Dr. Ludwig Hektoen, Chairman
Committee on Cancer Research
National Cancer Institute
Bethesda, Md.

Copy to Dr. OP Rhoads
Memorial Hospital
444 - East 68th
New York

Dear Dr. Hektoen:

In analyzing the result of a recently completed inhalation experiment on asbestosis I was startled to discover that a small group of 11 white mice that had been inhaling asbestos dust from 1.5-5.2 mg. showed an apparent (5.1.39) incidence of pulmonary cancer. This experience was quite at variance with the result in all previous long term dust exposures which were summarized in 1938 & published by Cornwall & Kerr in the American Journal of Pathology Jan. 39. I would have attached little significance to this recent finding because of the small number of animals involved but for the fact that the literature does contain some 10 reports of pulmonary cancer in cases of human asbestosis. Even these cases, however, are not a representative selection of material as it has been found no cases of pulmonary tumors in purely uncomplicated asbestosis workers. However Gloyne, Wiesner & other English observers contend that asbestos has a specific carcinogenic action on the lung.

The question is of considerable importance in industrial medicine because of the associated compensation aspects and from a scientific view point it interests me a great deal.

In view of this recent finding I have analyzed the results of a large number of dust inhalation experiments that have been carried on during the past 5 years to see if evidence of pulmonary tumors is shown in the animals killed. It would appear that except in mice pulmonary tumors is shown in the animals killed. It would appear that except in mice that have been generally uncommon in the strains of different species that we have used, there has been occasional adenomas of the lung, whose incidence is not increased by dust exposure to the type of dust involved. A white mice that survived for 15 or more months on dust rooms - various forms of lung tumors were much more frequent. The average incidence of such tumors in a group of mice exposed to 4 different quartz containing dusts was 12.8% but this figure would rise to the incidence of 81.8% - the asbestos mice. Dr. Gonyea mice that died or were killed after exposure of 10 or more months there was only one instance of lung tumor. Therefore either age or duration of dust exposure must be important

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2. One of the experiments was planned to study carcinogenic effects. Mice were only used as there was space in the dust rooms and many of these animals that died after short exposures were discarded without autopsy as they could have developed a sufficient amount of dust retention. The strain of mice kept in the laboratory has changed from time to time by importation of new stock. At one time we did receive from Dr Maud Slye some cancer susceptible stock but as these animals failed to react to inhaled quartz we lost interest in the early experiments.

Obviously under such conditions the results with asbestos mean nothing but in view of the considerations which I have cited (Kline) they should be checked. From what we have learned about the action of asbestos from a different angle this question would seem particularly relevant.

From what we have learned about the action of asbestos from mineral in the living body would not be surprised to discover that this mineral's carcinogenic effects are different from those of other minerals. Their crystallographic structure is unique. They abrasively act as mechanical irritants rather than chemically as in the case of quartz or other forms of free silica. On crushing or grinding, asbestos fibres lose practically all their cohering capacity, quartz on the other hand becomes more irritating as the particles size decreases. Asbestos produces fibrosis only in the lungs of certain species; quartz experimental reaction in any organ of any species of animal that has been tested. Asbestos seems to have no specific action for pulmonary epithelium but it causes an unusual type of diffuse fibrosis which confines and distorts the epithelial lined respiratory bronchioles but often fails to obliterate them. However, this mechanism would not appear to be the one responsible for the tumors for this is one of the strains which develops no fibrosis or effusions. Possibly the lack of reaction is due to superior respiratory protection against inhaled foreign bodies. The lungs of mice suffer respiratory protection against inhaled foreign bodies. The lungs of mice exposed to asbestos dust for two years appear very little if at all affected as the asbestos fibres are rapidly removed from that peculiar structure known as the alveolar sheet or basket to some other part of the body.

In order to verify our accidental discovery of possible carcinogenic action of fibrous asbestos I would like to repeat the above inhalation experiment under properly controlled conditions. I would need a large number of cancer susceptible mice, splitting each litter into three groups. Each second of the ages of each. One third of the offspring would be kept in a normal atmosphere as a control; another third would be exposed to quartz dust as a second control & the other third would be exposed to asbestos dust. We would attempt

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3/ to obtain 500 mice for each group. The experiments would either only have to be continued for 15 to 24 months. Our routine in such experiments provides for dusting 8 hours a day, 6 days a week. We have all the necessary equipment for such experiments & a trained laboratory personnel. Funds are lacking, however. Our previous study of asbestosis, which continued for a period of 7 years was financed by the Asbestos Association. Since this group of manufacturers, has already invested $30,000 I cannot ask them for further contributions. I discussed the matter w Dr. Rhoads at the Memorial Hospital who favored it & was of the opinion that it was worthy of consideration by your committee. I am therefore applying for a grant of $5000 to cover the cost of the first years expense. I had told Dr. Rhoads that I would be willing to do the entire experiment for this amount and ordinarily I should. However on my return from New York I found two proposals for investigations of the industrial dusts, each of which would yield the Laboratory $5,000 a year. As I have only only two dust rooms free for new work I cannot afford to tie up one of them for two years for half the amount.

Should you be formally informed with this proposal I would appreciate any criticisms or suggestions.

Sincerely yours,

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