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

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

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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.

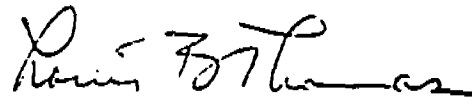
We want to emphasize that we do not think there is any single, histological feature either of the angiosarcomas or of the hepatic fibrosis which is pathognomonic of vinyl chloride exposure. For example, all the changes we've seen in the livers of the VC-PVC workers can apparently be produced by exposure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

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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

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TABLE 1

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

| COUNTRY                                                             | CASE # | BIRTH DATE | 1st VC<br>or PVC<br>EXPOSURE | DX<br>ANGIO-<br>SARCOMA | AGE<br>AT<br>DX | YRS<br>1st EXP<br>TO DX | TOT<br>YRS<br>EXP | DATE OF<br>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         |
| <del>COMPOUNDERS, FABRICATORS, ETC</del><br>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