CHEMICAL MANUFACTURERS ASSOCIATION

R&S 110412

December 13, 1979

To: Vinyl Chloride Research Coordinators

Subject: Dr. Stafford's Letter Transmitting to NIOSH the Report Covering the Study Conducted by the Institute of Occupational Medicine (IOM) on "An Epidemiological Study of Respiratory Disease In Workers Exposed to PVC Dust"

Gentlemen:

In accord with advices given to him by the Legal Division of ICI Americas, and with an earlier recommendation made by the Vinyl Chloride Research Coordinators, Dr. Stafford sent a copy of the IOM report to Dr. Anthony Robbins of NIOSH. A copy of Dr. Stafford's excellent letter to Dr. Robbins is attached. His letter presents a perceptive historical perspective as well as a thorough-going recapitulation of ICI's investigative work on PVC dusts.

Sincerely,

J. T. Seawell
Project Administrator
Vinyl Chloride

JTS:das

cc: Dr. John Stafford

Enclosure

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Imperial Chemical Industries Limited

Plastics Division

Dr Anthony Robbins
Director
NIOSH
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CC Mr John Lawrence SPI New York City

Mr J T Seawell CMA Washington, DC

Your ref.	Our ref	Tel ext	Date
	JS/SEW/DSO-16	3162	6 December 1979

Dear Dr Robbins

PVC DUST

In 1974 when vinyl chloride monomer (VCM) was found to give rise to angiosarcoma of the liver (ASL) in humans exposed to high concentrations of the gas over long periods, various international meetings were organised to review occupational health matters in the manufacture and use of this chemical. The principal use of VCM is of course in the manufacture of polyvinyl chloride (PVC) which is normally made as a finely divided, particulate material and which is normally considered to be "physiologically inactive" with an ACGIH hygiene standard of 10 mg/m^3, the standard for the generic classification of "nuisance particulates." At these meetings and seminars, consideration was given to PVC particulate matter but no specific risk to health was identified.

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Despite this finding, Imperial Chemical Industries Ltd (ICI), a large manufacturer of VCM and PVC inter alia in the UK, decided to investigate this area further by doing in vitro and in vivo work in its Central Toxicology Laboratory (CTL) and by doing full chest X-ray examinations of PVC dust exposed employees. To do the latter, ICI went to an independent body, the National Coal Boards' Radiographic Unit (NCB) which is skilled in investigating dust induced respiratory conditions. In 1975/6, the NCB examined about 450 employees and reported no unusual findings or undue level of respiratory ailments.

Over the years 1975-8 however, some papers appeared in the scientific literature suggesting that there were problems caused by PVC dust exposure. Vague and ill-defined abnormalities were reported in chest X-rays of PVC dust exposed men and in some cases, allegations of pneumoconiosis were made. At the same time, the in vitro and in vivo animal work gave a similarly confused picture. At ICI's CTL, the in vitro work demonstrated varying levels of cytotoxicity associated with the presence of certain types of surfactant but no notable effects were observed in animals. This lack of effect was also found in the three species animal work done under the aegis of NIOSH (Dr Trent Lewis). ICI tried to have the NCB work on our employees published but the lack of a suitable control group resulted in our abandonment of this idea.

Late in 1978, ICI approached the Institute of Occupational Medicine (IOM), an independent research organisation associated with the University of Edinburgh and asked them to carry out a health and hygiene survey in ICI's oldest established PVC factory at Hillhouse in Lancashire which has been in operation for nearly 40 years. Such a survey was done in early 1979 and on 19 November, we received the IOM's report TM/79/2 dated October 1979, a copy of which is enclosed for your attention. As you will note, the IOM have observed some radiographic abnormalities and changes in ventilatory capacity of the lungs associated with PVC dust exposure. These changes are slight and there is no evidence of substantial risk to health. In our view, the IOM have made a well-disciplined study in this field and provided evidence of changes in lung function associated with PVC dust exposure. However, we remain sceptical of their X-ray findings which of course must be further discussed and evaluated by the scientific community.

We are making the IOM report available to you as new information discovered in the course of what is clearly a continuing research programme. We are awaiting protocols from the IOM to decide how best to proceed in the next phase of this interesting study.

The IOM presented the results of these present researches on 18 September to our Hillhouse Factory employees. The IOM report has been made available to the UK government and to the relevant labour unions via the Trades Union Congress medical advisor. We have also given the information to our colleagues in the European PVC industry on 21 November and the USA to the CMA and SPI on 28 November. The report will shortly be sent also to the PVC Association in Japan. The IOM have filed the report in their Institute Library from which it may be freely obtained. The IOM are preparing a paper for publication and we hope it will be accepted by a reputable scientific journal in 1980. The report is also available in summary and complete form to employees in ICI's PVC factories.

Especially in view of the three species animal research studies financed by NIOSH and directed by Dr Treat Lewis, we feel sure you will be interested to receive the enclosed report of some complementary research work which you may wish to transmit to and discuss with other relevant US Government agencies. Naturally, we would be glad to have your comments and observations on this work. If you would find it helpful to have face to face discussions, my colleagues and I would be very pleased to meet with you at any mutually convenient time and place. Should you or any of your specialists in this area be visiting the UK in the near future, we would be delighted to visit the IOM with you so that you can speak directly with the leaders of this research project.

Yours sincerely

J Stafford
Division Manager
Health & Environment Protection

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CONFIDENTIAL

PVC DUST - EXECUTIVE BRIEF

For occupational health purposes, PVC dust is classified as a "nuisance dust" and is monitored against a TLV of 10mg/m3 on an 8 hour TWA. From time to time in the literature references have appeared to research which suggested that PVC was more active than a nuisance dust both in humans and animals. Studies were therefore initiated by ICI over the past 5 years to investigate the possible effects of PVC dust on humans and on animals. In 1975/6 ICI invited the NCB Radiographic Unit to survey PVC dust exposed workers at Hillhouse - no respiratory disease attributable to PVC was found. Periodic checks were made with other PVC producers in Europe and USA who had carried out similar chest X-ray surveys and again no adverse effects found. Animal tests were done at ICI's Central Toxicology Laboratory and no fibrosis found; some US Government sponsored work on 3 animal species was published about the same time and reported no adverse effects.

However early in 1978 a paper was published concerning a possible case of pneumoconiosis in a French factory worker who had been heavily exposed to PVC dust in past years. About this time also allegations of the occurrence of pneumoconioses in Italian PVC workers were being made. Despite the weight of evidence that PVC dust did not cause fibrosis of the lungs in animals or man, ICI Plastics Division decided to engage the Institute of Occupational Medicine (IOM) in Edinburgh to make a thorough investigation into the pulmonary health of past and present employees at its Hillhouse factory where PVC has been made and handled in powder form for 35-40 years.

The IOM carried out its health and hygiene examinations on 818 employees early in 1979 and they have just completed their statistical analysis. Oral reports of their findings were given to representatives of the Health and Safety Executive and in Edinburgh on 14 September, to the employees concerned on 18 September and ICI management on 19 September. The IOM are writing a paper on their work and will submit the paper to a professional journal for publication as soon as possible.

In short, their report has given the following conclusions:-

1 There was no evidence of a serious progressive form of pulmonary fibrosis except in one man out of the 818 whose disease may or may not be related to his work. This man is being investigated further.

2 Exposure to PVC dust does have a small but measurable effect on the ventilatory capacity of the lungs. This effect is related to degree of exposure to PVC dust and to cigarette smoking habits.

3 One of the three radiologists who read the X-ray films found small radiographic abnormalities in 50 of the population and these could be correlated with the observed reduction in lung function and the degree of exposure.

4 No excess of lung cancer was found in the population studied.

5 A comprehensive survey of dust in the atmosphere found present concentrations of respirable dust to range from 0.17 to 2.88mg/m3. In former years these concentrations were probably higher.

The depth and thoroughness of this study is probably unique in the field of nuisance dusts. The study has shown that exposure to PVC dust does have an effect on man but the effect is small and difficult to detect. This is particularly true of the X-ray work where only 1 out of 3 radiologists in this study observed the abnormalities which could be correlated with reduction in lung function. It may also be that such small or marginal effects are found with many other nuisance dusts when they are examined in great depth.

The outcome of the study is being considered and will be discussed with employees, government and colleagues in the UK, European and US PVC industries over the next few months.

JS/SEW/DSO-16
8 October 1979

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11/28/79

INSTITUTE OF OCCUPATIONAL MEDICINE

SUMMARY OF THE RESULTS OF A SURVEY* OF THE RESPIRATORY HEALTH OF WORKERS IN A FACTORY MANUFACTURING POLYVINYLCHLORIDE

Eight hundred and eighteen men selected from the present and past workforce of a factory manufacturing polyvinylchloride (PVC) were studied to determine whether PVC dust caused any measurable effects on the lungs of workers exposed to it. Respiratory symptoms such as cough or breathlessness, the results of breathing tests and appearances of the chest X-ray were compared with estimates of the amount of fine PVC dust to which each man had been exposed during his employment at the factory. In studying the effects of PVC dust, allowance was made for the known effects of ageing, smoking and physique on the lungs.

Shortness of breath on exertion

It was found that men who smoked cigarettes and who had also been exposed to higher amounts of PVC dust reported slight shortness of breath on exertion more often than smokers who had been exposed to lower amounts of dust. This symptom was associated more strongly with ageing and with smoking as [illegible]h. The dust effect was not seen among non-smokers and ex-smokers.

Breathing tests

There was a relationship between the amount of dust to which men had been exposed at work and their ability to perform well in breathing tests: in general, the higher the exposure, the poorer the breathing test. This was particularly noticeable among cigarette smokers. The diagram shows that for cigarette smokers the effect of the average exposure is small compared to the effect of ageing, and smaller than the effect of smoking itself. But addition of the estimated effect of higher than average exposures to the results of ageing and of smoking could be sufficiently great to contribute towards chest illness in some men.

Chest X-rays

Even highly trained doctors often disagree on the presence or absence of spots on a chest X-ray. All X-rays in this study were read independently by three readers all of whom had been shown previously to be able reliably to detect progressive degrees of change in response to dust exposure but [illegible]

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* For details of the study, Technical Memorandum TM/79/2 should be consulted.

differed from each other in their interpretation of what was just normal or just abnormal.

One reader recorded very few spots on the X-rays, regarding most X-rays as within normal limits. One reader recorded small spots in a larger number of men and found these spots were more common in older men. The third reader recorded spots in the largest number of men and we found that these X-rays on which he had recorded spots occurred more commonly in older men, but also in men who had been exposed to higher amounts of dust. We are confident from this that the more dust a man is exposed to, the more likely he is to have small spots on his X-ray. Having said this, the number of spots on any X-ray was relatively few and all films were on the borderline between what is just normal and what is just abnormal. Nevertheless, the breathing tests of men with spots on their X-rays were on average poorer than those of men without such spots, even when age and height had been taken into account.

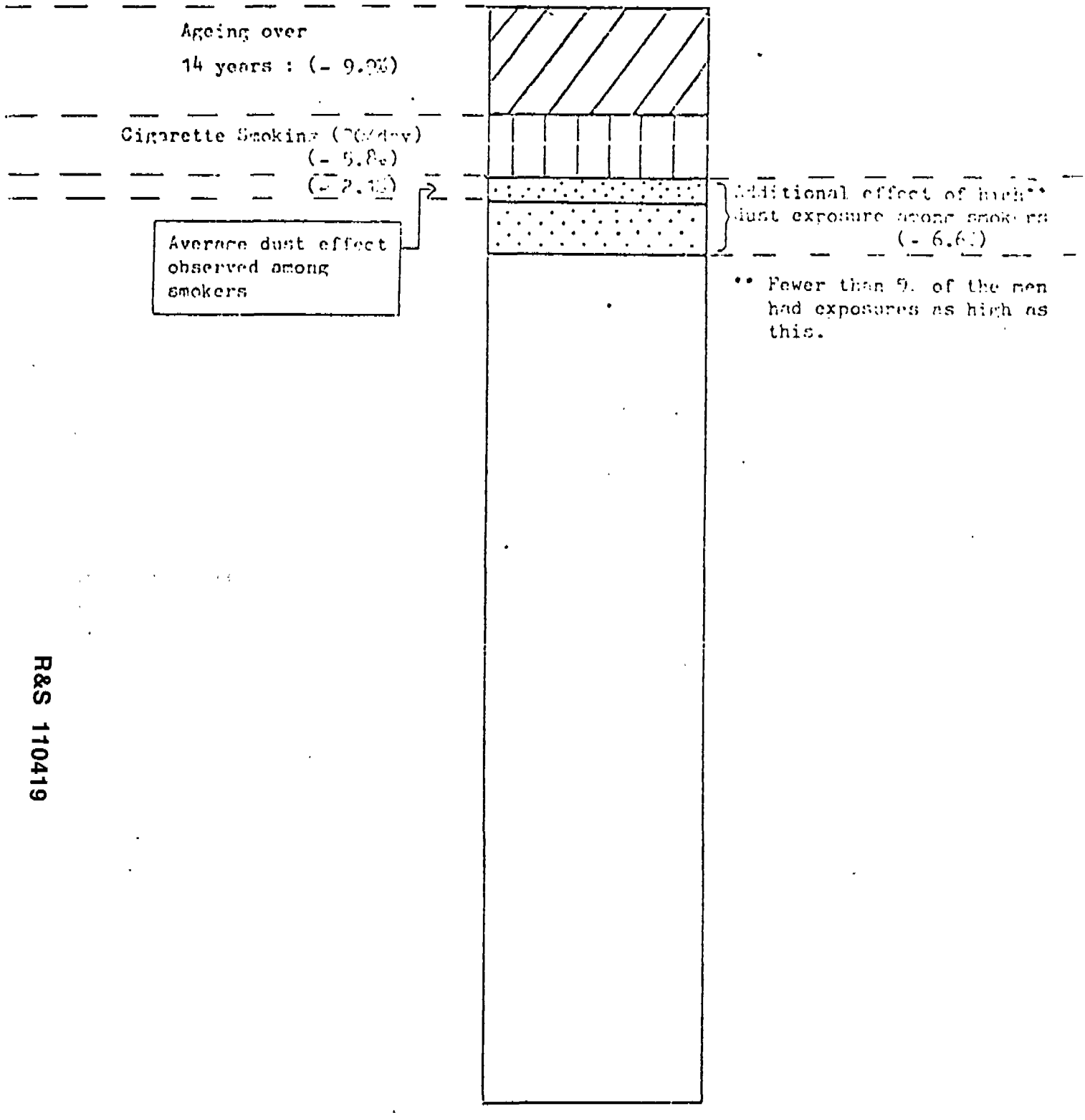
Conclusions

Careful selection and study of both current and past workers at the factory with measurement of current dust levels in different jobs in the production of PVC has allowed us to draw conclusions about the effects of PVC dust on the lungs. These effects stem from past dust levels which are generally believed to have been higher than they are now, but in the absence of knowledge of what these levels were it is sensible to regard them as potentially applying to the present levels. The effects are poorer breathing tests and spots on the chest X-rays of men exposed to higher amounts of PVC dust. The effect on breathing tests is most marked in cigarette smokers, in whom there was also a relationship between dust exposure and slight shortness of breath on exertion. These findings show that PVC is more than just a nuisance dust, having a specific, though usually slight, harmful effect on the lungs. It is accordingly recommended that efforts should be made to reduce dust levels further and to ensure that workers are exposed to as little as is practicable.

9 November 1979

ESTIMATED LOSS OF BREATHING CAPACITY OVER 14 YEARS* DUE TO AGEING, CIGARETTE SMOKING AND EXPOSURE TO PVC DUST AMONG CIGARETTE SMOKERS.

(The figures in this diagram are based on additional work which supplements that reported in 31/7/72. These results are included in a paper which is being prepared for publication.)



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* 14 years was the mean time worked in the factory by the men seen.

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL

March 17, 1980

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
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Received 6th May 1980 at 9.30 AM — presumably came by seamail. JS 6/5/80

R&S 110420

Dear Mr. Stafford:

Dr. Robbins forwarded to me a copy of the epidemiological report on respiratory disease in workers exposed to polyvinyl chloride dust for my review and comment. I must state initially that I am not an epidemiologist. My role on the NIOSH conducted PVC animal inhalation study was that of an interim manager, i.e., I assumed the responsibility of directing the study following its initiation by others. In this vain, David H. Groth, M.D., Pathologist, is the prime person in NIOSH who is compling the data on the PVC inhalation study and preparing the final report. (1)

The epidemiological study was well conducted and the conclusions are consistent with the results. As stated, this is one of several studies demonstrating evidence of an association of PVC dust exposure and the development of respiratory disease. Your study and the other reports indicate that PVC dust exposure leads primarily to chronic obstructive lung disease. (2)

My personal opinion is that the effect of PVC dust exposure is mainly a nonspecific effect on the distal terminal airways. The dust is being deposited in sufficient quantity around the respiratory bronchioles of one millimeter or less in diameter, producing a marked effect on conduction past these anatomical sites to the alveoli. The result is the formation of chronic obstructive airway disease in those specific areas without the development of a classical pneumoconotic disease syndrome.

Results from animal studies performed by members of my staff lead me to question the concept of a nuisance dust level, particularly at airborne concentrations of 10 mg/m^3 total, or 5 mg/m^3 respirable. Your studies, other epidemiological studies on dusts, and our own animal studies suggest that dust concentrations of 2 mg/m^3 can cause a reduction in FEV_1 and other physiological indicators of obstructive airway disease. Much more

information is needed on the time of onset, progression of response, reversibility and other clinical interests before one can adequately evaluate the risks. I strongly concur with the statement in the Conclusions and Recommendations portion of the report, which reads " . . . further measures to reduce individual dust exposure would be prudent."

Sincerely yours,

Trent R. Lewis

Trent R. Lewis, Ph.D., Chief
Experimental Toxicology Branch
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IMPERIAL CHEMICAL INDUSTRIES LIMITED
PLASTICS DIVISION—WELWYN GARDEN CITY

From: J STAFFORD
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R&S 110422

Dr Trent R Lewis, Ph.D.,
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JS/SEW/DSO-16 3162 6 May 1980

Dear Dr Trent Lewis

PVC DUST

Thank you for your letter of 17 March which alas reached me today - it must have come by seamail which can take anything between 1 and 3 months!

I am grateful to you for your comments and speculations about PVC dust which I am circulating to my colleagues. As you know Dr Groth spoke about the NIOSH inhalation studies at the Bethesda symposium 20/21 March. Dr Seaton, the Director of the IOM in Edinburgh, also gave a paper on the same programme. There were of course papers from other workers in the field which tended to confirm the prudent view that more care should be given to the handling of PVC dust.

We are committed to continue with further studies of our PVC dust exposed employees and for this work we have again engaged the IOM who, as you say, made a good job of their first investigation for us. As new results become available, we will make them available to you. I look forward to receiving Dr Groth's final report on his animal studies in due course.

Y urs sincerely

J Stafford
Division Manager
Health & Environment Protection

Circulation

Dr G Pigott	Dr D M Ferguson	Dr M N Johnson
Dr W G F Adams	Mr M J S Gibbons	Mr P Claus
Dr B Bennett	Mr D Ryerson	Dr J G Kammuller
Dr F W Best	Dr T R Torkelson	Mr J C Thomas
Dr D P Duffield	Mr J Lawrence	Dr R Mattiussi
Mr G J Sleddon	Mr J Seawell	Dr J P Tassignon

IMPERIAL CHEMICAL INDUSTRIES LIMITED
PLASTICS DIVISION—WELWYN GARDEN CITY

From: J STAFFORD
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To:

Dr T R Torkelson
Mr J Lawrence
Mr J Seawell
Dr M N Johnson

I am left speechless at the time delay but at least I have acknowledgment and comment of a sort.

J Stafford

Date: 6/5/80

: of onset, progression of response,
interests before one can adequately
oncur with the statement in the
ortion of the report, which reads
e individual dust exposure would be

Sincerely yours,

Trent R. Lewis

Trent R. Lewis, Ph.D., Chief
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R&S 110423