



MOUNT SINAI SCHOOL OF MEDICINE
of The City University of New York
FIFTH AVENUE AND 100TH STREET • NEW YORK, N.Y. 10029



Gustave L. Levy Distinguished Service Professor

November 1, 1975

Dr. Robert L. Woolridge
Chief, Prevention Branch
Division of Cancer Control and
Rehabilitation
National Cancer Institute, NIH
614 Blair Building
Bethesda, Maryland 20014

Re: Project site visit October 29-30, 1975

Dear Dr. Woolridge:

In the following please find an evaluation report on the Medical Surveillance Program carried out at the University of Louisville under contract No. N01-CN-55121. Drs. Louis B. Thomas and Elliot Alpert are in principle in agreement with this evaluation, however, they have not read or seen the report and I am sending them copies with the request to offer any supplementation or correction if they so wish.

This report is to cover a review of the 90-day definite work scope concerning the plan to implement a cancer control medical surveillance program in a cohort of workers exposed to gaseous vinyl chloride in the B.F. Goodrich plant in Louisville. This evaluation is based on the study of the First Quarterly Technical Progress Report and the Statement of Work as to Implementation and Assessment, and on the Initial Report of the contract, as well as on the additional material which you made available. It is furthermore based on the formal presentations during the site visit and on informal conversations with some of the physicians and scientists active in the program.

Overall, the group has admirably organized their activities. Basically, the proposed plan offers a most useful modality to appreciate the scope of the vinyl chloride problem and to develop the necessary screening procedures, and in addition provides a demonstration model for industrial surveillance in general, particularly for hepatic injury resulting from industrial exposure. It will furthermore generate important scientific information and permit identification of the disease entities created by vinyl chloride.

It appears that the following factors are of major importance in the success of this project:

Dr. John Creech deserves great credit for all the accomplishments. He has not only identified originally the connection between vinyl chloride

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exposure and hepatic angiosarcoma, but he continued to serve as a crucial stimulus in the project by combining an unusually sharp, observing mind, with scientific originality and dedication to the workers, who have great confidence in him. He appears to be the key factor in the success of this project. For instance, I was deeply impressed when he informed me that he studied the wild rats in the factory and that they failed to show any lesions in the liver. He assumes that rats in previous years (for instance four or five years ago) may have shown lesions and that their absence now indicates that in the last two years, the life span of rats, not enough vinyl chloride was in the air to produce a lesion.

The second factor is the excellent cooperation of management and labor. The voluntary expressions of the representatives of labor at the site visit and their understanding of scientific problems were most impressive.

The third factor is the enthusiasm of the physicians and scientists at the University of Louisville.

The examinations of the cohort population of the active workers and their documentation seems to be as well carried out as is possible at this time and represents an excellent example of an industrial surveillance. No recommendation can be made for further improvement. The attempt to obtain information on retired workers is underway, and since they represent an important subject of the study, not only for their own benefit but also for appreciation of the problem, it is strongly suggested that additional efforts be made to include as many of these workers as is possible and that the attempt be continued to obtain autopsy material on retired workers if it should become available. This will give important leads as to additional diseases which might be found in an unexpected incidence. I am raising particularly the question of an increased incidence of primary hepatic carcinoma, of which no case seems to have been reported. However, I learned on October 31 at the Workshop on Hepatocellular Carcinoma at the Fogarty International Center, sponsored by the Division of Cancer Treatment of the NCI, from a presentation by Dr. Thomas Mason that the state economical units around Louisville and around Niagara Falls, New York, have a relative high incidence of primary hepatic carcinoma, as reported in death certificates.

As to the laboratory screening and diagnosis of hepatic disorders, the difficulty still prevails that the "hepatic fibrosis associated with splenomegaly" is ill defined clinically and even functionally and morphologically. It is also at this time not known whether it indeed represents a precursor stage of the angiosarcoma. Since this hepatic fibrosis is not necessarily associated with injury of the hepatocytes, it is at this time questionable whether it will reflect itself in abnormalities of the results of conventional or even sophisticated so-called liver function tests. While obviously these tests have to be carried out,

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the high relative incidence of abnormalities even in preemployment tests, and the fact that unknown factors, viral hepatitis and mild alcoholic liver injury may account for abnormalities, make the evaluation of their results problematic even if they should reflect the hepatic fibrosis. It is therefore very important that the Louisville scientists are trying to obtain additional information on the value of liver enlargement as demonstrated by scanning, and of spleen alterations as recognized by scanning, since that might develop into an important parameter for recognition of vinyl chloride-induced organ injury. In addition, this may serve as an important parameter to recognize industrial injury from other agents in correlation with the exposure index which is being prepared. Correlation of the exposure index with both scanning and biochemical parameters appears to be an important avenue for further studies.

At the site visit there was no opportunity to discuss the results of light-microscopic and electron-microscopic examination of liver biopsy specimens to ascertain early vinyl chloride-induced alterations, and it is hoped that the studies underway in Louisville and elsewhere may serve to identify in the future the early injury.

In general, the hepatic studies seem to be very well planned and conducted and we are looking forward to additional information.

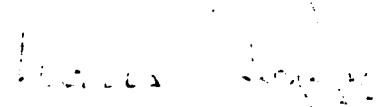
The pulmonary studies are still in an early stage, particularly since it is not known whether vinyl chloride exposure does cause inflammatory and degenerative airway changes. The suggestion of an increased tendency to bronchiogenic carcinoma requires attention by specific techniques, in view of histologic studies on autopsy material indicating a possible higher incidence of clear-cell carcinoma in the lung.

The cardiac studies are at this time obviously a "shot in the dark" and it is difficult at this time to evaluate whether they will be useful, elaborate as they have to be by necessity.

In toto, the progress of the work is most impressive and a better evaluation will only be possible when additional information has been obtained, as doubtlessly will be the case.

With best personal regards,

Very sincerely yours,


Hans Popper, M.D.

HP:lk

CC: Dr. Louis B. Thomas
Dr. Elliot Alpert

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