



Air Products and Chemicals INC

CHEMICALS GROUP

Five Executive Mall, Swedesford Road, Wayne, Pa. 19087

April 6, 1976

①
4/15
See attached letter
concerning a planning
item. Smith is what
he says. I will
be looking for
information. ② AF

RECEIVED

APR 7 1976

R. J. FLEMING, V. P.

Mr. J. R. Smith
Special Studies Staff
Environmental Protection Agency
National Environmental Research Center
Research Triangle Park, North Carolina 27711

Dear Mr. Smith:

This will furnish you further information on the subject of reported non-polymerization worker cases of angiosarcoma which we discussed by telephone on March 31 and April 2.

Some confusion seems to have arisen over the nomenclature applied to the reported cases of angiosarcoma in Connecticut. They have been variously called "community cases" or "neighborhood cases" in the media, in EPA documents (STAR Document, p. 1), and in the EPA hearing (cross-examination of Barry Castleman by Dr. William Marcus, hearing transcript p. 42, copy attached), "non-polymerization cases" by NIOSH, and "non-occupational cases" by CDC and in other places. Unfortunately, we seem to have added to the confusion by using both "non-occupational" and "non-polymerization" on page 19 of the Air Products' submittal to Dr. Goodwin, dated February 23, 1976.

I will hereinafter use the NIOSH designation of "non-polymerization" for employees not working in PVC plants and "non-occupational" for persons not employed in any part of the PVC industry.

The cases with which we are concerned are therefore "non-polymerization" cases. NIOSH does list these in "Table II" which they maintain. The latest listing of these cases is dated September 12, 1976, and is attached. It has not been distributed routinely with Table I over the last few months, and Drs. Adams and Smith of this company were informed earlier this year by Dr. Lloyd that it had been discontinued. This led to the statement in the submittals by Air Products and the Society for the Plastics Industry that these cases had been dropped. In a conversation today with Dr. Pierre Decauffle of NIOSH, he confirmed that this list is not normally distributed now, but that it is still in existence and will be maintained.

The burden of proof is on NIOSH to substantiate their listing of these cases, and to show their relationship to vinyl chloride. No one presently exercises this responsibility. Angiosarcomas do occur in populations not exposed to vinyl chloride. The CDC has recently published a survey of ten cases in Wisconsin which have no vinyl chloride relationship whatsoever (copy attached). The Connecticut cases would seem to fall into a similar classification except for the very casual relationship to fabrication operations. This type of correspondence is expected to occur on a statistical basis from time to time.

AP00011368

Mr. J. R. Smith

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April 6, 1976

Regarding the foreign cases listed in NIOSH Table II, Germany 03 filled aerosol cans where the exposure from leakage was reported to be high. We have no more information than NIOSH on Germany 07, or Great Britain 02. Italy 01 did not have primary liver angiosarcoma. Sweden 02 worked in an obsolete acetylene-process vinyl chloride plant where the exposure was high.

The two U. S. (Connecticut) cases are discussed by you in the footnotes to Table 6-19 of the STAR Document, where you quote Dr. L. B. Thomas of the National Cancer Institute. He states that both cases are uncertain. Furthermore, EPA has stated that their measurements of vinyl chloride around fabrication plants show it to be "almost negligible" (Preamble to Standard 40 FR 59534). The highest found was 6 ppb, and none was found at 3 of the 5 plants tested. Thus, these "non-polymerization" cases are doubtful in relationship to vinyl chloride, and do not support any concern for harm at "levels of exposure as low as 1-10 ppm" (STAR Document, p. 1).

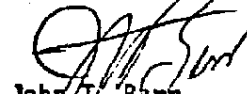
The exchange between Mr. Castleman and Dr. Marcus at the EPA hearing indicates that the EPA has reached the same conclusion. This is supported by the statement in Appendix E, page 5, of the Risk Assessment Document by A. M. Kusmak and R. E. McGaughy that, "This survey has produced no evidence that living around vinyl chloride plants is a risk factor in the occurrence of liver angiosarcoma."

Thus, we stand on our position that there is no demonstrated risk to persons not exposed to high concentrations of vinyl chloride for long periods of time, and therefore the proposed standard is unnecessary.

I hope that this clarification is of help to you, and apologize for any confusion to which we may have contributed. We will be happy to discuss any other part of our comments with you whenever you may wish.

Very truly yours,

AIR PRODUCTS AND CHEMICALS, INC.



John T. Barr
Technical Manager

Attachments

cc: Mr. G. Baise, Ruckelshaus, Beveridge, Fairbanks & Diamond, Wash., DC
Dr. D. R. Goodwin, EPA, Research Triangle Park, NC
Mr. J. Hadley, Keller & Heckman, Wash, DC
Mr. R. Harding, SPI, New York, NY

bcc: A. R. Adams
R. Fleming
R. H. Schenck
W. M. Smith
L. B. Tepper

AP00011369

TRANSCRIPT OF EPA HEARING ON
VINYL CHLORIDE, FEBRUARY 3, 1976

1 DR. MARCUS: Do you know of any evidence of the
2 increased risk in the general population, other than the
3 studies that have been done in work?

4 MR. CASTLEMAN: Aside from the fact that there
5 were apparently two neighborhood cases with no known
6 occupational exposure, no I don't.

7 DR. MARCUS: I would like to say that EPA
8 investigated very carefully those cases, and we consulted
9 with our expert doctor, Hans Popper of Mount Sinai, and
10 it was his expert opinion that these people did have
11 angiosarcoma, that was of a different type than that caused
12 by vinyl chloride monomer, and I must say, to date we
13 do not have any evidence that angiosarcoma has been
14 produced by vinyl chloride monomer in the general population.

15 MR. CASTLEMAN: I think it is important to
16 realize that only about one-fourth of the present PVC
17 plants were operating 20 years ago. The latency of this
18 disease is 20 years or more, and of these ten plants,
19 at least one-fourth of the present level of plants, which
20 is about ten, the total production rate is one-tenth of the
21 rate it is today. The population may also have been thinner
22 around the plants than it is today.

23 So, if you look at the present situation in terms
24 of how many people lived near the plants of a certain
25 size, it bears little resemblance to the situation 20

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1 years ago.

2 The mortality experience that we observe today
3 started 20 years ago. I don't think the absence of
4 cases is any proof of anything. Wouldn't you agree with
5 that?

6 DR. MARCUS: In general I would say that is a
7 very cogent comment. The only thing here is that vinyl
8 chloride happens to offer us a unique opportunity to
9 see an extremely rare cancer, which we can say is maybe
10 due to the substance in question, rather than an increased
11 rate of cancer, which is a very difficult thing to assess.

12 That is why I say, I was hoping somebody would
13 have some information about VCM induced angiosarcoma in
14 the general public, because we have not been able to find
15 it as yet.

16 MR. CASTLEMAN: I talk to the same people you do

17 CHAIRMAN DENNEY: Dr. McGaughy.

18 DR. MC GAUGHY: I just have one short question.

19 We are interested in getting as accurate a
20 picture as we can as to what the risk is to the population
21 due to vinyl chloride exposure. You mentioned there
22 were two or three factors that we have not considered.

23 Mainly the carcinogenicity of vinyl chloride and
24 other chemicals and the transplacental effects that might
25 caused to expectant mothers.

Acme Reporting Company

CENTER FOR DISEASE CONTROL

Morbidity and Mortality



Vol. 25, No. 8

WEEKLY
REPORT

For
Week Ending
February 28, 1976

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE

DATE OF RELEASE: MARCH 5, 1976 - ATLANTA, GEORGIA 30333

EPIDEMIOLOGIC NOTES AND REPORTS
ANGIOSARCOMA OF THE LIVER - Wisconsin

In the period June 1973-November 1975, 4 cases of angiosarcoma of the liver (ASL) were diagnosed at the Marshfield Clinic, Marshfield, Wisconsin. One was based on hepatic arteriography and 3 on tissue findings later confirmed by pathologic review at the National Cancer Institute (NCI).

An additional 6 cases, confirmed on pathologic review at NCI and identified through a national ASL case surveillance project initiated at CDC in 1974, have been diagnosed since 1964 in Wisconsin residents. This total of 10 cases is roughly twice as large as might be expected (5.5 cases), based on CDC surveillance estimates of crude ASL incidence for the entire United States. (Five additional cases had been re-

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ported for Wisconsin; 4 were not confirmed, and 1 was in a resident of another state.)

In view of this relative frequency of cases, together with the recent succession of cases at the Marshfield Clinic, epidemiologic information concerning each of these 10 cases

TABLE I. CASES OF SPECIFIED NOTIFIABLE DISEASES: UNITED STATES
(Cumulative totals include revised and delayed reports through previous weeks)

DISEASE	WEEK ENDING		MEDIAN 1971-1975	CUMULATIVE FIRST 8 WEEKS		
	February 28 1976	February 22 1975		February 28 1976	February 22 1975	MEDIAN 1971-1975
Aseptic meningitis	28	35	33	307	292	292
Brucellosis	7	2	2	38	21	15
Chickenpox	5,764	4,311	---	39,268	29,693	---
Diphtheria	4	14	6	62	64	23
Encephalitis	13	17	15	129	96	120
Primary	4	7	5	32	33	33
Post-infectious	242	210	172	1,935	1,568	1,314
Hepatitis, Viral	126	707	---	5,409	5,428	---
Type A	133	150	890	1,365	1,123	7,619
Type unspecified	3	6	6	43	42	42
Malaria	605	578	622	4,318	2,668	4,767
Measles (rubeola)	53	41	41	284	270	270
Meningococcal infections, total	53	41	40	281	263	263
Civilian	---	---	1	3	7	9
Military	1,366	1,425	1,092	9,366	11,136	14,246
Mumps	22	24	---	194	201	---
Pertussis	449	285	645	1,870	1,037	3,534
Rubella (German measles)	2	---	---	6	9	8
Tetanus	570	565	---	4,572	4,105	---
Tuberculosis	1	1	1	21	8	13
Typhoid fever	3	2	4	58	29	37
Typhus, tick-borne (Rky. Mt. spotted fever)	---	---	---	3	10	9
Venereal Diseases:						
Gonorrhea (Civilian)	28,313	17,273	---	151,748	141,258	---
Gonorrhea (Military)	562	419	---	4,708	4,776	---
Syphilis, primary and secondary (Civilian)	528	531	---	4,132	3,938	---
Syphilis, primary and secondary (Military)	8	3	---	64	52	---
Rabies in animals	39	45	56	249	284	448

TABLE II. NOTIFIABLE DISEASES OF LOW FREQUENCY

	Cum.		Cum.
Anthrax	2	Polio myelitis, total:	2
Botulism	4	Paralytic: N.Y.C. 1	2
Congenital rubella syndrome	5	Pittscois: Ohio 1, Calif. 3	19
Leptospirosis: Pa. 1, Calif. 2	20	Rabies in man:	---
Leptospirosis	7	Trichinosis: N.J. 1	33
Plague	---	Typhus, murine: Tex. 1	2

(Delayed Report for week ending 2/24/76)

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ANGIOSARCOMA — Continued

has been assembled through medical record review and family interview (Table 1). Particular attention has been given to potential occupational or environmental exposure to chemicals known to induce ASL (vinyl chloride, arsenic, and thorium dioxide).

Most cases (7 of 10) were diagnosed since 1970, probably reflecting better case ascertainment in recent years. Ages ranged from 36-71 (mean age 58 years). All but 1 patient were male, and all but 1 were white. Places of usual residence for all cases were widely scattered across the state, roughly corresponding with the state's population (Figure 1).

One patient had a history of prior thorium dioxide exposure. For none of the remaining cases was tumor etiology obvious. Occupations and histories of exposure to potential environmental toxins differed widely, with no more than 1 case associated with any particular industry or mode of exposure. In several instances, however, individual patient occupations or exposures were suggestive of possible oncogenicity (Table 1). Patient 10 had had exposure to a vinyl compound; he had worked in paper and plywood products with potential contact with various chemicals, including polyvinyl acetate. Two other patients gave histories of possible exposure to arsenic: patient 9, who had exposure to insecticides while farming, and patient 8, who worked with wood probably treated with arsenic preservatives in the manufacture of bleachers. All but 3 of the 10 patients were known to have lived on farms during their lifetimes, 2 for all of their lives (Table 1).

(Reported by J Flechtner, MD, C Reyes, MD, Marshfield Clinic; K Rentmesster, MPH, HG Skinner, MD, State Epidemiologist, Wisconsin State Dept of Health and Social Services; Office of Extramural Coordination and Special Projects, National Institute of Safety and Health; and the Cancer and Birth Defects Div, Bur of Epidemiology, CDC.)

Editorial Note

These data indicate no obvious common-source origins among recent cases of ASL in Wisconsin. The marked male preponderance among cases, however, suggests occupational

Figure 1
GEOGRAPHIC DISTRIBUTION OF CONFIRMED CASES OF
ANGIOSARCOMA OF THE LIVER IN WISCONSIN RESIDENTS,
1964-1975, BY PLACE OF USUAL RESIDENCE



exposure as the potential origin for at least some of the cases. Anecdotal histories of occupational and environmental exposures in several of the cases may warrant further investigation, particularly in relation to contact with arsenic. Although at present only vinyl chloride monomer (1), thorium dioxide (2), and arsenic (3-4) are clearly implicated as causes of ASL, investigations such as the one described here may well provide useful leads in defining further causes.

References

1. Ciesch JL, Johnson MN: Angiosarcoma of liver in the manufacture of polyvinyl chloride. *J Occup Med* 16:150-151, 1974
2. MacMahon HE, Murphy AS, Bates MI: Endothelial-cell sarcoma of liver following Thorotrast injection. *Am J Pathol* 23:585-595, 1947
3. Lender JJ, Stanley RJ, Sumner HW, et al: Angiosarcoma of the liver associated with Fowler's solution (potassium arsenite). *Gastroenterology* 68:1582-1586, 1975
4. Roth F: The sequelae of chronic arsenic poisoning in Moselle vintners. *Ger Med Mon* 2:172-175, 1957

Table 1
Cases of ASL in Wisconsin Residents 1964-1975

Case Number	Month and Year Diagnosis	Month and Year Death	Usual Town Of Residence	Age at Diagnosis	Race	Sex	Occupation	Comments	Farm Residence
1	4/64	2/65	Sheboygan	71	W	M	University Teacher	Lived near a chemical company which made plastics and resin	Youth
2	2/67	2/67	Oshkosh	61	W	M	Foundry Welder	Exposure to welding materials and resins	None
3	6/67	6/67	Necedah	36	W	F	Secretary	Infectious hepatitis in childhood, mother and sister had liver disease	Youth
4	7/71	7/71	Milwaukee	68	B	M	Hog Scaldier		None
5	4/72	4/72	Milwaukee	64	W	M	Unknown	Exposure to thorium dioxide	Unknown
6	4/74	6/74	Brown Deer	46	W	M	Lutheran Pastor	Lived near a paper mill, 1955-1959	Youth
7	7/74	7/74	Wausau	57	W	M	Rock Crusher; Glue-Liner for rubber raincoats, 1940s	Exposure to silica dust, rubber cement	Youth
8	9/74	9/74	Waupun	46	W	M	Postal Mail Carrier formerly employed by company that made bleachers	Contact with lumber, paints, wood preservatives, ammoniacal-copper-arsenate wood preservative (?)	Lifetime
9	8/74	8/74	Stratford	66	W	M	Retired Farmer	No tissue diagnosis; ASL diagnosed by hepatic arteriography	Lifetime
10	11/75	11/75	Marshfield	65	W	M	Press operator for paper and plywood company (23 years)	Contact with wood, plywood, glues, polyvinyl acetate, others	Youth

NIOSH
September 12, 1975

TABLE II

REPORTED CASES OF ANGIOSARCOMA OF THE LIVER AMONG
NON-POLYMERIZATION WORKERS EXPOSED TO VINYL 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	
Fed. Rep. Germany	03*	07-16-30	06-09-52	03-00-73	43	21	14	10-10-73	Note 6
Fed. Rep. Germany	07*	05-09-36	00-00-60	00-00-74	38	14	03	12-16-74	Note 9
Great Britain	02*	09-08-14	00-00-46	02-00-70	55	24	11	12-00-70	Note 1
Italy	01	06-15-34	00-00-65	04-19-71	36	6	3	04-16-71	Note 2 & 7
Sweden	02*	11-27-11	00-00-45	05-15-72	61	27	23	08-16-72	Note 3
United States	14	00-00-13	08-18-38	06-00-73	60	36	00	07-03-73	Note 4 & 8
United States	15*	00-00-25	00-00-00	07-00-72	47	00	00	02-15-73	Note 5

Note 1 Pouring PVC oil mixture onto fabric bases

Note 2 Production of PVC sacks

Note 3 Production of Vinyl Chloride

Note 4 Machine operator covering electrical wire with PVC plastic insulation

Note 5 Accountant at plant making PVC fabric

Note 6 Loading pesticide cans with VC propellant

Note 7 Angiosarcoma involving liver, lung, and pericardium. Although difficult to determine, primary site seems to be pericardium.

Note 8 Diagnosis: Sarcoma (possibly "angiosarcoma"), liver. Possibility of generalized neoplasm of the reticuloendothelial cell system cannot be ruled out.

Note 9 Assistant Factory Chemist

* Indicates microscopically confirmed angiosarcoma of the liver.

"00" Indicates unknown data.

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