

SHELL OIL COMPANY

VCM-MCA ^{REFERENCE}

DATE APRIL 16, 1974

TO MESSRS. W. G. EDDLEMAN
 R. H. FINDLEY
 This Copy For ~~R.~~ E. JOYNER, M.D.
 A. J. MARTIN
 R. L. MAYCOCK
 R. F. NELSON
 R. J. REYNOLDS
 H. E. WALKER

FROM MANAGER, INDUSTRIAL HYGIENE -
 HEAD OFFICE

SUBJECT VCM MEETING - APRIL 15, 1974

The meeting was held at the Industrial Bio-Test offices in Northbrook (Chicago), Illinois. Attendees are noted on Attachment 1. Dr. Goode, who is in charge of the inhalation work at the Decatur Lab reported on mortality results to date. These are shown as Attachment 2. He emphasized that the pathology was only in the mice. Grossly, the effects are manifested as subcutaneous masses, probable liver tumors and tan foci on the lungs. The first observed change in the animals is a swelling of the abdomen. Death may occur suddenly within 48 hours with no other apparent symptoms. Goode ascribes this to internal hemorrhage. To date there have been no gross observable effects on the control animals.

Dr. Gordon, the Bio-Test pathologist, then gave his impressions. He called attention to a higher incidence of tumors in the female mice. The compound-induced lung adenomas are indistinguishable from the spontaneous adenomas seen in these animals, but the incidence appeared to be dose-related. Although some strains of mice do show spontaneous hemangiosarcomas of the liver, Gordon has seen this occur spontaneously only once at IBT. Dr. Gordon, and Dr. Kociba who looked at the slides, agreed that the liver lesions are the same as seen and reported by Dr. Maltoni.

Gordon's data are presented in detail in Attachment 3. Note that there are some discrepancies with the gross data reported by Goode. This, however, was explained as a sex-identification error in the mice on a gross basis. Microscopic visualization of the gonads was used to verify Gordon's data. I asked about the discrepancies between the five-month and seven-month data. For example, six female mice at 2,500 ppm should have died of tumors in that period. Gordon's data show 15 females dying within that period. The IBT people were unable to explain the differences, but were going to check into it.

The consensus of the group was that despite these minor discrepancies, the tumors were real and they confirmed Maltoni's findings. On a ppm-hour basis, the tumors appeared at 1/40 the level that were noted in Maltoni's rats. This may be species- or strain-specific. Zwicker (BFG) and Kennedy (Conoco) both stated that there was a report circulating in Europe that Maltoni is seeing, "... avalanches of hemangiosarcomas in his mice." No data were available, but the feeling was that these new Maltoni results were similar to those at IBT.

*Not by list
 formed in
 surveillance
 (by experience)*

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The government people present would make no commitment about new levels. During lunch, however, I asked Lassiter what he thought the action might be. He felt that OSHA would have to review their position and could either now promulgate a proposed permanent standard sooner or could revise the emergency standard. He felt that the results reported would support the NIOSH recommendation of 1 ppm. Fairchild later agreed that any so-called "zero standard" would be based on feasible analytic techniques available. He stated that although NIOSH could analyze to levels under 1 ppm, the methods were not feasible for most installations.

The discussion then turned to the nature of follow-up research. Dr. Stara stated that he already has orders from EPA to start inhalation toxicity studies on VCM. His own attitude is that there should be no duplication of MCA work, but rather, there should be a coordinated government-industry approach. Fairchild also stated that NIOSH will not be doing any animal work - it preferred to see what MCA will be doing before taking any action. He also stated that there is an HEW committee to coordinate toxicology and related programs which is active. A subcommittee has been formed to recommend protocols for testing carcinogens. The recommendations of the subcommittee are to include methods of determining levels of exposure which would lead to socially acceptable risks from carcinogens. (Emphasis mine). The Federal representatives thought that they would prefer to wait until the report was out before embarking on animal studies. Expected date of publication is before the end of May.

With this the research coordinators recommended two action items. First was to cease mouse exposure at nine months. This will be equal to half a mouse's lifetime and would be comparable to a one-year exposure for rats and hamsters. Second, the coordinators recommended that MCA investigate the costs of doing animal studies on larger numbers of animals at lower levels. The exact levels will be determined later, probably in conjunction with the HEW subcommittee report. An offhand estimate was that such studies would add about \$200M-\$500M to the overall budget. Stara pointed out that EPA and FDA might help fund low-level toxicity studies. He suggested writing to Dr. Charles Edwards (Assistant Secretary of HEW for Health) and to Russell Train (EPA Administrator) for assistance in obtaining the cooperation of the National Toxicity Research Center (Pine Bluff, Arkansas) in kilo- and mega-mouse studies.

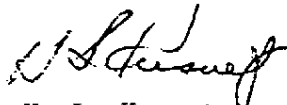
There was one other area of importance at the meeting. Jane Brodie of the New York Times phoned Dr. Fairchild at Northbrook. She seemed to know about the meeting, who would be attending, the agenda, and the results. She wanted a statement from Fairchild regarding the significance of the results and what the Government would be doing about it. Fairchild said that he was at the meeting to listen, and was not sure he could get back to her in time for her deadline. By the time he left at 3:00 p.m. CDT, he had not called her back.

MCA was preparing a statement for distribution on April 16. It was not completed at the meeting and would probably be done by Clark, Johnson, and

Blewitt on their flight back to Washington. It was agreed that the statement would be factual (rather than interpretive or speculative), would point out that the results were preliminary, and that the results had been made available to government (OSHA, NIOSH, and EPA) the same time as they were released to the industry sponsors. It was to be clear that any statements would come from MCA rather than from Bio-Test or from the individual company sponsors.

Blewitt also mentioned that CBS was preparing a one-hour special on vinyl chloride. They were sending a camera to Goodyear at Niagara Falls along with Dr. Selikoff for the program.

The meeting adjourned at 4:30 p.m. CDT.


H. L. Kusnetz

Attachments

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ATTENDEES

Zeb G. Bell	- PPG Industries
A. S. Cummin	- Borden Company
W. D. Harris	- Uniroyal Inc.
M. N. Johnson	- B. F. Goodrich
F. Kennedy	- Conoco
R. J. Kociba	- Dow
H. L. Kusnetz	- Shell Oil Company
W. E. Rinehart	- Ethyl Corporation
M. Smith	- Air Products
T. R. Torkelson	- Dow
R. N. Wheeler	- Union Carbide Corporation
B. F. Zwicker	- B. B. Goodrich
R. F. Blewitt	- MCA
A. C. Clark	- MCA
K. D. Johnson	- MCA
J. W. Goode	- IBT
D. E. Gordon	- IBT
M. L. Keplinger	- IBT
E. J. Fairchild	- NIOSH
D. V. Lassiter	- OSHA
J. F. Stara	- EPA

SEVEN-MONTH MORTALITY DATA - AS OF APRIL 15, 1974

(Deaths from all causes)

Species	Control M/F	50 ppm M/F	200 ppm M/F	2,500 ppm ^(b) M/F
Rat	4/4 (2/3) ^(a)	10/8 (5/1)	6/9 (6/1)	5/7 (3/4)
Mouse	16/5 (8/2)	31/9 (26/6)	7/13 (2/2)	18/13 (8/7)
Hamster	13/22 (9/18)	20/20 (16/6)	22/29 (16/20)	27/27 (15/15)

NOTES: (a) Nos. in () refer to corresponding five-month mortality data.

(b) In addition, one group of 100 female rats had been exposed to 2,500 ppm, but with food available ad lib. There have been no deaths in this group to date.

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Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

Summary of Mortality & Tumor Data Among Vinyl Chloride Mice
IBT Number 663-03222 (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%) 0

As of 10/15/67

1. Tumors listed are primary tumors only
2. Only the skin tumors are testicular
3. Numbers reflect #'s of tumors, not #'s of animals.

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Industrial BIO-TEST Laboratories, Inc.

1810 FRONTAGE ROAD

NORTHBROOK, ILLINOIS 60062

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				
1317 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
13 Female	AA (s)	HS (s)		4-5-74
1297 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
1404 Male	AA (s)	HS (s)		3-22-74
1 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
1537 Female	AA (s)	HS (s)		4-7-74
145 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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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) - refers to multiple