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DOCUMENT DESCRIPTION: Letters Between Dr. Gardner & Union Carbide Co. RE  
Proposed Study of the Relation between Incidence of Pneumonia and Exposure  
to Dusts Containing Manganese Dioxide

March 25, 1938

Dr. A. C. Cranch  
Union Carbide Company  
30 East 42nd Street  
New York City

51539

Dear Dr. Cranch:

I have just returned from a vacation to find your letter of March 3rd referring to the proposed study of the effect of manganese dioxide upon susceptibility to pneumonia. With certain modifications, your proposals are agreeable and satisfactory.

It will not be possible for us to expose animals to two concentrations of manganese dust simultaneously as this would necessitate devoting two dust chambers to this purpose. If you desire to use both low and high concentrations, we will have to make one after the other.

You suggest that we keep track of fertility, the blood picture and the urine. I do not think this would add much information and there are very good reasons for believing it might offer difficulties. We do not allow any of the animals exposed to dust to breed as this introduces a factor whose effect is hard to evaluate. Furthermore, it tends to overcrowd the cages, which we seek to avoid.

Blood counts in guinea pigs are of no value unless they are repeated at very frequent intervals and continued over long periods. These small rodents show great individual variation and occasional counts on different animals would be of no significance. It would prove too expensive an undertaking to warrant our doing so for the compensation which you propose.

Urine examinations cannot be made in these small animals unless we resort to catheterization and this I would hesitate to do because of the danger of infection. One cannot use metabolism cages for the collection of urine in a dust room. I would therefore suggest that this item be omitted.

Your other proposals are entirely satisfactory except that I might add that the tissues of all animals will be examined microscopically and that bacteriological studies

will be made of the lungs of any animals which show evidence of pneumonia.

With these modifications, the Saranac Laboratory will undertake the study which you propose for the sum of \$5,000 plus an additional sum of \$2,000 to cover the cost of erecting another dust room.

The snow is gone and the ground is sufficiently soft so that we could start excavating at any time. We will be ready to start the experiments as soon as we receive your authorization.

With very best regards,

Sincerely yours,

Leroy U. Gardner, M.D.  
Director

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# Union Carbide Company

Unit of Union Carbide **UCC** and Carbon Corporation

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CABLE ADDRESS "UNICARBIDE"  
CODES WESTERN UNION AND LIEBERS

*Carbide and Carbon Building  
Thirty East Forty-second Street  
New York*

March 28, 1938

Dr. LeRoy U. Gardner  
Box 551  
Saranac Lake, N. Y.

My dear Doctor Gardner:

Your letter of the 25th just received with reference to the proposed study of the effects of manganese dioxide dust upon susceptibility to pneumonia.

Regarding the points you bring up, can understand the difficulties that the study of two concentrations would present so in the revision of the proposed study I have substituted 10 mgms. per 100 liters as the concentration to be studied as this would be double the concentration noted under working conditions where the dust was under fairly good control. The 10 mgms. per 100 liters would approximate conditions existent in many manganese milling operations and I believe this figure would fairly represent the concentration, exposure to which has been charged with increasing the pneumonia incidence.

With regard to keeping track of fertility, this was suggested inasmuch as it has sometimes been charged that exposure to manganese dioxide dust inhibited reproduction. This is contrary to observations made in connection with cases with which I have had contact and I realize that to include this in the proposed study might complicate matters considerably so we will omit it as you suggest.

With regard to the blood picture, some observers have asserted that certain changes occur in humans under exposure. You point out, however, the unreliability of observations on blood changes in guinea pigs, a point which I know to be valid, so that it is very probable that blood changes noted would not represent anything conclusive as far as possible effects on human subjects might be concerned. This might, therefore, well be omitted in the present study.

With regard to observations on the urine, while we have usually included this in animal experimentation of this sort, I realize that in this particular instance the presence of the dust under conditions of the test would act as sufficient contaminant to urine collected in the usual way so

Dr. LeRoy U. Gardner

March 28, 1938

that examination would be quite impracticable. As for catheterization naturally this would present too many difficulties in proportion to any value in the inherent observation so that I agree that this observation also might well be omitted.

The determination of the bacteriology in the case of test animals showing evidence of pneumonia I believe would be quite vital to the study, and also the determination of the gross and microscopic changes of the lungs, and an estimation of the amount of manganese which might accumulate in the lung at the end of the test and a comparison of this amount with that found in the lung of animals retained one or two months after discontinuance of exposure. I believe that we should make an effort to determine the extent to which manganese collects in the lung and may be eliminated after exposure ceases.

In line with the above, I am enclosing a revision of the proposal sent you early in the month, incorporating the changes outlined in your letter. If the study as now revised is agreeable to you at the terms mentioned in your letter, I will submit it for consideration by the "Powers That Be" and let you know at the earliest possible date of what decision is made.

I am collecting some more translations of foreign articles bearing on this angle of the manganese problem. In case you have not had access to them, I will forward them if we undertake this study.

With very best regards, I am

Very sincerely yours,



INDUSTRIAL TOXICOLOGY DEPARTMENT

A. G. Cranch, M. D.

gk  
enc.

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PROPOSED STUDY OF THE RELATION BETWEEN INCIDENCE OF PNEUMONIA  
AND EXPOSURE TO DUSTS CONTAINING MANGANESE  
DIOXIDE.

March 28, 1938

The theory has been advanced that exposure to and inhalation of dusts containing manganese dioxide tends to produce an increase in the incidence and severity of pneumonia cases among those exposed.

To determine the degree to which this theory may be supported by observation the following study is proposed:

A review of all available literature on the subject.

A study of the incidence of pneumonia in guinea pigs exposed to various dusts as shown in the records of the Saranac Laboratory for the Study of Tuberculosis, with special reference to such pneumonias known to be due to pneumococcus infection. This study should show the percentage of animals exposed to the different dusts and which developed pneumonia during such exposure.

Exposure of 100 guinea pigs not less than 8 hours per day, 5 days per week for a period of not less than 8 months, to a concentration of manganese dust in the air approximating 10 mgms. per 100 liters of air; such dust to be obtained through the use of so-called 200-mesh milled ore containing manganese dioxide in known percentage. The maintenance of 100 guinea pigs as a control group for comparison with the above groups.

Observations to be made at suitable intervals, approximately 1 month, of weight changes. If no animals have died within the month then monthly one or two shall be sacrificed to determine pathology present. A sample of lung tissue shall be examined microscopically and if there is evidence of gross pathology in any other organs, microscopic examination of such organs shall be made.

At the end of the period of exposure a group of 10 to 20 animals shall be kept for a period of 1 to 2 months, at the end of which time they shall be examined to determine to what extent manganese in the lung may be eliminated after the exposure has ceased or to what extent the lung has recovered from damage, if any, noted because of the exposure.

Except for the recovery group just mentioned, all animals at the end of the exposure period, shall be killed and examined for pathological changes. Any organs showing such changes shall be examined microscopically. An adequate number of samples of lung tissue shall be examined microscopically to determine what changes may have occurred as a result of the exposure to the dust containing manganese dioxide. A determination should also be made in a few animals to show the amount of manganese dioxide present in the lungs of exposed animals for comparison with the similar determination in animals held for recovery period following the exposure to the dust.

Brief monthly progress reports would be requested by the Company and also permission to observe the progress of experiments at such time as might be desired.

It is understood that in connection with this study there will be no experimental human exposures and that the personnel to be engaged in this project shall not have the status of employees of the sponsor company and that they shall not be so regarded for any purpose under any state or federal law and that accordingly, such company shall be held harmless from any and all claims on the part of such personnel for any cause or reason whatsoever arising out of and in connection with

Proposed Study of Relation of Incidence of Pneumonia  
and Exposure to Dusts Containing Manganese Dioxide-  
Continued.

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this study.

If the contribution required by the sponsor company for the support of this study as originally estimated is insufficient for its completion, the company shall be under no obligation to make additional contribution unless it shall be duly notified as to the need for such further expense and agrees thereto.

If it is found practicable for the company considering the sponsorship of this study to support the above outlined project, full discretion would be granted as to the publication of the results as an objective study by the company but it reserves the right to review the manuscript of such a report prior to publication and to determine, if at all, in what manner the name of the sponsor company or any of its affiliates might be used in connection with such publication. The company would also wish to advise as to the publication in which the report shall appear and the time of issue.

If after receipt of the present estimate of the expense to the company for the above study it is decided to undertake same, then the understanding between the Laboratory and the company will be embodied in the form of a properly executed agreement, neither party to have any obligations in this connection until such agreement is executed.

March 31, 1938

Dr. A. G. Granch  
Union Carbide Company  
30 East 42nd Street  
New York City

Dear Dr. Granch:

I am pleased to have your letter of March 28th with comments on the proposals for our study of the effect of manganese dioxide.

The revised proposals are entirely agreeable to us and we will be willing to use them as the basis of an agreement which you may send us.

Very truly yours,

Leroy U. Gardner, M.D.  
Director

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