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MANUFACTURING CHEMISTS ASSOCIATION

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

April 17, 1974

To: TECHNICAL TASK GROUP ON VINYL CHLORIDE RESEARCH

Subject: Report on Conference with Industrial BIO-
TEST Laboratories, April 15, 1974

Gentlemen:

As a result of the telephoned information received by MCA from Industrial BIO-TEST personnel last week, a conference at the Northbrook, Illinois offices of IBT was set up at which an oral status report on the chronic inhalation studies with vinyl chloride was presented to MCA, industry and federal agency representatives.

Those in attendance, and their affiliations, are shown below:

Z. G. Bell, Jr.
A. S. Cummin
E. J. Fairchild
J. W. Goode
D. E. Gordon
W. D. Harris
M. N. Johnson, M.D.
Flynt Kennedy
M. L. Keplinger
R. J. Kociba
H. L. Kusnetz
D. V. Lassiter
W. E. Rinehart
W. M. Smith
J. F. Stara

T. R. Torkelson
R. N. Wheeler
B. M. G. Zwicker
R. F. Blewitt
A. C. Clark
K. D. Johnson

PPG Industries, Inc.
Borden, Inc.
NIOSH
Industrial BIO-TEST Laboratories
Industrial BIO-TEST Laboratories
UNIROYAL, Inc.
The B. F. Goodrich Company
Continental Oil Company
Industrial BIO-TEST Laboratories
The Dow Chemical Company
Shell Oil Company
OSHA
Ethyl Corporation
Air Products & Chemicals, Inc.
U. S. Environmental Protection
Agency
The Dow Chemical Company
Union Carbide Corporation
B. F. Goodrich Chemical Company
MCA
MCA
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Dr. Goode first presented the mortality data and gross observations, and then Dr. Gordon described the pathology observed in the mice. The data, as presented, are shown in the attached tables. There are apparent discrepancies between the total mortality data and the detailed listing of recent deaths. These will be resolved. No test-related pathology has yet been noted in any animals other than mice.

Dr. Fairchild, of NIOSH, reported that Dr. David Rall, of HEW, had appointed a committee to coordinate departmental toxicology and related programs, and that under this committee there has been named a subcommittee to develop a "white paper" on guidelines for research to determine "socially acceptable" levels of risk. A report from this subcommittee, which will cover both philosophical and statistical considerations, is expected in the next few weeks.

Dr. Stara expressed the view that the vinyl chloride problem presented industry with a unique opportunity to seek to demonstrate a "no effect level" of a human carcinogen with a sensitive animal model of well-documented validity.

Dr. Lassiter expressed a guarded judgment that the mouse data reported by IBT would not lead OSHA to modify the emergency temporary standard, but that it might well cause OSHA to accelerate the rule-making process for the development of a permanent standard.

Dr. Lassiter also reported briefly on the retrospective morbidity and mortality studies being conducted by NIOSH/CDC at nine or ten locations (six companies) around the country. No epidemiological data were presented.

In an afternoon session of the Research Coordinators, it was agreed that the exposure of the mice in the present project should be terminated at nine months, but that exposures of both rats and hamsters should proceed for the initially-planned twelve months.

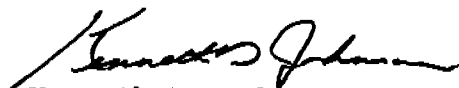
It was further moved, seconded and carried that the chairman appoint a group to begin investigating the cost and availability of facilities of new experiments to be conducted at lower levels of exposure, with larger groups of animals. He was asked specifically to seek to encourage the National Center for Toxicological Research, at Pine

Bluff, Arkansas, to offer to undertake such a program. Details of the test protocol are to be left open until after the Rall committee makes its report available.

The Research Coordinators asked MCA to call a meeting of the Technical Task Group on Vinyl Chloride Research as soon as the report of Tabershaw-Cooper Associates on their epidemiological study reaches them.

A copy of the MCA news release reporting the Industrial BIO-TEST mouse data has been sent to you in this morning's mail.

Sincerely,



Kenneth D. Johnson, Ph.D.
Secretary
Technical Task Group on
Vinyl Chloride Research

KDJ:mb

Tables Attached

cc : Mr. A. W. Barnes
D. P. Duffield, M.D.
Dr. Tiziano Garlanda
Vinyl Chloride Management Contacts

TABLE 1

Mouse Mortality Data

DATE	GROUP							
	<u>Controls</u>		<u>TI</u>		<u>TII</u>		<u>TIII</u>	
	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>
February 10, 1974	2	8	6	26	2	4	7	8
April 12, 1974	5	11	9	31	13	7	13	18

Industrial BIO-TEST Laboratories, Inc.

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NORTHBROOK, ILLINOIS 60062

TABLE II

Summary of Tumors in Vinyl Chloride Exposed Mice

IBT Number 663-03222-MCA

<u>Group, Animal No., Sex</u>	<u>Histopathologic Findings</u>			<u>Date of Death</u>
	<u>Lung</u>	<u>Liver</u>	<u>Skin</u>	
T-I				
1023 Male	AA (s)*	HS (s)**		
1110 Female	AA (s), Metastatic Skin Tumor		*** EC (para-aural)	3-20-74
1119 Female		HS (s)		3-24-74
1200 Female	Metastatic Skin Tumor		EC & MC+ (Femoral region)	3-30-74
T-II				
1347 Female	Metastatic Skin Tumor		EC (Abdomen)	3-5-74
1309 Female		HS (s)		3-18-74
1889 Male	AA (s)	HS		3-25-74
1382 Female		HS (s)		4-2-74
1350 Female	AA (s)	HS (s)		4-5-74
1299 Female	AA (s)		EC & MC (Inguinal Region)	4-9-74
T-III				
1538 Female	AA (s)	HS (s)		3-6-74
1532 Female	AA (s)		LS⊙	3-7-74
1562 Female	AA (s)	HS (s)		3-8-74
1598 Female	AA (s)	HS (s)		
1405 Male	AA (s)	HS (s)		2-25-74
1494 Male	AA (s)	HS (s)		3-22-74
1574 Female	AA (s)	HS (s)		3-22-74
1531 Female		HS (s)	EC & MC (Femoral region)	3-23-74
1588 Female		HS (s)		3-25-74
1593 Female	AA (s)	HS (s)		3-30-74
1505 Female	AA (s)	HS (s)		4-3-74
1565 Female	AA (s)	HS (s)		4-3-74
1409 Male	AA (s)	HS (s)		4-5-74
1543 Female	AA (s)	HS (s)		4-5-74
1544 Female	AA (s)	HS		4-5-74
1546 Female	AA (s)	HS (s)	MC (Axillary region)	4-5-74
1535 Female	AA (s)	HS (s)		4-7-74
1432 Male	AA (s)			4-8-74
1477 Female	AA (s) Metastatic Skin Tumor?	HS (s)	EC (Para-Aural) MC (Abdomen) EC (Pelvic region)	4-9-74

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TABLE III

*Industrial BIO-TEST Laboratories, Inc.*1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062Summary of Mortality & Tumor Data Among Vinyl Chloride Mice
IBT Number 655-02222 (MCA)

Group	No. Mortalities with Neoplasms	Location of Tumors			
		Lung	Liver	Skin	Metastasis → Lu
T-I	4 (1 Male, 3 Females)	2(50%)	2(50%)	2(50%)	2
T-II	6 (1 Male, 5 Females)	3(50%)	4(66.7%)	2(33%)	1
T-III	19 (4 Males, 15 Females)	17(89.5%)	17(89.5 %)	3(15.8%)	

Key to Symbols

- * Alveologenic Adenoma of Lung (AA)
- ** Hemangiosarcoma of Liver (HS)
- *** Epidermoid Carcinoma of Skin (EC)
- + Mammary Carcinoma of Skin (MC)
- ⊕ Lymphosarcoma of Thymus
- (s) Multiple tumors of indicated type

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INTERIM RESULTS OF EXPOSURE OF
RATS, HAMSTERS AND MICE TO VINYL CHLORIDE

M. L. Keplinger, Ph.D.,
J. W. Goode, Ph.D.,
D. E. Gordon, D.V.M., Ph.D.
and
J. C. Calandra, M.D., Ph.D.

Industrial Bio-Test Laboratories, Inc.
Northbrook, Illinois

The following data are partial results of a study in progress at the Industrial Bio-Test Laboratories, Inc. The studies are being coordinated for sponsoring companies by the Manufacturing Chemists Association. The data are very incomplete but because of their significance were first presented to EPA, NIOSH and OSHA on April 15, 1974.

In this study which was designed to complement Maltoni's studies, 100 rats, hamsters and mice of each sex (600 total per exposure group) are being exposed to either 0, 2500, 200 or 50 ppm vinyl chloride vapor 7 hours per day 5 days per week. Mice will be exposed for 9 months and kept for an additional 9 months. Rats and hamsters will be exposed for 12 months and kept for an additional 12 months.

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

Moribund and dead animals (when possible) receive gross autopsies and are photographed. The major organs of all animals are fixed for histological examination.

Only the tissues from a few animals have been examined so far. The table shows the results to date (about 8 months exposure).

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Note that no direct numerical comparisons can be made with the control groups as they have not been selected in the same way. Only mice with tumors have been examined in the exposure groups. No tumors have been observed grossly as yet in any of the control mice.

In addition to the tumors in mice a few tumors have been observed in rats and hamsters but because of autolysis the diagnosis at this time must be considered tentative. At this time it appears that angiosarcomas may have been observed in one male hamster and one male rat exposed to 2500 ppm and in one female rat exposed to 200 ppm. No tumors have been observed in rats or hamsters exposed to 50 ppm but one male control was found to have a dermal fibroma.

These tentative data need to be confirmed and will be reported in detail when the study is completed.

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