INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

April 15, 1965

TO:	Mr. Leon Horowitz	Certain-teed Products Corporation
	Mr. C. L. Shechter	Johns-Manville Corporation
	Mr. F. H. Edwards	Owens-Corning Fiberglas Corporation
	Dr. Lee E. Grant	Pittsburgh Plate Glass Company
	Dr. J. H. Wolfels	U. S. Rubber Company

Attached is an Industrial Hygiene Foundation asbestos and fibreglass three-year research project proposal incorporating suggestions made by those listed above who attended a research planning meeting in my office on April 12, 1965.

Also enclosed is a contractual agreement in an original and one copy; in the event that sponsorship of this project is approved, both should be signed, the carbon returned and the original retained for the sponsor's files.

Sincerely yours,

Robert T. P. deTreville

Robert T. P. deTreville, M.D.
Managing Director

deT:cjc

Enclosures

cc: Mr. Marshall Burch, Owens-Corning Fiberglas Corporation
Dr. G. S. Bishop, Owens-Corning Fiberglas Corporation



Attachment 2

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

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Prospectus for

An Investigation of:
a. The Specificity of Asbestos Bodies and
b. The Biologic Effect of Trace Substances Associated with Chrysotile Asbestos.

INTRODUCTION

Thomas[1] found that about 50% of the people that had died in hospitals in Capetown (200 consecutive autopsies) had "asbestos bodies" in the lungs. The same author[2] found a similar prevalence of "asbestos bodies" among the hospital deaths in Miami, Florida. Cawse, Totten and Gross[3] examined the lungs of 100 consecutive hospital deaths for which autopsy permission had been obtained, and found that 60% of these had "asbestos bodies" in their lungs. Ian Webster[4] recently reported a 67% prevalence in Johannesburg.

There is, at present, a reasonable doubt that "asbestos bodies" are specific indicators of the inhalation of asbestos fibers. Such bodies have been found in coal miners and talc workers where they have been called "pseudo-asbestos bodies." Recently Davis[5] and Collet[6] have demonstrated the intracellular development of "asbestos bodies" secondary to amorphous material.

Asbestos occupies an anomalous position in its ability to produce lung damage, causing diffuse fibrosis as well as the production of lung cancer. It is anomalous inasmuch as no other silicate has been shown to possess this ability. The fibrosis encountered in talcosis is limited to the tremolite variety, which is asbestoriform. On the other hand, the pneumoconiosis associated with the mining of mica (another silicate) has not been investigated experimentally, and the fibrogenic activity of the dusts coexisting with the mica has not been evaluated. Other silicates may evoke either minimal or relatively slight inflammatory changes, and certainly are incapable of producing lung cancer.

Inasmuch as certain polycyclic hydrocarbons and trace metals known to be potent cancer-producing agents have been demonstrated in asbestos, particularly nickel and benzopyrene, the possibility exists that the trace metal and/or the polycyclic hydrocarbon may be solely responsible for the observed carcinogenicity.

This possibility is suggested by two findings:

1. The report of Braun and Truan[7] which indicated that the prevalence of lung cancer among Canadian asbestos miners was no greater than that of the general population. This was in contrast to the report of Doll[8] which indicated a greatly increased risk of lung cancer among British workers exposed to asbestos dust while fabricating the asbestos.

2. In a recent investigation in the laboratory of the Industrial Hygiene Foundation, lung cancers were found in rats exposed for 18 months to high concentrations of chrysotile dust.[9] Because rats exposed to chrysotile dust by other investigators failed to develop lung cancer, there is a good probability

that the chrysotile dust that produced lung cancer was significantly different from that which did not have this effect. It is likely that this difference is caused by a coating of nickel steel alloy applied to the asbestos dust particles during the continuous hammer milling process used for rendering the dust respirable. This method has not been used by previous investigators. Nickel has been found capable of producing lung cancer in trace amounts.

Although asbestos and glass are both silicates, the industrial health experience with workers of these two materials has been vastly different. No pulmonary disease has been reported in workers exposed to glass dust.

However, the dust of fibrous glass has been labeled as highly dangerous in the lay press by association with asbestos. It is a fact that although the effect of flake glass dust on the lungs of animals has been reported, no similar study has been made of the dust of fibrous glass without an associated resin or filler.

PROPOSAL

Phase 1.

It is proposed to examine the response of animals lungs to different inorganic fibrous materials of contrasting chemical composition, and to characterize the differences and similarities in the responses.

Phase 2.

It is proposed to investigate the influence of trace minerals and polycyclic hydrocarbons (i.e., benzopyrene) associated with asbestos ore or the subsequent processing on the long-term response of the lung to the dust.

Another objective of this phase is to obtain definitive data on the long-term effect of dust derived from filamentous glass upon the lungs. Three varieties of such glass dust will be investigated:

1. with the phenol-formaldehyde-type of binder
2. with the binder used in textiles
3. without binder.

MATERIALS AND METHOD

Phase 1.

The following fibrous materials will be reduced to respirable particle size (< 3 μ) and will be injected in amounts of 3.5 mg. to 30 mg. as aqueous suspensions:

1. chrysotile dust (prepared by milling in Wright mill and with demonstrated carcinogenic potential)
2. chrysotile dust (unmilled synthetic)*
3. aluminum nitride
4. tricalcium phosphate (filamentous)
5. fibrous glass
   a. with phenol-formaldehyde-type binder
   b. with binder used for textiles
   c. without binder
6. magnesium hydroxide (brucite)
7. mineral wool
8. zinc oxide (filamentous)

These materials will be injected intratracheally into hamsters under ether anesthesia. Previous experience has demonstrated that asbestos bodies will form in response to chrysotile dust within five months. The animals will therefore be held for six months and then killed.

The lungs will be expanded with buffered formalin under a head of 10 cm. of water. Blocks removed from these lungs will be sectioned at 6 μ

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* Synthetic chrysotile has been prepared at Melion Institute by Dr. William Granquist. Electron photomicrographs show the characteristic tubular crystals.

after paraffin impregnation. These sections will be stained by different methods and photographed sequentially to provide means for studying more completely the tissue reaction to these various materials. Search for the so-called asbestos bodies will be made using routinely stained sections, and sections stained for iron. In addition, unstained cleared sections will be examined under dark-field conditions for asbestos bodies. The latter glow when examined in this manner.

The difference in tissue reaction between the synthetic chrysotile dust and that which is known to be fibrogenic as well as carcinogenic will point to the contribution to pathogenicity made by one or more of the various trace substances which may be associated with chrysotile asbestos dust as a result of processing.

The development of "asbestos bodies", better termed ferritin bodies (Wolfile) by dusts other than asbestos would point to the non-specificity of these structures and to the desirability of collecting such "asbestos bodies" from human lungs in order to subject them to electron-probe analysis. Such analysis could give information in regard to the chemical make-up of the dust responsible for the development of the ferritin ("asbestos") body.

Phase 2.

In order to explore the etiologic role of the various components of chrysotile asbestos in the production of lung fibrosis and lung cancer, six series of rats will be injected intratracheally with the following:

1. chrysotile dust known to be carcinogenic
2. synthetic chrysotile

3. synthetic chrysotile plus nickel
4. synthetic chrysotile plus nickel, plus benzopyrene
5. nickel alone or with carbon as carrier
6. benzopyrene with carbon as carrier.

These rats will be held for two years and then killed. The lungs will be prepared for examination and sections cut in the same manner as in Phase 1.

Three other series of rats will be injected intratracheally with the following dusts:

1. filamentous glass with phenol-formaldehyde-type binder
2. filamentous glass with the binder used for textiles
3. filamentous glass without binder.

These animals will also be held for two years and then killed. The lungs will be prepared and studies as in the preceding groups.

The number of animals per series will be such that there will be no doubt regarding the statistical significance of the results.

PROGRESS REPORTS

A progress report giving the results of Phase 1 will be submitted at the end of 12 months.

An interim report on Phase 2 will be submitted at the end of 24 months, and a final report will be submitted at the end of the third year.

COST

The cost of this investigation is $10,000 per year for three years, or $30,000 for each of the five participating companies.

SUPERVISION

Research will be performed under the direct supervision of Dr. Paul Gross, Director of the Foundation's Research Laboratory. The Foundation's studies on asbestos presently are being conducted under partial support of the U.S. Government through a National Institutes of Health grant and a contract with the U.S. Public Health Service, Division of Occupational Health (Dr. Lewis J. Cralley).

A list of Dr. Gross' publications in the pathology of pulmonary diseases, and a membership information booklet describing laboratory projects presently in progress, are attached.

REFERENCES

1. Thomson, J. G., Kaschula, R. O. C. and MacDonald, R. R. Asbestos as Modern Urban Hazard. S. Afr. Med. J. 36:759, 1962.

2. Thomson, J. G. Asbestos and the Urban Dweller in Biologic Effects of Asbestos. Annals of New York Academy of Sciences 132:196, 1965.

3. Cauna, D., Totten, R. S. and Cross, P. Asbestos Bodies in Human Lungs at Autopsy. J. A. M. A. 188:371, 1963.

4. Webster, L. and Chatzidakis. "Incidence of Asbestos Exposure" pp. 24-25 Annual Report on Medical Research 1963-1964. CSIR Special Report, Pretoria, S. Africa, 1965.

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6. Collet, A.. Personal communication to Dr. Cross, 1964.

7. Brown, D. C. and Truan, T. D. Epidemiological Study of Lung Cancer in Asbestos Miners. Arch. Indust. Health 17:634, 1958.

8. Doll, R. Mortality from Lung Cancer in Asbestos Workers. Brit. J. Indust. Med. 12:81, 1955.

9. Cross, P. and deTreville, R. T. P.: to be published.