

FILE NAME: Johns-Manville (JMA)

DATE: 1966-1968

DOC#: JMA213

DOCUMENT DESCRIPTION: Grant Application, Grant Award, Letter,
Memo

16547
BD
July 11, 1966

H. M. Jackson

Research Fibrous Dusts

Some time ago you asked me to review a proposal on this subject submitted by the Industrial Hygiene Foundation to five companies. After discussions with the Foundation staff, the proposal was revised to include additional dusts, thus broadening the scope of the research. Another sponsor was included.

Recently I met with Dr. Cralley of the U.S.P.H.S., Dr. Vorwald from Detroit, and Dr. Wright from Cleveland, to ascertain if they were undertaking any studies which would duplicate the proposed research in any way. Happily I am able to report that, while they are doing research, there will be no duplication.

Therefore, I strongly recommend that Johns-Manville join the other companies and be a co-sponsor in this research program. A copy of the project and the research agreement are attached.

Pittsburgh Plate Glass and Pittsburgh Corning already have signed their agreements with the Foundation. Mr. Edwards of Owens-Corning Fiberglas has stated that his company is willing to be a co-sponsor. Dr. Wolfis has indicated a similar intent on the part of U. S. Rubber. Certain-teed will follow the example of Johns-Manville.

If approval can be obtained this week, I shall be able to discuss several details with the I.H.F. staff and representatives of some of the other sponsoring companies while attending another meeting in Pittsburgh next week.

Kenneth W. Smith, M.D.

cc: C. W. Hite

Purpose

To obtain factual information concerning the biological effects of asbestos, glass and other materials. This information will be used to refute erroneous and misleading statements which are being made concerning the health hazards associated with the use of asbestos and related fibrous materials.

Scope

A research laboratory program is proposed to study the biologic effects of asbestos fibers, fibrous glass and related fibrous materials. Substances to be investigated will include naturally-occurring chrysotile, amosite, crocidolite asbestos fibers, synthetic chrysotile, fibrous glass, asbestos fibers known to cause cancer in animals, as well as trace elements on the surface of asbestos which may cause cancer.

Sponsors

Certain-teed Products Corp.
Johns-Manville Corp.
Owens-Corning Fiberglas Corp.
Pittsburgh Plate Glass Corp.
Pittsburgh Corning Corp.
U. S. Rubber Company

Research Agency

The Industrial Hygiene Foundation, Pittsburgh, Pa.
Dr. Paul Gross

Cost

Each sponsor will contribute \$20,000.00 per year for three years and \$10,000.00 for the fourth year. This cost may be reduced as the research progresses if additional companies agree to become sponsors.

Recommendation

It is strongly recommended that Johns-Manville be a co-sponsor in this research project. Approval is requested now so that the program may be initiated at once. Personnel, materials and facilities are available at the present time.

COPY

Chen
B. J.
File

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

June 3, 1966

Mr. Jerry Bishop
Wall Street Journal
30 Broad Street
New York, New York 10004

Dear Mr. Bishop:

With regard to my letter of May 27, the attached copies of letters from Dr. J. M. G. Davis and Dr. A. Collet agreeing with Dr. Paul Gross' stand against the Thomson article on asbestos which appeared in the May 1966 issue of the Journal of Pathology may be of interest.

Sincerely yours,

Robert T. P. deTreville

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

deT:sjc

Enclosures

bcc: ☒ Mr. Hugh Jackson

COPY

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

January 10, 1967

Johnson's Study

Dr. J. H. Wolfe
Corporate Medical Director
U. S. Rubber Company
Rockefeller Center
1230 Avenue of the Americas
New York, New York 10020

Dear Jack:

Thanks for your letter of December 23. I have approached the Asbestos Textile Institute (ATI) directly and received an invitation to attend the February 9 meeting of ATI's Board in Cherry Hill, New Jersey.

I will bring Mr. H. E. Sunbury's letter to the attention of our Board of Trustees on February 1 with the recommendation that Dr. Paul Gross' work be continued pending outcome of ATI's evaluation and decision.

By information copy, I am notifying Dr. Kenneth Smith (Johns-Manville), Dr. Joseph Goodman (Raybestos-Manhattan) and Mr. Leon Horowitz (Certain-teed) of this progress in our attempt to complete funding of our project for the Asbestos Industry.

Sincerely,

Bb

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

deTisje

cc: Mr. H. E. Sunbury
Dr. Kenneth Smith
Dr. Joseph Goodman
Mr. Leon Horowitz

PRODUCED
JM - 83

John Wright

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

February 1967

FIBROUS DUST STUDY

REPORT OF PROGRESS IN PHASES 1 & 2

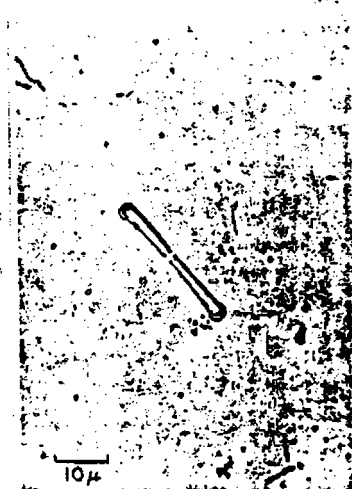
July 1, 1966 - December 31, 1966



Ferruginous Bodies
from lungs of asbestos
worker with asbestosis.



Ferruginous Body from
aluminum silicate fiber
experimentally produced
in hamster lung.



Ferruginous Body from
glass fiber experimentally
produced in hamster lung.

At the present stage of development, it seems certain that results of this study will demonstrate nonspecificity of "asbestos" bodies and justify changing their name to ferruginous bodies from known (e.g., asbestos) or unknown filamentous dusts.

Animals have been injected intratracheally with synthetic chrysotile dust according to the protocol.

Regarding Phase 3, experimental materials and equipment have been procured but purchase of animals is awaiting notification of funding. If funds do not become available, this phase must be set aside temporarily.

An additional aspect, Phase 4, has been added to the study. Electron-photomicrographic studies have been initiated with consideration of electron probe analysis, also.

SPONSORS: Johns-Manville Corporation; Owens-Corning Fiberglas Corporation; Pittsburgh Corning Corporation and Pittsburgh Plate Glass Company.

AN ASSOCIATION OF INDUSTRIES FOR THE ADVANCEMENT OF HEALTHFUL WORKING CONDITIONS

PRODUCED
JM - 83

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

February 1967

FIBROUS DUST STUDY

REPORT OF PROGRESS IN PHASES 1 & 2

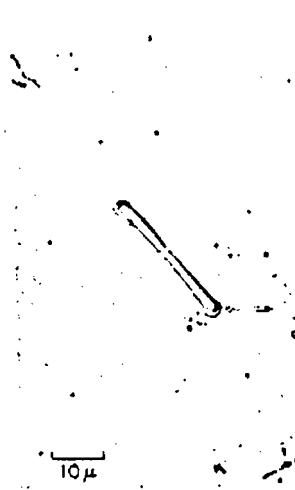
July 1, 1966 - December 31, 1966



Ferruginous Bodies
from lungs of asbestos
worker with asbestosis.



Ferruginous Body from
aluminum silicate fiber
experimentally produced
in hamster lung.



Ferruginous Body from
glass fiber experimentally
produced in hamster lung.

At the present stage of development, it seems certain that results of this study will demonstrate nonspecificity of "asbestos" bodies and justify changing their name to ferruginous bodies from known (e.g., asbestos) or unknown filamentous dusts.

Animals have been injected intratracheally with synthetic chrysotile dust according to the protocol.

Regarding Phase 3, experimental materials and equipment have been procured but purchase of animals is awaiting notification of funding. If funds do not become available, this phase must be set aside temporarily.

An additional aspect, Phase 4, has been added to the study. Electron-photomicrographic studies have been initiated with consideration of electron probe analysis, also.

SPONSORS: Johns-Manville Corporation; Owens-Corning Fiberglas Corporation; Pittsburgh Corning Corporation and Pittsburgh Plate Glass Company.

AN ASSOCIATION OF INDUSTRIES FOR THE ADVANCEMENT OF HEALTHFUL WORKING CONDITIONS

PRODUCED
JM - 83

Note on copy of Transactions:

APPENDIX D

Dr. Angevine —

Please see p. 111 for a picture of a ferruginous body produced by Dr. Gross.

RTP deT.

March 8, 1967

Dr. D. Murray Angevine
Chief Editor, Archives of Pathology
Department of Pathology
University of Wisconsin
School of Medicine
470 North Charter Street
Madison, Wisconsin 53706

Dear Dr. Angevine:

Regarding Dr. Thomson's reply, by way of review, it should be recalled that the following two basic assumptions in his paper (Arch. Path. 81:458, 1966) were challenged:

1. that histopathologists today do not believe that the asbestos body may be nonspecific, and
2. that it is now accepted by most that pleural plaques result from inhalation of asbestos.

In a paper given in October, ¹ Dr. Paul Gross reported early findings of his research² on production of ferruginous bodies with non-asbestos filamentous fibers of respirable size. Scientific questions are properly settled by consideration of such data, not by opinions. The very existence of Dr. Gross' research is adequate proof that Dr. Thomson does not speak for all histopathologists today concerning specificity of so-called asbestos bodies for asbestos inhalation.

Mourman's findings, mentioned by Dr. Thomson, are in accord with those published earlier³ by Dr. Kenneth Smith, who said, "If inhalation of the asbestos fiber alone could cause pleural plaques, one would expect to find plaques wherever the fiber is used." Mourman's conclusion that "the dust that induces the formation of asbestos bodies does not, however, seem to be the sole cause of plaque formation" does not appear to be consistent with the second assumption of Dr. Thomson.

Further work is certainly needed to shed light on this important area, as the occurrence of ferruginous (so-called asbestos bodies) has been found

PRODUCED
JM - 83

Dr. D. Murray Angevine
March 8, 1967
Page 2

in almost half (48%) of the individuals studied at autopsy in Montreal by Thurlbeck.¹ Fortunately, plans for such are being made through cooperative efforts involving industry, government, universities and private institutions, as was pointed out in a recent meeting held by Industrial Hygiene Foundation (IHF) and reported in IHF Medical Series Bulletin No. 11 entitled "Asbestos Bio-effects Research for Industry." A limited number of copies of this publication will be made available to readers of Archives of Pathology upon request without charge while the supply lasts.

Sincerely yours,

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

deT:sjc
cc: Dr. Paul Gross
bcc: Mr. E. K. Davison
Mr. Hugh Jackson

Enclosures: *All four references were sent to Dr. Angevine.*

1. Transactions of Industrial Hygiene Foundation 31st Annual Meeting, 1966.
2. Industrial Hygiene Foundation Medical Series Bulletin No. 11, "Asbestos Bioeffects Research for Industry," 1966.
3. The Pneumoconioses. A.J. Lanza, Editor. Grune & Stratton, Inc., New York, 1963.
4. The Incidence of Asbestos Bodies in the Lungs at Random Necropsies in Montreal. Lily Anjilvel and W. M. Thurlbeck. Can. Med. Assoc. J. 95, 1179-1182, Dec. 3, 1966.

PRODUCED
JM - 83



AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO, ILLINOIS 60610
PHONE (312) 527-1500 • TWX 910-221-0300

D. MURRAY ANGEVINE, MD,
Chief Editor
Department of Pathology
University of Wisconsin
School of Medicine
470 North Charter Street
Madison, Wisconsin 53706

JOHN H. TALBOTT, MD, Director
Division of Scientific Publications

ROBERT W. MAYO,
Executive Managing Editor
NORMAN O. RICHEY,
Managing Editor

ARCHIVES OF PATHOLOGY EDITORIAL BOARD

ARCHIE H. BAGGENSTOSS, MD, Rochester, Minn.
KENNETH M. BRINKHOUS, MD, Chapel Hill, N.C.
JOSEPH FELDMAN, MD, La Jolla, Calif.
SAMUEL P. HICKS, MD, Ann Arbor, Mich.
PAUL KOTIN, MD, Bethesda, Md.
PAUL E. LACY, MD, St. Louis
HENRY D. MOON, MD, San Francisco
JOHN L. SHAPIRO, MD, Nashville, Tenn.
C. BRUCE TAYLOR, MD, Evanston, Ill.

April 4, 1967

Robert T. P. deTreville, M.D.
Managing Director
Industrial Hygiene Foundation of America, Inc.
Mellon Institute, 4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213

Dear Dr. deTreville:

I wish to thank you for your letter of March 8 together with enclosures. After careful consideration, I do not believe it advisable to publish further correspondence on this matter in the Archives of Pathology. It would seem that after the initial exchange of opinions in print that further discussion should be by correspondence of participating parties.

I assure you that this is not a deliberate attempt to curtail debate but rather than a continuation of it may not be of large reader interest.

Sincerely yours,

D. Murray Angevine

D. Murray Angevine, M.D.
Chief Editor
Archives of Pathology

DMA:cg

PRODUCED
JM - 83

JOHNS-MANVILLE
RESEARCH & ENGINEERING CENTER

P.O. BOX 159 • MANVILLE, NEW JERSEY • TELEPHONE: (201) RANDOLPH 2-9000



April 12, 1967

Dr. Paul Gross
Director of Research Laboratory
Industrial Hygiene Foundation of America, Inc.
Mellon Institute
4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213

Dear Dr. Gross:

I am sending, under separate cover, two samples of synthetic chrysotile for use in your research. These samples were prepared by Dr. Julie Yang of our laboratory. The sample labeled "Synthetic Chrysotile" is the purest material we have been able to synthesize. The impurities which are present (see attached table of properties) were probably contaminants in the magnesium hydroxide used as a raw material. It is unfortunate that we were not able to grow longer fibrils, but this requires the use of a mineralizer which would introduce unwanted impurities into the system.

The sample labeled "Ni-containing Synthetic Chrysotile" contains 2.2 per cent nickel. The nickel is most probably in the divalent form and substituted for the magnesium in the chrysotile lattice. Electron micrographs of both samples are attached.

Very truly yours,

James P. Leinweber, Chief
Basic Chemistry Research Section

mac

Attachment

PRODUCED
JM - 83

ATTACHMENT

	Synthetic Chrysotile	Synthetic Ni-Chrysotile
X-ray Diffraction	Chrysotile	Chrysotile
Electron Micrographs		
A. Morphology	Fibrous	Fibrous
B. Size	Up to 5 microns	Up to 2 microns
Ignition Loss @ 1800F	13.2%	12.7%
Impurities* by Emission Spectrograph		
Al	0.018%	0.02
Ca	0.18%	0.14
Fe	0.017%	0.06
Cr	--	0.06
Cu	--	0.10
Ni	--	2.2

*Concentrations reported as element, not oxides

PRODUCED
JM - 83

July 11, 1966

H. W. Jackson

Research Fibrous Dusts

Some time ago you asked me to review a proposal on this subject submitted by the Industrial Hygiene Foundation to five companies. After discussions with the Foundation staff, the proposal was revised to include additional dusts, thus broadening the scope of the research. Another sponsor was included.

Recently I met with Dr. Gralley of the U.S.P.H.S., Dr. Vorwald from Detroit, and Dr. Wright from Cleveland, to ascertain if they were undertaking any studies which would duplicate the proposed research in any way. Happily I am able to report that, while they are doing research, there will be no duplication.

Therefore, I strongly recommend that Johns-Manville join the other companies and be a co-sponsor in this research program. A copy of the project and the research agreement are attached.

Pittsburgh Plate Glass and Pittsburgh Corning already have signed their agreements with the Foundation. Mr. Edwards of Owens-Corning Fiberglas has stated that his company is willing to be a co-sponsor. Dr. Wolfstie has indicated a similar intent on the part of U. S. Rubber. Certain-teed will follow the example of Johns-Manville.

If approval can be obtained this week, I shall be able to discuss several details with the I.H.F. staff and representatives of some of the other sponsoring companies while attending another meeting in Pittsburgh next week.

Kenneth W. Smith, M.D.

cc: C. W. Rite

14-83

Purpose

To obtain factual information concerning the biological effects of asbestos, glass and other materials. This information will be used to refute erroneous and misleading statements which are being made concerning the health hazards associated with the use of asbestos and related fibrous materials.

Scope

A research laboratory program is proposed to study the biologic effects of asbestos fibers, fibrous glass and related fibrous materials. Substances to be investigated will include naturally-occurring chrysotile, amosite, crocidolite asbestos fibers, synthetic chrysotile, fibrous glass, asbestos fibers known to cause cancer in animals, as well as trace elements on the surface of asbestos which may cause cancer.

Sponsors

Certain-teed Products Corp.
Johns-Manville Corp.
Owens-Corning Fiberglas Corp.
Pittsburgh Plate Glass Corp.
Pittsburgh Corning Corp.
U. S. Rubber Company

Research Agency

The Industrial Hygiene Foundation, Pittsburgh, Pa.
Dr. Paul Gross

Cost

Each sponsor will contribute \$20,000.00 per year for three years and \$10,000.00 for the fourth year. This cost may be reduced as the research progresses if additional companies agree to become sponsors.

Recommendation

It is strongly recommended that Johns-Manville be a co-sponsor in this research project. Approval is requested now so that the program may be initiated at once. Personnel, materials and facilities are available at the present time.

PRODUCED
JM - 83

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

AGREEMENT FOR SPONSORED RESEARCH

THIS AGREEMENT, made and entered into this fifteenth day of April, 1966, by and between JOHNS-MANVILLE CORPORATION hereinafter referred to as "SPONSOR", and INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC., a nonprofit corporation hereinafter referred to as "RESEARCHER".

WITNESSETH:

RECITAL OF FACTS:

SPONSOR desires the services of the RESEARCHER in the conduct of study, research, development and other work related to and for the purpose of gaining useful knowledge in the following matter:

dusts An investigation of the factors involved in the pathogenicity of asbestos dust, their applicability to filamentous glass dust, and the specificity of the so-called asbestos (ferritin) bodies. ?

hereinafter referred to as the PROJECT. RESEARCHER desires to undertake this PROJECT for the SPONSOR, both parties agreeing to the terms and conditions hereinafter set forth.

PRODUCED
100 - 83

NOW, THEREFORE, in consideration of the premises and of the mutual promises and covenants herein contained, the parties hereto agree as follows:

1. Undertaking.

SPONSOR engages RESEARCHER to carry out the PROJECT by conducting study, research, development and other work therein and thereupon, and the RESEARCHER agrees to undertake and carry out the PROJECT using its best efforts in performing such work and devoting to it such time and attention as is reasonably required for the sufficient progress of the PROJECT. The PROJECT will be under the direct supervision of the RESEARCHER'S Research Pathologist.

2. Effective Date, Term and Termination:

This agreement shall become effective on June 1, 1966 and shall terminate on May 31, 1969.

3. Progress Reports.

RESEARCHER agrees to make progress reports periodically as indicated, setting forth the findings and progress made in the course of the PROJECT and other information pertinent thereto. The final report will be submitted May 31, 1969.

4. Publication Rights.

It is also agreed that no advertising, promotional, or publicity matter containing any reference to the RESEARCHER or to any of its employees, shall be made use of by the SPONSOR or anyone in the SPONSOR'S behalf, unless and until the same shall have first been submitted to and received the approval in writing of the RESEARCHER. The RESEARCHER reserves exclusive right to publication of material developed in the Industrial Hygiene Foundation of America, Inc. Research Laboratory in suitable scientific *timing* journals if the results of the research merit publication; however, the RESEARCHER will not publish any findings in association with the name of the SPONSOR unless the SPONSOR gives permission.

5. Charges.

RESEARCHER'S charge for partial support of the Industrial Hygiene Foundation of America, Inc. Laboratory Research in carrying out the PROJECT and partially covering compensation to personnel engaged in carrying on the work, clerical and consultative services and preparation and printing of a report will be Ten Thousand Dollars (\$10,000) from *July* June 1, 1966 to May 31, 1967; Ten Thousand Dollars (\$10,000) from June 1, 1967 to May 31, 1968; and Ten Thousand Dollars (\$10,000) from June 1, 1968 to May 31, 1969.

6. Independent Contractor.

It is agreed and understood that the RESEARCHER is acting as an independent contractor in the performance of any and all work hereunder

and that the SPONSOR shall not be liable and responsible for the payment of any and all legal claims for damages made by the RESEARCHER'S employees or agents, or by any other person or persons, on account of any property damage or personal injury sustained or suffered by, or the death of, any person or persons arising or growing out of, or in connection with, the performance of this agreement, or any act or omission in connection herewith, and RESEARCHER hereby indemnifies and agrees to hold SPONSOR harmless against any and all such claims.

IN WITNESS WHEREOF, the parties hereto have executed this agreement on the day and year first above written.

JOHNS-MANVILLE CORPORATION

BY _____

SPONSOR

INDUSTRIAL HYGIENE FOUNDATION
OF AMERICA, INC.

BY



Managing Director

RESEARCHER

PRODUCED
83

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

June 1, 1966

Prospectus for

An Investigation of:

- a. The Specificity of Asbestos Bodies and
 - b. The Biologic Effects of Trace Substances
Associated with Chrysotile Asbestos.
-

INTRODUCTION

Thomson⁽¹⁾ found that about 30% of the people that had died in hospitals in Capetown (500 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. Cauna, Totten and Gross⁽³⁾ examined the lungs of 100 non-selected hospital deaths for which autopsy permission had been obtained, and found that 40% of these had "asbestos bodies" in their lungs. Ian Webster⁽⁴⁾ recently reported a 47% 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 and possibly also 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 asbestos-like. 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 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, chromium and benzopyrene, the possibility exists that the trace metals and/or the polycyclic hydrocarbons may be solely responsible for the observed pathogenicity.

This possibility is supported 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 possible 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.

Nevertheless, the dust of filamentous 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 filamentous glass which does not have 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 response.

Phase 2.

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

**PRODUCED
JM - 83**

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 binders used in textiles
3. without binder.

Phase 3.

A comparative study of the three main types of asbestos dust (chrysotile, amosite and crocidolite) is proposed to attempt to pinpoint the cause of biological activity—i. e., whether due to silicates per se or the associated trace metals or hydrocarbons. Positive findings would be a basis for identifying any possible health hazards and for suggesting specific engineering or other process controls to eliminate such hazards.

MATERIALS AND METHOD

Phase 1.

The following fibrous materials will be reduced to respirable particle size ($<3\mu$) 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)

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

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. Asbestos bodies will be sought in lung juice as well as in the lung tissues.

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 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 Ferruginous bodies, to 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 Ferruginous ("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⁽⁹⁾
2. synthetic chrysotile
3. synthetic chrysotile plus nickel
4. synthetic chrysotile plus chrome
5. synthetic chrysotile plus nickel, chrome and benzopyrene
6. nickel alone or with carbon as carrier
7. chrome alone or with carbon as carrier
8. 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 binders 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 studied as in the preceding groups, with special attention to asbestos bodies in lung tissues or juice.

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

**PRODUCED
JM - 83**

Phase 3.

SUPPLEMENTARY PROPOSAL

(Note: The following supplement has been added to the original proposal of April 15, 1966.)

INTRODUCTION

Because of the interest of a number of companies in biologic investigations similar to those planned for chrysotile asbestos, but using instead, amosite and crocidolite, an additional investigation is proposed to be undertaken concurrently with the one proposed April 15, 1966.

As in the proposal dealing with chrysotile asbestos, the purpose of the presently proposed concurrent investigation is to attempt to pinpoint the cause of the biologic activity of all three main types of asbestos dusts: whether this lies in the silicates per se, in the associated trace metals, or in the associated hydrocarbons.

Because neither amosite nor crocidolite is available as a pure synthetic material, the investigation proposed for these two types of asbestos is necessarily different from that proposed for chrysotile. Nevertheless, in order to make the investigation complete, it is desirable to include also chrysotile in the new investigation since different methods are involved.

Inasmuch as the biologic activity of asbestos seems to have two components: (a.) inflammatory—responsible for asbestosis, and (b.) neoplastic—responsible for lung cancer and mesothelioma, it is advisable to

PRODUCED
JM - 83

investigate both of them. This can readily be accomplished within the four year span contemplated for this investigation.

In order to determine whether the biologic activity of asbestos resides in the silicate, in the associated trace metals, or in the associated hydrocarbons, attempts will be made to remove the trace metals and the hydrocarbons from their respective silicates and to compare the biologic activities of such "purified" asbestos samples from which these associated materials have been removed.

PROPOSAL

As a prerequisite to any biologic testing (insofar as the lungs are concerned), it is necessary to reduce the asbestos to a respirable particle size. This will be done in the following manner: the amosite and crocidolite will be ball-milled and then fed into continuous hammer mills modified from a design by Holt and Young.⁽¹⁰⁾ The dusts emerging from the hammer mills will be collected in electrostatic precipitators. This method has been used successfully by us to reduce chrysotile asbestos to a particle size, 70% of which was respirable. A sufficient quantity of finely divided chrysotile dust is available for the purposes of this investigation.

All three types of asbestos dust will be deprived of the greater portion or of all of their hydrocarbon content in one of two ways:

1. by continuous extraction with various solvents
2. by heating beyond the decomposition point of the hydrocarbons.

The trace metals will be removed from the three types of asbestos dust by treatment with aqua regia followed by treatment with EDTA (ethylene diamine tetraacetic acid, a chelating agent).

**PRODUCED
JM - 83**

One batch of each type of asbestos dust will be subjected to both procedures, i.e., removal of trace metals and removal of hydrocarbons.

Accordingly, each of the three types of asbestos dust will consist of five batches, each with a different composition:

1. the unaltered dust as collected in the precipitators
2. the dust minus the hydrocarbons (heat-treated). Here, it is anticipated that there may also have been some change in the chemical structure of the asbestos through loss of some molecules of water of hydration.
3. the dust minus the hydrocarbons (solvent extraction). Here, it is anticipated that the extraction may not be 100% complete.
4. the dust minus trace metals
5. the dust minus trace metals then subjected to solvent extraction to remove most of the hydrocarbons.

In order to investigate the inflammatory component of the various (15) batches of asbestos dust, these will be injected intratracheally into rats and hamsters. The lungs of these animals are expected to show definitive changes within one year after the intrapulmonary introduction of the dusts.

In order to explore the lung cancer aspect of the neoplastic component of the biologic activity of asbestos dust, additional rats will be injected with the same batches of dust as above and allowed to live out their lives. Most of the animals, however, will have died before the end of the third year.

The other (mesotheliomatous) aspect of the above neoplastic component will be investigated by injecting the 15 different batches of asbestos dust within the pleural cavity of rats and hamsters and allowing them to live out their lives. Most of these animals will also have died before the end of the third year.

For the investigation of the inflammatory component of asbestos dust, a large enough number of animals will be put on test to allow sampling at intervals throughout the year and still have an adequate number remaining to represent the 12 month old lesion.

A tabular summary of the protocol is attached.

REPORTS

Definite trends in regard to the inflammatory component are expected to be demonstrable in animals that will be killed prior to the 12 month period (as indicated under footnote (b) in the Tabular Summary). An interim report covering the findings in these 420 animals will, therefore, be issued at the end of the first year.

Because few, if any, tumors are expected to develop prior to 24 months, no interim report on the neoplastic component will be issued until the end of the third year. The final report covering the entire investigation will be issued toward the end of the fourth year. This report will probably be in the form of several manuscripts suitable for publication.

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).

PRODUCED
JM - 83

TABULAR SUMMARY OF PROTOCOL

Type of Asbestos	Batch (a)	Dust Injected Intratracheally		Dust Injected Intrapleurally	
		for		for	
		Inflammatory Component		Lung Cancer	
		No. Rats (b)	No. Hamsters (b)	No. Rats (c)	No. Hamsters (c)
Chrysotile	1	20	20	20	20
	2	20	20	20	20
	3	20	20	20	20
	4	20	20	20	20
	5	20	20	20	20
Amosite	1	20	20	20	20
	2	20	20	20	20
	3	20	20	20	20
	4	20	20	20	20
	5	20	20	20	20
Crocidolite	1	20	20	20	20
	2	20	20	20	20
	3	20	20	20	20
	4	20	20	20	20
	5	20	20	20	20
TOTALS		300	300	300	300

(a) The following batches are identified:

No. 1 = dust as collected from electrostatic precipitators

No. 2 = dust extracted with solvents

No. 3 = dust heated to decompose hydrocarbons

No. 4 = dust treated with aqua regia and EDTA

No. 5 = dust treated as with No. 4 and No. 2

(b) Two animals killed immediately after the dust injection

Four animals killed 4 days after the dust injection

Four animals killed 1 month after the dust injection

Four animals killed 6 months after the dust injection

Six animals killed 12 months after the dust injection

(c) All animals allowed to live out there lives

PRODUCED
JM - 83

REFERENCES

1. Thomson, J.G., et al. Asbestos as Modern Urban Hazard. S. Afr. Med. J. 37:77-81, 1963.
2. Thomson, J.G., et al. Asbestos as an Urban Air Contaminant. Arch. Pathol. 81:458-464, May 1966.
3. Cauna, Dzidra; Totten, Robert S.; and Gross, Paul. Asbestos Bodies in Human Lungs at Autopsy. JAMA 192:371-373, May 3, 1965.
4. Webster, Ian. Report of progress quoted in the Annual Report of the Pneumoconiosis Research Unit of the South African Council for Scientific and Industrial Research. 1965.
5. Davis, J.M.G. Electron-Microscope Studies of Asbestosis in Man and Animals. Ann. N.Y. Acad. Scie. 132:98-111, 1965.
6. Collet, A. Personal Communication, 1965.
7. Braun, Daniel C. and Truan, T. David. An Epidemiological Study of Lung Cancer in Asbestos Miners. AMA Arch. Ind. Health 17: 634-653, June 1958.
8. Doll, R. Mortality from Lung Cancer in Asbestos Workers. Brit. J. Ind. Health 12:81, 1955.
9. Gross, P. and deTreville, R.T.P. Experimental Asbestosis: Studies on the Progressiveness of the Pulmonary Fibrosis Caused by Chrysotile Dust. To be published.
10. Holt, P.S. and Young, D. K. A Dust-Feed Mechanism Suitable for Fibrous Dust. Ann. Occ. Hyg. 2:245, 1960.

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

REC'D

PITTSBURGH, PA. 15213

June 3, 1966

1HF Fibrous Dust Study

TO: Mr. Leon Horowitz
Mr. C. L. Sheckler
Mr. F. H. Edwards
Dr. Lee B. Grant
Dr. J. H. Wolfstie

Certain-teed Products Corporation
Johns-Manville Corporation
Owens-Corning Fiberglas Corporation
Pittsburgh Plate Glass Company
U. S. Rubber Company

Regarding my letter of April 14, during the past month it has become apparent that the Foundation's original proposal for an investigation of the specificity of asbestos bodies and the biologic effects of trace substances associated with chrysotile asbestos was not sufficiently comprehensive, in that it did not cover the amosite and crocidolite forms of asbestos which are of interest to industry. It will be recalled that the original study depended on the availability of synthetic chrysotile (through Mellon Institute); inasmuch as synthetic amosite and crocidolite are not available, Dr. Gross suggests that a separate, additional study (attached) be performed concurrently.

The supplemental study requires more animals and will be extended an additional year. It is thus estimated that the original budgetary requirements will be \$100,000 during the first three years and \$50,000 in the fourth for a total of \$350,000. Each sponsor listed above would thus pay \$20,000 during the year July 1, 1966 to June 30, 1967. The Foundation is prepared to undertake these studies if sponsors listed will sign both copies of the Revised Agreement for Sponsored Research, returning one copy and retaining the other for sponsor's files.

It now appears that support for the second, third and fourth years may very well develop on a broader base; Dr. Gross has been invited to present our proposal before the Asbestos Textile Institute on June 9 and a similar briefing will be scheduled for the National Insulation Manufacturers Association (and also any other large asbestos manufacturing companies not covered under these industrial associations).

From informal discussions during the past month, it is our impression that each company receiving this letter wishes to keep on schedule, and have the Foundation initiate work on July 1. A prompt response, indicating approval, would provide Dr. Gross with a stronger proposal to present to the Asbestos Textile Institute on June 9, in hopes of extending the base of support; this would, of course, be very advantageous from many respects.

Please call Dr. Gross or me if further questions arise.

Sincerely yours

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

Enclosures

AN ASSOCIATION OF INDUSTRIES FOR THE ADVANCEMENT OF HEALTHFUL WORKING CONDITIONS

PRODUCE
JM - 83

CHQ

June 8, 1966

H. M. Jackson

cc: Dr. K. W. Smith ←

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA
STUDY OF FIBROUS MATERIALS

I received a revised copy of the IHF proposed study and contract forms. It appears that this proposal includes amosite and crocidolite forms of asbestos.

The financial aspects of the IHF study is somewhat confusing. Originally, there were five corporations involved with the request that each corporation pay \$10,000 a year for a three year period and the USPHS would supplement that sum over a three year period. The cost between the April 14th letter and present date has increased to \$20,000 a year per corporation for three years plus \$10,000 for one additional year or as I interpret the contract, the total per corporation would now be \$70,000 for three years instead of \$30,000 for the same period.

The additional research work concerning amosite and crocidolite fibers certainly could not possibly increase the cost over double.

I am very much concerned that this new proposal has priced itself right out of existence. I doubt very much that Certain-teed Products, U. S. Rubber and Pittsburgh Plate Glass will agree to an expenditure of this size, considering that their interest in amosite and crocidolite is minimal. Unless, this is a joint industry study with at least the five original corporations participating it could very well result in being labelled biased and we would find ourselves in the same position at the Ethyl Corporation and their lead studies.

I have forwarded the June 3rd IHF letter, proposal and contracts to Dr. Smith.

C. L. Sheekler

PRODUCED
UM 83

6/1/66
INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

IHF Fibrous Dust Study

PITTSBURGH, PA. 15213

REVISED AGREEMENT FOR SPONSORED RESEARCH*

THIS AGREEMENT, made and entered into this first day of June, 1966, by and between JOHNS-MANVILLE CORPORATION hereinafter referred to as "SPONSOR", and INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC., a nonprofit corporation hereinafter referred to as "RESEARCHER".

WITNESSETH:

RECITAL OF FACTS:

SPONSOR desires the services of the RESEARCHER in the conduct of study, research, development and other work related to and for the purpose of gaining useful knowledge in the following matter:

An investigation of the factors involved in the pathogenicity of asbestos dusts, and of filamentous glass dusts, and the specificity of the so-called asbestos (ferruginous) bodies

hereinafter referred to as the PROJECT. RESEARCHER desires to undertake this PROJECT for the SPONSOR, both parties agreeing to the terms and conditions hereinafter set forth.

* Supersedes Agreement for Sponsored Research dated April 15, 1966.

PRODUCED
JM - 83

NOW, THEREFORE, in consideration of the premises and of the mutual promises and covenants herein contained, the parties hereto agree as follows:

1. Undertaking.

SPONSOR engages RESEARCHER to carry out the PROJECT by conducting study, research, development and other work therein and thereupon, and the RESEARCHER agrees to undertake and carry out the PROJECT using its best efforts in performing such work and devoting to it such time and attention as is reasonably required for the sufficient progress of the PROJECT. The PROJECT will be under the direct supervision of the RESEARCHER'S Research Pathologist.

2. Effective Date, Term and Termination.

This agreement shall become effective on July 1, 1966 and shall terminate on June 30, 1967. At the termination of each contract year, agreements for continued support for subsequent years will be submitted.

3. Progress Reports.

RESEARCHER agrees to make progress reports periodically as indicated, setting forth the findings and progress made in the course of the PROJECT and other information pertinent thereto. The final report will be submitted June 30, 1970.

4. Publication Rights.

It is also agreed that no advertising, promotional, or publicity matter containing any reference to the RESEARCHER or to any of its employees, shall be made use of by the SPONSOR or anyone in the SPONSOR'S behalf, unless and until the same shall have first been submitted to and received the approval in writing of the RESEARCHER. The RESEARCHER reserves exclusive right to publication of material developed in the Industrial Hygiene Foundation of America, Inc. Research Laboratory in suitable scientific journals if the results of the research merit publication; however, the RESEARCHER will not publish any findings in association with the name of the SPONSOR unless the SPONSOR gives permission.

5. Charges.

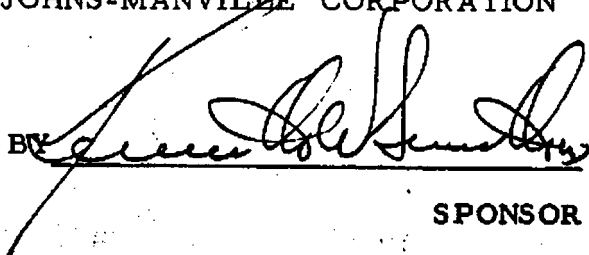
RESEARCHER'S charge for partial support of the Industrial Hygiene Foundation of America, Inc. Laboratory Research in carrying out the PROJECT and partially covering compensation to personnel engaged in carrying on the work, clerical and consultative services will be Twenty Thousand Dollars (\$20,000) for the period extending from July 1, 1966 to June 30, 1967. (Continued support for the period extending from July 1, 1967 to June 30, 1970 will be a maximum of \$20,000 per SPONSOR per year for the second and third years and \$10,000 for the fourth year. It is hoped that additional SPONSORS will support the project in the second, third and fourth years, thereby reducing the total cost per SPONSOR in subsequent years.)

6. Independent Contractor.

It is agreed and understood that the RESEARCHER is acting as an independent contractor in the performance of any and all work hereunder and that the SPONSOR shall not be liable and responsible for the payment of any and all legal claims for damages made by the RESEARCHER'S employees or agents, or by any other person or persons, on account of any property damage or personal injury sustained or suffered by, or the death of, any person or persons arising or growing out of, or in connection with, the performance of this agreement, or any act or omission in connection herewith, and RESEARCHER hereby indemnifies and agrees to hold SPONSOR harmless against any and all such claims.

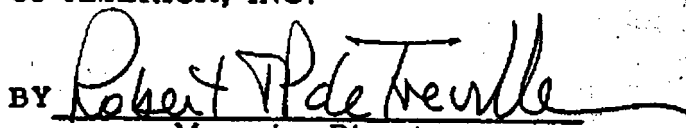
IN WITNESS WHEREOF, the parties hereto have executed this agreement on the day and year first above written.

JOHNS-MANVILLE CORPORATION

BY 

SPONSOR

INDUSTRIAL HYGIENE FOUNDATION
OF AMERICA, INC.

BY 

Managing Director

RESEARCHER



ESTABLISHED 1935

(412) 687-2100

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

5231 CENTRE AVENUE

PITTSBURGH, PA. 15232

December 23, 1968

TO THE SPONSORS OF IHF FIBROUS DUST STUDY:

✓Mr. Hugh M. Jackson
Mr. Russell Brittingham
Dr. Lee B. Grant
Dr. Jon L. Konzen
Dr. Joseph L. Goodman

Johns-Manville Corporation
Pittsburgh Corning Corporation
PPG Industries
Owens-Corning Fiberglas Corporation
Raybestos-Manhattan, Inc.

In the past our reports of progress usually have been submitted to sponsors on dates specified in our research agreements.

We are now considering instituting quarterly reports, and our first such attempt is enclosed herewith. To supplement the written text we have developed a new system of tabulation, which we hope will aid its comprehensibility.

Your comments, pro or con, are solicited to guide our future efforts in your behalf.

Best wishes for the holiday season and New Year.

Sincerely,

Robert T. deTreville

Robert T. P. deTreville, M.D.
President

deT:ejd

Enclosure

cc: Mr. C. L. Sheckler

PRODUCED
JM - 83