Letter to the Editor

Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women

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Dear Editor:

The role of a scientific journal is to publish papers that contribute to the body of scientific knowledge, are technically correct, and appropriately reviewed and edited. The role of the editor is to ensure that the content, writing, format, and references meet the standards of the journal. The role of the peer reviewers is to assess whether the work is new and contributes to the knowledge in the field, ensure that the writing fairly represents the current knowledge in the field, and that the citations are accurately cited. The role of the authors is to provide a full disclosure of their work, including sufficient detail about data and methods so that independent investigators can assess the credibility of their work. The reader relies on the journal editor and his/her selection of reviewers to ensure these standards are met. In the matter of the subject paper, the editor, the reviewer(s), and the authors, failed to meet these standards, resulting in the publication of a paper that is scientifically unacceptable.

Gordon *et al.*¹ undermine the scientific method, the integrity of the scientific peer-review process, and the ASTM Standardization process. The subject matter of the paper is at issue in on-going litigation where the authors have been retained by plaintiffs and Lab D (the undersigned) by defendant. All laboratories found the samples to consist primarily of platy talc particles characteristic of cosmetic grade talc. However, the authors made multiple errors leading to the misidentification of trace levels of accessory minerals as asbestos in the talcum powder. The authors presumed that they could use visual pattern recognition to identify selected area electron diffraction (SAED) patterns as a particular mineral, without performing any tests on minerals that were likely to pose interferences to establish the reliability of their method. The authors presumed that the particles they counted by transmission electron microscopy (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 failed to compare and contrast their interlaboratory

results, which varied dramatically. For example, in one bulk sample that Lab C analyzed three times, the results varied from nondetect to 202 million fibers per gram on a single sample. In the same bulk sample, Lab A found a single fiber only after analyzing between 400 and 500 grid openings, which Lab A extrapolated to 11 400 fibers per gram on the same sample. They left the reader with the mistaken impression that “three independent laboratories” had validated each other’s work.

The paper does not disclose key portions of Lab B’s methodology – that it attempted to extrapolate to exposure using indirect preparation methods – or the fact that the analysis of glove box air samples Lab B prepared by direct preparation yielded statistically insignificant fiber concentrations. Moreover, the authors misrepresented the work performed by the laboratories. The authors suggest that the identity of the product was verified, but in reality the samples were collected from a variety of sources and none were in as-manufactured condition. Contrary to what is written in the paper, both Lab A and Lab C analyzed samples for which they found no countable structures. Lab B made no independent bulk analysis as implied in the paper, but reported no asbestos in four of the 20 Lab D samples reviewed. Lab A never did releasability testing or quantitative SAED as claimed in the paper.

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. They claim that Lab D’s definition of asbestiform is incorrect, ignoring the fact that the method was accepted by EPA and was, in fact, published in a peer-reviewed journal. The authors claim that Lab D’s analyses were in error, but base their argument on a “consensus” among themselves, not on analytical data, and give no indication of the error rate they attribute to Lab D. The authors also incorrectly quote or ignore relevant peer-reviewed literature, including their own and that of RJ Lee Group (RJLG).^{2–4} In short,

their paper misstates the facts, and misrepresents their own work, the conclusions of the references cited, and the work by Lab D (RJLG).

ASTM is a developer and provider of consensus-based standards. ASTM developed testing methods that are a critical part of the means by which the scientific community ensures that test results are reliable and repeatable. The authors, two of whom are members of the ASTM committee charged with developing methods for asbestos analysis, claimed to have used methods developed by the committee, but failed to perform critical steps required by ASTM in the identification of amphiboles. They also ignore the fact that the same ASTM committee has a draft method for the identification of asbestos in talc under development. This method provides a means for separating asbestos from nonasbestos because of the complex mineral assemblage encountered that could have been used in their analysis. Producing results which are purported to have been performed according to a standard method, but not following critical portions of the method undermines the integrity of the process.

The primary issues in the underlying litigation are determining whether cosmetic talcum powder is contaminated with asbestos and deciding whether exposure to cosmetic talc was the causative factor for the mesotheliomas at issue. The authors claim to have shown that exposure to asbestos-contaminated talc is that causative factor, but support their argument with incorrect methodology and faulty data. They also ignore the science, as expressed by IARC,⁵ which did not identify a causative link between exposure to talc, free of asbestiform minerals, with lung cancer or mesothelioma. Cosmetic talc, including the source mines at issue, has been recognized as being free of asbestos.^{5,6} Finally, the authors ignore the presence of amosite, found by Lab D (RJLG) in the TEM analysis of the diseased lung tissue. Amosite, a commercial asbestos fiber, has never been found to be a contaminant of cosmetic talc, but is a well-recognized causation agent for mesothelioma. A conclusion contrary to the existing body of knowledge requires a detailed analysis with well laid-out experimental procedures, measurements, and statistics, and not hand-waving arguments.

The authors and Lab D (RJLG) have been investigating the potential occurrence of asbestos in cosmetic talc in a series of cases in which the plaintiffs argue that usage of cosmetic talc led to the induction of mesothelioma. The interlaboratory debate boils down to whether the laboratories accurately identified the amphiboles they claimed to and if so, whether those amphiboles were asbestiform. It is well recognized that elongate mineral fragments do not have the same biological activity as asbestos fibers.^{7,8} The known elongate minerals found at trace levels in cosmetic talc include a mixture of magnesium silicates (e.g. sepiolite), including talc fiber (some of which are talc plates viewed on edge), transitional intergrowths of talc and anthophyllite, nonasbestos tremolite, and nonasbestos

anthophyllite. The issue is whether the authors establish the presence of anthophyllite asbestos and to a lesser extent tremolite asbestos, as claimed in the paper, given these acknowledged background interferences.

The first issue is whether the analytical methods, as the authors used them, were reliable for the purpose and used properly. One of the authors claimed to have followed a modified Yamate⁹ protocol, but had no record of which grids were analyzed, and recorded no fiber count data sheets showing the grid opening in which a fiber was found or TEM grid maps as required by the method. Another claimed to have followed Yamate as well, but provided no record to relate the individual particles counted to the corresponding analytical data. The third claimed to have followed D6281,¹⁰ a method for identifying asbestos in air in locations, but which acknowledges that nonasbestos amphiboles may be included in the fiber count. The authors write that they did not need to perform quantitative zone axis identification, suggesting that Yamate says it is “optional” and “useful,” when, in fact, it is expressly required by both Yamate Level III and D6281.

Because of the extensive milling in cosmetic talc, amphibole minerals are often found as particles having elongated aspect ratios (>5:1) and parallel sides thus requiring a detailed characterization to properly define them as either asbestos fibers or nonasbestos fragments. The characterization must comply with accepted definitions of what is asbestos and what is not asbestos. Of the methods supposedly used by the authors, only EPA 600/R-93/116¹¹ (R-93) has an explicit analytical definition of asbestos. This definition is consistent with other published work.^{2,12–15} Under R-93, if most of the individual fibrils are thick (i.e. >0.5 µm in width), the population is not asbestos. Also, per R-93: “If a sample contains a fibrous component of which most of the fibers have aspect ratios of <20:1 and do not display the additional asbestiform characteristics, by definition the component should not be considered asbestos.” In this case, the PLM optical data from Lab C and the data from Lab D (RJLG), both using R-93, conclude that the amphibole particles present are not asbestos. This last fact alone should have led the authors to reconsider their findings since 90% of all the particles identified in the talc samples were optically visible, and if asbestiform, should have been observed in the optical analysis.¹⁶

The authors cite a lack of accepted procedures for identifying asbestos fibers from nonasbestos fragments by electron microscopy. In fact, a review of the literature, including Van Orden *et al.*¹² and Wylie,¹⁶ shows that there are well-defined characteristics of asbestos that differentiate it from the nonasbestos mineral fragments in the TEM. The authors claim that Van Orden’s method is a scanning electron microscopy (SEM) method that was not validated for the purpose of distinguishing between asbestiform and cleavage populations. As seen in Van Orden *et al.*, the method was validated, and is a TEM – not an SEM – method as stated in their paper.

Asbestos is identified by its habit by looking at a population of particles. If most of the particles in a population of particles longer than 5 μm have an aspect ratio less than 20:1, or if the average aspect ratio is less than 20:1, it should be classified as nonasbestos.^{2,11,15,17} “Elongated particles [...] that did not come from a population of asbestos fibers are sometimes called cleavage fragments.”¹⁸ Lab A did not report dimensional data for the particles counted, but the paper indicates that the majority of its counted fibers had aspect ratios less than 20:1. The particles Lab C identified in the bulk talc as anthophyllite had average aspect ratios less than 20:1 in samples with four or more particles. The aspect ratio of the tremolite particles reported by Lab C were greater than 20:1, but only four particles were identified as tremolite of the 13 bulk samples analyzed. In no sample were a sufficient number of tremolite particles identified to characterize as a population. Moreover, review of the images provided indicates one of the particles fall in the category of particles which cannot be identified as asbestiform or cleavage based on a single particle and the other three are nonasbestos cleavage fragments. The particles identified as anthophyllite by the author–reviewer, during the review of Lab D bulk analysis, had higher aspect ratios but proved to be fibrous talc or clay upon reexamination. Four of the five particles illustrated in their paper had aspect ratios less than 20:1. The upper image in Fig. 6 is unambiguously a cleavage fragment. Thus, the authors have not demonstrated that an asbestiform amphibole population was present in the talc.

The authors premise their conclusions on visual inspection of SAED patterns to identify amphiboles with (0.53nm) row spacing as is permitted by Yamate Level II for environments known to contain asbestos. The major analytical problem with this approach is that magnesium silicates, talc fibers, and mineral intergrowths found in talc can have SAED patterns with row spacing (0.53nm), or other patterns, that are very similar to those produced by anthophyllite or tremolite. This gives rise to significant interferences. In order to unambiguously identify such particles, it is necessary to tilt the fibers to multiple orientations, record the SAED patterns, and make quantitative measurements of the d-spacings and angles constituting the basis vectors in the pattern.^{9,10} These measurements should then be compared not only with the suspected mineral but also with potential interferences by other amphibole and nonamphibole minerals. Two of the authors, after repeated criticism, produced a number of zone axis SAED patterns measurements that they compared with zone axis data for anthophyllite and tremolite. They reported matches in a number of cases. Our independent re-analysis of their claimed anthophyllite pattern measurements indicate that a number of other minerals, including talc and clays, have a comparable or better fit.

The authors criticize Lab D’s (RJLG) analysis, suggesting that they missed or ignored countable asbestiform structures and misidentified amphibole structures as talc

or transitional minerals. To support their argument, they provide pictures, SAED patterns, and EDS spectra from particles they found in their re-analysis of Lab D grids in Fig. 12. Typical of the data from Labs A and B, in Fig. 12, there are four unlabeled and unindexed SAED patterns, three unlabeled EDS spectra, and two unlabeled images, making it impossible to relate the pieces of data. The particles in Fig. 12 have aspect ratios of about 10:1, not characteristic of asbestiform structures. The EDS spectra do not match the EDS spectra of particles found in the lung. There is indication in the SAED patterns (left center in Fig. 12) that at least one of the particles is multiphase or transitional. The morphology of the exemplar particles is not asbestiform, nor does the data provided support the claimed identification. Their exemplars do not provide evidence that Lab D (RJLG) was incorrect or that the particles in the lung match the particles in the talc.

We have examined the TEM grids prepared by the authors, as they did ours. Except where the documentation was nonexistent (Lab A), we have successfully relocated most of the particles greater than 5 μm in length in Lab B and Lab C samples. We did confirm the presence of non-asbestos tremolite identified by the authors in some cases, but in others found that the particles were intergrowths with talc. With minor exception, however, their identifications of anthophyllite have been incorrect. When subjected to quantitative zone axis SAED analysis, the particles identified by the authors as anthophyllite have proven to be talc, talc/anthophyllite intergrowths, or amorphous clays. Thus, the authors have not provided the requisite analytical data, required by the protocols used, to demonstrate the products analyzed contained the minerals they claim to have found.

We also searched for and relocated particles for which data were provided from the authors’ reevaluation of Lab D grids. We were able to relocate the upper particle in Fig. 12. It is not a fiber overlapped by other particles but a single coherent intergrowth between talc and tremolite and should not be treated as a respirable particle or asbestiform fiber. The authors reviewed 20 samples originally analyzed by Lab D. In most of those, the reviewers either explicitly agreed with the analysis or identified no particles within the area analyzed by Lab D that they believed were incorrectly identified. Of the six particles he reported that had been analyzed by Lab D, the reviewer agreed with the identification of five. We have been unable to relocate eight particles analyzed by the reviewer because no map was provided. The remainder, those outside the Lab D analyzed areas, but for which location data were provided, we were unable to locate two, but eight (four claimed anthophyllite, two claimed chrysotile/antigorite, and two claimed tremolite) were relocated and quantitatively analyzed. Only one (nonasbestiform) tremolite particle was found to be correctly identified by the reviewer. The remainder of the particles were intergrowths, talc, or clay fibers. The authors have not demonstrated that Lab D’s mineral identifications were incorrect as claimed in the paper.

In attempting to link cosmetic talcum powder to mesothelioma, the authors argue that the asbestos bodies found in the lung tissue are derived from the talc; yet, the morphology of the particles in the talc was not consistent with the morphology of the asbestos bodies found in the lung. The two asbestos bodies in Fig. 11 have aspect ratios over 100:1, are less than a micrometer in diameter, and have highly parallel sides. They have a dramatically different morphology than the five particles used by the authors to illustrate their product testing findings. In fact, very few if any, of the 1000 plus particles characterized by the four laboratories during product testing have the morphology of the asbestos bodies found in the lung by Lab D or the two asbestos bodies shown in the paper. Finally, in drawing the causative link between allegedly contaminated talc and causation of mesothelioma, Gordon *et al.* ultimately relies on the identification of the mineral core of an asbestos body in the lung tissue. They ignore any possible iron content of the mineral fiber, instead assigning that to the iron coating on the fiber. But they fail to recognize the large number of uncoated amosite fibers that were also present in the lung tissue as possibly causative of the disease or that these fibers are dimensionally and morphologically similar to those that are coated in the asbestos bodies. Thus, contrary to the claims in the paper, the authors have not established the connection between the talc samples and asbestos disease in the lung tissue.

The authors cite a number of publications supposedly supporting their claims that consumer cosmetic talc usage has been linked to the occurrence of malignancy. Citations as to causation of mesothelioma are used to support the arguments of the authors, but these studies¹⁹ – for which Gordon was one of the authors – showed no relationship between talc exposure and the presence of asbestos in ovarian tissue, even though more than 60% of those studied had known exposures to talc. In 74 of the 75 ovary samples studied in their references, any asbestos found in the ovaries was identified as chrysotile, amosite, and/or crocidolite¹⁹ (see also Refs. 4 and 5 in the paper) – not anthophyllite or tremolite as characterized in this study. Tremolite was reported in one sample. Thus, the findings of the references cited as a basis for claiming that asbestos in cosmetic talc has been related to ovarian cancer or mesothelioma in the past are misrepresented.

Gordon *et al.* cite several books and other studies to suggest that talc ore deposits are known to be contaminated with asbestos fibers. However, the cited references^{20,21} do not report asbestos in any talc ore sample. As noted by Rohl and Langer: “because no methods exist to distinguish between possible differences in fiber surface, we do not refer to anthophyllite and tremolite fibers in these talcums as asbestos. Instead they are referred to as asbestiform.”²⁰ Pooley’s study of northern Italian talc²¹ indicates that tremolite does not occur in the talc ore, but in the surrounding country rock and when crushed, the tremolite is shorter and thicker than asbestos. Berg²² was clearly aware of the

potential significance of asbestos, noting that the communities are sensitive to asbestos issues, but in none of his analyses of Montana talc ore samples did he report any asbestos fibers. The other references cited make no mention of asbestos in cosmetic talc ores. Thus, these citations do not support the premise that the mines from which the products analyzed were produced contain asbestos anthophyllite or tremolite.

There are a number of additional errors in this paper that should have been caught by the editors. For example, the Yamate protocol is extensively discussed, but never formally referenced in the paper. On a number of occasions, a citation is made that is incorrect: Pooley study as Reference 18 when it is actually 17 in the published paper; Reference 22, an analytical method, is cited to indicate that the talc is contaminated with asbestos; Reference 8 is a study of industrial grade talc miners and has nothing to do with cosmetic grade talcum powder users as described in the paper. No quantitative comparison of the data from Labs A, B, and C was presented.

In summary, this paper purports to demonstrate a causal link between the usage of cosmetic talc as a personal care product and the incidence of mesothelioma. This would be a significant finding if the underlying data and arguments were to withstand scrutiny and their results able to be replicated. In this case, neither the underlying data nor the references support the arguments of the authors. The authors contradict prior writings and testimony without explanation. As a result, the editors should require the paper be withdrawn.

Disclaimer statements

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Conflicts of interest - Both authors have participated in talc litigation.

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