LETTER TO THE EDITOR

Response to Second Letter by Lee et al. of 2016

Response to second Letter to the editor by Dr. Lee et al. OEH472 to Manuscript Entitled, “Asbestos in talcum powder as a cause of mesothelioma in women” By Gordon, Fitzgerald & Millette 2014 [1].

I would like to thank the Journal for giving me the opportunity to respond to Dr. Lee’s bizarre reply to my response to his initial criticisms.

Dr. Lee criticized my response to his opinion letter in three basic areas. The first of which is a multiple page diversion to a reference that had nothing to do with the manuscript in question but was a critique about previous publications regarding talcum powder, and ovarian and gynecologic tumor developments. The second are comments on my ability to properly analyze bulk minerals. The third is to defend his analysis of phantom fibers not at all in the tissue from the patient published in this original article based on an exhaustive analysis.

Unfortunately, we submitted errata to correct the issues created by the manuscript reviewer and editorial suggested exclusions which were missed upon the last review prior to publication. This has been corrected by the publication of a Corrigendum [2]. In every case we have not misquoted anything and our claims are reliable, easily duplicated, and highly accurate.

It is apparent that the focus of half of his letter refers to a single reference to talc in gynecologic tissues and organs in the Introduction and Discussion of our manuscript. Their premise represents a misinterpretation of the reference and the claims that our manuscript does not tell the complete story. However, that was not the focus of the published work regarding the contamination of Cashmere Bouquet talcum powder with asbestos. The purpose was clearly defined to correlate the finding of the same types of asbestos found in the containers of talcum powder given to us directly by Colgate as well as containers that were received, factory sealed, with the asbestos found in the lungs and lymph nodes of the patient that used the Colgate brand of cosmetic talcum powder. In addition, we also tested the ability to find and confirm that the use of the talcum powder confirmed the presence of asbestos by documented sampling in air testing in a glove box and a simulated bathroom conditions. The air testing confirmed that respirable asbestos could be deposited in the lungs of those using the talcum powder. The data presented in no way reflects anything in the ovaries or gynecologic tissue. To distort our work in this forum the way Lee has clearly driven by his clients or their lawyers and totally inappropriate. Lee’s goal was not to advance the science of cancer causation so that lives may be saved by sound scientific research, but rather addressed other legal issues he faces in his defense of talc which has no place in published commentary and has even less to do with our 2014 published manuscript [1] to which Lee et al. refers. Dr. Gordon will in fact address this in a new manuscript to be

written. It should be noted that the data for this manuscript was available at the time of the writing and publication of our article being criticized here.

In the references to the gynecological studies, I did not look at 70 patients at the electron microscopy level. This is a fatal flaw in Lee’s review of our work. I also did not look at the talc used by the patients for its content. Again, the authors of this letter are trying to address issues that are not presented or contained in the manuscript that they are criticizing. It may sound like science, but it is not sound science.

I will only briefly respond to the criticisms of the correlation of data previously published on gynecologic tissues. The study was initiated to study the presence of talc in these tissues to determine if these women were developing tumors related to exposure to cosmetic talcum powder. Not only did we find cosmetic talcum powder in the gynecologic tissue, we also found asbestos, a class one carcinogen. We found talc not only in the user group, but also in the control group of women that did not use the talcum powder in their perineal areas. Not reported, however, was the use of talcum powder cosmetics in other areas of the subjects’ bodies. We did find asbestos in women that had partners who were exposed occupationally to asbestos. Lee et al. indicated that we did not report anthophyllite type asbestos. This was true at the time of publication of those articles. However, as with the talcum powder and the human tissues studied, the amount of tremolite and anthophyllite was relatively small and required greater sensitivity to detect. This was the case with the studies analyzed in the Heller work [3–5]. When the manuscript is published, honest reviewers will reach their own conclusions. This should never have been addressed in this forum because it has no impact with regard to issues presented in this manuscript in question.

Talc and its effects on gynecologic tissues, will be further discussed in a future manuscript to be written by me and other concerned scientists.

Lee’s letter is a personal attack. His gratuitous and unsubstantiated use of the terms such as “sloppy” and “incompetent” is irresponsible and doesn’t negate our research or its conclusions. It may satisfy Lee’s need to get the last word, but without foundation, it is as unhelpful as it is unscientific. Like any conscientious scientist, I have no problem with critical review of our research. In fact, we welcome honest commentary and rely upon it to improve the final product, just as that final product improves the lives of its subjects by answering critical questions with practical implications for prevention. In my opinion, rebuttals and sur-replies, the likes of which are carried out by Dr. Lee only in the interest in hiding the truth and covering up facts, than it is answering the critical questions surrounding the cause of some cancers. I have personally witnessed Dr. Lee pulling the wool over the eyes of a judge to disqualify one

of the most honest and careful scientists/minerologists I know. This was done in a court proceeding when the other side was not able to question his explanations.

I have published over 200 peer reviewed manuscripts on many subjects. I know and understand the scientific method. In some analyses, I may not use the scientific method per se in testing as the Lee lab does. Our protocols are a matter of testing and the use of many protocols for testing approved by various agencies. However, in the testing of talcum powder there are no uniform testing protocols. There are suggested methods. My research and methods have increased the sensitivity of testing to find smaller amounts of asbestos by looking at more material. To do that, more material is tested by techniques dependent on a greater sensitivity. I have the same capability to test bulk samples by techniques such as PLM or PCM or XRD. However, the literature and numerous replicable test results already published reveals that such tests are inadequate in identifying asbestos in talcum powder. In other words, if one does not want to find them, he can make that happen. Using TEM techniques has the sensitivity to identify these structures provided the specimens are studied with adequate sensitivity by looking at more and more of the material. It is well documented now that even small amounts of asbestos can cause cancer and in particular mesothelioma in the pleura of the lung and in the abdomen. Tests performed and reported in our paper show that the asbestos released from talcum powder can be breathed and as a result may cause these cancers whether it stays in the lungs or is dissolved or transported out of the lung. To be sure, as with all asbestos-related diseases, the latency is very long which may be due to the level of exposure and relative size of the fibers.

Lee also claims our lab should use the Draft Yamate method [6] and criticizes our choice not to do so in these circumstances. The Draft Yamate [6] method was developed in the 1980s to meet specific criteria for the percentage of asbestos in air, water, or a bulk sample. As most earnest researchers know when a sample has very little asbestos and where the fibers are relative small, the Draft Yamate [6] method is not adequate due to sampling and sensitivity. Further, the concept that tilting or zone axis analysis is required, in SAED analysis is ridiculous since differentiating between talc and anthophyllite is clear without ever doing zone axis tilting. Millette clearly stated this in his 2015 publication, "Procedure for the Analysis of Talc for Asbestos" [7]. Talc always appears as talc even with tilting, anthophyllite, however, appears as amphibole asbestos on a flat plane, but when tilted to certain angles it can appear as talc. That is the deception promoted by the Lee lab during its documentation. In our testing of the grids that were prepared by the Lee Lab, we found significant asbestos fibers which were confirmed by SAED. Lee found tremolite and anthophyllite but called them cleavage fragments no matter what the size and what all other agencies criteria defined. An asbestos fiber by any other name is still an asbestos fiber.

The allegation that I have not been formally trained in mineralogy is absurd. I have learned all the techniques over many years of doing this work and I am more than competent in identifying asbestos fibers and typing them. I may not know how to identify all minerals, but I am well

educated in identifying asbestos type minerals. As I stated, it is more difficult when modified by a human than just looking at a mineral.

This is not a game. This public jousting serves only to sow doubt, but doubt can be the product some want. A client may not need to prove asbestos isn't in their products, they just need a lab willing to provide the reasonable doubt the company needs in court. My motivation is that sound science will show the way to cancer prevention. Prevention is the most reliable cancer cure. Talc undeniably causes granulomatous lung disease in some individuals and it is used for just that purpose with talc pleurodesis. Whether it is a carcinogen or co-carcinogen in its own right is yet to be determined. However, there is substantial evidence that talc can cause an inflammatory process. In that respect alone, it is acting as a potential cancer promoter.

Lee also claims that I have found asbestiform fibers in product testing, and that the "asbestiform fibers" are not asbestos, but are rather intergrowths or cleavage fragments. Lee is wrong, it is impossible to identify a cleavage fragment when there are single fiber identifications. Lee is wrong on the cleavage fragments vs asbestos fiber front for three reasons. First, I have identified fibers in samples that I received from Dr. Nolan tested by Drs. Rohl and Langer. I found asbestos that any laboratory would call asbestos fibers because they had an aspect ratio greater than 20:1 and in a few instances were greater than 100:1. All human health related agencies provide that if a particle is found that has the typical characteristics of a fiber, is greater than 5 μm , has aspect ratios of greater than 3:1 and fits the EDS and SAED criteria of a type of asbestos, it has to be considered an asbestos fiber. It should be noted that asbestiform is the criteria that has been used because it is clear that from a biologic standpoint there is no difference. Secondly, my work on these specimens was confirmed in two other mineralogy laboratories. Regardless of what Dr. Lee claims, Dr. Langer told him in an unsubstantiated conversation, that conversation is meaningless given he communicated the opposite to me in an email I have maintained. The laboratory they worked in was clean and there was no chance of contamination as suggested by Colgate attorneys. Langer was very careful not to contaminate his lab or the specimens. I visited Dr. Langer's Laboratory and saw how careful he was to not cross contaminate any samples. And although Dr. Langer has done some back pedaling with regard to those samples and the possibility of being cleavage fragments. Drs. Langer and Nolan were asked to reanalyze those specimens. Their report was never produced by the Colgate attorneys, a common litigation strategy when results do not support an attorney's litigation necessity. From a health perspective there is no difference. Dr. Lee et al's statements in this letter regarding the biologic effects of fragments vs fibers have been totally and unequivocally refuted by the EPA in a document dating back to 2006 [8]. I will not go any further since I do not care to personally attack Drs. Lee and Sanchez and Mr Van Orden. It is unfortunate that they do not understand where mineralogy ends and biologic effects begin or where they intersect. I offer as additional proof that other minerals not termed asbestos and have fibrous appearance have been implicated as causative in the

development of fibrosis, lung cancer, and mesothelioma, and possibly other types of cancer.

After seeing many reports on tissue fiber burden analyses and on bulk product testing, and after reading depositions related to Lee's laboratory procedures, it is apparent that Lee does not perform their testing based on their own SOP. Lee is inconsistent and picks and chooses the techniques and protocols he will use. Further, although his lab claims to use the Draft Yamate III protocol [6], I have yet to see a report among the many I have reviewed that confirms he used it. His lab frequently uses SEM as a means of analyzing for asbestos not approved by any agency. My lab protocols conversely meet suggested methodology.

Lee advocates that even if these fibers are found, regardless of size, they are cleavage fragments not asbestos fibers. Such was the testimony of Dr. Sanchez. Their position is not supported by any agency that considers human health effects. The EPA published a specific document that clearly indicates that Dr. Lee's position is totally unreliable [8]. Lee's work suffers from publication skepticism, because it in no way defines specifics of his criteria. Lee's cleavage fragment defense does not in any way allow for human tissue interactions with asbestos fragments or fibers and its consequences. In the end, all that results is confusion of the issue of what is asbestos. Lee's lab ignores the definition and criteria of every agency that provides guidance on asbestos analysis. Their criteria may suit their purposes but it is not the criteria for reliably identifying asbestos. All agencies include TEM as an optional/recommended tool when studying bulk samples for the presence of asbestos. Lee claims that cleavage fragments can be defined by SEM techniques by what criteria? All agencies require TEM analysis for the determination of Taos contaminated by those minerals. SEM is not an acceptable methodology unless one is trying not to find asbestos. When Lee's lab does find what is clearly an asbestos fiber he calls it by any other name. Cleavage fragment is Lee's favorite pseudonym for asbestos, but all the agencies indicate that when in doubt it is to be defined as an asbestos fiber. The Lee lab has taken the opposite approach, criteria be damned. The reader can be the judge as to why one who defends asbestos companies uses a technique that will not reliably find asbestos fibers in his clients' products.

Let's be clear, these mistakes alleged by Lee are mistakes of his own making, not Gordon et al. [1]. Lee claims that my expertise is with tissue digestion and not mineralogy. He questions my analysis of finding anthophyllite vs amosite based on reduced Mg ratio to iron. Lee is ignorant of what happens to these fibers in the human body over many years. They actually show a documented fiber of amosite based on their analysis. As I stated earlier, I believe that there is a good chance that whoever gave them the tissue may have contaminated it with a specimen from a patient that may have had an amosite exposure or contamination in their own lab. I looked at all the tissue, not just a representative sample of the tissue by the same technique, SEM, that was used by Lee et al. and did not find one amosite type asbestos fiber or asbestos body. Further, there is a big difference between what is determined as an anthophyllite fiber from tissue that greatly differentiates it from what a mineralogist will identify. It is well documented that the main changes

associated with human on asbestos fibers is the subtraction by the leaching of magnesium and the addition of iron. When one looks at a fiber directly from the mine or at least not in contact with human or animal cells, there is a constant and documented ratio of Mg, Si, and Iron, the same components seen in anthophyllite and in amosite. One distinguishing factor for amosite is the presence of Mn in most amosite fibers. Clearly there was none in the EDS demonstrated. Further, Mg is higher in anthophyllite. However, in the fiber produced in this letter, they show an intermediate amount of Mg. This best supports, along with our assessment, that it is anthophyllite not amosite based on reduced Mg due to leaching. The fiber is coated with iron that could not be seen in this TEM visually, but is present increasing the iron peak. This is best demonstrated when you do multiple EDS analyses along the length of the fiber. When the ratios of both iron and Mg change, it is clearly more likely to be anthophyllite than amosite just based on EDS. When at Lee's lab studying Dr. Lee's prepared grids on this case, Sean Fitzgerald did the same analyses of SAED and determined that all the fibers we were able to identify, not all due to time constraints by EDS and SAED, were found to be anthophyllite. Further, Sean Fitzgerald is a mineralogist that formerly worked in Dr. Lee's lab. All this information was contained, but ignored by Lee in my original response. Based on the size of the fiber, I refuse to believe that the SAED produced in this letter is not from the fiber represented in the photo represented by Lee in his final letter. Many of the same samples that I studied were confirmed by not one, but two mineralogists that were authors on this paper. Not only did they find it in the talc product, but they identified it in air samples from the containers by two different methods with the same results I had.

The most recent manuscripts both before and after publication clearly indicate that the criteria used by myself for identifying the fibers as asbestos and not cleavage fragments are correct. In addition, it has been stated by Lee et al. that dual axial tilting as part of identifying anthophyllite from other amphiboles and in particular talc is necessary. However, they have never described why and yet in a very recent publication by Dr. Millette, he indicated that doing such are time-consuming and do not add relevant data to the identification. Thirdly, the EPA does not recognize Lee's argument regarding the identification of cleavage fragments. He, and the lawyers who helped, encouraged, or wrote his response can continue the personal attacks, but I do not undertake talc testing for litigation purposes. I am doing it to promote our knowledge of how asbestos at various environmental levels impact the development of disease in humans. I do not only accept specimens from individuals, other pathologists and plaintiff attorneys alone, I will accept them from anyone that will send them to me for analysis.

In summary, it is clear that a couple of statements appearing in the introduction and discussion of this the manuscript at question is that this manuscript looks at pleural mesotheliomas not gynecologic tissues. The basis for Lee et al. arguments here on both product testing and human tissue demonstrate their bias not mine. We have reported our findings that they disagree with and they have expressed why and I hope that the reader will take

into account our rejection of their criticisms and our basis for such rejection. Dr. Lee et al's criticisms miss the mark. Sound science is more important than sounding like science. I encourage them to continue their review of this very important work with this in mind and thank them for their comments.

References

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