SAINT LUKE'S HOSPITAL
of the Methodist Church
11311 SHAKER BOULEVARD
CLEVELAND, OHIO 44104

April 8, 1969

Mr. Frank Zimmerman
National Gypsum Company
325 Delaware Avenue
Buffalo, New York 14202

Dear Frank,

Enclosed is a copy of the proposal that has been submitted to our Scientific Committee by Doctors, Weill and Ziskind of New Orleans. Our Committee has not looked at this officially as yet, and will not do so until sometime in May. It has been circulated.

As I indicated to you on the telephone today, I hope that you will look at this, especially from the point of view of whether or not there is anything there that might be troublesome for National Gypsum Company, and which we could avoid by making the necessary adjustments at the outset. I can only repeat that these are two very high-caliber people, and they are as anxious as I am to do the work properly and without causing disturbance where it is at all avoidable.

I will be in town on Monday, the 14th, and if there are any problems will appreciate knowing about it on that day. I will be seeing Bill Duncan on the 18 and 19th and will talk to him about it.

With best wishes,

Sincerely yours,

George W. Wright, M.D.
Director of Medical Research

GWW:vk
Enclosure

A STUDY OF THE HEALTH EFFECTS RELATED TO ASBESTOS EXPOSURE IN WORKERS OF THE INDUSTRY AND OTHER RESIDENTS OF NEW ORLEANS

Introductory Statement

New Orleans is well represented in the manufacture of asbestos cement products, an industry which accounts for the major use of asbestos fiber in the United States. There has been increasing interest in the role of long term asbestos fiber inhalation in the production of pulmonary and pleural neoplasms. This interest extends not only to the workers in the manufacturing plants using asbestos materials but also to the community at large, particularly those individuals living in areas adjacent to the industrial installations where the fiber is used. Carcinogenic or co-carcinogenic properties of asbestos have become apparent since improved industrial hygiene techniques have led to dust suppression with the result that workers incur a smaller risk of early development of diffuse pulmonary fibrosis and cor pulmonale. In addition, the better control of infectious diseases has also resulted in greater longevity for the workers and larger numbers are surviving to develop malignancies. Since pleural mesotheliomas have been adequately associated with prolonged exposures to asbestos dust, these tumors in addition to the pulmonary and gastrointestinal carcinomas and peritoneal mesotheliomas must be sought for in populations thought to be at increased risk due to their occupational or geographic proximity to the asbestos industry.

Although the clinical, radiographic, and pulmonary physiologic abnormalities encountered in classical cases of asbestosis have been recognized for many years, several patterns of diffuse lung disease have emerged in local plant workers. These different radiographic and physiologic patterns are undoubtedly related to varying mixed dust exposures, although all of these workers who develop diffuse pulmonary infiltrations with or without respiratory functional impairment are labelled as having "asbestosis". The investigators have evidence that a significant number of these workers may actually have simple silicosis or silico-asbestosis as a result of exposure to silica dust in the plants which produce asbestos cement products. There is an obvious need for identifying these individuals with abnormal deposits in their lungs, correlating the x-ray, clinical and physiologic changes with the exact nature of their work exposures and properly identify their pulmonary disease. It is of interest to note that inhalation of asbestos dust has been thought to foster the retention of quartz dust with a resultant pulmonary disease which followed sooner and attained a more serious grade than could have been expected on the basis of mere additive action. Whether this experimental finding has clinical application in the production of disease in workers of this industry should be investigated. The importance of correlating radiologic changes with pulmonary functional impairment is further demonstrated by the finding that where this mixed dust exposure produced widespread nodulation (as seen in workers from the local manufacturing installation) it was associated with little or no clinical symptoms and normal pulmonary function.

Research Plan:

It is proposed that this investigation be conducted in two phases, one involving the workers of the Johns Manville and National Gypsum Plants in New Orleans, and the other dealing with selected portions of the New Orleans population outside the plant. During the first year, the Phase I investigation will be actively started as outlined below. The community study, or Phase II, will undergo intensive planning during the first year with full employment of consultative resources so that a meaningful active program can be started at the beginning of the second year, aimed at assessing the risk of the development of pulmonary or pleural neoplasia outside the plant but as the result of prolonged environmental exposure to asbestos dust. Marked stability of residence in the New Orleans population will significantly aid the follow-up of the study groups.

I. Phase I

The aim of this portion of the investigation is to determine the frequency, functional effect, and extent of abnormal diffuse pulmonary infiltrations secondary to occupational dust exposures in the Johns Manville and National Gypsum plants which in New Orleans produce a variety of asbestos cement products. Current chest x-ray films, including the PA, right anterior oblique and left anterior oblique projections, will be carefully examined in all workers for the presence of abnormal parenchymal infiltrations. Individuals with abnormal lung fields will be further studied in the Pulmonary Function Laboratory, Department of Medicine, Tulane University School of Medicine.

At this time, complete clinical information will be gathered with particular emphasis on the detailed occupational history, the presence of respiratory or cardiovascular symptoms, and the physical examination. These individuals will then have complete studies of pulmonary function including the measurements of lung volume; ventilatory capacity, including the parameters of air flow rates; pulmonary mechanics, including compliance and airway resistance, arterial blood gas measurements at rest and during exercise; and determination of the pulmonary diffusing capacity, using the carbon monoxide single breath method. Clinical, radiographic, and physiologic data obtained will be correlated with the length and type of work exposure. Plant records and previous medical history will be fully utilized for this purpose.

The incidence of pleural fibrosis and/or calcification will be determined in this group of workers. Pulmonary function studies will also be completed in those individuals with pleural changes but no detectible infiltrations in the lungs. All the workers will have a brief questionnaire administered in order to survey the presence of respiratory symptoms and, in addition, simple ventilatory tests performed in order to detect the presence and severity of diffuse airways obstruction so that this process will not be confused with the potential effect of prolonged dust exposure.

An important part of this investigation will be its prospective aspects, which will include the careful clinical, physiologic, and radiographic follow-up of all of these workers in future years, whether they continue employment in

the plant, retire, or change to another type of work. The late development of pleural or pulmonary changes will thus be detected even though asbestos exposure has not been continuous. It is suggested that all future employees at these two plants be included in this study and have pre-employment radiographic and ventilatory examination. In this way changes related to the development of chronic obstructive pulmonary disease can be separated from dust effects on the lungs.

The identification of pulmonary, pleural, or abdominal malignancies in these workers will, of course, result from the study as outlined above. In addition, individuals who have worked in these plants in the past will be carefully traced and their current health surveyed. In those workers who have expired, an energetic attempt will be made to ascertain the cause of death and, when possible, autopsy data will be reviewed and the worker's physician contacted. Because of the imperfections known to be associated with the collection of this type of retrospective data, the prospective aspect of the search for malignant change in asbestos workers will be strongly emphasized. During the long-term period of this study, every effort will be expended to obtain autopsy or other pathologic documentation of the cause of death in workers who have been employed in these plants. Information gained from the plant work records will lead to correlation of the onset of the malignant disease with the onset of occupational exposure, the years of exposure, any latent period during which

the occupational exposure had ceased, and the residential history. Particular attention will be directed toward individuals who develop thoracic or abdominal malignancies and who had very short exposures to asbestos fiber twenty or more years ago.

Another aim of this investigation will be to characterize the present and past plant conditions in regard to dust exposure and measures undertaken for its control and to detect any consequent change in incidence or type of disease. Workers and executive personnel who have been employed in these plants for long periods of time will be carefully questioned in this regard and attempts will be made to quantitate impressions of changing dust concentrations with actual particle counts obtained in the past. Jobs resulting in high dust exposures will be identified in order to correlate disease patterns with various jobs which are associated with different degrees of dust exposure. It is anticipated that particle and fiber counts will be made in these two plants periodically in the future and that the resulting data will be made available to the investigators.

II. Phase II

The aim of the community investigation will be to provide data which will help to assess the risk of individuals outside the plant developing malignancies related to asbestos fiber exposure. The complexity of this problem requires a detailed planning stage which is projected for the first year of this overall program. During this period discussions will be conducted by the investigators and consultantive advice will be sought both in New Orleans

and from workers in other areas. It is expected that a workable and productive epidemiologic design will result from this planning phase and that the active part of the community investigation will begin in the second year. The advisability of implementing a citywide "ferrugenous body" survey will be considered and this, together with a system for reporting pleural mesotheliomas, will be discussed with local pathologists. Case detection of mesotheliomas can be increased by a systematic search of the hospital records. An attempt will also be made to gain information regarding the incidence of this tumor and geographic location of these patients from past and present cancer surveys which are being conducted in this city. In future years other occupational exposures to asbestos materials may also be considered and a more definitive plan of investigation involving insulation workers will be discussed during Phase II of this proposal. Early in this investigation the application of modern statistical and computer techniques will be planned for the collection, retrieval and analysis of data relating to the plant and community study groups.

b. Data collected from a careful prospective study of the asbestos cement industry will be highly significant if it helps to answer some of the difficult questions posed by the incomplete information on human health effects resulting from this exposure. Can the early diffuse changes of asbestosis be detected by x-ray or modern pulmonary function testing so that further deterioration of function as a result of advancing disease will be prevented?

Will the acknowledged reduction of dust concentrations in the industry over the past several years have an effect on the incidence of fibrotic and neoplastic disease? Is bronchogenic carcinoma of asbestos workers seen only in those individuals who are also cigarette smokers, as has been suggested, and does this increased incidence of bronchogenic carcinoma in exposed subjects, also include individuals without the parenchymal changes of asbestosis? We hope that this investigation will provide useful information on these problems to industry and others interested in occupational health. This study will help to evaluate the usefulness of new tools for the study of this environmental exposure such as ferrugenous body counts, atmospheric fiber counts, and selected pulmonary physiologic parameters. Certainly, recent studies have provided conflicting opinions concerning many of these vital points. It has been evident that an integrated approach has usually been lacking and often information regarding environmental occupational conditions is available but not correlated with human health effects, or the reverse is true. It is this common pitfall which we hope to avoid in our proposed investigation.

c. The Human Rights Committee of the Tulane Medical School will review this proposed study. Only standard and accepted methods for the collection of clinical, radiographic, and physiologic data will be used.

d. The facilities of the Tulane Pulmonary Diseases Section and Pulmonary Function Laboratory will be fully utilized for this investigation. The well equipped and modern Pulmonary Function Laboratory contains the following pieces of major equipment: Several spirometers and gas analyzers

for the measurement of lung volumes and ventilation; blood gas analyzers with P_{O_2}, P_{CO_2} and pH electrodes, Scholander gas analyzers for analysis of expired air; appropriate pneumotachygraph screens; electrical transducers; pre-amplifiers, integrators, and oscilloscope for the measurement of pulmonary compliance; body plethysmograph and appropriate attachments for the measurement of airway resistance and thoracic gas volume; gas chromatograph and carbon monoxide infrared analyzer for alveolar gas analysis in measurement of pulmonary diffusing capacity. A second system for the collection of alveolar gas samples in diffusing capacity measurements is being requested in the budget, in addition to two portable waterless spirometers for use in the plants.

III. Previous work done on this project

a. The investigators have conducted a number of studies in the field of occupational and environmental respiratory disease. A bibliography and selected reprints are included with this application. Additionally, a number of cases from the local asbestos cement industry demonstrating varying patterns of diffuse respiratory disease has come to the attention of our group. Cases of pleural mesotheliomas from within and outside the plant have also been identified.

IV. Personal Publications

Weill, H., Ziskind, M.M., Dickerson, R.C. and Derbes, V.J.: Allergenic air pollutants in New Orleans. J. Air Pol. Control Assn. 15:467, Oct., 1965

Weill, H., Buechner, H.A., Gonzalez, E., Herbert, S.J., Aucoin, E., Ziskind, M.M.: Bagassosis: A study of pulmonary function in 20 cases. Ann. Int. Med. 64:737, 1966

Foreman, Spencer, Weill, Hans, Duke, Roy, George, Ronald and Ziskind, Morton: Bullous disease of the lung: Physiologic improvement following surgery. Ann. Int. Med., 69:757, 1969

Weill, Hans, George. Ronald, Munsokul, Narong, Ziskind, Morton, and Buechner, Howard: Management of acute respiratory failure in chronic obstructive pulmonary disease. Submitted for publication

Weill, Hans, George, Ronald Schwarz, Marvin, Ziskind, Morton: Evaluation of pulmonary function after acute exposure to chlorine gas. Am. Rev. Resp. Dis., March, 1969

V. Results obtained by Others

1. Selikoff has found a very high incidence of asbestosis in insulation workers after twenty years of exposure. Additionally, he found pleural calcification in one-fourth of these workers exposed for more than twenty years. These investigators also found a significantly increased incidence of bronchogenic carcinoma and mesotheliomas in these workers.

2. Thomson and Bader in separate studies confirmed that asbestosis results in reduction in lung volume, disturbance of gas transfer and increased stiffness of the lungs (reduced pulmonary compliance). Evidence of airways obstruction was only rarely encountered.

3. McVittie showed that intra-thoracic malignancy accounted for 40% of the deaths in a group of asbestos workers.

4. Thomson found that 30% of urban males living in Cape Town, South Africa, or Miami, Florida, had asbestos bodies demonstrated in the lungs at autopsy, an indication of the wide exposure to asbestos fiber among the general population. Attention has recently also been directed to the possible role of talc and other

fibers in the production of ferrugenous bodies by Cralley.

5. Knox and Doll have found that with the decreasing dust concentrations in an asbestos textile plant the current risk of developing bronchogenic carcinoma is considerably less and may perhaps not be above the expected general incidence.

These are brief illustrations of recently reported studies. The current literature indicates an increasing public concern regarding the association of asbestos exposure and neoplasia. There is also the strong indication that diffuse pulmonary fibrosis is now occurring later in the life of an asbestos worker and its incidence may be decreasing.

VI. Biographical Sketches are attached.

PROPOSED BUDGET *

Personnel			
Hans Weill, M.D., Principal Investigator	25%	$ 4,500	
Morton Ziskind, M.D., Co-Investigator	25%	5,000	
Research Associates (3)	30%	-	
Carmel Wagenspack, Field Coordinator	100%	11,000	
Pulmonary function technician	100%	7,000	
Clerk	100%	4,000	
TIAA		2,460	
FICA		1,091	$ 35,051
Consumable Supplies			
Analyzed gases		1,500	
Parts for gas chromatograph		500	
Electrodes for blood gas analysis		500	
Esophogeal balloons (at $8.00 each)		500	
Chemicals, buffers, etc.		500	
Glassware and tubing		500	
Maintenance of equipment		1,500	
Clerical and secretarial supplies, telephone		2,000	
Photographic and reproduction expense		1,000	8,500
Other Expense			
Biostatistical and computer consultations		1,000	
Travel and other expenses for Field Coordinator and study subjects		3,000	
Travel for investigators, meetings and conferences		2,000	
Radiologic expenses ($20 for each complete chest survey)		2,000	8,000
Sub-total			51,551
Overhead Rate (45.2% of S&W			14,238
Permanent Equipment			
Box balloon-spirometer collecting system for pulmonary diffusion measurements		2,500	
Jones Pulmonar Spirometers, 2 at $300 each		600	3,100
Total			$ 68,889

* The first year budget is largely devoted to the initiation of the plant study and planning for the non-industrial phase of the investigation. Future budget requirements will in addition include the cost of carrying out the community studie