Letter to the Editor

Response to RE: Gordon R, Fitzgerald S, and Millette J. Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women. *Int J Occup Environ Health*. 2014;20(4):318-332

Ronald E. Gordon

Professor and Director, Icahn School of Medicine at Mount Sinai, New York, USA

Dear Editor:

Thank you for the opportunity to reply to the letter you received from by Dr. Lee and Mr. Van Orden.¹ It is clear that Dr. Lee and Mr. Van Orden have no idea of what constitutes a true academic journal submission. As you are well aware, this manuscript² was submitted online and reviewed by at least two reviewers and at least two editors. The authors have included references or discussion of all methodology used in the studies performed. Further, the original paper represents a unique presentation of data documenting the presence of asbestos from the talc mines to a particular brand of talcum powder product. The original paper further demonstrated that similar types of asbestos were found in a patient using this brand of talcum powder and shows exactly how the patient was able to inhale the asbestos. The patient developed mesothelioma and ultimately died from this cancer. This manuscript confirms that the asbestos findings in prior testing of the talcum powder product and documents the presence of asbestos in the mines from which the talc for this product was sourced. The fact that the authors of the letter claimed that they had not found any asbestos based on their cursory testing of the talcum powder does not make the published manuscript scientifically unacceptable. In fact, it is their methodologies that are scientifically unacceptable. The authors of the article in question and their asbestos analysts are all very familiar with the analysis of asbestos-forming minerals and their potential interferences. In fact, all three authors are well-known recognized authorities on the identification and science of asbestos analysis with decades of asbestos laboratory experience

and dozens of contributions to the peer-reviewed body of literature on the subject. In this letter to the editor, the writers openly admit their identity as the outlier of the four laboratories that analyzed this material. Their laboratory was the only one that did not identify asbestos in the products, and the missive constitutes a blatant attempt to create doubt in the results of the other three laboratories by evoking inadequate, sometimes antiquated methods. This letter to the editor provides intentionally misleading information.

Dr. Lee and Mr. Van Orden are wrong in suggesting that the results in the published paper are biased. I am an academic who prides himself in being extremely honest and straight forward and will not manipulate data under any circumstances. I operate a pathology-based core facility laboratory at the Icahn School of Medicine at Mount Sinai, New York City, NY, USA. The laboratory has been licensed by the state and the College of American Pathologists and has never been cited on an inspection. I have been a member of that department for over 35 years and only publish work that is relevant and that adds to the scientific literature as in this case. Although the initiation of this publication was in light of testing done for legal issues, it was not the reason for the article publication whatsoever. I did not do this testing because it is the primary source of my income. I did it as a service to the institution as well as for attorneys and other clients that seek my counsel. I do not discriminate as to who can send me samples for testing. I will not manipulate data or alter methods so as to conform to what the client would like to find or not find. I use existing methodology and/or further develop that methodology to answer the demands of the project and not just employ techniques that will give only positive results, as insinuated by the letter. The work reported in this published manuscript was only an

Correspondence to: Ronald E. Gordon, Core Pathology Electron Microscopy Facility, Department of Pathology, Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Place, New York, NY 10029 USA. Email: Ronald.Gordon@mountsinai.org

extension of some previous published work that reported on the gynecologic effects of talcum powder in the development of ovarian and other gynecologic tumors; disease genesis very similar in derivation to mesotheliomas. Our study also gave insight into the issues of talcum powder that we had not been aware of in previous studies. Further, the other two authors confirmed my findings of asbestos in a number of the specimens that I tested. In addition, they did testing on whether fibers could be released into the air through use of this product and detected countable asbestos structures in the breathing zone of the person using it. One of Dr. Lee's criticisms is that Lab C was not able to confirm Lab A's work, which in retrospect is just not true. Although the initial analyses of Lab C did not find asbestos fibers in a few of the bulk samples, subsequent analyses at greater analytical sensitivities did find asbestos fibers whether they were by light microscopy of bulk samples or electron microscopy, thereby confirming the findings of Lab A by Lab C.

All the work that was performed for the published manuscript was done based on accepted methodologies. The fibers were identified as asbestos fibers using morphology, elemental composition by energy dispersive spectroscopy (EDS) and crystal structure by selected area electron diffraction (SAED) as is standard confirmation of asbestos. These methods used in the published paper were all based on methods accepted by the National Voluntary Laboratory Accreditation Program, the Environmental Protection Agency, the Occupational and Safety and Health Administration, and others. Dr. Lee *et al.* stated that SAED amphibole structure confirmation was only done visually, which is not completely true. Any visual determination that was questionable was evaluated either by an overlay method with SAED from Union Internationale Contre Le Cancer controls or actually *d*-spacing measurements made to confirm. In all cases, not one fiber was ever "presumed" to be confirmed – it was confirmed. There is no evidence that Dr. Lee's Lab, R J Lee Group (RJLG), has ever reported an asbestos fiber or structure in any of the subject brand samples that he tested. When two of the authors of the published manuscript went back to the grids prepared and analyzed by RJLG, not only was asbestos observed and documented on the RJLG grid preparations but also countable asbestos structures were repeatedly found in the same grid openings (filter preparation area) examined by RJLG. Apparently, these asbestos fibers were not seen or not reported by Dr. Lee or the technicians that analyzed them. Furthermore, on review of the testing, none of the R J Lee Group (RJLG) analyses of this product were conducted by either Dr. Lee or Mr. Van Orden.

I was asked by the attorneys to determine if there was asbestos in containers of one particular brand of talcum powder and to determine if asbestos would be released into the breathing zone of users if used in a manner consistent

with product intent, as were my co-authors. It was understood that I would not be limited to relatively small samples or to a methodology that might miss shorter asbestos fibers. I looked at larger samples of the talcum powder and confirmed them to be asbestos containing. My testing included multiple testing of the same sample and different samples from the same container. The results of my analyses were expressed in terms of the number of fibers per gram of powder. It is important to report results in terms of number of fibers per gram, as it is individual fibers that will ultimately lead to development of fibrosis, lung tumors, or mesotheliomas, pleural or peritoneal. Further, this methodology has been reported in the literature by myself as well as other investigators numerous times and accepted without question.³⁻⁶ In no way was the reader deceived with regard to the validity of the work, since the number of specimens of talc that were examined by each lab was stated in the paper. In addition to finding the same types of asbestos in those specimens of talcum powder many additional specimens were looked at by laboratory B and the findings of asbestos present correlated with the initial results of Lab A. This gave the authors significant confidence that asbestos was present in all the specimens from the one producer because asbestos was found using different methods and because the results were so reproducible.

Regarding Dr. Lee's assertion that the author's "undermine the ASTM Standardization process," Dr. Lee insists that the authors should have relied upon a Draft ASTM method for asbestos in talc knowing full well that this was not the proper thing to do. Having been involved with ASTM for many years, Dr. Lee should know that Draft ASTM methods are not to be relied upon as one would rely on the authority of published ASTM Standards. As a draft, the method has not been accepted by the ASTM committee of experts and asbestos specialists, and can be changed at any time. Furthermore, in making his statement, Dr. Lee apparently either did not really know what the current ASTM Draft method on talc actually states regarding appropriateness of use, or decided to blatantly disregard the policy of use as stated, Witness the following statement found on the top of every ASTM ballot:

"This document is under consideration within an ASTM International technical committee. The revisions proposed have not received all approvals required to become an ASTM standard. You agree not to reproduce or circulate or quote, in whole or in part, this document outside ASTM Committee/Society activities, or submit it to any other organization or standard bodies (whether national, international, or other) except with the approval of the Chairman of the Society. If you do not agree with these conditions please immediately destroy all copies of all documents."

Dr. Lee did neither obtain the approval of the Chairman of the Committee having jurisdiction over the Draft method for asbestos in talc nor did he request written authorization of the President of the Society. It is Dr. Lee who is attempting to "undermine the ASTM Standardization process" by introducing an ASTM Draft method in support of his litigation opinions, not the authors.

Yes, it is true that Lab A did not do releasability testing, but it was never stated that it had. However, SAED was confirmed on every fiber that was found. Further, when analyses of these same specimens were repeated the findings of asbestos fibers were confirmed by SAED. Dr. Lee also claims that “The authors presumed the particles they counted by TEM were regulated amphibole asbestos, even though they found no evidence of asbestos by Polarized Light Microscopy (PLM), and in the face of contradictory findings by Lab D.” The authors carefully identified amphibole asbestos by TEM using acceptable methods. It is well known that asbestos fibers can be smaller than those seen by PLM. The Rohl *et al.* article of 1976⁷ concluded that for talc PLM could only be used as a screening procedure. Rohl cited earlier work by Stanley and Norwood in 1973⁸ who concluded that “light microscopy was helpful only in screening samples with large particles and high concentrations of objectionable fibers.” In fact, a negative finding of asbestos using PLM is not considered a sufficient cause to classify a number of products (e.g. floor tiles) as non-asbestos containing material. Such products must be analyzed by TEM if found negative by PLM. It is not required that asbestos be found by PLM before it can be counted by methods using other microscopes. Ironically, the PLM analyses conducted by Dr. Lee’s laboratory did identify the asbestos-forming minerals anthophyllite, tremolite, and serpentine – just not optically considered asbestiform by his analyst(s). The determination of asbestiform is a visual assessment, and low levels of asbestos content especially in talc cannot be determined as non-existent by light microscopy (PLM) alone.

In this study, three laboratories using independent techniques found asbestos in the samples of talcum powder. Their results contradicted those of lab D (Dr. Lee’s lab) because his lab uses different, novel approaches to define asbestos that have not been accepted. In fact, Dr. Lee condones the use of SEM techniques that are not supported by any governmental agency that promulgates methods for testing products or materials for asbestos. Further, there is still no convincing evidence or documentation that cleavage fragments of sizes similar to asbestos fibers do not cause disease.

The entire concept that Dr. Lee is proposing is that the original manuscript was submitted and published for the sole purpose of gaining advantage in ongoing litigation. This was not at all the reason for this study. The manuscript was submitted for publication because it provides the results of the scientific work performed by three laboratories on an important health concern related to the use of vintage talcum powder. The authors understand that Dr. Lee has a different opinion; essentially that none of the mines and none of the processed talc contained asbestos. We encourage Dr. Lee to submit his findings for peer review as the authors have. We have shown in

the manuscript beyond a reasonable degree of scientific certainty that the cosmetic talc that was tested, in fact, contained asbestos, to include anthophyllite asbestos, tremolite asbestos, or chrysotile asbestos or a combination of the above. We based our analytical procedures and asbestos criteria on approved methods including sanctioned and seasoned standards of the EPA, OSHA, NIOSH, ISO, and ASTM International.

There is significant documentation from the talc suppliers and their own employees that the mines known to be used to supply the talc for this product contained asbestos. As described in the original manuscript, the talc sources predominately used for manufacture of this product were shown to contain asbestos and the asbestos-forming minerals in or in proximity to the talc mined, consistent with the known geology and mineralogy, and confirmed in historic and contemporary testing of those source ores.

It is important to note that a number of women who used the talcum powder that is the subject of the published paper exclusively developed mesothelioma. These women, from all over the country, had no other known exposure to asbestos-containing products. While it is true that I did not and do not maintain count sheets or identify the specific grid openings in which I identify asbestos, I do document every fiber that I count by all the criteria: morphology, chemistry by EDS, and crystalline structure by SAED. Further (and much more extensively than as is the practice of the letter authors), I examine every grid opening in a minimum of five grids 10–100 times greater area of analysis than the minimum typically specified for air sampling, for example. Since I am not doing air or water sampling, those suggested guidelines are not an issue, and not necessarily sensitive enough to detect the relatively low ratio of asbestos to obfuscating talc particulate in these powders. As to the criticism that Dr. Lee’s laboratory was unable to verify my grids, it is frequently fruitless to go back to these grids in projects where I have tested talc because the carbon support film breaks. The primary reason that the replica does not store well is that my preparations are specifically designed to maximize particle load, so that I am maximizing the amount of material I am looking through for each grid. Further evidence of the fragile nature of carbon film grids was found when I looked at two grids containing filters supplied by Dr. Lee. All the grid openings were blown making it impossible to analyze.

The results of the testing of the lungs of the individual described in our original paper confirmed that asbestos fibers associated with the talc were present. There was nothing faulty about the methodology used to determine the presence of asbestos fibers and their identity. Dr. Lee believes his criteria, and unapproved SEM methodologies, which have not been accepted by any agency, the only criteria by which asbestos presence can be confirmed. He proves his ignorance of tissue-modified asbestos fibers in his claim that he found amosite in the lung tissue of the

woman in this case. In fact, I have shown by re-examination of his (or, his laboratory, as we know that none of the actual analyses were his) own preparations that it was not amosite that he identified but anthophyllite that had been coated with iron and protein, which we as clinical pathologists usually identify as asbestos bodies. We found most of these fibers and bodies in his TEM and SEM samples that we looked at in his facility (RJLG). We were able to prove that the fibers were not amosite by determining the relative peak heights for the iron. In the case of amosite, it generally has a peak height as a pure fiber of a minimum 2/3 to 3/4 of the silica peak. If it had some coating because of the biological interaction in the human lung that there would be more iron present, however, there would not be less. When we found these fibers on the RJLG TEM grids, we were able to get EDS spectra that significantly varied along the fiber length with many sites being as little as 1/3 of the silica peak or less. When we identified asbestos bodies that the RJLG report indicated were amosite bodies, we were able to find sites along the body that were less coated and we could get iron peaks that were 1/2 or less in height compared to the silica peak. We also found that the magnesium peak was larger than would be expected for amosite. These chemical variances and inconsistencies in the mineral fraction isolated from the lung tissue of the woman at issue in this case were therefore clear indicators that the dominant asbestos type in the tissue was anthophyllite, wrongly identified by the laboratory of the author of the letter to the editor as amosite.

In my opinion, there is no debate as to whether there were asbestos fibers in the subject talc – it just comes down to how much was present. The fact that only one fiber was found in a set of five grids does not constitute insignificance. Significance and correlation were determined by getting the same results in analyzing the same samples over and over again. The determination is based on reproducible findings no different than any hematology, chemistry lab test for blood, urine, or other bodily fluid or even homogenized tissue or cells. All these test methods have been proven to be statistically accurate. Dr. Lee's methods of determining the mass of asbestos (or should I say his claim, since he never finds asbestos) are meaningless to the correlation with inhalation and disease causation in humans. It is clear that he has no understanding of the concept of the correlation of inhaled fibers and disease causation. The literature indicates a universally accepted principle that the greater the number of fibers the greater the chance of developing an asbestos related disease. For just that reason I determined and reported the number of fibers per gram of talcum powder.

Another issue for which Dr. Lee developed criteria, which not one agency has been willing to accept specifies whether particle are certain true asbestos fiber structures or cleavage fragments. As he stated,⁹ when the talc is finely ground, it becomes impossible to determine if any single fiber is an asbestos fiber or a cleavage fragment.

Further, the entire concept that an asbestos fiber is only considerable as such if it has to a length-to-width ratio of $>20:1$ is totally misleading. Regarding Dr. Lee's use of aspect ratios $>20:1$ to define asbestos, he fails to specify that the asbestos definition he is quoting to create doubt is from the Glossary of EPA 600/R-93/116 (R-93),¹⁰ which is specific to light microscopy rather than TEM.

Dr. Lee also fails to explain that the R-93 definitions and, in fact, the whole R-93 document has never been officially adopted by EPA. While there is general consensus among analysts that R-93 contains good information about how to perform polarized light microscopy of bulk samples for asbestos, it is not legally binding. In 2010, Mr. Van Orden, a senior staff member and signee of this letter of the RJ Lee Group, published a paper¹¹ with attorney co-authors where they argue that the EPA-600/R-93/116 is not a legally binding test method. Specifically, they claim: "What remains the single, legally binding test method was originally promulgated in 1982..."¹² It may be that EPA has not adopted R-93 officially, in part, because there are discrepancies in the method. Dr. Lee could have easily quoted Table 2.2 in R-93 concerning the Optical Properties of asbestos fibers where it says, in reference to anthophyllite asbestos morphology and color: "straight to curved fibers and bundles; aspect ratio typically $>10:1$," inconsistent with his $20:1$ assertion.

Further, Dr. Lee claims that the R-93 definition of asbestos is "consistent with other published work." He cites five articles as evidence. Two of the citations are of his writing (Letter references 12 and 14) and one, reference 13, is a title of a presentation at a meeting, which has no proceedings, and therefore, has not been published. Reference 2 is the paper with the original suggestion of the mineralogical definition that was modified for inclusion into EPA R-93 and the last reference (reference 15) is an old "Absence of Asbestos" method that the U.S. Food and Drug Administration has requested be modernized.¹³ The Expert Panel charged with the task of updating the method concluded that the method, as currently written, could lead to false-negative results, which could allow talc samples with asbestos contamination to pass. In addition, the Panel further concluded the lack of identification procedures by optical microscopy could lead to false-positive results. Therefore, Dr. Lee's reference 15 is an old method under much-needed revision in order to assure that PLM analysis is not considered adequate for the determination of the absence of asbestos in talc, and cannot be considered an authoritative scientific reference.

Dr. Lee has not considered bundles of fibrils that are broken from longer fibers and have ratios $<20:1$. The paper by Illgren¹⁴ that was quoted by Dr. Lee as a reference makes a clear distinction between the asbestos fiber and the cleavage fragment. All of the fibers that I identified in the subject talcum powders fit the criteria Illgren claimed as asbestos in his review. Wylie makes a point about size and aspect ratio, but never requires $>20:1$ aspect to be

asbestiform, just that – asbestos fibers are more likely to be greater.¹⁵ The OSHA Method says “when in doubt, count.”¹⁶ I would ask of Dr. Lee, why is it acceptable to create doubt in order to not count asbestos?

In the manuscript, I reported that the majority of the asbestos fibers I identified had aspect ratios of >15:1 and many were above 20:1 to quote the article accurately. The systematic use of size alone indicates that the greater the aspect ratio the more likely it will be an asbestiform fiber not a cleavage fragment. In almost every case, the fibers I identified were asbestos fibers by both Dr. Lee’s and my criteria to the extent I can determine his criteria.

Even in 1976, McCrone stated that once talc is ground it is difficult if not impossible to see the smaller asbestos fibers by light microscopy and Electron Microscopy has to be employed. The New York State Department of Health stated that if the light microscopy is negative for some products where light microscopy has been repeatedly proven inadequate, TEM confirmation is required. It appears that Dr. Lee speaks out of both sides of his mouth. In one assertion, he claims that there has to be a population of fibers to call it asbestos. In another assertion, individual fibers are discounted as cleavage fragments. We are left with no possibility by which asbestos presence can be allowed. He quotes papers that have stated that for fibers to be considered asbestos they have to be >5 µm in length and have an aspect ratio of 20:1 or greater. However, there is no agency in this country or for that matter any country that has ascribed to a definition of asbestos where only those fibers with aspect ratios >20:1 are asbestos. Even the papers that Dr. Lee quoted indicate that if the fibers are that size and aspect ratio they are more likely to be asbestos.

In the dozens of analyses of the talcum powder products in question, Lab A only counted fibers 5 µm in length or greater. Aspect ratios in those analyses were mostly 15:1, or >20:1. The majority of scientists involved in asbestos analysis consider 5:1 as a realistic aspect ratio to consider as asbestos. Further, most investigators do not ascribe to the statement in the letter to the editor regarding the letter authors’ laboratory, RJLG (Lab D), to wit: “The authors criticize the work of Lab D, arguing that Lab D’s definition of cleavage fragment is not generally accepted, ignoring the fact that these same definitions are part of the literature and methods they cite.” The key insinuation here is that Lab D’s definition of cleavage fragment is parts of the literature and parts of methods that the authors’ cite. To the contrary, Lab D’s definition is cobbled together from various methods to produce a definition that suits Lab D: a definition that consistently and repeatedly is used to refute

the obvious presence of asbestos. Finally, Dr. Lee’s arguments are totally irrelevant in light of the fact that people that inhaled the talcum powder have repeatedly developed mesothelioma.

Disclaimer Statements

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Conflicts of interest Dr Lee and Dr Gordon are working for attorneys on opposite sides of a civil law suit.

Ethics approval Not required.

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