL 068590



MEMORANDUM

164
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

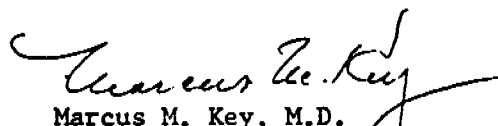
DATE: August 22, 1974

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

SL 068591

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTE OF HEALTH
BETHESDA, MARYLAND 20814

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
Communicable Disease Center. 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
megaleucytosis 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. Mulvey's section. Thus we do not
think his hepatic angiosarcoma is characteristic of the
angiosarcomas seen in the VC-PVC workers. Also [REDACTED]

SL 068592

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 histologic feature, i.e. the cells of the angiosarcomas 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.

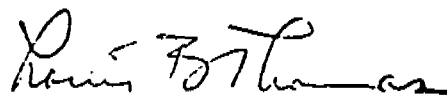
We want to emphasize that we do not think there is any single, histological feature either of the angiosarcomas or of the hepatic fibrosis which is pathognomonic of vinyl chloride exposure. For example, all the changes we've seen in the livers of the VC-PVC workers can apparently be produced by exposure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

Page 3 - Dr. Philip Landrigan

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,

A handwritten signature in dark ink, appearing to read "Louis B. Thomas". The signature is fluid and cursive, with the first name "Louis" and last name "Thomas" clearly distinguishable.

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

SL 068594

June 25, 19

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	04-09-64
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
CONFIRMED CASES OF LIVER ANGIOSARCOMA AMONG WORKERS EXPOSED TO VINYL CHLORIDE OR POLYVINYL CHLORIDE 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

SL 068595



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
Vinylidene 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 vinylidene 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

SL 068596



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

OCT 20 1975

NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES
P.O. BOX 12133
RESEARCH TRIANGLE PARK, N.C. 27709

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

SL 068597

October 8, 1975

OCT 20 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.

SL 068598

LIST OF PROJECTS

1. 5 R01 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 R01 ES 01150-01
VAN DUUREN, Benjamin L.
New York University Medical
Center
New York, New York

Carcinogenic Intermediates and Metabolism of Vinyl Chloride and
Analogues.

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 R01 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.

Page 2 - LIST OF PROJECTS

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.

SL 068600



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,

A handwritten signature in dark ink, appearing to read "Robert M. Hehir", is written over the typed name.

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

Attachment

SL 068601

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