

# SAINT LUKE'S HOSPITAL

*of the Methodist Church*

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CLEVELAND, OHIO 44104



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Dear Dr. Powell:

Thank you very much for the material which you brought to me. Before commenting generally on it I will respond to your specific questions.

You have asked me to cite the case reports or epidemiologic studies which indicate that the emergency limit of 5 fibers/cc (TWA) should be lowered, and if so, to what number. Although there are numerous case reports in the literature, I don't believe that any of these provide valid information on which to alter or base a TLV. There are no lung or pleura abnormalities peculiar to and therefore solely related to asbestos. Each of the abnormalities that we associate with asbestos on an epidemiologic basis occur with some frequency in persons never known to have been exposed to asbestos in any way. Although the discovery of isolated examples of pulmonary fibrosis, lung cancer or mesothelioma in persons who have also experienced an asbestos exposure, usually slight, may suggest a need for epidemiologic study it does not establish that a casual relationship exists between the pathology observed and the exposure to asbestos, and in no way establishes a TLV. In fact, the occasional case of lung cancer or mesothelioma observed in a person who has had a very slight and almost casual exposure to asbestos is far more likely to represent a coincidence, since these opportunities for slight or casual exposure to asbestos are virtually universal in our society, and since these various pathological processes occur for other reasons or in what might be termed the general and non-asbestos exposed population. The "number" which characterizes a TLV indicates the level of the agent below which an excess of a particular biological manifestation will not occur even though a person be exposed for a working lifetime. Epidemiologic studies relating "measurement of exposure" to the level at which the excess of disease occurs are essential in establishing a TLV. This kind of information obviously does not exist in isolated case reports.

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The only published epidemiologic study known to me which suggests a lower TLV for asbestos than the recently set "emergency limit" is the one upon which the British TLV is based. It was a study of only 290 men currently employed in 1966 in a single textile mill, and who had worked ten or more years after being employed subsequent to 1933. In this study no dust counts were available until after 1951, and no counts in modern terms were available until after 1960. Large amounts of crocidolite as well as some chrysotile were used in this mill. Rales and x-ray changes were used as the evidence of asbestosis. The study is based upon scant numbers of workers and less than adequate knowledge of exposure since only the last six years of exposure in the mill were measured in modern terms. This mill was known to have been quite dusty, especially between 1930 and 1950. In my opinion, while this study has value it gives only a first approximation to a TLV and even the authors make no pretense that it is exact. The liberal "regulations" governing the operation of the TLV based on this study is eloquent evidence of the uncertainty associated with it. These regulations appear to me to state 2 fibers/cc as a goal more than to indicate a strict TLV. I know of some ongoing and as yet incomplete evidence which indicates a TLV of 10 fibers/cc is probably too high and that some number near 5/cc over a forty year period would likely be adequate to prevent an excess of bronchogenic cancer and meaningful asbestosis. All things considered, there seems to be reason to prevent persistent exposure of unprotected workers in asbestos environments to ~~the~~ TWA's above 5/cc, but not require a lower TLV by law. It is clear that anyone who complies with a 5/cc TLV must actually operate at a TWA which in all circumstances would be substantially less than 5/cc. Such a level would constitute a large reduction in dustiness in comparison to conditions under which workers were employed over the past forty years when environments twenty to fifty times that high in fiber concentration must have been fairly common. Concentrations of fiber four to six times higher than such a TWA exist even now under some circumstances.

There is no simple or certain answer to your question about feasibility in terms of time required for achieving a 2 or a 5 fibers per cc TWA. I would be inclined to put mining and milling, asbestos textile and asbestos cement products in a quite different category from that of either industrial or marine insulation application. Insulation application is a far more intermittent type of asbestos exposure than is asbestos production or the manufacture of asbestos containing products. There is a less need for fixed dust control apparatus in insulation application. From what I know of insulation application, and I must indicate that I have less experience with this than with the other kinds of exposures, I should think that it would require less time for them to achieve the kinds of control to reach either 5 or 2 fibers than would be

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the case in other kinds of asbestos exposure. I say this because there would be little or no relocation or rebuilding of machinery and for the most part it would be a matter of getting the proper kind of equipment and then teaching and motivating the workers to use it. Of great importance with respect to the future of insulation application is the fact that the amount of asbestos being incorporated into the materials used is progressively being decreased. Realistic estimates made by those who should know, would indicate that, with some rather minor exceptions, there would be no asbestos contained in the materials being used for insulation after approximately the next five years. I believe that achievement of a time weighted average of either 5 or 2 fibers per cc could be accomplished in the insulation industry within the time required to purchase the necessary kind of equipment and the teaching of the workers as to how to use it. I would think that two years would be a reasonable estimate for this.

The problem is far more difficult in those situations where asbestos is being produced, or is being used in the manufacture of the material. The problem here is one of substantial effort to be expended in discovering how to design equipment to operate within these TWA's, plus the time required to build the necessary equipment, and in some places to completely relocate the entire manufacturing system in order to accomplish the desired TWA. I know of one textile mill that has been redesigning, rebuilding and relocating machinery over the past four years in an effort consistently to reach 6 fibers/cc TWA. They have accomplished this goal by the methods indicated, but have also been forced to abandon some processes and products with the result that the work force has dropped from around 250 at the outset to less than 75 now. A considerable reduction of the ambient fiber concentration has been achieved by attaching various ventilation devices to existing equipment, by introducing wet or dampening processes, by abandoning entirely some processes, and by upgrading fiber to remove its dustiness before it is used, and by trying to operate with lower intensities of energy application. This last factor is quite important and oftentimes has gone in the opposite direction. My own experience with those who have been trying hard in the last few years to reduce the fiber concentration in the ambient air of the worker, suggests to me that 5 fibers per cc might be reached by attaching better exhaust equipment, by dampening processes and redesign of, but still utilizing, essentially the same manufacturing equipment. The designing and installation of this kind of alteration could probably be accomplished under most circumstances within two years. To reach a 2 fiber per cc level would escalate the effort involved in an exponential manner, and in most instances would actually require considerable if not total rebuilding of machinery, relocating the machinery, and essentially building

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new plants. The outside walls of the factory might not be changed, but the inner construction would have to undergo extensive alterations. In some circumstances, the engineering required to do this doesn't even exist at the present time and would have to be developed in an experimental manner. There are, of course, some operations of a manufacturing variety that could be brought into the 2 fiber level rather quickly because knowhow for this already exists, but even under these circumstances there would have to be a considerable amount of rebuilding and relocating of equipment if old and new operating plants are to be utilized. The time required for this, I think, would be substantially more than two years, and I base this on what I have been observing in a company that has been trying to achieve this kind of reduction for the past several years.

All of this, from a time point of view, would be dependent also on the availability of exhaust systems and the competition for this kind of equipment is very great at the present time. To reach 5 fibers per cc would, in my judgement, be more likely achievable without great alteration of basic equipment than would be the case if 2 fibers per cc is desired. I would hold out some hope of being able to achieve 5 fibers within two years, but for 2 fibers I think one is talking about something on the order of three, four, or even five years. In saying this I am fully aware that there are operations now in the industry where the fiber count is below 2, but I believe that where this does exist the plant or the equipment is newer and those involved have been working on it for a long time, or the process by the very nature is not one of the more dusty varieties.

Feasibility depends, of course, first on engineering aspects, but of equal importance in the real world is the economic aspect. I don't know how much more it might cost to get down to 2 fibers than to get to 5. I would think that it would be more expensive to the degree that equipment would have to be moved or markedly altered. I don't believe that I am competent to judge the financial impact of achieving a TLV of 2 versus one of 5.

As is true of the other questions, I don't believe we have the information necessary to answer your query about whether or not there should be lower limits for crocidolite and amosite. The only information suggesting that amosite is related to an excess of bronchogenic cancer and mesothelioma is that recently given orally by Selikoff at the Bucharest meeting. While it may ultimately be shown to be correct, it would be well to wait until the study is finished and its validity can be assessed before acting upon it. From what was presented orally one could conclude that an excess of both bronchogenic cancer and mesothelioma did occur in that particular factory utilizing amosite as its only form of asbestos, but there was nothing in the study to indicate that amosite

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per se, was more likely to do this than was chrysotile. From what was said it would appear that the exposures were unusually heavy. On the other hand, there is some evidence of an epidemiologic nature, which rather strongly suggests that crocidolite may be related to a greater excess of mesothelioma than is true of other forms of asbestos. The predominant way in which crocidolite is used in this country is as a portion of the total asbestos (chrysotile plus crocidolite) mix. Under most circumstances it makes up about one-fourth of the total asbestos mix. If a TLV of 5 is chosen, then crocidolite under most circumstances would be approximately 1 fiber per cc, and if the TLV is 2 it would be the order of one-half fiber per cc. One might make a choice between these two and insert into the TLV that when crocidolite is used it should not exceed one-half or one fiber per cc, depending on what choice is made. I would delay doing anything about amosite until more information is available to indicate that it is in fact, more hazardous than chrysotile.

I am not at all sure that I know what you mean in asking me for "the next two significant limits lower than 5 fibers per cc (TWA)". In part an answer to this would be related to the reliability of counting techniques. I don't believe we know the reliability of counting techniques at low levels with a high degree of certainty, but we do know that it would take much more effort in terms of time to count at the range of 2 fibers per cc than it would at 5 fibers per cc. This may be of some significance. It may also be that the distribution of fibers on the millipore filter would cause more error at 2 fibers per cc than at 5. These are technical matters that may have to be explored further in your considerations. If one can, in fact, count with a reliability such that the standard deviation of the estimate is at or below 0.2 fibers, then one could think in terms of significant numbers as being any unit, such as one, two, three, four or five. With a larger standard deviation one can get into difficulties and might have to go to units such as one, three and five. There is, of course, another way in which the matter of significant numbers can be considered. It is quite apparent that knowledge, with respect to the biological effects of asbestos, especially in human beings, is fragmentary and lacking that degree of completeness upon which one would like to base reliable TLV numbers. As I indicated earlier, I believe there is evidence to rather strongly suggest a level of 10 fibers per cc over a working life of a man is too high to protect him against excess of bronchogenic cancer. Moreover, there may be some differences posed by not only the number of fibers, but the geometry of the fibers. In this situation it is obvious that setting a TLV is to a large degree a matter of opinion, even though it may be a rather informed opinion. In those circumstances where exposure data having at least a semblance of reliability exists,

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it is clear that a rather large portion of the working population exposed for many years have developed little or no overt evidences of a biological response. This indicates that some individuals tolerate rather large intensities of exposure for long periods of time. It is our obligation, however, to protect those with less tolerance either in the specific meaning of that word, or because they cleanse their lungs less well. One might set as a goal the ability to utilize asbestos with zero exposure to the fibers, even though this is, in a modern sense, rather unrealistic. One must choose, therefore, in the real world a value somewhere between, let us say, 10 fibers per cc and zero. Even when the exposures were as much as 25 fibers or more per cc, there was a substantial portion of the population that did not develop overt evidences of biological reactions. At 10 fibers per cc some, although probably relatively few, did develop overt biological reactions and if one would go to 5, it would be reasonable to expect that even fewer and perhaps none, would develop overt evidences of asbestos related disease. This level is already much lower than the levels to which people have been exposed in the past. It is probably that a TLV of 4, 3, 2, or 1 would lead to an accumulation of a smaller amount of asbestos fiber in the lungs of persons working for years in contact with this material than would a TLV of 5. Whether a reduction below 5 would be biologically important is in my judgment, unknown. Those having the responsibility of setting a TLV are in a difficult position. There are some studies underway at the present time which very likely will, in the next few years, afford more information on which to base a change of the TLV from 5 to either a lower or perhaps even a higher level.

You have asked whether or not a lower limit is needed to protect against mesothelioma than against fibrosis, and I must say that I don't think there is any useful evidence bearing on this. It appears to be rather clear that you must have a lower limit to protect against either fibrosis or mesothelioma than against bronchogenic cancer. Mesotheliomas are reported in individuals who do not show evidences of fibrosis clinically, and who have minimal evidences histologically. On the other hand, the bulk of the mesotheliomas appear to occur in those people who also have overt evidence of pulmonary fibrosis. I have never seen a breakdown of the data to indicate the nature of the exposure in those individuals who have mesothelioma and minimal pulmonary fibrosis. Likewise, I have never seen any information to indicate the degree to which evidences of fibrosis were sought for in persons with mesothelioma. When one introduces long, thin asbestos fibers into the lungs of an experimental animal by intratracheal injection, one can always see a slight tissue reaction in the immediate neighborhood of aggregates that contain even just a few fibers. These tiny lesions would not appear on the x-ray and they might be missed by cursory

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histologic examination at autopsy. In most populations with a variable exposure to asbestos fiber far and away the majority of those who develop overt evidences of pulmonary fibrosis never develop mesothelioma. In fact, the lack of a relationship between the degree of fibrosis --- which can be thought of as a measure of asbestos fiber retention --- and the frequency of occurrence of mesothelioma is one of the strongest pieces of evidence to suggest that asbestos per se has little or nothing to do with the development of mesothelioma. One can, of course, postulate that the size and shape of asbestos fiber which causes pulmonary fibrosis may be very different from that which causes mesothelioma, but I think one might equally well say that there is some other factor associated with asbestos exposure which is the true determinant of whether or not mesothelioma occurs. I don't have any information at this time to answer the numerous questions with respect to the inconsistency between asbestos exposure and mesothelioma. There is, in fact, no evidence whatsoever to indicate that asbestos per se is a carcinogen in the sense of being an initiator. In my opinion there is no evidence which will tell us what the TLV should be in order to protect against mesothelioma.

There may be times when a daily average exposure would be preferred to a time weighted average, but I know of no information in the literature that would relate these two kinds of measurement. It seems to me that if the collecting period embraces all of the normal operations of the worker, a time weighted average is indicative of the eight hour exposure. It may be that sampling soon after the start up of an operation might be different from sampling towards the end of the work period due to the "build up" factor. If this situation is suspected to be present, then one might sample at the beginning and again at the end of the work period, but this would not require an eight hour sampling period.

The question of just what constitutes a life work span for an American employee is relevant in establishing a TLV or standard. That work span, of course, would be the one that is anticipated for the young man going into industry at the present time. Although I don't know of any particular study of this matter, I believe that inquiry would show most young persons entering industrial life are now close to twenty-five years of age. It may be that in the near future they will be a little bit younger. The trend suggests that retirement will occur at an earlier age in the future and perhaps at the age of approximately sixty instead of sixty-five. On the basis of this approach, I would think that the anticipated work cycle would be less than forty years and might realistically be put somewhere between thirty and thirty-five. If one then removes some time for those periods

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of layoffs for one reason or another, I think that thirty-five years would be a realistic upper limit and perhaps the ACGIH limit of thirty years for a period of exposure is acceptable. I would think that thirty-five years would be entirely appropriate and include a factor of safety in calculating total work exposures.

The wearing of respirators and protective clothing does have a useful role, but in my judgement would be permitted, except for brief periods, only when the regulating agency knows the specific conditions under which these mechanisms are to be used. An operation which normally complies with the standard, and which gets out of control should be shut down until the needed repairs or alterations are made. The wearing of masks during the start up after repairs and until it has been shown that the operation is within the limits of the standard might be permitted without a variance. Other circumstances, however, where masks, etc. are to be used, should be known to the regulating agency, and the agency in turn should exercise judgement and moderation in permitting the variance so as not to penalize either the worker or the industry. Special attention might be given to maintenance workers. These individuals oftentimes have an unusual exposure to whatever may be present because they work during times of abnormal operation and in circumstances under which TLV standards are often not thought applicable. There is considerable evidence that maintenance operators without regard to whether asbestos is in the picture or not, tend to have higher exposures than the regular operators of any piece of machinery. Consideration might be given to requiring a special set of recommendations with respect to protection of maintenance workers.

The question of when to require the use of a respirator if a delayed standard is adopted at the level of 2 fibers per cc, is relevant. I would think it appropriate to require respirators whenever the fiber count is known to be over 10 per cc, but I would not think it necessary to wear them so long as the time weighted average was 5 or under.

I would now like to pass on to comments on the criteria document and begin with Section III. Failure on my part to comment in complete detail should not be interpreted as meaning that I am in complete agreement with all of the statements or interpretations made. I think I could be of most help by indicating some of the places where misinterpretations or conclusions that are perhaps not quite warranted might be drawn from some of the things stated or, in some instances, omitted entirely from the document.

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Item C in the last paragraph on page 8 of Section III seems rather confusing to me. The parenthetical expression might be interpreted to indicate that chrysotile is the chief and almost sole type of asbestos utilized in those circumstances where an excess of bronchogenic cancer has been reported. I doubt if the writer means to imply this since in the British textile factories and shipyards crocidolite made up a large part, and in many circumstances the bulk of the type of asbestos to which the workers were exposed. Producers of anthophyllite have also reported an excess of bronchogenic cancer. It seems quite clear that all four of the major varieties of asbestos have been implicated, or at least no one of them can be separated out as being free of an association with an excess of bronchogenic cancer.

On page 9 of Section III, the middle paragraph suggests that a dose response relationship with respect to bronchogenic cancer is poorly defined. Perhaps the intent was to indicate that the level of exposure below which bronchogenic cancer excess would not occur has not been agreed upon by all. Actually, the data that has been presented by Newhouse, by Knox and his associates, and by McDonald cannot be interpreted in any other way than to indicate a dose relationship. All of them have shown that an excess of bronchogenic cancer occurs only in those most heavily exposed, and McDonald has actually shown what the cut-off point is in terms of millions of particles per cubic foot years. I am in agreement that the evidence for a dose response relationship for mesothelioma is somewhat tenuous at this time, although Newhouse's data strongly suggests there is one. Insofar as I know, although there is some suggestion of an increase of gastro-intestinal cancer in some populations exposed to asbestos, it is totally lacking in others and there has been no general acceptance of the conception that this form of tumor is clearly related to asbestos. Under these circumstances, it is only natural that a dose relationship would be lacking. None of what I have just been referring to seems to come through as clearly as I would have thought it might in the writing on pages 8 and 9 of Section III.

On page 12 of Section III, I find myself in disagreement with the last sentence of the very first paragraph. Since Knox has not shown an occurrence of excess bronchogenic cancer in those exposed to average fiber concentrations of 4 to 6, I fail to see any reason whatsoever for a statement to the effect that his work suggests that levels below this may be necessary in order to eliminate the risk of bronchial carcinoma. I wonder if the writer has some such evidence.

It seems to me that that portion of the document devoted to the information with respect to bronchogenic cancer and mesothelioma suffer some because of the omission of McDonald's study

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and also a failure to indicate that a surprisingly high proportion of mesotheliomas in the series that had been reported by Gilson, Wagner and others, have had no relationship to asbestos exposure even though thorough efforts were made to disclose such a relationship. When one takes this in conjunction with the recent report from Nigeria of a series of cases of mesothelioma, none of which had any discloseable evidence of asbestos exposure, one has to have some reservation as to whether or not asbestos per se is indeed the cause of mesothelioma. Perhaps there is some circumstance co-existing with asbestos exposure that leads to it. I would have thought that a better balance would have been achieved in this document if this kind of evidence had been presented instead of being omitted.

On page 13 of Section III, the expression of exposures by Gardner, and by Vorwald, and by Gross, in terms of fiber per cc needs some clarification. I know that neither Gardner nor Vorwald made any fiber counts in terms of modern methods, and I don't believe that Gross did either. Since a great deal of this document has to do with fibers per cc, the inference is that the writers are talking about these animal exposures in terms of human exposure, and I wonder if that is the intent. If so, I think they should indicate how they arrived at figures such as 1,400 and 5,000 fibers per cc with reference to Gardner and to Vorwald's work.

On page 14 of Section III, I would agree that one cannot extrapolate from animal experiments to estimates of work place air standards for asbestos, or for anything else for that matter. I don't believe, however, that the first point of the sentence of the second paragraph is entirely consistent with the facts. Insofar as I have evidence, I don't know of anyone who has shown an excess of pleural thickening, pleural plaques, or pleural or peritoneal mesothelioma in inhalation experiments with animals. I consider this to be quite an important fact, and I am a little surprised that it is not referred to.

In the last paragraph on page 14 of Section III, I am rather surprised to find that whereas some of the work from Wagner and his group is referred to in terms of relative disease producing potency of various forms and types of asbestos, there is a lack of any reference to the important finding of Wagner and Timbrell that chrysotile by the inhalation route was far less fibrogenic than was crocidolite in experimental animals. In fact, it was this observation that led to the theory that straight thin fibers of crocidolite penetrate further than thicker fibers or than curly fibers, and hence mesothelioma might occur in humans with greater frequency with this kind of crocidolite than with thicker crocidolite of the Transval. I consider this to be

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a very important omission.

The rather extensive comments about fiber length and whether or not "motes" can cause fibrosis in experimental animals fails to point out a most important observation. In all of the experiments that I am familiar with, the dust clouds to which the animals were exposed, or with which they were injected intratracheally, contained long fibers along with the other sized materials. Even though there was a relatively low percent of long fibers in some of the clouds, the concentration of the clouds was so great that the number of long fibers to which the animals were exposed was substantial. None of the experiments quoted would have any valid bearing on the question of whether or not "motes" are capable of producing fibrosis. Those who have taken the trouble to expose animals to materials in which there are no long fibers (greater than 5 microns in length) have seen no consequent pulmonary fibrosis. Work in my own laboratory at this time, with carefully prepared materials with respect to fiber size appears to be confirming this observation. To the degree that one can with validity extrapolate from animal to human experience, I would not anticipate fibers less than 5 microns long or "motes" to produce fibrosis in the lung.

On page 17, Section III, the paragraph referring to bundle size and biologic response confuses me. I wonder whose work is being quoted.

I believe that I have been misquoted on page 19 of Section III where it is indicated that I have written that there was no augmented frequency of bronchogenic cancer in mining and milling. In that general survey article I quoted others but indicated that more adequate studies were under way and the question was still unresolved.

On the same page I find myself at loss to know the relevance of the last paragraph, and in addition, would like to know whether these were Canadian mines and mills or U.S., or just where they were from. I must say that I am surprised by the low levels of fibers because such levels have certainly not been my experience.

The comments in reference to McDonald's presentation at the top of page 20 of Section III, again are a misquoting. At the place where McDonald states that "even heavy exposure to asbestos in mining and milling carries only a modest risk of contracting lung cancer", he is referring to the combined studies in Russia, Italy and in Canada, and not just to his own. Also, the quotation is taken a little out of context because he shows in the

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body of his paper that at the heaviest (approximately 5% of the total group under observation) there is more than a modest risk, but that in the exposure of the group just below the very heaviest there is only a very modest risk and in the four other categories below the top two there is no excess risk. I think the quotation, or reference to the quotation is a little out of context and somewhat unbalanced as it is presented. One important word is also left out having to do with the risk of contracting malignant mesothelioma, because his quote actually reads "only modest risk of contracting lung cancer and less still risk of contracting malignant mesothelioma". It is true that he reported five cases of mesothelioma, but this is from the total population of 9,000 employees and is surely a much lower risk than for bronchogenic cancer.

Towards the middle of page 20, Section III some comments by Selikoff on McDonald's paper are made, and I presume they have reference to McDonald's first and fully published paper. Since I have not seen Selikoff's letter, I don't know how correctly he is quoted, but some comments setting it in a more nearly correct light seem to me appropriate. First of all, it was only in McDonald's "heaviest" exposed group that the figures in the tables showed five times as much lung cancer as in the "lightest" exposed group. This is quite different from the inferences of heavily exposed and lightly exposed workers as quoted in the document. Moreover, if the paper is quoted properly, it would be noted that McDonald finally concludes that because of some reporting problems, it is more likely that the most heavily exposed group has only three times as much bronchogenic cancer as the lightest exposed. It is also very important to note that it was only in the heaviest exposed group that there was this large excess and that in the lowest four categories, including some that were heavily exposed in ordinary meaning of that term, there was no excess of bronchogenic cancer. None of this is reflected in the comments in the document and I think that there is a rather unbalanced representation of the true state of affairs and in fact the true meaning of McDonald's study, compared to the insulation workers is totally lost. It is also of some interest that Selikoff's group shows on the average, that is lumping all of his insulation workers that he has reported together, a frequency of bronchogenic cancer approximately seven times greater than in the general or non exposed population. There is a misquote in that the facts are that McDonald did compare his group to a non exposed population, namely the general public of the neighboring province. He found that the total number of excess bronchogenic cancers in that group of heaviest exposed was too small to be reflected in the comparison. I find that it is interesting that Selikoff comments on the fact that McDonald's heavily exposed

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group did have five times as much lung cancer and that his own group had even more. This strongly suggests that if total exposure has any meaning, Selikoff's group must be even more exposed than the most heavily exposed of McDonald's. It is, of course, true that exposure may not be the cause for the tremendous difference between the insulation working population of Selikoff and the mining and mill workers of McDonald.

The next to the last paragraph on page 20 of Section III does not seem to take into account the already published information. If one simply uses the raw data from McDonald's study and from Selikoff's study, it is clear that if the mine and mill population had the same experience as the insulation workers, McDonald should have found 432 rather than 97 cases of lung cancer and 132 rather than 3 cases of mesothelial tumors. It seems inescapable to me, and I must say the same opinion seems to be held by most others, that McDonald's study clearly shows that the experience in mining and milling of chrysotile in Canada is vastly different than that in insulation workers in New York City, or for that matter in British textile workers, who, incidentally, were exposed largely to crocidolite.

The last paragraph at the bottom of page 20, Section III and carrying over to the top of page 21, does not seem clear to me. First of all, there is evidence which will soon be published in a paper now in press by McDonald, that at 12 fibers or its equivalent in millions of particles per cubic foot years, there most assuredly is a degree of asbestosis and the term that he assumes this is not very relevant. I certainly would agree that the mechanisms for converting from millions of particles per cubic foot years to fibers leaves much to be desired, but I think it should be said that this is equally true for all of the other references elsewhere in the document where such an attempt is made. The assumption that the fiber content is in the neighborhood of 10% is based on actual analysis of the fiber count in the dust clouds, and is therefore not quite an assumption, but I am sure McDonald would indicate, if he were asked, that the range of variation is considerable and he has struck an average when he used 10%. Nowhere in McDonald's paper does he refer to using a Kfactor for purposes of conversion. I am totally at loss to understand what is meant by number 3 in that paragraph. In my judgement the greatest value flowing from McDonald's paper with respect to carcinogenesis is that at levels below 200 million particles per cubic foot years there is no evidence of excess bronchogenic cancer, and in fact even at a level of 400, the evidence is very slight, indeed. This simply goes to the fact that McDonald's data, as is true of others who have looked at ranges of exposure, have found that bronchogenic cancer occurs only in those more heavily exposed. To my way of thinking this kind of evidence

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should be brought out and stressed because it gives great hope that asbestos can be used in a controlled fashion without a risk of excess bronchogenic cancer. To fail to do this I think is a mistake.

Information with respect to the total exposure required to produce the earliest evidences of asbestosis is badly needed. In this regard the paper of Murphy et al, discussed on page 21 of Section III, is of interest. This paper demonstrates the difficulties of recognizing the presence or absence of asbestosis in any given individual, since a rather surprising number of their controls gave evidences of each of the manifestations that have conventionally been used to establish the presence or absence of asbestosis. For example, twenty percent of the controls were categorized as having slight asbestosis by x-ray. It is of interest that they conclude none of their cases revealed any evidences of asbestosis in the group exposed to sixty or less million particles per cubic foot years. In fact it required 75 to produce some of such evidence. As suggested by the writer of this document, there is some reason to question the way in which the data were averaged. If one discards the unusually low (abberant) count of 0.8 and utilizes the others, it can be calculated that there are no abnormalities in the way of asbestosis until more than 85 million particles per cubic foot years have been achieved. Even at the two million particles per cubic foot level of the recent past standard for TWA, it would thus require almost forty years to produce the earliest evidences of abnormality. If one looks at the konimeter data reported in this paper and makes suitable calculations from the percent of fibers observed, it would appear that exposures of better than an average of 8 fibers per cc represents the kind of exposure to which these men have been subjected. I would not infer too strongly that any of these relationships have great reliability, but since we have so few such data, I would have thought some of these points would be brought out a little more strongly in the writing of this document. To me, this paper suggests that something in excess of 2 fibers per cc might be tolerated for thirty to thirty-five years without the production of asbestosis.

The data referred to on page 22, Section III, indicated as being from an unpublished paper by Williams et al, is so out of line with what occurred in the majority of textile mills throughout the country that I would like to see the crude data before accepting the contention that from 1930 on in the one plant the exposures were below 5 million particles per cubic foot and that in both of them they were for the most part below 2 million particles per cubic foot. I would agree fully with the

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authors that asbestos dust must be stringently controlled in the working environment in order to prevent asbestosis, but it doesn't take any of this sort of data to prove that. Before accepting their contention that a level lower than 2 million particles per cubic foot is needed, I would like to see the crude information in order to evaluate the reliability of such data in plants going back that far. I look forward to seeing the published data from these authors.

The case reports referred to on page 23, Section III, and also those of Murphy on page 24 of this section, have little relevance to the problem in hand, since most assuredly we have no factual information about their total exposures. Moreover, an isolated case of mesothelioma can occur in almost anyone who may or may not have had some exposure to asbestos. After all, a rather substantial proportion of all the mesothelioma cases reported thus far by various investigators have had no definable exposure to asbestos whatsoever. The matter of exposures in floor tile sanding is surely open to a great deal of question. The low levels observed in the mock exposure, after a few minutes of sanding by Murphy and his co-workers, is surely not to be taken seriously as a true indicator of the exposure that those individuals may have experienced. I had the occasion to speak to Dr. Burgess who took part in these, and he was astonished at the thought that anyone would take such a study as a serious indicator of the kind of exposure that the individual may have had. Their only interest, actually, was to see whether some fibers were released.

The environmental data discussed in Section IV as indicated, represents quite recent measurements at a time when many procedures to lessen the exposure had already been put into effect. In spite of this, it is of interest to see the tremendous potential for high peak exposures in all operations, and especially in the insulation industry. The possibility that peak exposures may be just as, or even more important than the lower level, more continuous exposures must be seriously considered and should be stressed. There is no information to bear on this at the present time. Insulation work is an itinerant kind of work, and the people who ply this trade can also become involved in "moonlighting". I have had the occasion to take the occupational history of a number of insulation workers and have learned that some have been involved to a far greater extent than is generally inferred in the process of tearing out of old insulation. Most of this is not on board ship, although some is done in that kind of work. The fiber counts of insulation workers in Finland and in England run considerably higher than those reported in this

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section, and I would have thought it worthwhile to report those since they form a part of the total picture. The finding of higher counts in textile and insulation manufacture is an anticipated and in fact, I am surprised that many of the counts were not higher than actually indicated.

I have some doubts about the statement at the bottom of page 4, Section XIV. The fact that many of the counts in this very scant field study are low could mean that extensive controls are already in force rather than that it should be easy to do even better. I would agree, however, that these measurements suggest strongly that the engineering procedure is feasible, although perhaps it would not be economically so. I would agree also that because of the marked intermittency of exposure it should be possible to control the insulation worker time weighted exposure relatively easily, but that textile and insulation manufacture might be more difficult. I would also agree that warehousing and mixing constitute about the only problem in some types of manufacturing such as asbestos cement products.

The "editorial" by Gee, referred to on page 8 of Section V, does not seem to me to have any scientific or practical bearing on the matter in hand. Nothing specific is said other than that there should be a change. One can ask what is meant by "reasonable probability" - surely this is a highly personal opinion and does little other than to confuse the problem.

In comparing the British standards to the current emergency standard, as done on page 9 and 11 of Section V, a further factor should be recognized. A fixed, or stationary sampling device was used in deriving the data upon which the British standard is set. The "personal sampler" upon which the USA standard is set averages approximately 20% higher for any given operation. For this reason the British trend was to underestimate the condition and they therefore arrived at a lower standard than would have been the case had a personal sampler been used. Because of this, I would estimate that the British standard is more nearly 120 fiber years in terms of the USA equivalent. On the basis of thirty years exposure and utilizing the factor just referred to, a 4 fiber per cc standard is more nearly the equivalent of the current British standard derived on the basis of a fifty year anticipated exposure.

I do not consider myself competent in the theoretical aspects of carcinogenesis, but I would think the comments on page 12 and 13 of Section V, should be buttressed by evidence that asbestos is an "initiator". Some competent persons, for example Webster and Churg, have expressed a doubt that asbestos per se is a carcinogen in bronchogenic cancer, and Webster, among others,

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feels rather strongly that it is not the carcinogen in mesothelioma. I would think that for purposes of balance such views should be expressed and some evidence given supporting the concept of asbestos as an initiator.

Is it possible that the last paragraph on page 13 of Section V might suggest to some that without any further evidence an additional reduction to 1,0.5 or less, might be anticipated in the near future?

The second paragraph on page 4 of Section VI, says that the "current standard" (established Dec. 7, 1971) has not provided complete protection ---therefore, we need a new one. I would agree that there is some retrospective evidence that the old one of 12 fibers per cc is too high. What is the evidence that the current standard of 5 fibers per cc "has not provided complete protection"?

In the third paragraph of page 4, Section VI, what is meant by "data that had just become available" and "present state of the art"? To my mind, this is far too indefinite and non-specific to use in so important a document. If this kind of recent evidence is available, it surely deserves a few lines of description.

In line 4 of the third paragraph on page 4, Section VI, it is pointed out that "it is necessary to make recommendation based on available studies and data". Items 1, 2, 3 and 4 which immediately follow that paragraph state clearly to me that no adequate or valid studies or data are available. One has a right to wonder why the above quoted phrase is used in view of the subsequent statements.

From what is presented in this document I get the strong impression if not actual conviction, that the decision to go to 2 fibers per cc is essentially an opinion and rather arbitrary in nature. If this is, indeed, the situation, why not frankly say so? I would think this kind of frankness better than trying to buttress the choice of 2 fibers per cc by stretching scant data and by non scientific extrapolations. I get the added impression that since the British set the standard at 2 fibers per cc, we should too. Perhaps we should, but if we envisage a thirty year rather than a fifty year life work cycle and use personal samplers for monitoring, we would be setting our kind of 2 fibers per cc lower than that of the British by almost 100%. An added remark is made in the document to the effect that achieving these levels is possible from the standpoint of engineering

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techniques. I don't doubt that for a moment, but I am not at all certain that it is possible to reach these levels in a manner that is feasible economically.

What are the "considerations" that indicate the need for a safety factor as stated in the last paragraph of page 5, Section VI? If the TWA must be lowered by two and one-half times as a "safety factor" - why is the "peak" kept the same as it was before? Is there evidence that the peak exposure is so much less hazardous than the TWA?

The requirements with respect to medical surveillance set forth on page 3 of Section I, are undoubtedly desirable. It should be pointed out, however, that there has been little experience with this kind of requirement in circumstances where the requirements might have to be met on such a broad scale and under such varied circumstances. Does this recommendation mean that everywhere where asbestos fibers might be released into the ambient air, no matter how intermittent or trivial, it will be necessary to have evidence developed to show that the average exposures are less than one fiber per cc and peaks below 5 fibers per cc? I doubt if that is the intent and I wonder if some way might be found to clarify this. There will also be a great deal of difficulty in obtaining some of the desired observations on such a broad scale, and this, too, makes it desirable to limit such observations to those populations where it is truly meaningful.

I wonder also about the statement that medical surveillance is "required". Perhaps "recommended" would be a better term at the outset of such a program. It is difficult to know what to do with the information once it is obtained. Who is to be notified, who is to keep the records, how long should the films be stored, what about privileged information, etc. Many of these things will come up and perhaps should be given some attention before such a strong recommendation is made.

I trust that it will be understood that I have referred to those things which I think deserve further consideration and that my reaction to this document is not totally negative. Quite the contrary, there are many places where I am in full agreement with what is said, but to detail these would at least double the length of this already too long reply to your letter. The comments made and the questions raised by me should be construed as the kind of reflection a person of some knowledge in the field might have to this document. I do not have the responsibility of setting this standard -- though I am fully cognizant of the great responsibility borne by those who will have to do so, and of

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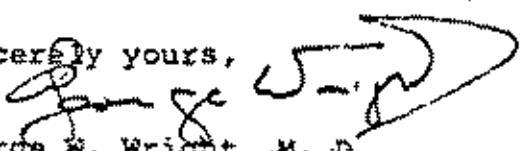
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the enormous difficulties posed by having to arrive at some final judgement. I have considered it my role to help in making the optimum choice and also in presenting that choice in the most supportable manner possible.

It should be clear that I don't believe a strong case, on scientific grounds, has been made for the choice of 2 fibers per cc TWA, with a 10 fiber peak. Taking into consideration the anticipated work life of the USA citizen and the methods of monitoring the fiber concentration in the air, I believe a standard of 4 or 5 fibers per cc would be more realistic. If stringently enforced, the actual exposure would be substantially less than that since no process can be carried out deliberately at a predetermined level of fibers in the air. If a standard is set, the operator must introduce a "safety factor" in order to be reasonably certain of compliance. Thus, a standard of 2 becomes an actual operating standard if  $1 + 0.5$  and a standard of 5 becomes more nearly  $3+1$ . I think this would prevent an excess of bronchogenic cancer and the development of a meaningful degree of fibrosis. In my opinion a standard relating reliably to mesothelioma cannot be set at this time, and to say that it can would be misleading. A standard of 4 or 5 fibers per cc TWA, would, if stringently enforced, produce an environment far less dusty than that to which workers have been exposed in the past, including those occupations where mesothelioma has been reported in excess, and I would anticipate that this level also would prevent mesothelioma.

With best wishes,

Sincerely yours,

  
George W. Wright, M. D.  
Head, Medical Research  
Division

GWW/b

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