What Are You "Talcing" About?

Malignant Mesothelioma and Its Non-Asbestos Causes: Cosmetic Talc Does Not Create Occult Asbestos Exposure

Eric D. Cook
Willcox Savage PC
440 Monticello Avenue, Suite 2200,
Norfolk, Virginia 23510
(757) 628-5500 Main
(757) 628-5566 Fax
www.willcoxandsavage.com
ecook@wilsav.com

Eric D. Cook of Willcox Savage, P.C., in Norfolk, Virginia is an expert in medical and state-of-the-art issues associated with asbestos and talc litigation. He routinely handles expert development, depositions, and trial examination issues (including Daubert/Frye). He has been assigned as trial counsel throughout the country and won multiple defense verdicts in mesothelioma cases, and several successful appeals.

TABLE OF CONTENTS

I. Introduction

Fiber burden studies can identify the type of fiber present in tissues, the amount of each type of fiber present, provide evidence of the concentration of exposure (with limitations), and to a lesser extent, potential sources of asbestos fibers.

It is not unusual for an individual to have experienced exposure to commercial amphibole asbestos fiber above background and have no recollection of such exposure. For example, Kelly Butnor, Thomas Sporn and Victor Roggli's study styled "Exposure to Brake Dust and Malignant Mesothelioma: A Study of Ten Cases with Mineral Fiber Analyses" found that excess commercial amphibole fibers were detected in all of the cases with elevated uncoated asbestos fiber tissue content, with amosite being the principal commercial amphibole in four of the cases and crocidolite predominating in the fifth case. Since occupational exposure information was obtained by direct patient interview and through review of the medical records and only cases in which occupational contact with brake dust was the sole recognized source of asbestos exposure were included in the study, Dr. Roggli and his colleagues concluded, in part, that elevated lung levels of commercial amphibole asbestos in some brake workers suggested that unrecognized exposure to these fibers plays a critical role in the development of their diffuse malignant mesothelioma. Kelly J. Butnor, Thomas A. Sporn, and Victor L. Roggli, "Exposure to Brake Dust and Malignant Mesothelioma: a Study of Ten Cases with Mineral Fiber Analyses," *Ann Occ Hyg* 47:325-330(2003).

II. The Historical Development of Fiber Burden Studies

The historical development of modern day fiber burden studies can be traced back to two important events – the first being a study on asbestos bodies in the lung tissue of Johannesburg, South Africa urban residents by Thomson, et al., in 1963 and secondly, the International Union Against Cancer meeting which immediately followed the New York Academy of Sciences meeting in 1964.

A. Early Studies of Ferruginous Bodies/Uncoated Fibers in Urban and Rural Residents

Early studies of asbestos bodies focused on examination of sputum of asbestos factory workers. A study published in 1963 gained widespread attention because it identified a significant percentage of the population of an urban area that had asbestos bodies in their lung tissue. Thomson, J.G., et al., "Asbestos as a Modern Urban Hazard," *South Afr Med J* 27:77 (1963). In *Thomson* the researchers found asbestos bodies in the lung tissue of 25% of Cape Town residents examined.

In 1969, Selikoff and Hammond reported an even higher percentage of New York City Residents with asbestos bodies in lung tissue – 51% of males and 39% in females. Selikoff, I.J. and Hammond, E.C., "Asbestos Bodies in the New

York City Population in Two Periods of Time," *Id.* Shapiro, H., Editor, *Pneumoconiosis: Proceedings of the International Conference, Johannesburg*, London Oxford University Press 99-105 (1969). In a subsequent publication reporting the results of 3,000 consecutive autopsies in the New York City area from 1966 to 1968, Langer, Baden, Hammond, and Selikoff reported that just over 50% of males had asbestos bodies in lung tissue as compared to 42% in females. The percentage of cases where asbestos bodies were found increased with age, with 2.8% of males and 3.8% of females under the age of one having asbestos bodies as compared to 57% of males and 54% of females over the age of 80 having asbestos bodies identified in lung tissue. Langer, Baden, Hammond, Selikoff Presentation at Inhaled Particles III, Proceedings organized by the British Occupational Hygiene Society in London, (September 23, 1970).

In 1977, Churg and Warnock initiated an important series of studies outlining the frequency and nature of asbestos bodies in general autopsy populations, demonstrating that asbestos bodies could be found in the lung tissue of 96% or more of autopsies. *See generally* Churg, A. and Warnock, M.L., "Correlation of Quantitative Asbestos Body Counts and Occupation in Urban Patients," *Arch Pathol Med* 101:629-634 (1977); Churg, A. "Fiber Counting and Analysis in the Diagnosis of Asbestos-Related Disease," *Human Pathology* 13:381-392 (1982). Subsequent studies by Dr. Bruce Case confirmed that a majority of urban residents had asbestos bodies in lung tissue and that such concentrations are significantly correlated with increase in age. Case, B.W., et al., "Lung Fiber Analysis in Accident Victims: A Biological Assessment of General Environmental Exposures," *Arch Envir Health* 43(2): 178-179, 1988.

B. The Report of the International Union Against Cancer (UICC) Meeting in 1964 Emphasized the Need for Asbestos Fiber Burden Studies

At the close of the 1964 New York Academy of Sciences Symposium on the Biological Effects of Asbestos, the Working Group On Asbestos and Cancer met to make recommendations for future asbestos research. The working group was divided into three subgroups which focused on issues of epidemiology, pathology, and chemistry and physics. Among the recommendations from the pathology section was a recommendation to "develop a standard method of assessing semi-quantitatively the amount of asbestos fibers and/or bodies in sputum, fresh lungs and fixed tissues." The physics and chemistry section report included a recommendation to "suggest standard methods for identification of types of asbestos in the lung in a (A) large samples, and (B) tissue sections." Selikoff and Churg, editors, *Biological Effects of Asbestos NYAS Annal* 132 (Appendix I) (1965); *Arch Environ Health* 11:221-29 (1965). The questions to be addressed by such studies included correlation of dose with the extent of disease present in asbestosis, lung cancer and mesothelioma, and the type of fiber implicated in its causation. Significantly, the epidemiology work section in its report emphasized the need to study workers exposed to single types of fibers.

As a result of these recommendations, the medical and scientific community benefitted from the asbestos fiber burden and asbestos body studies of Dr. Arthur Langer in the United States, and Dr. Fred Pooley in Great Britain, as well as the pioneering work of Dr. J.C. McDonald and his research team at McGill University focusing on chrysotile asbestos miners and millers in Quebec. (*See generally* Langer A.M., Selikoff I.J., Sastre A: "Chrysotile asbestos in the lungs of persons in New York City," *Arch Environ Health* 22:348-361, 1971.; Langer A.M., et al., "Chemical characterization of asbestos body cores by electron microprobe analysis," *J Histochem Cytochem* 20:723-734, 1972; Langer A.M., et al., "Chemical characterization of uncoated asbestos fibers from the lungs of asbestos workers by electron microprobe analysis," *J Histochem Cytochem* 20:735-740, 1972; Langer, A.M., et al., "Identification of asbestos in human tissues," *J Occup Med* 15:287-295, 1973; Langer, A.M., et. al.; "Electron microscopical investigation of asbestos fibers," *Environ Health Perspect* 9:63-80, 1974.; Pooley F.D., "The identification of asbestos dust with an electron microscope analyser," *Ann Occ Hyg* 18:181-186, 1975).

J.C. Wagner and Fred Pooley began to study the mineral fiber content of lung tissue in the 1960s and reported initial results at the International Conference on Pneumoconiosis in Johannesburg, South Africa in 1969. Their paper "The Detection of Asbestos in Tissues" described three integrated studies:

> The purpose of the investigation was to establish the present incidence of asbestos in the lungs of the general population; to determine if this incidence had changed over the last four decades; and, finally, to confirm that the bodies that the pathologists were recording were definitely formed around asbestos fibers.

Pooley, Oldham, Um and Wagner, "The Detection of Asbestos in Tissues," H.A. Shapiro, Editor, *Proceedings of the International Conference on Pneumoconiosis*, Johannesburg 1969, 108 (Cape Town, Oxford University Press, 1970). Pooley, Wagner and colleagues collected samples from numerous cities throughout the United Kingdom and as of the time of this presentation, nine centers had completed, or virtually completed, the collection of cases and about three-quarters of the available material had been examined. The proportion of cases with asbestos bodies varied from 0 in 25 cases in Dublin to 62 out of 158 (39.2%) in Finland. As for whether the incidence had changed over the last four decades, Pooley and Wagner studied samples from the Whittington Hospital in London from individuals dying in 1936 and females dying in 1946. The overall percentages of positive cases rose steadily to 20% in 1966, a figure which was close to the 17% positive ratio from a current study for residents of London, as well as under other industrial cities in the multi-city survey. *Id*. at 109. As for whether the asbestos bodies were truly formed on asbestos cores, Drs. Pooley and Wagner found that "an examination of bodies from several samples using [their

digestion technique] revealed the presence of a fiber core identical in character to fibers of the commercial amphiboles." *Id.* at 115.

C. Research to Identify the Core of Asbestos Bodies

More sophisticated techniques were available by the 1970s to determine the core of a ferruginous body, i.e., whether asbestos, and, if so, what type of fiber. Dr. Paul Gross, in a study published in Paul Gross, et al., "Pulmonary Ferruginous Bodies in City Dwellers – A Study of Their Central Fiber," *Arch Environ Health* 19:186-188 (1969) analyzed the cores of asbestos bodies to determine whether they were formed on chrysotile asbestos. Dr. Gross and colleagues noted that their prior study of digested lung tissue found a 97% prevalence of lungs positive for ferruginous bodies among randomly selected autopsied hospital patients in Pittsburgh. Utidjian, M.D., Gross, P. and deTreville, RTP, "Ferruginous Bodies in Human Lungs: Prevalence at Random Autopsies," *Arch Environ Health* 17:327-333 (1968). He hypothesized that since chrysotile was the type of asbestos used 95% of the time, the cores of "asbestos bodies" should be composed of chrysotile fibers. He discovered that virtually none of the asbestos bodies were formed on a chrysotile core, and therefore questioned whether "the asbestos bodies" found by other researchers were in fact formed on asbestos fibers.

Subsequently, it was confirmed by multiple researchers that the vast majority of asbestos bodies are formed on amphibole asbestos fibers, principally amosite. *See generally* Roggli, V.L., Pulmonary Asbestos Body Counts and Electron Probe Analysis of Asbestos Body Cores in Patients with Mesothelioma," Cancer 50:2423-2432 (1982) (98% of asbestos bodies formed on amphibole cores); Dodson, R.F., O'Sullivan, M., Corn, M. McLarty, J.W., Hammar, S.P.," Analysis of Asbestos Fiber Burden in Lung Tissue from Mesothelioma Patients," *Ultastructural Patholog*y 21:321-336 (1997) (97.6% of asbestos bodies formed on amphibole cores). *See also* Roggli, V.L., Pratt, P.C., Brody, A.R., "Asbestos Content of Lung Tissue in Asbestos Associated Diseases: A Study of 110 Cases," *Br J Ind Med* 43:18-28 (1986); Dodson, R.F., et al., "Relationships between Ferruginous Bodies and Uncoated Asbestos Fibers in Lung Tissue," *Arch Environ Health* 51:462-466 (1996).

III. Methods for Analysis of Tissue Mineral Fiber Content

As Dr. Roggli points out in his chapter on analysis of tissue mineral fiber content (Chapter 11), there are three areas to be addressed in described methods for analysis of mineral fiber content: tissue selection, digestion technique and fiber identification and quantification. *See generally* Roggli, V.L. and Sharma, A. "Chapter 11 Analysis of Tissue Mineral Fiber Content," *Id.* Oury, T.D., et al., (eds.), Pathology of Asbestos-Associated Diseases, Springer: New York, 2014, at 253-293.

A. Tissue Selection

The vast majority of asbestos fiber burden studies have been performed on lung tissue, although there are a few published studies on asbestos fiber content of extrapulmonary tissues such as pleura, pleural plaques, omentum and mesentery as well as lymph nodes. Dr. Roggli points out in his chapter, however, that since far fewer fibers would be expected to be found in extrapulmonary tissue, the closer the concentration of fibers approaches the background range of the laboratory, the bigger the potential of contamination significantly affecting the results.

> "In this regard, it should be noted that the expected levels of fibers in extrapulmonary tissues would be at or below the limits of detection for current techniques, and background contamination can be a considerable problem." *Id*. at 254.

In selecting lung tissue for examination, tissue unaffected by tumor and other lung conditions should be selected, and to the extent sufficient tissue is available, selection of tissue from the upper and lower lobes of each lung would be ideal, with each weighing 0.25 to 0.35 gram or less of wet tissue. "However, analyses may be performed on as little as 0.1 gram or less of wet tissue." *Roggli supra* at 254.

B. Digestion Technique

Digestion technique includes the dissolution and removal of the lung tissue in which the asbestos fibers are imbedded, and the collection of such fibers in such a manner that they can be examined for fiber identification and quantification by electron microscopy. Dissolution of lung tissue involves either wet chemical digestion with a variety of agents, including sodium or potassium hydroxide, hydrogen peroxide, sodium hypochlorite solution (commercial bleach). While tissue ashing is an alternative approach, tissue ashing in a high temperature furnace can break down fibers and consequently a higher count of fibers is counted than would otherwise be identified. *See generally Roggli, supra* at 255, 258. Once digestion is complete, the residue needs to be collected in a form in which it can be examined by electron microscopy. This involves some kind of filtration resulting in the inorganic residue being collected on a filter. As Roggli points out:

> "Use of a pore size which is too large in relation to the size of the fibers to be analyzed can result in significant loss of fibers and underestimation of the mineral fiber content of the sample." *Roggli supra* at 255, *Citing* O'Sullivan, M.F., Corn, C.J., Dodson, R.F., "Comparative Efficiency of the Nuclepore Filters of Various Pore Sizes as Used in Digestion

Studies of Tissue," *Environ Research* 43:97-103 (1987).

C. Fiber Identification and Quantification

Chapter 11 "Analysis of Tissue Mineral Fiber Content" in Dr. Roggli's textbook provides a summary of different methods of fiber identification and quantification. *See generally*, Roggli, V.L. and Sharma, A. "Chapter 11 Analysis of Tissue Mineral Fiber Content," *Id.* Oury, T.D., et al., (eds.), Pathology of Asbestos-Associated Diseases, Springer: New York, 2014, at 253-293.

Asbestos bodies are typically identified and quantified by light microscopy with the results reported as numbers per gram of wet lung tissue. When sufficient lung tissue is available, "a piece of lung tissue adjacent to the one actually analyzed can be dried to constant weight to obtain a wet-to-dry weight ratio, and the results reported as asbestos bodies per gram of dry weight." *Roggli, Pathology of Asbestos-Associated Diseases, supra*, at 312. Electron microscopy may be applied in an attempt to ascertain the core of the asbestos bodies identified and quantified by light microscopy.

Fiber identification and quantification by electron microscopy is performed utilizing either scanning electron microscopy (SEM) or transmission electron microscopy (TEM). Researchers typically use one technique or the other (SEM or TEM) consistently.

D. Factors Affecting the Results of Fiber Burden Studies

Dr. Roggli in his chapter "Analysis of Tissue Mineral Fiber Content" in the third edition of his textbook, provides a useful table identifying the factors effecting fiber burden data.

Table 11.1 Factors affecting fiber burden data

I. Digestion procedure
(A) Wet chemical digestion (alkali, enzymes)
(B) Low-temperature plasma ashing
(C) Number of sites sampled
II. Recovery procedure
(A) Use of centrifugation step
(B) Use of a sonication step
(C) Filtration step (type of filter, pore size)
III. Analytical procedure
(A) Microscopic technique (LM, PCLM, SEM, TEM)
(B) Magnification used
(C) Sizes of fibers counted and other "counting rules"
(D) Numbers of fibers or fields actually counted
IV. Reporting of results
(A) Asbestos bodies or fibers (or both)
(B) Sizes of fibers counted
(C) Concentration of fibers (per gram wet or dry lung or per cm^3)

Reprinted from Ref. [1]

LM light microscopy, *PCLM* phase-contrast light microscopy, *SEM* scanning electron microscopy, *TEM* transmission electron microscopy

(at 258).

Case and Sebastien noted, "The most common deficiency of tissue analytical studies of "environmentally exposed" individuals is poor definition of the target population. It is often difficult or impossible to exclude the possibility of occupational exposure, and misclassification inevitability occurs. Interpersonal variation in smoking habits, inhaled fibre dose, and respiratory clearance patterns further complicate the picture." Case and Sebastien, "Fibre levels in lung and correlation with air samples," *Non-Occupational Exposure to Mineral Fibres* IARC, Bignon, J., et al., (Eds.) pp. 207-218, (1989) at 210.

IV. Asbestos Bodies/Uncoated Fibers in the General Population

A. Overview

As Dr. Roggli pointed out in his analysis of tissue mineral fiber content chapter, "[d]etermination of background levels of fibers to be expected in the

general population is an extraordinarily difficult task, since it is no simple matter to define what is normal or to exclude unknown exposures." Roggli,V.L., and Sharma, A. "Chapter 11 – Analysis of Tissue Mineral Fiber Contents" in *Pathology of Asbestos-Associated Diseases* at 273.

The Helsinki Criteria recommended guidelines to identify individuals with probability of occupational exposure from the results of fiber burden studies:

> "Analysis of lung tissue for asbestos fibers and asbestos bodies can provide data to supplement the occupational history. For clinical purposes, the following guidelines are recommended to identify persons with a high probability of exposure to asbestos dust at work: over 0.1 million amphibole fibers (greater than 5 microns) per gram of dry lung tissue or over 1 million amphibole fibers (greater than 1 micron) per gram of dry lung tissue as measured by electron microscopy in a qualified laboratory or 1,000 asbestos bodies per gram of dry tissue (100 asbestos bodies per gram of wet tissue) or over one asbestos body per milliliter of bronchoalveolar lavage fluid, as measured by light microscopy in a qualified laboratory." *Helsinki, supra* at 311.

As you can see, the reference values are roughly one to two million fibers per gram dry lung for total amphibole fibers and 100,000 fibers per gram dry lung for amphibole fibers longer than 5 microns.

B. Evidence that No Background Exposures Cause or Contribute to any Asbestos-Related Disease, Particularly Mesothelioma

As early as 1971 when the National Academy of Sciences Committee on Biological Affects of Atmospheric Pollutants published its report styled "Asbestos-The Need for and Feasibility of Air Pollution Controls" there has been a general consensus in the medical and scientific community that there is no evidence that background exposures to asbestos cause or contribute to the development of asbestos related disease in general and mesothelioma in particular.

In the National Academy of Sciences Report, the committee concluded the following regarding non-occupational exposures to asbestos:

> The most important question in the case of persons with non-occupational exposures to asbestos is whether there is an increased risk of malignancies . . . The major potential

> for a risk appears to lie in those with indirect occupational contact, household contacts, or residence in the immediate neighborhood of an asbestos source; and even there, the actual risk is poorly defined. The appearance of a gradient of effect in such groups, however, suggests that there are levels of inhaled asbestos without detectable risk. It is not known what range of respirable airborne asbestos fibers will ultimately be found to have no measurable effects on health. At present, there is no evidence that the small numbers of fibers found in most members of the general population affect health of longevity. *The National Academy of Sciences, Committee on Biological Effects of Atmospheric Pollutants, Asbestos: The Need for and Feasibility of Air Pollution Controls* at 31(National Academy of Sciences, Washington, D.C. 1971).

A report by the Advisory Committee on Asbestos Cancers to the Director or the International Agency for Research on Cancer closely followed in 1973. In that report, which was published as part of the proceedings of the conference styled "Biological Effects of Asbestos" held in Lyon, France the following question was posed and answer given regarding background levels of exposure to asbestos and the risk of mesothelioma from such exposures:

> Q: Is there evidence of an increased risk of mesothelioma cancers at low levels of exposure to asbestos, such as have been encountered by the general population in urban areas?
>
> A: There is evidence of an association of mesothelioma tumors with air pollution in the neighborhood of crocidolite mines and the factories using mixtures of asbestos fiber types. The evidence relates to conditions many years ago. There is evidence of no excess risk of mesotheliomas from asbestos air pollution which has existed in the neighborhood of chrysotile and amosite mines . . . There is no evidence of risk to the general public at present. Report of the Advisory Committee on Asbestos Cancers to the Director of the IARC, *Brogofski, P. Gilson, J.C. Timbrell, V., Wagner, J.C., Editors, Biological Effects of Asbestos*, 342-343 (Lyon, IARC 1973).

In Canada, the Royal Ontario Commission concluded that ambient asbestos fibre concentrations present no health risk. "Asbestos in the Environment," Chapter 11 In: *Report of the Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos in Ontario* at 666 (1984)

(citing to exposure levels in the range of 0.03 f/cc). Similarly, David Ferguson, formerly Convenor of The Australian Mesothelioma Surveillance Program noted:

> Urban residents in Sydney (and presumably also in other Australian cities) have asbestos fibres in their lungs up to one million fibres per gram of dried lung. These fibres are mainly amphiboles because chrysotile is much more readily cleared from the lungs. The fibres arise from geological weathering and from attrition of asbestos cement and friction, insulation and fire retardant asbestos products. The low incidence of mesothelioma combined with universal lung fibre content suggests that people harbour fibres of this order without harm. The great majority are shorter than 5 μm. Ferguson D., "Low-level asbestos – the priorities are wrong," *The Medical Journal of Australia*, Vol. 152 , 617-18 (June 18, 1990).

Ferguson's statement above echoes the conclusion of the Canadian Royal Commission. These conclusions directly illuminate the issue of ambient asbestos exposure and disease causation. Despite the existence of background levels of asbestos, there is no epidemic of mesothelioma or any other asbestos-related disease among those with nonoccupational asbestos exposures. If indeed the low doses of asbestos in every breath of ambient air cause asbestos-related disease, one would expect such an epidemic.

V. Fiber Burden Studies-Overview

Dr. Andrew Churg's chapters on neoplastic asbestos-related disease and non-neoplastic asbestos-related diseases provide an overview of lung fiber burden analyses in asbestos-related disease cases by fiber type. As he points out:

> "Despite laboratory-to-laboratory variations in numeric values, a reasonably consistent correlation of fiber burden and disease has emerged from examination of populations with occupational asbestos exposure [cites omitted]. These correlations are shown in figure 9.3 which illustrates the fact that disease always appears with fiber burdens considerably greater than those seen in the general population and that different diseases typically appear at different fiber burdens.
>
> Furthermore, this pattern varies from chrysotile to amosite and crocidolite; for amphibole asbestos, the lowest burdens are seen in members of the general

population; those with pleural plaques and mesothelioma have about the same mean burden; and those with asbestosis have a considerably greater burden. For chrysotile exposure, the lower burdens are again seen in persons in various general populations; plaques occur at higher burden; and cases of mesothelioma and asbestosis occur only at very high and roughly comparable fiber burdens." Churg, supra at 294.

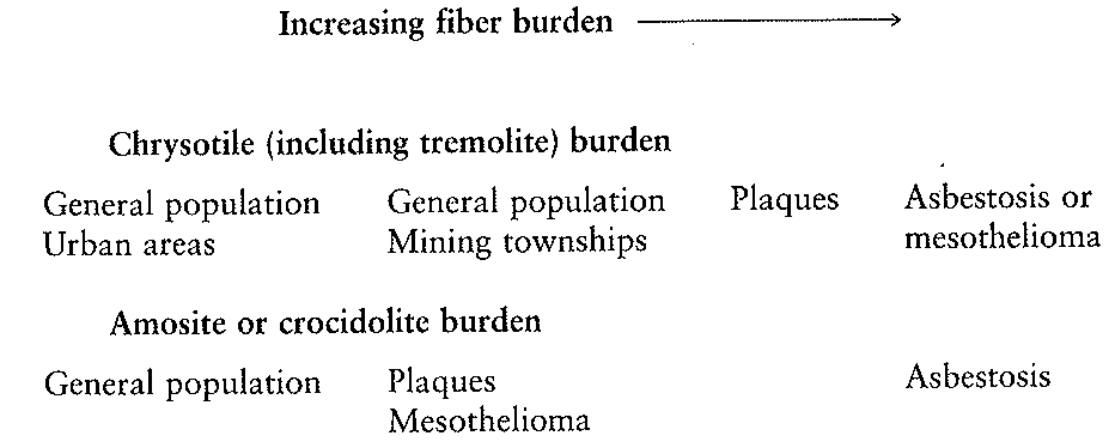

FIGURE 9.3
Relation between fiber burden and disease in those with chrysotile or amphibole (amosite or crocidolite) exposure.

In the non-neoplastic disease chapter, Dr. Churg also includes a chart identifying the geometric mean fiber concentration by disease category in workers with heavy amosite or chrysotile exposure. The results are revealing:

TABLE 9.10
Geometric Mean Fiber Concentration by Disease in Workers with Heavy Amosite or Chrysotile Exposure

	CHRYSOTILE MINERS AND MILLERS		SHIPYARD WORKERS AND INSULATORS AMOSITE
DISEASE	CHRYSOTILE	TREMOLITE	
Asbestosis	30	140	10.0
Airway fibrosis	27	120	4.3
Mesothelioma	34	180	0.9
Pleural plaques	15	75	1.4
Lung cancer	13	49	1.1
No disease	2	9	0.7

Values as millions of fibers per gram of dry lung.

(at 295).

The mean burden of chrysotile plus tremolite in the lungs of miners and millers with asbestos is 17 times the amosite burden in the lungs of shipyard workers with asbestosis. Similar differences are seen for pleural plaques. For mesothelioma, the difference is even more marked (almost 200 fold). These findings reinforce epidemiological data pertaining to fiber potencies. Churg, A., "Non-neoplastic Disease Caused by Asbestos," Chapter 9 in *Pathology of Occupational Lung Disease*, Churg, A., and FHY Green (Eds), Williams and Wilkins, Baltimore, MD pp. 277-338 (1998).

The predominant fiber type identified in patients with mesothelioma is amosite or crocidolite. Roggli, Chapter 11, "An Analysis of Tissue Mineral Fiber Content" *supra*, at 325 and numerous cites contained therein. In a study of 94 cases from the United States published in 1993, Roggli, et al., found that 58% of more than 1,500 fibers analyzed were amosite, whereas only 3% were crocidolite. Roggli, V.L., Pratt, P.C., Brody, A.R., "Asbestos Fiber Type in Malignant Mesothelioma: An Analytical Scanning Microscopic Study of Ninety-Four Cases," *Am J Ind Med* 223:605-614 (1993). Interestingly, Dr. Roggli reported increased detection of crocidolite more recently than in his earlier studies. Roggli, V.L., Vollmer, R.T., "Twenty-Five Years of Fiber Analysis: What Have We Learned?" *Human Pathology* 39, 307-315 (2008). This increase was consistent across all disease categories studied, i.e., asbestosis, lung cancer, and mesothelioma. *Id.*

VI. Additional Contributions Fiber Burden Studies Have Made to the Advancements of Knowledge Regarding Asbestos-Related Diseases

The results of fiber burden studies have made enormous contributions to the advancement of knowledge of asbestos related diseases, the persons at risk, and persons not at risk. This section contains but a few of the examples.

A. Contrary to what one might expect given the percentage of total asbestos consumption for crocidolite usage in the United States, a considerable percentage of individuals with asbestos-related diseases have elevated levels of crocidolite in their lung tissue

While we are conditioned not to expect to find crocidolite in the tissues of persons with asbestos-related disease, a paper by Langer and Nolan published in 1998 shows that there is evidence of more crocidolite in the U.S. than one would expect. The authors obtained tissue from autopsy or biopsy from 81 workers and two household persons who had died of various allegedly asbestos-related diseases. Thirty-three were mesotheliomas, 35 were lung cancers, 12 were asbestosis, and three died from other cancers. Twenty-three of these were insulators or pipe coverers, 28 were shipyard workers in various trades, were persons in other trades, and only two were housewife family members of insulators. The surprising finding in this study was the much higher incidence of crocidolite in the tissues of these people. Crocidolite was found in 39 percent of the tissue specimens obtained from individuals who had some history of shipyard work. This included one wife of an insulator who developed lung cancer. In that case, the wife had 700,000 crocidolite fibers per gram of lung tissue, but the counts for amosite and chrysotile were below the level of detection. The appendix on crocidolite consumption information pertinent to the United States is of interest.

The authors noted that tremolite occurs with the highest concentrations in lungs of plasterers. They noted that:

> Patching, taping, and spackling compounds marketed in the U.S.A. are known to have contained tremolitic talc in addition to chrysotile, although the actual materials have been shown to contain cleavage fragments rather than asbestos.

Further, they noted that while tremolite may be associated with chrysotile, it is also associated with other types of commercial amphibole asbestos and that calcic-amphibole contamination of amosite needs to be considered as well. Langer, A.M. and Nolan, R.P., "Asbestos in the Lungs of Persons Exposed in the USA," *Monaldi Arch Chest Dis.* 53(2):168-80 (1998).

Dr. Victor Roggli, in his summary of 25 years of fiber analysis published in 2008, reviewed the results of his fiber analyses in the first $12^1/_2$ years compared

to the more recent period prior to publication. While there was a decrease in asbestos body and amosite concentrations over time consistent with the banning of asbestos from insulation products, crocidolite showed an increased detection frequency from Group 1 (the first half of the period) to Group 2 (the second half of the period). For all three disease categories studied – asbestosis, lung cancer and mesothelioma. Roggli, V.L., Vollmer, R.T., "Twenty-Five Years of Fiber Analysis: What Have We Learned?" *Human Pathology* 39:307-315 (2008).

B. Fiber burden studies of insulators have universally found commercial amphibole fiber, primarily amosite

Amosite has been found to be universally present in tissues obtained from United States insulators. Accordingly, the U.S. insulators should be considered an amphibole asbestos exposed workforce. *See generally* Langer, A., et al., "Asbestos in the Lungs of Persons Exposed in the USA," *Minaldi Arch Chest Dis* 53(2):168-180, 1998; Kohyama and Suzuki, "Analysis of asbestos fibers in Lung Parenchyma, Pleural Plaques, and Mesothelioma Tissues of North American Insulation Workers," *Annals of New York Academy of Sciences* 643:22-52 (1991) (100% of insulators' lungs examined had elevated levels of amosite with the mean concentration measured at 150.2 million fibers per gram dry lung; 54% had elevated crocidolite in their lungs with a mean concentration of 11.4 million fibers per gram dry lung).

C. Fiber burden studies helped establish a link between erionite fiber and mesothelioma

Fiber burden studies were instrumental in helping establish that erionite was a separate and distinct cause other than asbestos of diffuse malignant mesothelioma in certain villages of Cappadocia, Turkey. *See generally* Baris, I., Simonato, L., Pooley, F., et al., "Epidemiological and Environmental Evidence of the Health Effects of Exposure to Erionite Fibers: A 4-Year Study in the Cappadocian region of Turkey," *International Journal of Cancer* 39:10-17 (1987). While airborne fiber levels were generally low, the villages affected by malignant mesothelioma had higher proportions of erionite fibers in the air than villages with no increased rate of mesothelioma. The same pattern was confirmed by analysis of the fiber content in the lung tissues of sheep from several villages, both affected and unaffected by malignant disease. The three villages with the highest proportion of erionite fibers had high rates of malignant pleural mesothelioma, malignant peritoneal mesothelioma and lung cancer. While there had not been (as of yet) a full scale investigation of human lung fiber contents, data from two mesothelioma cases clearly indicated an accumulation of erionite fibers in the lungs, both in absolute terms and in relation to other types of fiber. *See also* Sebastien, et al., "Ferruginous Bodies in Sputum as an Indication of Exposure to Airborne Mineral Fibers in the Mesothelioma Villages of Cappadocia," *Archives of Environmental Health* 39:18-23 (1984) (reporting a significant correlation between the presence of ferruginous bodies, previously

identified by the same authors as "zeolite bodies" in the sputum and in the place of residence of inhabitants of the affected villages).

More recently, Dr. Fred Pooley and Dr. E.B. Ilgren published the first confirmed case of erionite-related mesothelioma in North America. Ilgren, EB, et al., "First confirmed erionite related mesothelioma in North America," *Letter to the Editor – Indoor Built Environment*, 17:567-568 (2008). Ilgren had previously identified two pleural mesotheliomas in a small village in the northern part of the State of Jalisco, Mexico, which revealed high occupational level (greater than 1 million fibers per gram dry lung) of fibrous erionite.

D. Fiber burden studies have helped establish that a percentage of diffuse malignant mesotheliomas are unrelated to asbestos

The case records of Massachusetts General Hospital, published regularly in the New England Journal of Medicine, provides solid evidence of a background rate of mesothelioma unrelated to a history of asbestos exposure. In answering questions concerning a female diagnosed with mesothelioma, Dr. Kazemi noted the following:

Finally, the Case Records in Massachusetts General Hospital published regularly in The New England Journal of Medicine provide solid evidence of a background rate of mesothelioma unrelated to a history of asbestos exposure. In answering questions concerning a female diagnosed with mesothelioma, Dr. Kazemi noted the follows:

> When cases of mesothelioma from large institutions are reviewed, however, 20 to 30% of the patients give no history of exposure to asbestos or have no evidence of asbestos exposure at autopsy or at biopsy [cite omitted].
>
> . . . . .
>
> Several of my colleagues and I have reviewed the cases of mesothelioma seen at this hospital since the diagnosis was first made by the Department of Pathology in the early 1950s. We have reviewed 115 cases of pleural mesothelioma or peritoneal mesothelioma or both . . . In our review the outstanding finding was the fact that 30% or more of the patients with a mesothelioma gave no history to exposure to asbestos and on pathological examination had no evidence of asbestos fibers in the lungs or other changes consistent with exposure to asbestos. Therefore one must conclude that not all mesotheliomas result from exposure to asbestos.

> Robert Scully, Editor, Case Records of the Massachusetts General Hospital," *The New England Journal of Medicine* 323:659,666(1990).

In summarizing his discussion of fiber burden studies and a background rate of mesothelioma independent of asbestos exposure, Dr. Roggli noted:

> "The distribution of asbestos body counts in patients with mesothelioma appears to be bimodal, suggesting that there are the two distinct populations. … One group has elevated tissue asbestos content and is asbestos related, while the other has a tissue asbestos content indistinguishable from a reference population and may be considered to be 'spontaneous' or idiopathic. Analysis of tissue asbestos content in an individual case can thus provide useful information with regard to an etiologic role for asbestos in the production of a mesothelioma."

Roggli, V., *Pathology of Asbestos-Associated Diseases, supra,* at 268-269. *See also* Attanoos, Richard L., et al., "Malignant mesothelioma and its non-asbestos causes," *Archives of pathology & laboratory medicine* 142.6 (2018): 753-760; Attanoos, Richard L., et al., "In Reply to "Malignant Mesothelioma and Its Nonasbestos Causes," *Archives of pathology & laboratory medicine* 143.8 (2019): 911-914; Tomasetti, C. and B. Vogelstein, "Stem cell divisions, somatic mutations, cancer etiology, and cancer prevention," *Science*, 355: 1330-1334, 2017; Carbone, M., et al., "Mesothelioma: Scientific Clues for Prevention, Diagnosis, and Therapy," *CA Cancer J Clin* 0: 1-28, 2019.

E. Fiber burden have demonstrated that asbestos textile worker cohorts originally thought to have only chrysotile exposures, were exposed to either crocidolite and/or amosite

The Rochdale asbestos textile workers in Great Britain were originally thought to have chrysotile-only exposures and, therefore, the mesotheliomas identified among that cohort were originally thought to be chrysotile induced. However, it was later discovered that all the cases of mesothelioma in the cohort had elevated levels of crocidolite in their lung tissue. Additional investigation revealed that all of them worked in a portion of the plant that utilized crocidolite fiber as well as chrysotile. Langer, Arthur and Robert Nolan, "Fiber type and mesothelioma risk," University Energy and University Environmental Policy Center, *Symposium on Health Aspects of Exposure to Asbestos and Buildings*, December 14-16, 1988, pp. 91-140; Pooley, F.D., and Mitha, R., "Fiber types, concentrations and characteristics found in the lung tissues of chrysotile-exposed cases and controls," *Accompl Oncol* 1, 1-11 (1987a); Pooley, F.D. and Mitha, R.,

"Determination and interpretation of the levels of chrysotile asbestos in lung tissue," *Accompl Oncol* 1, 12-18 (1987b).

A number of fiber burden studies have likewise demonstrated that a significant percentage of workers at the South Carolina asbestos textile plants studied by J.C. and A.D. McDonald as well as Dr. John Dement had elevated levels of amosite or crocidolite in their lung tissue. In 1989, Dr. Patrick Sebastien and colleagues found non-trivial concentrations of amosite and crocidolite in 32% of the specimens from Charleston. In the Charleston asbestos textile cases, amphibole asbestos was detected only in cases hired before 1940; no crocidolite was detected in cases hired after 1940.

In 1997, a number of researchers, including Dr. John Dement, Dr. Fred Pooley, and Dr. Russell Harley conducted a further study of the Charleston, South Carolina asbestos textile plant that began operation in 1896 to produce asbestos packing materials for steam engines and pumps. Asbestos textiles were first produced in 1909. The authors noted that "chrysotile was the only type of asbestos processed as a raw material, although a small amount of crocidolite yarn was woven into a tape or made into a braided packing beginning in the 1950s and ending in about 1975. Crocidolite was never carded, spun or twisted and the total quantity of crocidolite processed was extremely small (less than 1,000 kg)." Green, FHY., Harley, R., Vallyathan, V., et al., "Exposure and Mineralogical Correlates of pulmonary fibrosis in chrysotile asbestos workers," *Occup Environ Med* 54:549 (1997). The researchers found that pulmonary fibrosis was correlated with cumulative exposure to asbestos and the concentration of asbestos fibers in the lung. The concentration of tremolite fibers in the lung provided a better estimate of lung fibrosis than did the concentration of chrysotile. Further, 23.8% of the workers were found to have between 100 and 1 million amosite/crocidolite fibers per gram, 21.4% had between 1 million and 10 million amosite/crocidolite fibers per gram and 7.1% of the workers had between 10 and 100 million amosite/crocidolite fibers per gram dried lung. *Id.* at 553.

Subsequently, Drs. Case, Dufrene, McDonald and Sebastien published an additional analysis of lung tissue from Charleston, South Carolina asbestos textile workers in an article styled, Case, BW, et al., "Asbestos Fiber Type and Length in Lungs of Chrysotile Textile and Production Workers: Fibers Longer than Eighteen Microns", Inhalation Toxicology, 12 (Suppl 3): 411-418 (2000). Lung fiber concentration and dimension were assessed by transmission electron microscopy and energy-dispersive x-ray spectrometry for autopsy samples from 64 textile workers and chrysotile miners and millers (32.5% of 508). These amosite/crocidolite fibers were present in the lungs of workers who ceased employment prior to the first use of such fibers recorded in the textile industry. The investigators cautioned:

> "Finally, as in two previous studies, we found that the 'chrysotile-only' textile workers had a high proportion of individuals with lung tissue

containing amosite and/or crocidolite. Sebastien, et al. had noted that these fibers were present in 'non-trivial' concentrations in 32% of workers examined. Green, et al. found commercial amphibole in 28% of 35 textile workers lungs examined. Our findings our similar for the proportion of workers exposed: 19 of 50 males and 3 of 14 females and 32% of all fibers counted in the lungs of textile workers were amosite or crocidolite. Finally, 12 of the 22 textile workers having commercial amphibole in the lungs stopped working between 1938 and 1947, long before any such documented exposure in the textile plant. For 15 of the 22, amosite and crocidolite formed the majority of all fibers present. This subset of the Charleston textile workers does not support the hypothesis that this is a 'pure chrysotile' cohort (WHO, 1988). More generally, the exposure experience of textile workers is clearly unique and should not be used to assess risks of lung cancer in miners, cement workers, or friction product workers, regardless of fiber type." *Id*. at 417.

F. Fiber burden studies have helped demonstrate that the lungs revealed increased levels of crocidolite fiber in mesothelioma cases from asbestos cement plant workers predominantly exposed to chrysotile

Dr. Fred Pooley collaborated with researchers in a number of countries, including Austria and Sweden to perform asbestos fiber burden studies on lung tissue from mesothelioma cases. Chrysotile was the predominant fiber used at these plants, but the cases of mesothelioma had increased levels of crocidolite, even though only small amounts of crocidolite were utilized. For example, Pooley collaborated with the University of Lund to examine the lung tissue from diseased asbestos cement workers mainly exposed to chrysotile asbestos but also to small amounts of commercial amphibole in Sweden. The plant in which the workers were employed made asbestos-cement products from 1907 to 1977. Although chrysotile was the major asbestos type used, small amounts of crocidolite were used in certain products (1 to 4%) until 1966. Small amounts of amosite were used until 1956 but not on a regular basis. F.D. Pooley, "Investigation of the Importance of Tremolite in the Production of Asbestos-Related Disease and Its Relevance as A Long-Term Indicator of Chrysotile Exposure" – a Report to the British Health and Safety Executive (1990) at 30; Albin, M., Johansson, L., Pooley, F.D., et al., "Mineral fibers, fibrosis and asbestos bodies in lung tissue from diseased asbestos cement workers," *Br J Ind Med* 47:767-74 (1990). Asbestos cement workers with mesothelioma had significantly higher total fibers, all asbestos, chrysotile, crocidolite, tremolite, and anthophyllite levels, as compared to controls. However, comparison between

exposed workers with and without mesothelioma showed significant differences for total fibers, and all asbestos "and particularly for total amphiboles, crocidolite, tremolite and anthophyllite. The mesothelioma cases did not have significantly higher levels of chrysotile or amosite." *Id*. at 31.

Likewise, Pooley examined the lung tissue of diseased asbestos cement workers at the Rhoose British asbestos cement factory. There crocidolite was used only between 1932 and 1935, and when the factory changed ownership in 1935, chrysotile was the exclusive fiber used until the closure of the plant in 1980. In the two cases of pleural mesothelioma, the lung tissue revealed excess concentrations of crocidolite as well as chrysotile and tremolite. *Id.* at 7.

G. Fiber Burden Studies Have Provided a Limited Amount of Information Regarding Exposures to Asbestos in Buildings

As an example, one case of a woman who worked in a building with asbestos-containing materials was found to have an unusual number of high aspect-ratio tremolite fibers in her lungs. The authors, including Dr. William Longo, noted there was "no evidence of exposure to cosmetic talc" and concluded the acoustical ceiling plaster from the building in which the patient worked was the most likely source of the tremolite asbestos fibers identified. They further indicated that, "[a]dditional studies are necessary in order to determine whether (cases of exposures to acoustical ceiling plasters) such as these occur with sufficient frequency to be of public concern." Roggli, V., et al., "Mineral Fiber Content of Lung Tissue in Patients with Environmental Exposures: Household Contacts versus Building Occupants," *Annals of the N.Y Academy of Science*, 643(1991):511- 18.

VII. Claims of Occult Asbestos Exposure from Cosmetic Talc Are Not Well-Founded

Dr. Gordon is an exemplar proponent of the belief that the use of cosmetic talc creates occult asbestos exposure, and his tissue digestions are repeatedly cited by Plaintiffs in this regard. E.g. Gordon, R.E., Fitzgerald, S. & Millette, J., "Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women," *Intl J Occ Environ Health*, 20(4):318-348 (2014); Lee, R. & Van Orden, D., "Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women, Letter to the Editor" *Intl J Occ Environ Health*, 21(4):337-341 (2015); Gordon, G., "Response to RE: Gordon R, Fitzgerald S, and Millette J. Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women," *Intl J Occup Environ Health*, 21(4):342-346 (2015); c. Lee, R., Van Orden D., Sanchez M. "Response to Gordon 2016, Letter to the Editor."*Intl J Occ Environ Health*, 23(2): 172-176 (2017); Gordon, Ronald E. "Response to Second Letter by Lee et al. of 2016," *Intl J Occ Environ Health*, 23(2): 177-180 (2017); *see e.g.* Moline, Jacqueline, et al., "Mesothelioma Associated with the Use of Cosmetic Talc," *Journal of occupational and environmental medicine* (2019); Finkelstein, Murray M. "Malignant Mesothelioma and Its Nonasbestos Causes." Archives of pathology & laboratory medicine 143.6 (2019): 659.

Dr. Gordon's belief is subject to a number of flaws. This paper focuses on two. First, Dr. Gordon testified that his analyses of minerals in human tissue do not attempt to differentiate between a mineral that grows or crystallizes in the asbestiform habit v. another habit.

> Q. Okay. Does your analyses that you do of human tissue make any attempt to differentiate between a mineral that grows or crystallizes in the asbestiform habit versus a different habit?
>
> …
>
> A. No.

May 4, 2018 Gordon Dep. at 127-128. Although he does not have an opinion as to what percentage of amphiboles are asbestiform or asbestos minerals, he generally agrees that the great majority of tremolite on earth is nonasbestiform. Nov. 29, 2018 Gordon Dep. at 97-98; May 4, 2018 Gordon Dep. at 125.

Second, Dr. Gordon's control group does not provide a reliable baseline for evaluating asbestos exposure. His original control group included fiber burden results for more than 200 people. July 13, 2016 Gordon Dep. at 130-132; Sept. 11, 2017 Gordon Dep. at 128-129. Dr. Gordon began omitting people from that control group whose tissue had even a single amphibole fiber greater than 5 microns. (Sept. 11, 2017 Gordon Dep.) at 131:13-15. Now, Dr. Gordon's control group is down to 35 individuals with a decreased background level in which he considers any fibers greater than 5 microns to be in excess of background. Oct. 16, 2017 Gordon Dep. at 143; Sept. 11, 2017 Gordon Dep. at 132. Dr. Gordon would now claim that a *single* asbestos fiber over five microns long is a "significant" above-background exposure that is a substantial, contributing cause of the plaintiff's mesothelioma. Mar. 20, 2015 Gordon Dep. at 109-110; Feb. 17, 2021 Gordon Dep. at 47.

Dr. Gordon claims that his control group with zero asbestos background fibers was properly curated because anyone with asbestos fibers greater than five microns long has appreciable asbestos exposure and should not be included in a control group. *Id.* But this assumes what it sets out to prove. By removing from the control group everyone whose results were inconsistent with his hypothesis (or preconceptions), Dr. Gordon ensured the result he set out to achieve, essentially creating a self-fulfilling prophecy.

No other laboratory has adopted Dr. Gordon's control group or reported anything remotely similar as a benchmark for determining whether a given fiber burden is significant. July 12, 2017 a.m. Frye Hr'g at 27. Dr. Gordon's "control group" has never been tested, validated, or published in the peer-reviewed literature. Sept. 29, 2016 Gordon Dep. at 193; (March 20, 2015 Gordon Dep.) at 114:9-13.

Dr. Gordon's elimination of anyone with an asbestos fiber greater than five microns from his control group as "occupationally exposed" renders his methodology inherently unreliably. It depresses the commonly accepted background level of exposure so that asbestos fibers resulting from everyday life look like the result of an unusual contamination. (E.g. Dodson, R.F., et al., *Asbestos Content in the Lymph Nodes of Nonoccupationally Exposed Individuals*, Am. J. Indust. Med., 37:169-74 (2000)) at 171, Tbl. I (finding up to 460,000 fibers/gram in non-occupationally exposed individuals' lymph tissue and up to 58,000 fibers/gram in non-occupationally exposed individuals' lung tissue).

Dr. Gordon's control group failed *Daubert* challenge on multiple occasions. E.g. *Jackson v. Colgate Palmolive Company*, 2019 WL 3603547, August 6, 2019; *Hanson v. Colgate-Palmolive Company* 353 F. Supp. 3d at 1289. The court in *Jackson* recently cited to *Hanson* in excluding Dr. Gordon's opinion, and summarizing flaws inherent in Dr. Gordon's approach.

> [W]ith respect to the first Helsinki criterion, Dr. Gordon's finding of above-background asbestos levels in Mrs. Hanson's lungs relies on a control group of his own creation for which there are too many unanswered questions and hallmarks of impropriety. Dr. Gordon's current control group consists of thirty-five patients who have been "documented" not to have any evidence of asbestos exposure based on "histories taken by trained individuals, trained MDs...." (*Id.* at 128:9-16.) But Dr. Gordon does not have any documentation of their medical or exposure histories. (*Id*. at 139:2-11.) Documentation is limited to age range, gender, a list of "means and ranges," and fiber analysis worksheets. (*Id.* at 139:9-11; 140:23-141:16.) Dr. Gordon has never submitted his control group to the scientific community or had the group peer reviewed. (*Id.* at 136:25-138:1.)
>
> While it is true a valid control group must consist of persons without lung disease who have no history of exposure to asbestos, Dr. Gordon's entire control group is pristine with respect to asbestos, meaning no one returned a tissue sample with any countable asbestos fibers. (Gordon Brandt Testimony 7/12/2017, doc. no. 67-3, p. 28:2-4.) Dr. Gordon admits there is no control group in the world other than his where the members have no countable asbestos fibers. (*Id.* at 27:4-15.) Dr. Gordon explains "no other laboratory depends on results that are even current" and "if they did it the way I

did it, they probably would" have no countable asbestos fibers in their control group. (*Id.*)

Dr. Gordon's control group previously exceeded 200 people and had members with countable asbestos fibers. (*Id.* at 16:23-25.) Dr. Gordon admits "some" of the decrease from 200 to thirty-five occurred when he discovered members had countable asbestos fibers, and he further admits none of those removed suffered an asbestos-related disease necessitating their removal from the control group. (*Id.* at 18:5-8.) Dr. Gordon explains the reduction from 200 to thirty-five patients was warranted because he never found anybody with countable asbestos fibers caused by background sources since the 1980s. (*Id.* at 17:5-10.) Nevertheless, Dr. Gordon has co-authored studies where countable asbestos fibers were detected in tissue of the background group. (*Id.* at 18:9-12.)

Dr. Gordon admits the amount of background asbestos can vary depending on where a person lives. (Gordon Dep. 5/1/2017, p. 135:3-6.) Nevertheless, even though asbestos would be part of the ambient air for a person living near a factory using or producing asbestos products, according to Dr. Gordon, the person could not represent "true background." (*Id.* at 130:14-20.) Thus, Dr. Gordon testified only people who have "never had any contact with asbestos of any kind" can create "true background levels." (Id. at 131:6-8.) As a result, a finding of a single countable asbestos fiber exceeds the background established by Dr. Gordon's current control group. (*Id.* at 127:14-16.)

Dr. Gordon's control group appears from the circumstances to be a creation of his own making designed to generate a pristine environment where a single countable asbestos fiber exceeds background levels. The control group has not been peer reviewed, and Dr. Gordon's penchant for little to no documentation of his work makes it impossible for defense experts to conduct a meaningful review of the selection process for the original group of 200 or the winnowing to the current group of thirty-five. The Court has no reasonable assurance the control

> group accurately reflects background levels in the general population.

Jackson at 8-9. A Nebraska court similarly excluded Dr. Gordon's fiber burden opinion due to a "lack of transparency, peer-review, and general acceptance" of "selectively removing part of the [control group] because [of] their higher levels of fiber burden," rendering his control group "not sufficiently reliable." (*Cade v. Union Pac. R.R.*, No. CI 12-393 (Neb. Dist. Ct. Feb. 18, 2015)) at 6. The *Cade* court went through each of the relevant factors under *Daubert* and held that "[n]one of the *Daubert* factors support inclusion of information about Dr. Gordon's control group." A court in Pennsylvania reached a similar conclusion. (Mem. Opinion, *Brandt v. The Bon-Ton Stores, Inc., et al.*, No. 2987.

VIII. Dr. Roggli's Fiber Burdens Studies Demonstrate Cosmetic Talc Does Not Create Occult Asbestos Exposure

Dr. Roggli and coauthors analyzed lung tissue samples from a large series of malignant mesothelioma patients to examine the question of whether talc exposure plays a role in the development of mesothelioma. Roggli, et al., "Talc and mesothelioma: mineral fiber analysis of 65 cases with clinicopathological correlation", Ultrastructural Pathology, https://doi.org/10.1080/01913123.2020.1737286 (2020) ("Talc and mesothelioma"). The values were compared with their controls in which talc was reported in approximately 55% of the controls. Srebro SH, Roggli VL, Samsa GP., "Malignant mesothelioma associated with low pulmonary tissue asbestos burdens: A light and scanning electron microscopic analysis of 18 cases," *Mod Pathol* 1995;8:614; Roggli V.L., Sharma A., Butnor K.J., Sporn T., Vollmer R.T., "Malignant mesothelioma and occupational exposure to asbestos: A clinical pathological correlation of 1445 cases," *Ultrastruct Pathol* 2002;26:55. Of 609 mesothelioma patients, talc fibers reportedly exceeded control values in 65 or 11%, including 48/524 men (9.2%) and 17/85 women (20%). "Talc and mesothelioma" focuses on these 65 cases.

Of the 65 with elevated talc levels, amosite and/or crocidolite were elevated in 52 of 65 (80%), and tremolite, actinolite or anthophyllite were reportedly elevated in 41 of 65 (63%). Both were elevated in 52%. A history of working in industries associated with asbestos exposure and increased mesothelioma risk was identified in 75% of the men (36 of 48), and a history of exposure as household contacts of an occupationally exposed individual was identified in 71% of the women (12 of 17). The authors concluded that the vast majority of mesothelioma patients had talc levels indistinguishable from background.

Table 3 from "Talc and mesothelioma" reports the median and range of talc 'fiber' concentrations for the 65 malignant mesothelioma cases with increased talc levels, along with the 11 controls.

Table 3. Talc fiber content in 65 malignant mesothelioma cases with increased talc levels.

	No. of Cases	Talc Content
Males	48	18,800 (11,000–138,000)
Females	17	20,100 (11,500–70,200)
Total	65	19,500 (11,000–138,000)
Controls	11	1130 (<100-10,500)

Values shown are median concentration in fibers per gram of wet lung tissue with ranges indicated in parentheses. Values shown for controls are for the 11 cases where talc was detected.

Table 4 from "Talc and mesothelioma" focuses on the 17 women with mesothelioma and increased talc levels. Eleven of the 17 (65%) had elevated commercial amphibole asbestos fibers reported. Twelve of the 17 (71%) had elevated asbestos body counts. Twelve of the cases had a history of exposure as a household contact of an asbestos worker including in industries such as (i) shipbuilding, (ii) insulation, (iii) railroad during the steam era, (iv) power plant, and (v) chemical plant. For one woman, her former husband's work was not identified, but he died of asbestosis and mesothelioma.

Table 4. Malignant mesothelioma in women with elevated talc content.

Case	Age	Dx	Exposure	PPP	Asb	↑AB	↑AC	↑TAA	Talc
1	82	PI	HHC (husband)	+	-	-	+	+	70,200
2	80	EPI	HHC (husband)	+	ND	+	+	+	57,200
3	73	BPI	Si plant/pattern	-	-	+	-	+	46,100
4	79	EPI	HHC (husbands)	-	-	-	-	+	37,200
5	68	EPI	HHC (F,H)	ND	-	+	-	+	29,900
6	75	SPI	HHC (husband)	+	+	+	+	+	28,000
7	66	SPI	HHC (son)	-	-	+	-	-	22,500
8	49	BPI	HHC (insulators)	-	-	+	+	-	21,700
9	34	EPI	Bldg. occupant	ND	-	-	-	-	20,100
10	62	EPI	HHC (husband)	-	-	+	+	+	20,000
11	75	BPI	HHC (husband)	-	ND	-	+	+	17,100
12	68	EPI	Tile sort/Press op	-	-	+	+	+	15,900
13	80	EPI	HHC (husband)	-	-	+	+	-	13,400
14	65	SPe	HHC (husband)	-	-	+	+	+	12,000
15	76	EPI	HHC (husband)	-	-	+	+	+	11,900
16	59	EPI	Publishing/art	ND	ND	-	-	-	11,700
17	61	EPI	Photographer	+	-	+	+	-	11,500

Talc values are fibers of 5 μm or greater in length per gram of wet lung tissue; age = years.
AB = asbestos bodies/gm; AC = commercial amphibole fibers/gm; asb = asbestosis; B = biphasic; Bldg. = building; E = epithelial; F = father; H = husband; HHC = household contact; ND = no data; op = operator; Pe = peritoneal; PI = pleural; S = sarcomatoid; Si = silica; sort = sorter; TAA = noncommercial amphibole fibers/gm; + = present; - = absent.

Table 5 from "Talc and mesothelioma" focuses on the seven mesothelioma cases in which both talc and noncommercial amphibole fibers were present in elevated concentrations, but in which amosite and/or crocidolite were not detected. Case Nos. 1, 2, and 7 were reported previously. Roggli V.L., Vollmer R.T., Butnor K.J., Sporn T.A., "Tremolite and mesothelioma," *Ann Occup Hyg* 2002;46:447; Srebro S.H., Roggli V.L., "Asbestos-related disease

associated with exposure to asbestiform tremolite," *Am J Ind Med* 1994;26:809. "Case 1 was a painter and plasterer for 38 years who worked extensively with joint compound containing chrysotile, which was likely a major source of the noncommercial amphibole tremolite and anthophyllite." "Talc and mesothelioma" at 214. "Case 2 worked for 34 years in the pattern shop of a silica plant with extensive exposure to industrial grade talc, which was likely the source of the noncommercial amphibole tremolite and anthophyllite." *Id*. Cases 3 and 4 were "household contacts of individuals who worked with asbestos." *Id.* Case 5 "was a painter and sandblaster who also had pleural plaques." *Id.* at 215. Case 6 "worked in a shipyard for 6 months." *Id.* at 214. "Case 7 was a household contact from his parents for 18 years, with his father working as a toolgrinder and his mother at a glass manufacturing plant." *Id*.

Table 5. Malignant mesothelioma cases with elevated talc and TAA content.

Case	Age	Dx	Exposure	PPP	Asb	↑AB	↑AC	↑TAA	Talc
1	56 M	BPI	Painter/plasterer	-	-	-	-	+	60,600
2	73 F	BPI	Si plant/pattern	-	-	+	-	+	46,100
3	79 F	EPI	HHC (husbands)	-	-	-	-	+	37,200
4	68 F	EPI	HHC (F,H)	ND	-	+	-	+	29,900
5	52 M	EPI	ND	-	-	+	-	+	14,400
6	67 M	BPI	Shipyard work	-	-	+	-	+	13,300
7	54 M	EPI	HHC (parents)	ND	-	+	-	+	13,100

Talc values are fibers of 5 µm or greater in length per gram of wet lung tissue.
Age in years with gender indicated (male or female).
Other abbreviations are same as in Table 4.

Table 6 focuses on the six mesothelioma cases in which only talc was present in elevated concentrations. "Case 1 was the son of a pipefitter who was likely exposed to asbestos, and this patient had elevated asbestos body counts by light microscopy." *Id.* at 215. "Case 5 was a painter and sandblaster who also had pleural plaques. " *Id.* Cases 2, 3, 4, and 6 "did not work in industries in which there is a known increase in mesothelioma risk." *Id.*

Table 6. Malignant mesothelioma cases with elevated talc only.

Case	Age	Dx	Exposure	PPP	Asb	↑AB	↑AC	↑TAA	Talc
1	66 F	SPI	HHC (son)	-	-	+	-	-	22,500
2	34 F	EPI	Bldg. occupant	ND	-	-	-	-	20,100
3	76 M	EPI	Security guard	ND	-	-	-	-	15,000
4	83 M	EPI	Shade tree mech.	ND	-	-	-	-	13,600
5	67 M	SPI	Paint/sandblast	+	-	ND	-	-	12,800
6	59 F	EPI	Publishing/art	ND	ND	-	-	-	11,700

Talc values are fibers of 5 µm or greater in length per gram of wet lung tissue.
Age in years with gender indicated (male or female).
Mech. = mechanic; paint = painter; sandblast = sandblaster. Other abbreviations are same as in Table 4.

The data in "Talc and mesothelioma" is consistent with a number of other fiber burden studies which fail to establish cosmetic talc as a source of asbestos exposure. For example, many female mesothelioma patients have fiber burden and asbestos body counts that do not exceed background and "no evidence for any increased mesothelioma risk from mineral fibers in these North American

women…" Attanoos, R.L., Letter to Editor, In Reply to "Malignant Mesothelioma and Its Nonasbestos Causes," *Arch Pathol Lab Med* 143: 911-913 (2019); Kraynie A., de Ridder G., Sporn T., Pavlisko E., Roggli V.L., "Malignant mesothelioma not related to asbestos exposure: analytical scanning electron microscopic analysis of 83 cases and comparison with 442 asbestos-related cases," *Ultrastruct Pathol* 2016;40(3):142–146. As Dr. Roggli, et al., remind us:

> … in 2002, we published a case series of patients with mesothelioma and elevated concentrations of tremolite fibers. Among 312 cases for which a fiber burden analysis had been performed, we identified 14 for which noncommercial amphibole fibers were the only fiber type present in excess levels. **Every case had an identified occupational or para-occupational exposure to asbestos.** Actinolite and anthophyllite were always identified in cases where another amphibole fiber type was present in excess levels, with the exception of one case in which actinolite was the only fiber type present in excess, and this was in a patient with environmental exposure in Turkey.

Victor L. Roggli , John M. Carney , Thomas A. Sporn & Elizabeth N. Pavlisko (2020) Response to letter regarding "Talc and mesothelioma: mineral fiber analysis of 65 cases with clinicopathological correlation", Ultrastructural Pathology, 44:4-6, 524-525, DOI: 10.1080/01913123.2020.1795019 citing Roggli V.L., Vollmer R.T., Butnor K.J., Sporn T.A., "Tremolite and mesothelioma," *Ann Occup Hyg* 2002;46:447–453 (emphasis added).

Ultimately, there is "no evidence for any causative role of cosmetic talc in malignant mesothelioma." Attanoos, R.L., Letter to Editor, In Reply to "Malignant Mesothelioma and Its Nonasbestos Causes," *Arch Pathol Lab Med* 143: 911-913 (2019).