THE STATE OF SOUTH CAROLINA
In The Court of Appeals

APPEAL FROM RICHLAND COUNTY
Court of Common Pleas
Jean H. Toal, Circuit Court Judge

Appellate Case No. 2025-000065
Civil Action No. 2023-CP-40-04072

Michael L. Perry and Lonnie Long,..... Respondents,

v.

American International Industries et al.

Of whom Johnson & Johnson; LLT Management, LLC f/k/a LTL Management, LLC; Kenvue, Inc.; and Johnson & Johnson Holdco (NA), Inc. are the ..... Appellants.

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I certify that this Designation does not contain any matters which are irrelevant to this appeal.

- MAS Analysis Report of Avon Products, prepared by William E. Longo, PhD, dated 15 November 2022.
- MAS Supplemental Report Talcum Powder Analysis of Avon Powder Products, Project M71560 & M71562, prepared by William E. Longo, PhD, CEO dated 19 November 2022.
- MAS Talcum Powder Analysis of Avon Somewhere Powder, prepared by William E. Longo, PhD, CEO dated 20 September 2023.
- MAS Talcum Powder Analysis of Avon Split, prepared by William E. Longo, PhD, CEO dated 21 September 2023.
- MAS Avon Talcum Powder Analysis, prepared by William E. Longo, PhD, CEO dated 21 September 2023.
- MAS Talcum Powder Analysis of Solomon, Beth – Talc Splits, prepared by William E. Longo, PhD, CEO dated 16 February 2024.
- MAS Analysis Report of Avon Unforgettable Perfumed Talc, prepared by William E. Longo, PhD, dated 21 April 2017.
- Expert Report of Steven P. Compton, PhD, Investigation of Italian Talc Samples for Asbestos, dated 01 August 2017.
- Expert Report of Steven P. Compton, PhD, Investigation of Vermont Talc Samples for Asbestos, dated 23 April 2018.
- Expert Report of Steven P. Compton, PhD, Investigation of Montana Talc (American International Industries Microtalc 1745) for Asbestos, dated 15 March 2019.
- Expert Report of Steven P. Compton, PhD, Examination of Avon Talcum Powder for Asbestos Gail Welch Case, dated 29 May 2020.
- Expert Report of Steven P. Compton, PhD, Examination of 907 Talc Powder for Asbestos, dated 26 January 2024.
- Expert Report of Steven P. Compton, PhD, Examination of Vintage Avon Bunny Fluffpuff Talc in Rabbit-shaped Puff container for Asbestos, dated 19 May 2023.
- Expert Report of Steven P. Compton, PhD, Examination of Vintage Avon Unforgettable Talc in Shaker Container for Asbestos, dated 19 May 2023.
- Expert Report of Jennifer S. Pierce, MS, PhD, in the matter of Michael Perry regarding Avon, Inc., dated 19 June 2024.
- Affidavit of R. Mark Bailey, on behalf of Johnson & Johnson, dated 30 October 2023, with exhibits 1 through 16.
- MAS Expert Analysis Report of Estee Lauder Products by William E. Longo, PhD, CEO, dated 16 December 2022.
- Expert Report of R. Mark Bailey, PG, Transmission Electron Microscopy Analytical Test Report of Johnson & Johnson Baby Powder, dated 06 May 2021.

- Expert Report of R. Mark Bailey, PG, Transmission Electron Microscopy Analytical results for 3 talc archive batch samples on behalf of Johnson & Johnson, dated 08 September 2021.
- MAS 4th Supplemental MDL Report, Analysis of Non-Historical J&J's Talcum Powder Consumer Product Containers and J&J Chinese Historical Talc Retain Samples, by William E. Longo, PhD, CEO, dated 29 April 2024.
- MAS Supplemental #2 Expert Report on Below the Waist Application of Johnson & Johnson Baby Powder by William E. Longo, PhD, Mark W. Rigler, PhD, and William B. Egeland, MS, PG, dated January 2018.
- MAS Expert Report Rev #1 on Talcum Powder Application to Baby and Diaper Change II: A Hygiene Study by William E. Longo, PhD, William B. Egeland, MS, PG, and Martin Bennett, dated 28 June 2019.
- MAS Expert Report on Johnson's Baby Powder Application to Baby and Diaper Change: A Hygiene Study Supplemental by William E. Longo, PhD, William B. Egeland, MS, PG, and Martin Bennett, dated May 2020.
- Declaration of William Longo, PhD, dated 21 September 2021.
- Expert Report of Jennifer Sahmel, PhD, CIH, CSP, FAIHA, on behalf of Vi-Jon, dated 20 June 2024.
- Expert Report of Paul A. Nony, PhD, CIH, CSP, on behalf of Estée Lauder, dated 26 June 2024, *with* References.

Other:

- Social Security Records of Michael Perry, 1979 through 2000.
- Social Security Records of Michael Perry, 1987 through 2023.
- Work History Affidavit.

Medical Documents/Materials:

- PERRY - MUSC 2.8.23-11.17.23
- PERRY - RSFP ROPER 2022-2023
- PERRY ROPER 5.19.17-7.1.23
- SC-PERRY MUSC radiology link
- Perry, Michael - Roper St. Francis (Dx Pathology Report 07.05.23) PERRY_SC_000014-000015 (3065538)
- Admission to Medical University of South Carolina dated 080823
- Admission to Palmetto Digestive Health Specialists dated 062623
- Cardiac testing
- Office notes of Charleston Oncology

- Office notes of Medical University of South Carolina (reverse chron)
- Office notes of Roper St. Francis Physician Partners
- Pathology reports
- Radiology reports
- Perry, Michael - Dr. Brian M. Lingerfelt (Medical 07.07.23)
- Perry, Michael - Edgepark Medical Supplies (Medical 07.07.23)
- Perry, Michael - Medical University of South Carolina (Pathology)
- Perry, Michael - MUSC (Pathology Report 08.18.23)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 1)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 2)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 3)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 08.22.23 - 12.26.23 Vol 1 - UC)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 08.22.23 - 12.26.23 Vol 2)
- Perry, Michael - MUSC Medical University of South Carolina (Medical Affidavit 07.08.23 - 08.18.23)
- Perry, Michael - Palmetto Digestive Disease Endoscopy Center (Medical 06.19.17 - 06.26.23)
- Perry, Michael - Palmetto Digestive Disease Endoscopy Center (Medical Affidavit 06.19.17 - 06.26.23)
- Perry, Michael - Pulmonology at MUSC Health Hollings Cancer Center (Medical 07.15.23 - 07.24.23)
- Perry, Michael - Pulmonology at MUSC Health Hollings Cancer Center (Medical Affidavit 07.15.23 - 07.24.23)
- Perry, Michael - Roper Hospital (Medical 03.01.21 - 06.30.23)
- Perry, Michael - Roper Hospital (Pathology)
- Perry, Michael - Roper St. Francis (Dx Pathology Report 07.05.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical Vol 1 01.11.21 - 07.12.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical Vol 2 01.11.21 - 07.12.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical

- Admission to Medical University of South Carolina dated 07.24.23.
- Admission to Palmetto Digestive Health Specialists dated 04.10.19.
- Admission to Palmetto Digestive Health Specialists dated 06.05.23.
- Admission to Palmetto Digestive Health Specialists dated 06.19.17.
- Admission to Palmetto Digestive Health Specialists dated 07.12.17.
- Admission to Palmetto Digestive Health Specialists dated 08.09.17.
- Admission to Palmetto Endoscopy Center dated 01.20.14.
- Admission to Roper Hospital dated 06.30.23.
- Office notes of Medical University of South Carolina.
- Pathology reports; 02.25.10.
- Radiology reports; 06.11.17.
- Office notes of Medical University of South Carolina (reverse chron).
- Radiology reports; 12.05.23.
- Radiology Materials – Refer to **APPENDIX C** for list of studies received on disc format
    - 03 disc(s) on 10 May 2024 from Medical University of South Carolina.
    - 01 disc(s) on 04 June 2024 from Medical University of South Carolina.

APPENDIX B: LITERATURE CONSIDERED, REPORTS REVIEWED AND OTHER RELIANCE MATERIALS.

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APPENDIX C: RADIOLOGY STUDIES, AS RECEIVED ON COMPACT DISCS.

Medical University of South Carolina, 20 studies:

- NM Pulmonary Ventilation Perfusion VQ, Accession Number: 21078587, dated 07/14/2023.
- MRI Brain W WO Contrast, Accession Number: 21076525, dated 07/17/2023.
- MRI Chest W WO Contrast, Accession Number: 21076526, dated 07/17/2023.
- PET CT Skull Base to Midthigh, Accession Number: 21053965, dated 07/18/2023.
- XR Chest 1 View Portable, Accession Number: 21178471, dated 08/08/2023.
- XR Chest 1 View Portable, Accession Number: 21178636, dated 08/08/2023.
- XR Chest AP Portable, Accession Number: 21178863, dated 08/09/2023.
- XR Chest AP Portable, Accession Number: 21182695, dated 08/10/2023.
- XR Chest AP Portable, Accession Number: 21187659, dated 08/11/2023.
- XR Chest AP Portable, Accession Number: 21192101, dated 08/12/2023.
- XR Chest 2 Views, Accession Number: 21194509, dated 08/13/2023.
- XR Chest 2 Views, Accession Number: 21195964, dated 08/14/2023.
- XR Chest 2 Views, Accession Number 21200519, dated 08/15/2023.
- XR Chest 2 Views, Accession Number: 21201843, dated 08/15/2023.
- XR Chest PA and Lateral, Accession Number: 21266398, dated 09/01/2023.
- CT Chest W Contrast, Accession Number: 21290447, dated 09/29/2023.
- CT Chest W Contrast, Accession Number: 21567301, dated 12/05/2023.
- RAD ONC PLANNING, Accession Number: 21555596, dated 01/02/2024.
- RAD ONC PLANNING, Accession Number: 21873777, dated 01/31/2024
- CT Chest W Contrast, Accession number: 21822953, dated 04/29/2024.

Exhibit B

STATE OF SOUTH CAROLINA	)	IN THE COURT OF COMMON PLEAS
	)	
COUNTY OF RICHLAND	)	FOR THE FIFTH JUDICIAL CIRCUIT
SARAH J. PLANT and **PARKER PLANT,**	)	**C/A NO. 2022-CP-40-01265**
Plaintiff,	)	*In Re:* Asbestos Personal Injury Litigation Coordinated Docket
v.	)	
AVON PRODUCTS, INC., et al.	)	
Defendants.	)	

STATE OF SOUTH CAROLINA	)	IN THE COURT OF COMMON PLEAS
	)	
COUNTY OF RICHLAND	)	FOR THE FIFTH JUDICIAL CIRCUIT
KELLY PAYNE CLARK and **SHANNON PAYNE LANCASTER**, as Co-Executors of the Estate of **SHELBY LINVILLE PAYNE,** Deceased**,**	)	**C/A NO. 2022-CP-40-01281**
Plaintiffs,	)	*In Re:* Asbestos Personal Injury Litigation Coordinated Docket
v.	)	
3M COMPANY et al.	)	
Defendants.	)	

ORDER GRANTING IN PART AND DENYING IN PART PLAINTIFFS' MOTION IN LIMINE TO EXCLUDE THE TESTIMONIES OF DR. GREGORY DIETTE, DR. DAVID WEILL & DR. ALLEN FINEGOLD

Plaintiffs in both of the above-captioned cases moved this Court, pursuant to Rules 702 and 403 of the South Carolina Rules of Evidence, for an Order excluding the expert testimonies of Dr. Gregory Diette, Dr. David Weill and Dr. Allen Finegold. The Court finds that the motion is well taken and should be, and therefore is, GRANTED IN PART and DENIED IN PART. Each

of these experts will be excluded from testifying at trial about the cause of mesothelioma in either Ms. Plant or Ms. Payne. Each of these experts will be excluded from testifying at trial that either Ms. Plant or Ms. Payne's mesothelioma was "idiopathic" or "spontaneous" or "naturally-occuring". These experts will be permitted to otherwise testify about talc and asbestos to the extent it falls within their qualifications, disclosure and subject to trial objections to specific questions.

RELEVANT FACTS

Drs. Diette, Weill and Finegold are medical doctors offered by multiple defendants including, Avon Inc. ("Avon"), Chanel, Inc. ("Chanel"), Colgate Palmolive, Inc. for Mennen ("Mennen"), Whittaker Clark & Daniels ("WCD") and Color Techniques, Inc. to give expert testimony in both of the above-captioned cases. They intend to opine that both Ms. Plant and Ms. Payne's mesotheliomas are not the result of exposure to asbestos, but instead occurred "spontaneously" or were "naturally occurring".

APPLICABLE LAW

Rule 702 of the South Carolina Rules of Evidence provides that "[i]f scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise." The trial court must act as a gatekeeper over scientific evidence and make three preliminary findings before expert testimony may be admitted. *Watson v. Ford Motor Co.,* 389 S.C. 434, 446, 699 S.E.2d 169, 175 (2010). The Court must find "that expert testimony is necessary to assist the jury in resolving factual questions, the expert is qualified in the particular area, and the testimony is reliable." *Id.* at 446-47, 699 S.E.2d at 175. "In South Carolina, a trial court minding the Rule 702 gate must assess not only (1) whether the expert's *method* is reliable (i.e., valid), but also (2) whether

the *substance* of the expert's testimony is reliable." *State v. Warner*, 430 S.C. 76, 86, 842 S.E.2d 361, 365–66 (Ct. App. 2020), *aff'd in part and remanded*, 436 S.C. 395, 872 S.E.2d 638 (2022). A trial court does not abuse its discretion under Rule 702 by excluding the testimony of medical experts whose conclusions were not supported by the data and experiments upon which they relied. *Id.* (citing *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). '"A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.'" *Id*. (quoting *Joiner*, 522 U.S. at 146).

Courts evaluating the admissibility of scientific expert evidence "must find the evidence will assist the trier of fact, the expert witness is qualified, and the underlying science is reliable." *State v. Council*, 335 S.C. 1, 20, 515 S.E.2d 508 (S.C. 1999). In considering the admissibility of scientific evidence the Court looks at several factors, including: (1) the publications and peer review of the technique; (2) prior application of the method to the type of evidence involved in the case; (3) the quality control procedures used to ensure reliability; and (4) the consistency of the method with recognized scientific laws and procedures. *State v. White*, 382 S.C. 265, 274, 676 S.E.2d 684 (S.C. 2009) (citing *Council*, 335 S.C. at 19).

This type of evidence is also subject to attack for relevancy and prejudice. *Id.* at 19–20, 515 S.E.2d at 517.

a. *Drs. Diette, Weill and Finegold may not offer opinions about the cause of Ms. Plant or Ms. Payne's mesothelioma.*

The Court finds that these doctors have not made an attempt to determine the products at issue contined asbestos at all. They did not make an attempt to determine the fiber type of asbestos potentially associated with any talc product at issue in this case. Furthermore, these doctors have not reviewed any studies relating to the products at issue in this case either purporting to demonstrate the presence or lack of presence of asbestos in the products or for purposes of

determining the amount of asbestos released from the normal and expected use of these products. These doctors do not have any information sufficient to testify in these two particular cases about the cause of mesothelioma in either Sarah Plant or Shelby Payne.

b. *Drs. Diette, Weill and Finegold may offer testimony about talc and asbestos generally, including testimony about their opinions relative to the rates of "spontaneous" or "idiopathic" mesotheliomas in women.*

The Court does not preclude at this time opinions regarding the rates of mesothelioma cancer in women which are "spontaneous" or "naturally-occuring".

CONCLUSION AND ORDER

WHEREFORE after reviewing the evidence submitted and arguments of counsel, both through the briefs and oral argument, this Court GRANTS IN PART and DENIES IN PART the Plaintiffs' Motion to Exclude Drs. Diette, Weill and Finegold. These experts will not be permitted to testify about the cause of either Shelby Payne or Sarah Plant's mesothelioma cancer, or testify that either womans' cancer was "spontaneous" "idiopathic" or "naturally-occuring".

AND IT IS SO ORDERED.

This Order memorializes an earlier ruling of Febraury 15, 2023 and acknowledges all objections made thereto.

[JUDGE'S E-SIGNATURE PAGE FOLLOWS]

Richland Common Pleas

Case Caption: Sarah J Plant , plaintiff, et al vs Avon Products Inc , defendant, et al

Case Number: 2022CP4001265

Type: Order/Other

So Ordered

Jean H. Toal

Exhibit C

Gregory B. Diette, M.D., M.H.S.

02 July 2024

Gregory B. Diette, M.D., M.H.S.
8805 Columbia 100 Parkway
Suite 101
Columbia, Maryland 21045

Ms. Lucy Willson, Esq.
Willcox & Savage, PC
440 Monticello Avenue, Suite 2200
Norfolk, Virginia 23510

RE: Perry, Michael v. Johnson & Johnson, *et al.*

Dear Ms. Willson,

This supplemental report has been prepared at your request as an updated summary of my opinions regarding claims that M. Michael Perry developed pleural mesothelioma as a result of asbestos exposure. I have reviewed the materials, in this case, to determine the potential role, if any, of cosmetic talcum powder containing products from Johnson & Johnson ("Johnson's Baby Powder" and "Shower to Shower") that were allegedly purchased at Wal-Mart locations, Avon ("Avon Deep Woods," "Avon Musk," "Avon Spicy," "Timeless," "Soft Musk," "Cotillion," "Birds of Paradise," and "Skin So Soft"), Vi-Jon ("Equate"), Estée Lauder Companies ("ELC" for "White Linen"), Gold Bond and Ammens products allegedly bottled by PTI Union LLC, and cosmetic talc allegedly produced by IMI-Fabi, LLC, IMI Fabi (USA), LLC and IMI Fabi (Diana) LLC, allegedly containing asbestos, as a cause of Mr. Perry's disease. This supplemental report reflects additional materials that I have received and reviewed since the submission of my initial report on Mr. Perry on 27 June 2024 and should be read in conjunction with that report.

Please refer to the appendices at the conclusion of this supplemental report for an updated list of case materials that I have received and reviewed in this matter.

EXPERT REPORTS.

Peterson, Michael, M.E.M., DABT.[1]

Mr. Peterson reviewed case materials pertaining to Mr. Perry. It is Mr. Peterson's opinion that the scientific evidence does not support that exposure to Gold Bond and Ammen's cosmetic talc products increases the risk of mesothelioma. Mr. Peterson opined that even if Gold Bond and Ammen's cosmetic talc did contain trace asbestiform amphibole or serpentine minerals, this would not materially impact his conclusions. Mr. Peterson further notes that if he assumes that asbestiform amphibole or serpentine minerals were present in cosmetic talc products, then he would have to assume that the same non-talc minerals would be present in the cosmetic- and industrial-type talcs used in animal studies, as well as the talc to which miners and millers were exposed. He noted that given the negative results of the animal and epidemiology studies, and assuming that non-talc minerals were present in cosmetic talcs, he reasonably concludes that the levels were so low as to not increase the risk of mesothelioma. Mr. Peterson noted that this finding is consistent with risk calculations performed in the regulatory and peer-reviewed literature using conservative assumptions. Mr. Peterson stated that systematic review of the relevant scientific and peer-reviewed literature and the evidence from animal toxicology, epidemiology, exposure, and mechanistic studies of talc, it is his opinion that exposure to Gold Bond and Ammen's cosmetic talc products could not have increased Mr. Perry's risk of mesothelioma.

Mr. Peterson also identified possible occupational exposure to commercial amphibole asbestos during hotel renovations which occurred during his employment at various hotels. He noted that he was not able to determine the types of asbestos Mr. Perry might have been exposed to during his employment. Mr. Peterson opined that assuming Mr. Perry was exposed to at least some commercial amphibole asbestos (amosite and/or crocidolite) during the renovations, these exposures may have increased his risk of mesothelioma. If these exposures can be ruled out, it is likely that his mesothelioma occurred spontaneously. Mr. Peterson also noted that there is also the possibility that Mr. Perry has a genetic predisposition to cancer, as multiple first-degree relatives were also diagnosed with cancer.

Druschel, Gregory, PhD.[2]

Dr. Druschel evaluated plaintiffs' experts' reports on their findings of alleged asbestiform amphibole and chrysotile in commercial talc products and other samples assessing the veracity of the analytical approaches used and if they support positive identification of asbestiform amphiboles or chrysotile in talc samples. Dr. Druschel evaluated reports regarding Gold Bond powder products. Dr. Druschel opined that Dr. Longo's techniques lack sufficient precision, and are extremely susceptible to false positives for asbestos minerals in a talc matrix. Dr. Druschel further opined that the scientific evidence presented in plaintiffs' experts' reports is inconsistent, often with a low level of analytical quality, with a lack of precision necessary for the task, often done so poorly as to render the information useless, and does not support the conclusion, in any instance, of asbestiform amphibole or chrysotile presence in the samples analyzed.

[1] Expert Report of Michael Peterson, M.E.M., DABT, on behalf of PTI Union, LLC, dated 27 June 2024.
[2] Expert Report of Dr. Gregory K. Druschel, Ph.D., on behalf of PTI Union, LLC, dated 26 June 2024.

With regard to the likelihood of trace asbestiform amphiboles or chrysotile associated with the talc deposits of SW Montana or SW China, Dr. Druschel opined that thermodynamics dictates amphibole mineralization in impossible at these conditions, tectonics dictates chrysotile formation is impossible at these conditions. Further, he stated that if trace amphiboles or chrysotile are found in these samples (and here he noted that analytical work he has reviewed to date shows NO evidence of either) it is far more likely that small amount of asbestos mineral came from airborne dusts not related at all to the ore deposits, but rather contamination of the material sometime between excavation and analysis of the bottles in question.

ASSESSMENT AND CONCLUSIONS.

The allegation in this case is that Mr. Perry has pleural mesothelioma that was caused by cosmetic talc believed to also contain asbestos. I have assumed that the diagnosis of pleural mesothelioma is correct. Based on the materials available in this case, Mr. Perry does not have conditions such as diffuse pleural thickening or bilateral calcified pleural plaques which, if present, could be compatible with prior asbestos exposure. He does not have asbestosis.

In particular, I assessed the evidence in this case that asbestos as a potential contaminant of cosmetic talc produced and/or distributed by Johnson & Johnson, Avon, Vi-Jon, Estée Lauder, Gold Bond, Ammens IMI-Fabi, LLC, IMI Fabi (USA), LLC, and/or IMI-Fabi (Diana) could have been responsible for causing pleural mesothelioma in Mr. Perry. In this case, there is no objective evidence available that shows that Mr. Perry had any asbestos exposure from his alleged use of cosmetic talc produced and/or distributed by Johnson & Johnson, Avon, Vi-Jon, Estée Lauder, Gold Bond, Ammens, IMI-Fabi, LLC, and/or IMI-Fabi (Diana). There is no epidemiological evidence that the use of cosmetic talc produced and/or distributed by Johnson & Johnson, Avon, Vi-Jon, Estée Lauder, Gold Bond, Ammens, IMI-Fabi, LLC, IMI Fabi (USA), LLC, and/or IMI-Fabi (Diana) causes mesothelioma.

According to the testimony of Mr. Perry, his exposure to Johnson's Baby Powder was from his own personal use, his application to his husband, his husband's application to himself in his proximity, his mother's application to herself in his proximity, and his mother's application directly to him. Mr. Perry's exposure to Avon cosmetic talcum powder products was from playing with his father's container of powder and from being in proximity to his mother while she applied powder to herself. Mr. Perry's exposure to Vi-Jon cosmetic talcum powder products was from his application to himself and his application to his husband, and his husband's application to himself in Mr. Perry's proximity. Mr. Perry's exposure to Estée Lauder cosmetic talcum powder products was from being in proximity to his mother while she applied powder to herself. Mr. Perry's exposure to Gold Bond and Ammens cosmetic talcum powder products was from his own personal use and from applying powder to his shoes. Mr. Perry's exposure to cosmetic talc allegedly produced by IMI-Fabi, LLC, IMI Fabi (USA), LLC, and/or IMI Fabi (Diana), LLC was from talcum powder products since 2001.

Mr. Perry likely had no asbestos exposure from cosmetic talc produced and/or distributed by Johnson & Johnson, Avon, Vi-Jon, Estée Lauder, Gold Bond, Ammens, IMI Fabi (USA), LLC, and/or IMI Fabi (Diana), LLC, but even worst-case estimated exposures would have been to a dose too low to elevate his risk for mesothelioma. It is not plausible that his alleged exposures

from cosmetic talc produced and/or distributed by Johnson & Johnson, Avon, Vi-Jon, Estée Lauder, Gold Bond, Ammens, IMI-Fabi, LLC, IMI Fabi (USA), LLC, and/or IMI-Fabi (Diana) caused his mesothelioma.

I have not seen evidence in this case of any significant exogenous exposure (including asbestos) that would raise his risk of developing pleural mesothelioma, though I cannot rule out a contribution from his claimed occupational exposures. If Mr. Perry did not have significant exogenous exposure from commercial amphibole asbestos, it is most likely that his mesothelioma developed spontaneously or was naturally occurring.

It is possible that Mr. Perry had an inherited genetic risk factor for cancer especially given his young age, and personal and family history of malignancies. However, there is no germline testing result available to confirm that.

This supplemental report is based on the information available to me at this time. Should additional information become available, I reserve the right to determine the impact, if any, of the new information on my opinions and conclusions, to revise my opinions and conclusions if necessary, and to rebut the opinions of any other experts that formulate an opinion in this matter.

Respectfully submitted,

Gregory B. Diette, M.D., M.H.S.

APPENDIX A: CASE MATERIALS AND OTHER DOCUMENTS RECEIVED.

Legal Documents/Materials:

- Summons and Complaint
- First Amended Summons and Complaint
- Second Amended Summons and Complaint
- Plaintiff's Responses to Defendants' Master Set of Interrogatories and Requests for Production (Ex. 2)
- Plaintiffs' Responses to Defendants' Standard Interrogatories
- Plaintiffs' First Supplemental Responses to Defendants' Standard Interrogatories
- Plaintiffs' First Supplemental Responses to Defendants' Master Set of Interrogatories and Requests for Production (Ex. 2)

Depositions:

- Video-recorded Deposition of Michael L. Perry, Volume I, taken 10 October 2023, *with* Exhibits 1 through 14.
- Video-recorded Deposition of Michael L. Perry, Volume II, taken 11 October 2023, *with* Exhibits A through D.
- Video-recorded Deposition of Michael L. Perry, Volume III, taken 12 October 2023.
- Video-recorded Deposition of Michael L. Perry, Volume IV, taken 13 October 2023.

Expert Reports & Materials:

- Expert Report of Matthew S. Sanchez, on behalf of Johnson & Johnson, dated 06 June 2024.
- Expert Report of Matthew S. Sanchez, on behalf of Estée Lauder, dated 06 June 2024.
- Expert Report of Alan M. Segrave, PG, dated 17 June 2024.
- Expert Report of Christy A. Barlow, PhD, on behalf of Johnson & Johnson, dated 18 June 2024.
- Expert Report of R. Mark Bailey, PG, Laboratory Test Results for Avon Pavi Elle Perfumed Talc, Floral Fantasy, and 2 Odesseys, dated 27 December 2021.
- Expert Report of R. Mark Bailey, PG, Montana Talc Report on behalf of Avon, dated 12 June 2015.
- Expert Report of R. Mark Bailey, PG, Analysis of Avon Cotillion, dated 17 December 2019.
- Expert Report of R. Mark Bailey, PG, Laboratory Test Results for Avon Soft Musk and Topaze Perfumed Talc, dated 13 October 2021.
- Expert Report of R. Mark Bailey, PG, Laboratory Test Results for Avon To a Wild Rose, dated 19 January 2024.

- Murphy, Noth Carolina Talc Chart of Documents for Mark Bailey, PG, dated 20 August 2021.
- Expert Report of R. Mark Bailey, PG, on Asbestos in Talc Products from the Fontane Mine, Val Germanasca, Italy for Avon, dated 12 June 2020.
- Expert Report of R. Mark Bailey, PG, on Asbestos in Talc Products from the Hammondsville Mine, Vermont, USA for Avon, 16 November 2020.
- MAS Talcum Powder Analysis, Jeannine Henderson- Avon Wild Country, prepared by William E. Longo, PhD, CEO dated 25 October 2023.
- MAS Analysis of Avon Night Magic Talcum Powder, prepared by William E. Longo, PhD, and Mark W. Rigler, PhD, dated January 2019.
- MAS Report on Avon Talcum Powder Analysis with both Automated FESEM and ATEM, dated 12 March 2019.
- MAS Analysis Report of Chinese Talc Research Samples, prepared by William E. Longo, PhD, CEO dated 16 September 2020.
- MAS Analysis Report of Avon Occur Perfumed Talc, prepared by William E. Longo, PhD, dated 18 August 2021.
- MAS Talcum Powder Analysis of Avon and Clinique Containers, prepared by William E. Longo, PhD, dated 05 September 2021.
- MAS Talcum Powder Analysis of Montana Micro-Talc 1745 Retain Samples, prepared by William E. Longo, PhD, CEO dated 10 June 2022.
- MAS Talcum Powder Analysis of Avon Splits, prepared by William E. Longo, PhD, CEO dated 01 June 2022.
- MAS Talcum Powder Analysis of Historical Avon Splits: Wild Rose 1965, Cotillion 1961, & Persian Wood 1958, prepared by William E. Longo, PhD, CEO dated 01 June 2022.
- MAS Pfizer Treasure Mine Talc Analysis, prepared by William E. Longo, PhD, CEO dated 01 June 2022.
- MAS Talc Ore Samples Collected from the Eclipse Mine in Death Valley: Analyzed for Amphibole Asbestos by Transmission Electron Microscopy, prepared by William E. Longo, PhD, CEO dated 12 June 2022.
- MAS Talcum Powder Analysis of Rita Chapman Avon Powder Containers, prepared by William E. Longo, PhD, CEO dated 01 June 2022.
- MAS Supplemental Report Avon Talcum Powder Container Analysis for Asbestos, prepared by William E. Longo, PhD, CEO dated 30 September 2022.
- MAS Talcum Powder Analysis of Avon Powder Products, Project M71387 & M71587, prepared by William E. Longo, PhD, CEO dated 15 November 2022.
- MAS Talcum Powder Analysis of Avon Powder Products, Project M71560 & M71562, prepared by William E. Longo, PhD, CEO dated 15 November 2022.

- MAS Analysis Report of Avon Products, prepared by William E. Longo, PhD, dated 15 November 2022.
- MAS Supplemental Report Talcum Powder Analysis of Avon Powder Products, Project M71560 & M71562, prepared by William E. Longo, PhD, CEO dated 19 November 2022.
- MAS Talcum Powder Analysis of Avon Somewhere Powder, prepared by William E. Longo, PhD, CEO dated 20 September 2023.
- MAS Talcum Powder Analysis of Avon Split, prepared by William E. Longo, PhD, CEO dated 21 September 2023.
- MAS Avon Talcum Powder Analysis, prepared by William E. Longo, PhD, CEO dated 21 September 2023.
- MAS Talcum Powder Analysis of Solomon, Beth – Talc Splits, prepared by William E. Longo, PhD, CEO dated 16 February 2024.
- MAS Analysis Report of Avon Unforgettable Perfumed Talc, prepared by William E. Longo, PhD, dated 21 April 2017.
- Expert Report of Steven P. Compton, PhD, Investigation of Italian Talc Samples for Asbestos, dated 01 August 2017.
- Expert Report of Steven P. Compton, PhD, Investigation of Vermont Talc Samples for Asbestos, dated 23 April 2018.
- Expert Report of Steven P. Compton, PhD, Investigation of Montana Talc (American International Industries Microtalc 1745) for Asbestos, dated 15 March 2019.
- Expert Report of Steven P. Compton, PhD, Examination of Avon Talcum Powder for Asbestos Gail Welch Case, dated 29 May 2020.
- Expert Report of Steven P. Compton, PhD, Examination of 907 Talc Powder for Asbestos, dated 26 January 2024.
- Expert Report of Steven P. Compton, PhD, Examination of Vintage Avon Bunny Fluffpuff Talc in Rabbit-shaped Puff container for Asbestos, dated 19 May 2023.
- Expert Report of Steven P. Compton, PhD, Examination of Vintage Avon Unforgettable Talc in Shaker Container for Asbestos, dated 19 May 2023.
- Expert Report of Jennifer S. Pierce, MS, PhD, in the matter of Michael Perry regarding Avon, Inc., dated 19 June 2024.
- Affidavit of R. Mark Bailey, on behalf of Johnson & Johnson, dated 30 October 2023, with exhibits 1 through 16.
- MAS Expert Analysis Report of Estee Lauder Products by William E. Longo, PhD, CEO, dated 16 December 2022.
- Expert Report of R. Mark Bailey, PG, Transmission Electron Microscopy Analytical Test Report of Johnson & Johnson Baby Powder, dated 06 May 2021.

- Expert Report of R. Mark Bailey, PG, Transmission Electron Microscopy Analytical results for 3 talc archive batch samples on behalf of Johnson & Johnson, dated 08 September 2021.
- MAS 4th Supplemental MDL Report, Analysis of Non-Historical J&J's Talcum Powder Consumer Product Containers and J&J Chinese Historical Talc Retain Samples, by William E. Longo, PhD, CEO, dated 29 April 2024.
- MAS Supplemental #2 Expert Report on Below the Waist Application of Johnson & Johnson Baby Powder by William E. Longo, PhD, Mark W. Rigler, PhD, and William B. Egeland, MS, PG, dated January 2018.
- MAS Expert Report Rev #1 on Talcum Powder Application to Baby and Diaper Change II: A Hygiene Study by William E. Longo, PhD, William B. Egeland, MS, PG, and Martin Bennett, dated 28 June 2019.
- MAS Expert Report on Johnson's Baby Powder Application to Baby and Diaper Change: A Hygiene Study Supplemental by William E. Longo, PhD, William B. Egeland, MS, PG, and Martin Bennett, dated May 2020.
- Declaration of William Longo, PhD, dated 21 September 2021.
- Expert Report of Jennifer Sahmel, PhD, CIH, CSP, FAIHA, on behalf of Vi-Jon, dated 20 June 2024.
- Expert Report of Paul A. Nony, PhD, CIH, CSP, on behalf of Estée Lauder, dated 26 June 2024, *with* References.
- Expert Report of Michael Peterson, M.E.M., DABT, on behalf of PTI Union, LLC, dated 27 June 2024.
- Expert Report of Dr. Gregory K. Druschel, Ph.D., on behalf of PTI Union, LLC, dated 26 June 2024.

Other:

- Social Security Records of Michael Perry, 1979 through 2000.
- Social Security Records of Michael Perry, 1987 through 2023.
- Work History Affidavit.

Medical Documents/Materials:

- PERRY - MUSC 2.8.23-11.17.23
- PERRY - RSFP ROPER 2022-2023
- PERRY ROPER 5.19.17-7.1.23
- SC-PERRY MUSC radiology link
- Perry, Michael - Roper St. Francis (Dx Pathology Report 07.05.23) PERRY_SC_000014-000015 (3065538)

- Admission to Medical University of South Carolina dated 080823
- Admission to Palmetto Digestive Health Specialists dated 062623
- Cardiac testing
- Office notes of Charleston Oncology
- Office notes of Medical University of South Carolina (reverse chron)
- Office notes of Roper St. Francis Physician Partners
- Pathology reports
- Radiology reports
- Perry, Michael - Dr. Brian M. Lingerfelt (Medical 07.07.23)
- Perry, Michael - Edgepark Medical Supplies (Medical 07.07.23)
- Perry, Michael - Medical University of South Carolina (Pathology)
- Perry, Michael - MUSC (Pathology Report 08.18.23)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 1)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 2)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 07.08.23 - 08.18.23 Vol 3)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 08.22.23 - 12.26.23 Vol 1 - UC)
- Perry, Michael - MUSC Medical University of S. Carolina (Medical 08.22.23 - 12.26.23 Vol 2)
- Perry, Michael - MUSC Medical University of South Carolina (Medical Affidavit 07.08.23 - 08.18.23)
- Perry, Michael - Palmetto Digestive Disease Endoscopy Center (Medical 06.19.17 - 06.26.23)
- Perry, Michael - Palmetto Digestive Disease Endoscopy Center (Medical Affidavit 06.19.17 - 06.26.23)
- Perry, Michael - Pulmonology at MUSC Health Hollings Cancer Center (Medical 07.15.23 - 07.24.23)
- Perry, Michael - Pulmonology at MUSC Health Hollings Cancer Center (Medical Affidavit 07.15.23 - 07.24.23)
- Perry, Michael - Roper Hospital (Medical 03.01.21 - 06.30.23)
- Perry, Michael - Roper Hospital (Pathology)

- Perry, Michael - Roper St. Francis (Dx Pathology Report 07.05.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical Vol 1 01.11.21 - 07.12.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical Vol 2 01.11.21 - 07.12.23)
- Perry, Michael - Roper St. Francis Healthcare (Medical
- Admission to Medical University of South Carolina dated 07.24.23.
- Admission to Palmetto Digestive Health Specialists dated 04.10.19.
- Admission to Palmetto Digestive Health Specialists dated 06.05.23.
- Admission to Palmetto Digestive Health Specialists dated 06.19.17.
- Admission to Palmetto Digestive Health Specialists dated 07.12.17.
- Admission to Palmetto Digestive Health Specialists dated 08.09.17.
- Admission to Palmetto Endoscopy Center dated 01.20.14.
- Admission to Roper Hospital dated 06.30.23.
- Office notes of Medical University of South Carolina.
- Pathology reports; 02.25.10.
- Radiology reports; 06.11.17.
- Office notes of Medical University of South Carolina (reverse chron).
- Radiology reports; 12.05.23.
- Radiology Materials – Refer to **APPENDIX C** for list of studies received on disc format
    - 03 disc(s) on 10 May 2024 from Medical University of South Carolina.
    - 01 disc(s) on 04 June 2024 from Medical University of South Carolina.

APPENDIX B: LITERATURE CONSIDERED, REPORTS REVIEWED AND OTHER RELIANCE MATERIALS.

Abelmann A, Glynn ME, Pierce JS, et al. "Historical ambient airborne asbestos concentrations in the United States – an analysis of published and unpublished literature (1960s-2000s)." *Inhalation Toxicology.* 2015;27(14):754-766.

Acheson ED, Gardner MJ, Pippard EC, et al. "Mortality of Two Groups of Women who Manufactured Gas Masks from Chrysotile and Crocidolite Asbestos: A 40-year Follow-Up." *British Journal of Industrial Medicine.* 1982;39:344-348.

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Andrion A, Bosia S, Paoletti L, et al. "Malignant Peritoneal Mesothelioma in a 17-year-old Boy with Evidence of Previous Exposure to Chrysotile and Tremolite Asbestos." *Human Pathology.* 1994;25:617-622.

Armstrong BK, de Klerk NH, Musk AW, Hobbs MS. 1988. Mortality in miners and millers of crocidolite in Western Australia. Br J Ind Med. 45(1): 5–13. doi: 10.1136/oem.45.1.5.

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Attanoos RL, Churg A, Galateau-Salle F, et al. "In Reply to Malignant Mesothelioma and Its Nonasbestos Causes." *Archives of Pathology & Laboratory Medicine.* 2019;143;911-914.

Attanoos RL, Churg A, Galateau-Salle F, Gibbs AR, Roggli VL. "Malignant Mesothelioma and Its Non-Asbestos Causes." *Archives of Pathology & Laboratory Medicine.* 2018;142(6):753-760.

Attanoos RL, Gibbs AR. "Primary malignant gonadal mesotheliomas and asbestos." *Histopathology.* 2000;37(2):150-159.

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APPENDIX C: RADIOLOGY STUDIES, AS RECEIVED ON COMPACT DISCS.

Medical University of South Carolina, 20 studies:

- NM Pulmonary Ventilation Perfusion VQ, Accession Number: 21078587, dated 07/14/2023.
- MRI Brain W WO Contrast, Accession Number: 21076525, dated 07/17/2023.
- MRI Chest W WO Contrast, Accession Number: 21076526, dated 07/17/2023.
- PET CT Skull Base to Midthigh, Accession Number: 21053965, dated 07/18/2023.
- XR Chest 1 View Portable, Accession Number: 21178471, dated 08/08/2023.
- XR Chest 1 View Portable, Accession Number: 21178636, dated 08/08/2023.
- XR Chest AP Portable, Accession Number: 21178863, dated 08/09/2023.
- XR Chest AP Portable, Accession Number: 21182695, dated 08/10/2023.
- XR Chest AP Portable, Accession Number: 21187659, dated 08/11/2023.
- XR Chest AP Portable, Accession Number: 21192101, dated 08/12/2023.
- XR Chest 2 Views, Accession Number: 21194509, dated 08/13/2023.
- XR Chest 2 Views, Accession Number: 21195964, dated 08/14/2023.
- XR Chest 2 Views, Accession Number 21200519, dated 08/15/2023.
- XR Chest 2 Views, Accession Number: 21201843, dated 08/15/2023.
- XR Chest PA and Lateral, Accession Number: 21266398, dated 09/01/2023.
- CT Chest W Contrast, Accession Number: 21290447, dated 09/29/2023.
- CT Chest W Contrast, Accession Number: 21567301, dated 12/05/2023.
- RAD ONC PLANNING, Accession Number: 21555596, dated 01/02/2024.
- RAD ONC PLANNING, Accession Number: 21873777, dated 01/31/2024
- CT Chest W Contrast, Accession number: 21822953, dated 04/29/2024.

Exhibit D

IN THE CIRCUIT COURT OF COOK COUNTY, ILLINOIS

COUNTY DEPARTMENT, LAW DIVISION

STEPHANIE SALCEDO, Individually and as Administrator of the Estate of Theresa M. Garcia, Deceased,	)	
Plaintiff,	)	
v.	)	No. 20 L 4505
AVON PRODUCTS, INC., et al.,	)	
Defendants.	)	

REPORT OF PROCEEDINGS at the trial of the above-entitled cause before the Honorable Patrick J. Sherlock, Judge of the said Court, at Richard J. Daley Center, 50 West Washington Street, Room 2007, Chicago, Illinois, commencing at 10:20 a.m. on the 20th day of March, 2024.

Reported by: Deborah Habian, CSR, CRR, RMR

License No. 084-02432

where they exist?

A. Well, sure, as one -- right, because what you know is that asbestos, as an environmental exposure, impedes a number of genes, not only the growth control genes, but the genes that run the death pathway and other important genes like that, sure.

Q. We haven't talked about this yet, but in addition to asbestos being a complete carcinogen that promotes and initiates cancer and harms our defenses, do they also just inherently create more replication, more opportunities for that error?

A. Yeah, they do. Asbestos initiates through several different mechanisms, particularly inflammation and its ability to attract other cells, causes cell division. I mean, we've written a whole series of papers in my laboratory about how asbestos causes those cells to grow. In fact, the most recent paper -- I think you were going to show it -- how asbestos causes scarring and cancer, we looked at some data that we got on these animals that inhaled asbestos for a short time

and looked at the pleura. And the mesothelial cells were obviously dividing at an increased rate within 48 hours after exposure, and it lasted for eight days.

So for -- I mean, these are short-term experiments, but the answer to your question does asbestos inhalation help regulate cell division and increase rates of division, the answer is yes. And we know, as I showed you, dividing cells are more likely to become cancer cells.

Q. Is the rate in which replication occurs related to how often you would expect a natural-occurring spontaneous mesothelioma?

A. So because they're so rare, naturally occurring spontaneous from our endogenous errors, they occur. Any kind of cancer can be spontaneous. What controls that is hard to say. I really can't answer that question very well.

Q. Is the fact that -- let me start off with more basic questions.

Are certain cancers known to occur spontaneous or naturally occurring more than others?

REPORTER CERTIFICATE

I, Deborah Habian, a Certified Shorthand Reporter within and for the State of Illinois, do hereby certify:

That the foregoing report of proceedings was reported stenographically by me, was thereafter reduced to printed transcript by me, and constitutes a true record of the testimony given and the proceedings had;

That the said report of proceedings was taken before me at the time and place specified;

That I am not a relative or employee of attorney or counsel, nor a relative or employee of such attorney or counsel for any of the parties hereto, nor interested directly or indirectly in the outcome of this action.

IN WITNESS WHEREOF, I do hereunto set my hand this 21st day of March, 2024.

DEBORAH HABIAN, CSR, RMR, CRR, CLR
IL CSR NO. 084-02432
MO CCR NO. 1409

Exhibit E

IN THE SUPERIOR COURT OF THE STATE OF WASHINGTON
IN AND FOR THE COUNTY OF KING

WENDI J. HIRSHBERG and RICHARD)
HIRSHBERG, Wife and Husband,)
)
Plaintiffs,)
) No. 20-2-05603-1 SEA
vs.)
)
JOHNSON & JOHNSON, et al.,)
)
Defendants.)
)

VIDEOCONFERENCE DEPOSITION UPON ORAL EXAMINATION

OF

ARNOLD BRODY, PH.D.

Witness located in
Boca Raton, Florida

(ALL PARTICIPANTS APPEARING VIA VIDEOCONFERENCE)

DATE TAKEN: FEBRUARY 22, 2021
REPORTED BY: ANITA W. SELF, RPR, CCR #3032

length, but they -- we show varying fiber lengths. In other words, there were short fibers and long fibers binding to the membranes, and interacting with the membranes. And so, I think that's the point that I was trying to make right there.

Q. Okay.

And if we turn over to page -- let's see -- page No. 10, paragraph 18.

A. Okay.

Q. "Any form of cancer can occur spontaneously that is without an external cause," and that would include mesothelioma, correct?

A. That's right.

Q. And that's, in part, because cells are replicating. Obviously cells, depending on the organ, can replicate at a faster rate or a slower rate, but as they replicate, there are errors, and if they're not caught, the errors accumulate as mutations, correct?

A. That's correct.

Q. And an accumulation of mutations from these internal errors in cell replication can, in some individuals, result in cancer, correct?

A. That's right.

MS. DEAN: Object to form. Overly broad.

C E R T I F I C A T E

STATE OF WASHINGTON)
) ss.
COUNTY OF KING)

I, ANITA W. SELF, a Certified Shorthand Reporter in and for the State of Washington, do hereby certify that the foregoing transcript is true and accurate to the best of my knowledge, skill and ability.

IN WITNESS WHEREOF, I have hereunto set my hand and seal this 5th day of March 2021.

Anita W Self

ANITA W. SELF, RPR, CCR #3032

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Exhibit F

STATE OF SOUTH CAROLINA	:	IN THE COURT OF COMMON PLEAS
COUNTY OF RICHLAND	:	FOR THE FIFTH JUDICIAL CIRCUIT
MICHAEL L. PERRY and	:	
LONNIE L. LONG,	:	
Plaintiffs,	:	C/A No.
v.	:	2023-CP-40-04072
AMERICAN INTERNATIONAL	:	
INDUSTRIES, et al.,	:	
Defendants.	:	

CERTIFIED COPY

Deposition of

GREGORY B. DIETTE, MD, MHS

Via Zoom Videoconferencing

Wednesday, July 3, 2024

10:00 a.m.

Reported by:

Adam D. Miller, Registered Professional Reporter

tumor?

A I did.

Q Okay. So that means, fundamentally, Mr. Perry does not have a BAP1 germline mutation, but he could possibly have another unspecified germline mutation that could play a role in the development of mesothelioma; is that accurate?

A Absolutely.

Q Okay. All right. I know -- again, I'm going to page 3 now. You note in Mr. Perry's past medical history, one of the things that he had had was a colectomy due to some chronic inflammation from the diverticulitis; right?

A That's right.

Q You don't have an opinion that the inflammation associated with the diverticulitis played any role in causing his mesothelioma; right?

A I don't believe it did.

Q Okay. Going down to page 4 of your report and employment history -- and this is Mr. Perry's employment history; correct?

A That's right.

C E R T I F I C A T I O N

I, ADAM D. MILLER, Registered Professional Reporter, certify that the foregoing is a true and accurate transcript of the foregoing deposition, that the witness was first sworn by me at the time, place and on the date herein before set forth.

I further certify that I am neither attorney nor counsel for, not related to nor employed by any of the parties to the action in which this deposition was taken; further, that I am not a relative or employee of any attorney or counsel employed in this case, nor am I financially interested in this action.

/s/ Adam D. Miller
Registered Professional Reporter
and Notary Public

STATE OF SOUTH CAROLINA	)	IN THE COURT OF COMMON PLEAS
	)	
COUNTY OF RICHLAND	)	CIVIL ACTION NO. 2023-CP-40-04072
MICHAEL L. PERRY AND LONNIE L. LONG,	)	*In Re:* Asbestos Personal Injury Litigation Coordinated Docket
Plaintiffs,	)	**JOHNSON & JOHNSON DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION *IN LIMINE* NO. 19 TO EXCLUDE THE 1986 LETTER FROM H. W. SWANSON TO PHILLIPPE DOUILLET**
vs.	)	
AMERICAN INTERNATIONAL INDUSTRIES, ET AL.,	)	
Defendants.	)	

Defendants Johnson & Johnson ("J&J"), LLT Management LLC, Johnson & Johnson Holdco (NA) Inc. ("Holdco"), and Kenvue, Inc. ("Kenvue"), (collectively "J&J Defendants") hereby, oppose Plaintiffs' Motion *In Limine* No. 19 as follows:

INTRODUCTION

Plaintiffs move to exclude the FDA's 1986 letter response denying a citizen's petition to require a warning label on talc ("1986 FDA Response"), because they believe it is "false" and inadmissible hearsay. They are wrong on both fronts.

The 1986 FDA Response, which is reattached here with the FDA's certificate of authenticity (Ex. A), has been admitted routinely in trials involving J&J Defendants' talc products.[1] This Court is one of the many courts that has admitted the citizen's petition before. *See* Ex. B 2018.11.09 *Boyd-Bostic* Trial at [1276:3-1278:7]. Plaintiffs' arguments raise no new facts requiring a different decision.

ARGUMENT

[1] Counsel is not aware of any trial court excluding the 1986 FDA Response in a trial involving its talc products.

In the 1986 FDA Response, the FDA rejected a citizen's request to include an asbestos warning label on talc after reviewing dozens of studies, concluding that they were "of questionable reliability." *See* Ex. A at 3. The response also states "…that even when asbestos was present, the levels were so low that no health hazard existed." *See* Ex. A at 4. The 1986 FDA Response both rebuts Plaintiffs' claims that the defendants had reason to believe that talc was contaminated with harmful levels of asbestos and reflects on the reasonableness of the J&J Defendants' decision to continue selling talc without a warning label. *See* 2d Am. Compl. ¶40 (alleging J&J "failed to warn" its products "contained asbestos").

Even so, Plaintiffs want to exclude the 1986 FDA Response because Plaintiffs believe it is "demonstrably false." Indeed, Plaintiffs spend five pages of their motion arguing about what they believe certain facts demonstrate. In addition to being wrong, these arguments are properly made to the jury in attacking the weight (not admissibility) of the document. Plaintiffs also make a conclusory argument that the 1986 FDA Response is inadmissible hearsay. But they fail to acknowledge that the response letter offered into evidence has been authenticated, meets an exception to the hearsay rule, and is offered for purposes other than proving the truth of the matters asserted.

I. Plaintiffs' Subjective Belief that the 1986 FDA Response is False Does Not Make It Unfairly Prejudicial.

The fact the 1986 FDA Response contradicts Plaintiffs' theory of the case and reflects on the reasonableness of the J&J Defendants' conduct, does not make the evidence "unfairly" prejudicial. As the movant seeking to exclude evidence under Rule 403, Plaintiffs have the burden to establish this evidence is inadmissible. *State v. King*, 424 S.C. 188, 200, 818 S.E.2d 204, 210

(2018). But Plaintiffs merely offer argument supported by their *subjective* interpretation of the facts to support their position.

"Evidence is unfairly prejudicial if it has an undue tendency to suggest a decision on an improper basis, such as an emotional one." *State v. Williams*, 430 S.C. 136, 151 (2020) (citing *State v. Wilson*, 345 S.C. 1, 7 (2001)). Evidence is not unfair merely because Plaintiffs disagree with the evidence or its value. And each of the four points Plaintiffs make simply reflects argument properly considered by the jury in determining the weight of the evidence.[2]

First, Plaintiffs claims the document is simply wrong, pointing to prior J&J testing Plaintiffs believe contradicts some of the data the FDA *may* have relied on in formulating its response. But the FDA response was based on decades of data and tests conducted by independent agencies—including the FDA itself. *See* Ex. A 1986 FDA Response (describing the FDA surveillance activities which began in the 1970s). Even if Plaintiffs were able to prove the J&J data was flawed, which they have not, they certainly have not established as a matter of law that one flawed data set would have changed the FDA's response in 1986. Regardless, Dr. Goudie's "misleading" report is not misleading at all. Plaintiffs allege that J&J Defendants misled the FDA by failing to provide complete information, including an earlier 1972 report by Dr. Goudie labeled "Do Not Use this Report/Replaced By Another Version" that reported tremolite in two samples of Johnson's Baby Powder. Plfs' MIL 19 at 3. Plaintiffs fail to inform the Court about a follow-up letter that explains the earlier reports of tremolite could not be substantiated under the light microscope, which required an update to the testing report. *See* Ex. C 11/15/72 letter to Dr. Goudie (DX7052). At best, the earlier report creates a fact dispute potentially relevant to determining the

[2] In listing the reasons Plaintiffs believe the 1986 Response Letter is false, Plaintiffs' brief purports to list five separate reasons, but skips the fourth one. ***See*** Plfs' MIL 19 at 5-6 (skipping from the "third" point to the "fifth" point).

weight of the final report. Plaintiffs also accuse J&J Defendants of using a slide in another trial to "falsely claim" the FDA's conclusions, despite the fact the language of the slide was taken *verbatim* from the FDA's own language in the 1986 FDA Response. *See* Plf. Mtn. at 4.

Similarly, like Plaintiffs' mischaracterization of Dr. Goudie's report, Plaintiffs' representation to the court that asbestos has been found in Johnson's Baby Powder "over 400 times" is misleading. *See* J&J Defendants' MIL No. 5 (requesting exclusion of Plaintiffs' "Decades of Evidence" summary chart). Plaintiffs' "Decades of Evidence" chart is replete with their counsel's cherry-picked selection of words from the underlying records presented in a summary fashion—without context—to push the false narrative that there are decades of evidence of asbestos in J&J Defendants' products. For instance, at least nine entries refer to samples taken from parts of talc mines that never made it into the finished product, while one entry relates to test results of non-talc rock samples. *Id.* at 4-5 (detailing flaws in the Decades of Evidence chart). At least forty entries do not relate to cosmetic talc products sold by J&J Defendants. *Id.* And the "source" documents supporting the chart even include expert reports prepared by Plaintiffs' counsel for litigation—not independent, objective evidence of asbestos contamination. *Id.* at 2.

Plaintiffs' argument raises a factual dispute impacting the weight the jury should place on the evidence.

Second, Plaintiffs argue the letter was based on insufficient data. This is yet another jury argument that does not amount to unfair prejudice. The procedure for citizen petitions is similar to that of many other informal agency adjudications. Petitioners supply a detailed factual and legal statement, "including all relevant information and views on which the petitioner relies." 21 C.F.R. § 10.30(b) (2021). Any "interested person may submit comments" on a public docket, which becomes part of the petition's formal record. 21 C.F.R. § 10.30(d) (2021). And, after careful

consideration and independent review, FDA issues a response, either approving or denying the petition, dismissing it as moot, or providing a "tentative" explanation "indicating why the agency has been unable to reach a decision," such as the "need for additional information." 21 C.F.R. § 10.30(e) (2021). FDA's petition responses are deeply researched and scientifically grounded regulatory documents that bring to bear the agency's full multidisciplinary expertise. *See, e.g., Serono Lab'ys, Inc. v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir. 1998) (holding that FDA's denial of a citizen petition "rests on the 'agency's evaluations of scientific data within its area of expertise,' and hence is entitled to a 'high level of deference'") (citation omitted). Plaintiffs' criticisms about the length of some of the studies or how J&J later represented the FDA Response Letter again goes to the weight of the evidence—not its admissibility.

Third, Plaintiffs claim the letter was an "inside job" because one person at the FDA allegedly had decided to deny the petition before the official publication. But even if one individual had made an early decision, it would not amount the fraud Plaintiffs claim. In fact, the FDA has never found any fraudulent activity related to the 1986 Response Letter nor accused the J&J Defendants of fraud on the FDA. The response letter has never been recanted and a warning label never required.

Fourth, Plaintiffs claim that the FDA's 2019 test finding trace amounts of asbestos in one bottle of Johnson's Baby Powder somehow renders the FDA's response letter from thirty-three years ago false and misleading. A random sampling in 2019 does not diminish the value of the 1986 FDA Response which reflects both on the quality of talc in the U.S. market at and before the response was issued, as well as the state of the scientific knowledge about the detection of asbestos in talc. The mere fact that the FDA found asbestos in one bottle of talc thirty-three years after this

letter, when Defendants were using different talc mines, is a weight argument; it is not an argument that should govern the exclusion of clearly relevant evidence.

Plaintiffs' motion includes biased argument reflecting counsel's personal theories about the 1986 FDA Response. The FDA has never found the studies it relied on to be falsified, nor has it ever claimed the J&J Defendants (or the CTFA) committed fraud on the FDA. The motion to exclude should be denied.

II. The 1986 FDA Response to the Citizen Petition Is Not Inadmissible Hearsay.

Plaintiffs also wrongly claim that the 1986 FDA Response is inadmissible hearsay.

First, as reflected in the certified copy attached here, the FDA Response letter is over thirty years old, fitting neatly with the ancient documents exception to the hearsay rule. S.C.R.E. 803(16) ("Statements in a document in existence twenty years or more the authenticity of which is established.").[3] The letter itself and the material contained therein exceed the 20-year threshold. Notably, the basis for the ancient documents exception also address the substantive issue Plaintiffs have with the FDA denial of the citizen's petition. The Court of Appeal of South Carolina noted "[t]he same trustworthiness that age lends for the purpose of identification is present as to contents. If parties have acted in a manner inconsistent with contents of the document, the fact is subject to proof and an issue of fact is raised." *Johnson v. Pritchard*, 302 S.C. 437, 444, 395 S.E.2d 191, 195 (Ct. App. 1990).

Second, the 1986 Response Letter will be offered for a variety of reasons in addition to the truth of the matter asserted. For instance, Plaintiffs allege that J&J Defendants failed to include a warning on their product, that they knew that harmful levels of asbestos were in talc, and that they

[3] Additionally, as a domestic public document under seal, that also comes with a notarized affidavit, the document is self-authenticating under S.C.R.E Rule 902 (1) & (8).

recklessly and wantonly continued to sell their product—without a warning label. Plaintiffs seek punitive damages against the J&J Defendants for this conduct. But the fact that the FDA issued a response letter refusing to require a warning label on the product and finding that, even if trace levels of asbestos were present it would not be harmful, goes directly to the reasonableness of J&J Defendants' decision to continue selling its product without a warning label. Thus, the fact that the FDA conducted an investigation and issued a conclusion finding no significant risk and no need for a warning, whether or not the FDA's findings later proved to be accurate, is relevant to resolving Plaintiffs' claims against the J&J Defendants.

This document has been admitted routinely. This Court admitted this document in the Boyd Bostic II trial. *See* Ex. B 2018.11.09 *Boyd-Bostic* Trial at [1276:3-1278:7]. It was admitted in the *Lee* Trial that Plaintiff's counsel tried in Oregon against Defendants. *See* Ex. D 2024.05.23 *Lee* Trial [2665:20-2666:21]. It was even admitted in the Garcia trial where trial counsel in this case for both Plaintiffs' and defendants appeared. *See* Ex E 2024.03.22 *Garcia* trial [127:7-16]. Plaintiffs' motion should be denied.

CONCLUSION

For the foregoing reasons, the Defendants respectfully requests that the Court deny Plaintiffs' Motion *in Limine* No. 19.

Respectfully submitted,

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Columbia, South Carolina

July 24, 2024

Exhibit A

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

CERTIFICATE

Pursuant to the provisions of Rule 44 of the Federal Rules of Civil Procedure, I hereby certify that, John Wright, Division of Dockets Management, United States Food and Drug Administration, whose affidavit is attached, has custody of official records of the United States Food and Drug Administration.

In witness whereof, I have, pursuant to the provision of Title 42, United States Code, Section 3505, and FDA Staff Manual Guide 1410.23(1)(A)(6)(b), hereto set my hand and caused the seal of the Department of Health and Human Services to be affixed this 4th day of December, 2015.

Dynna Bigby,
Supervisory Administrative Proceedings Officer
Division of Dockets Management
FDA/Office of the Executive Secretariat (OES)

By direction of the Secretary of
Health and Human Services

AFFIDAVIT

John G. Wright, first duly sworn, deposes, and says:

1. I am, Administrative Proceedings Specialist, Division of Dockets Management, Office of Management, United States Food and Drug Administration.

2. In this capacity I have custody of official records of the United States Food and Drug Administration.

3. Enclosed is a reproduced certified copy of documents requested by LexisNexis CourtLink classified by the FDA as FOIA Request 2015-9061.

4. Copies of the administrative record are part of the official records of the United States Food and Drug Administration.

John G. Wright, JD

County of Montgomery
State of Maryland

Subscribed and sworn to before me this 4th day of December, 2015

Yatta Florence Yarjah, Notary Public
My Commission Expires 4/16/2018

JUL 11 1986

1986 JUL 21 PM 3:09

Phillippe Doullet
One Holyoke Lane
Stony Brook, New York 11790

Re: Docket No. 83P-0404

Dear Mr. Doullet:

This responds to your November 8, 1983, petition requesting that cosmetic talc be labeled with an asbestos warning statement, information on asbestos particle size, and the proportion of talc impurities in the product.

You assert that, because the mining of talc almost invariably includes the mining of asbestos as well, cosmetic talc may contain significant amounts of asbestos particles that present an inhalation hazard to humans. Also, you cite references to substantiate that significant amounts of asbestos have been found in commercial talc samples, that asbestos inhalation is hazardous to humans, and that asbestos contaminants in talc will produce toxicological responses when inhaled.

FDA recognizes that asbestos inhalation over extended periods is hazardous to humans. The agency is also aware that some cosmetic talc produced in the 1960s and early 1970s did contain asbestiform minerals. However, your petition has not persuaded us that the cosmetic talc that is presently being produced contains significant amounts of asbestiform minerals.

During the early 1970s, FDA became concerned about the possibility that cosmetic talc did contain significant amounts of this material. The agency received several reports about such contamination. However, at that time, the analytical procedures for determining asbestos in talc were not fully developed, and most of the analytical work was conducted without scientific agreement as to which methods were well-suited for the identification of asbestiform minerals in talc. Consequently, FDA considered all analytical results to be of questionable reliability. This assessment proved to be correct because many questions were subsequently raised about results reported in the literature in the early 1970s (see enclosed copy of National Bureau of Standards Special Publication 506 entitled "Misidentification of Asbestos in Talc"). Because of the questionable nature of the analytical results, the agency was not able to assess reliably the levels of asbestiform minerals in cosmetic talc then in the marketplace.

83P-0404

PDN1

Under these circumstances, FDA decided that the most appropriate actions that it could take to protect the public health would be to make the reports public and to request assistance from the affected industry in developing acceptable analytical procedures. This approach apparently has led to considerable improvement in the quality of this talc.

After FDA took these actions, many cosmetic manufacturers began to analyze their talc for asbestiform minerals as part of their quality control programs, and talc suppliers began to sell higher purity talcs to the cosmetic industry. By 1976, asbestos analytical methodology was sufficiently developed that the Cosmetic, Toiletry, and Fragrance Association (CTFA) could issue a specification (copy enclosed) for cosmetic talc. This specification required that such talc be free of fibrous amphibole (e.g., asbestos in the form of asbestiform tremolite) using a CTFA method of analysis that is capable of detecting 0.5 percent of amphibole asbestos. This specification contributed to the continued improvement of cosmetic talc quality.

In addition, FDA surveillance activities that were conducted in the latter portion of the 1970s showed that the quality of cosmetic talc had significantly improved, and that even when asbestos was present, the levels were so low that no health hazard existed. Our scientists recently reviewed data from these surveillance activities and concluded that the risk from a worst-case estimate of exposure to asbestos from cosmetic talc would be less than the risk from environmental background levels of exposure to asbestos (non-occupational exposure) over a lifetime.

Consequently, we find that there is no basis at this time for the agency to conclude that there is a health hazard attributable to asbestos in cosmetic talc. Without evidence of such a hazard, the agency concludes that there is no need to require a warning label on cosmetic talc.

FDA should also point out that, in reviewing your petition, we found several problems with the information on which you relied. The publication "Asbestiform Impurities in Commercial Talcum Powders," which you cite in your petition, appears to contain a number of significant errors that lead us to question the accuracy of the findings that were reported. For your information, we have enclosed a copy of a June 8, 1973, rebuttal of this publication that was written by the Chief Mineralogist of the Colorado School of Mines Research Institute in Golden, Colorado. Also, your petition's 1978 book reference to the Mt. Sinai School of Medicine findings is too old to reflect present contamination levels. Further, we are not convinced that the Mt. Sinai findings pertained to cosmetic talc. Your reference states that common commercial talcs were analyzed, but it does not specify whether these commercial talcs were industrial grade or cosmetic talc.

For all of these reasons, your petition is denied. This denial is without prejudice to the future filing of a petition on this matter, accompanied by all relevant data in support of the petition.

Sincerely yours,

H. J. W. Swanson

Acting Associate Commissioner
for Regulatory Affairs

Enclosures

cc: HFC-1
HFC-200 (#G-86-182)
HFC-220 (Rogers/file)
HFF-1
HFF-100
HFF-152
HFF-300
HFF-302
HFF-310
HFF-440
GCF-1 (Horton/Derfler)
HFA-224
HFA-305

Prepared:JRTaylor:5/15/86
Initialled:JRTaylor:5/15/86, 6/5/86
EJCampbell:5/15/86, 6/5/86
HJEtemann:5/16/86, 6/9/86
JAWerninger:5/19/86
WGFlamm:5/29/86, 6/9/86
IRLake:5/29/86, 6/12/86
RJLenahan:5/29/86, 6/10/86
LBBrock:6/10/86
RWGill:6/12/86
F/T:JRTaylor:sag:6/4/86
Concurred:EBrisson:6/27/86
Retype:RLSpencer:cdk:6/27/86:disk 26 (#1.32)
Revised:PSDerfler:7/3/86
Retype:RLSpencer:cdk:7/7/86
Concurred:PDerfler:7/8/86
Revised:Concurred:LHorton:7:9/86
F/T:RLSpencer:bka:7/10/86

CTFA Specification
TALC COSMETIC

Issued: 6-1-42
Revised: 3-23-62
6-30-7[illegible]
10-7-76

COSMETIC TALC

CTFA Adopted Name:
TALC

DEFINITION: Cosmetic Talc is an essentially white, odorless, fine powder, ground from naturally occurring rock ore. It consists typically of 90% hydrated magnesium silicate, having the ideal formula $Mg_6[Si_8O_{20}](OH)_4$, with the remainder consisting of naturally associated minerals such as calcite, chlorite, dolomite, kaolin and magnesite, and containing no detectable fibrous, asbestos minerals.

TEST	SPECIFICATION	METHOD
Color	As specified by the buyer and showing no change after heating	Heat 1 to 2 g at 200°C for 5 minutes
Odor	As specified by the buyer	
Identification	Positive: 1. Close match to CTFA Spectrum—IR with no indication of foreign materials *OR* 2. (Alternate) Close match to X-ray Powder Diffraction File No. 19-770, published by ASTM, showing the most intense reflections at d values about 9.35, 1.53 and 4.59 Å	CTFA G 3-1 ASTM D 934-74
Slip	As specified by the buyer	
Lustre	Do.	
Water-Soluble Iron	Passes test	USP XIX, page 487
Screen Test	100% through 100 mesh 98% minimum through 200 mesh Finer grades: as specified by the buyer	CTFA C 6-1
Water Soluble Substances	0.1% maximum	USP XIX, page 487 See test for "Reaction and Soluble Substances"
Acid Soluble Substances	As specified by the buyer 6.0% maximum	CTFA E 32-1
Loss of Ignition	5.0% maximum	USP XIX, page 487
Arsenic (as As)	3 ppm maximum	CTFA F 1-1, Parts I-A and II
Lead (as Pb)	20 ppm maximum	CTFA F 2-1, Parts I-A and II
Fibrous Amphibole (Asbestiform Tremolite et al)	None detected	CTFA J 4-1
Free Crystalline Silica (Quartz)	As specified by the buyer	CTFA J 5-1 (DTA) Alternate: CTFA J 6-1 (X-ray)

* * * * *

National Bureau of Standards Special Publication 506. Proceedings of the Workshop Asbestos: Definitions and Measurement Methods held at NBS, Gaithersburg, MD, July 18-1977. (Issued November 1978)

MISIDENTIFICATION OF ASBESTOS IN TALC

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Abstract

Both optical microscopy and x-ray diffraction (XRD) are widely used to detect minerals associated with talc. Optical microscopy can determine the morphology of a particle, but cannot always fully identify the specific mineral. Although XRD is an excellent screening technique for the detection of minerals associated with talc, the method can misidentify minerals due to interferences, interpretive errors, and the inability to determine morphology.

Methods for reduction or elimination of these problems include special techniques of sample preparation and x-ray diffraction, combined with microscopic examination (both optical and electron).

Key Words: Amphiboles; asbestos; chlorite; electron microscopy; fiber; morphology; optical microscopy; x-ray diffraction; talc.

Introduction

There are many ways to analyze and study any naturally occurring material. The conclusions reached will often vary widely depending on the expertise and specific interest of the investigator. That situation sums up the present status of "asbestos"; it is also the status of minerals which are associated with "asbestos"; and it is becoming the status of other minerals which can be naturally associated with talc.

Popular methods of analysis can give the wrong answer – namely that asbestos is present when it certainly is not. That problem (misidentification) is not so much one of limitations of the methods, but rather one of misinterpretation of data, and failure to recognize the mineralogical background required to certify mineral purity, for example, when analyzing sheet silicates for asbestos. Unfortunately, one main factor is that asbestos has now developed variable definitions, depending on whether the point of view is mineralogical, industrial, medical, or regulatory. The medical definition is most concerned with whether or not the particles are biologically active; the industrial definition is dependent upon flexibility and weavability; the mineralogical definition upon crystallography; and the regulatory definition upon size and aspect ratio.

The word "asbestos" stems from ancient Greek and has always referred to a very fibrous industrial mineral product. Since asbestos has historically related to a mineral exploited as an important industrial commodity, we think a combined mineralogical and industrial definition should take precedence [1,2][1]. Other presentations during this

[1]Figures in brackets indicate the literature references at the end of this paper.

workshop have amply covered the aspects of asbestos terminology, and it is not our intent to provide comprehensive coverage of that subject. Our primary objective is to review some of the basic principles of analysis, and to point out problem areas where identification of "asbestos" has been abused.

Analysis Methods and Misidentification of Asbestos

It is useful to categorize the various analytical methods which have been applied to talc to highlight inherent principles which lead to misidentifying asbestos as being present. We offer the following general comments on the three principle determinative properties (chemical composition, morphology, structure).

Chemical Composition

It is well known that every mineral has a specific chemical composition, and that each mineral has an ideal theoretical chemical formula (configuration). Unfortunately, many investigators overlook the fundamental point that chemical composition does not identify a specific mineral. A simple example will bring that point into focus:

> A pearl, an oyster shell, a slab of marble, a piece of chalk, and the minerals aragonite and calcite are obviously different materials, and yet each will be identified as calcium carbonate. That is to say, chemical analyses will identify them all as the same substance, where everyone knows that a pearl is not a piece of chalk.

The same situation exists in certain phases of asbestos analysis. For example, chrysotile, antigorite, lizardite, sepiolite, chlorite, and talc are all hydrous magnesium silicates. But a Meerschaum pipe (sepiolite) is certainly not chrysotile asbestos in spite of the fact that chemical analysis alone could lead to that misidentification.

Accordingly, chemistry alone does not identify a mineral, nor do those sophisticated instrumental methods which are based on chemical principles, such as:

- Wet Chemical Analysis
  - Classical (gravimetric, volumetric)
  - Instrumental (atomic absorption, flame emission)
- Microprobe (electron and ion)
- Emission Spectrograph
- Mass Spectrograph
- X-Ray Fluorescence

Morphology

Although the shape of a mineral particle is one of the key characteristics in the identification of a mineral, shape alone cannot be the sole determinant of a specific mineral species. There are hosts of minerals in different mineral classes whose particles have the same shape. They exist across the spectrum of all classes of minerals and the possibilities are beyond comprehension. Even if we limit ourselves to minerals which occur in the true fibrous state, we would estimate there are up to 100. There have been instances where nonasbestos particles have been misidentified as chrysotile in talc because shape alone was the index used.

Methods based on morphology include:

- Optical Microscopy
- Automated Image Analyzers
- Electron Microscopy (SEM and TEM)

Structure

The configuration of atoms in the crystal lattice of a mineral does not necessarily determine a mineral species. The atomic arrangement at the molecular level does not always carry through to the external visible physical form. That is to say that methods based on molecular structure can misidentify a mineral. For example, chrysotile asbestos is classified with the sheet silicates because of its crystal structure arrangement, but it certainly does not occur in flat sheets like the micas or its sibling, antigorite.

Methods of identification which relate to molecular structure are:

Infrared Spectroscopy

Differential Thermal Analysis

X-ray Diffraction

Electron Diffraction

In general then, no single property defines a mineral, and no single method which depends on one property can identify a specific mineral.

Conversely, methods which depend on a single factor or characteristic of a mineral can give misidentifications.

Two Popular Methods

Optical microscopy and x-ray diffraction methods require some additional discussion primarily because they have received widespread attention by industry and government laboratories as possible monitoring techniques.

Although both these methods are fundamental to the science of mineralogy and are highly reliable in the hands of experts, complications arise when shortcuts are taken in the professional procedures.

Optical Microscopy

When an experienced optical mineralogist or crystallographer identifies a mineral with a petrographic microscope, he can come to a remarkably accurate conclusion. The reason for high accuracy is that not one but several specific properties are determined, such as refractive indices, extinction angle, birefringence, and optical orientation. Specific training and wide mineralogical background are required to get the right answer.

In contrast, current optical methods in federal regulatory proposals relating to asbestos presume that asbestos is present in the first place. The analyst then merely observes the mineral particle for size/shape. Consequently, those methods which depend solely on aspect ratio give misidentification. They misidentify the presence of asbestos by such simple oversights as looking at a platelet on edge and counting it as an asbestiform particle. It is not necessary to elaborate on the other shortcomings of those methods in view of the recent NBS report on the analysis of 80 industrial talcs [3] evaluating that methodology. The same shortcomings were also recently corroborated in a study conducted by Harvard University and NIOSH [4].

However, there are a few rare cases where abnormal crystal habit can be misleading and subtly can lead to a misidentification. Optical microscopy is most vulnerable to this type of misidentification. For example, talc normally occurs as micaceous plates, but rare acicular talc does exist, and one must be very careful to avoid misidentifying the rare occurrence as asbestos. As an example, our XRD examination of an industrial acicular talc sample has identified the presence of significant amphibole (probably tremolite). However, when the material was subjected to thorough petrographic examination it was found to be composed of free grains of columnar amphibole and acicular talc and composite talc-amphibole. The significance is that an erroneous conclusion could be reached by misidentifying such a rare talc variety as asbestos, if only aspect ratio and simple optical microscopy were used.

Thus, simple optical microscopy can determine the morphology of a particle, but if used alone it cannot always fully identify the specific mineral observed.

X-Ray Diffraction

Although x-ray diffraction (XRD) is a valuable technique, it cannot determine the physical shape of a mineral particle, and for that reason it cannot determine whether or not a sample is asbestos. Furthermore, it cannot distinguish between two mineral varieties in the same mineral class in cases such as the asbestos minerals and their nonasbestiform analogues. It is surprising that such a basic shortcoming continues to be overlooked by responsible investigators alleging to have identified asbestos by XRD.

One result of the inability of powder XRD to differentiate between the asbestiform and nonasbestiform varieties of a mineral is the potential error of prejudging an XRD detected phase to be the asbestiform variety. For example, preparing calibration standards of mixtures of talc plus chrysotile could have the effect of causing a serpentine peak in an unknown sample to be prejudged as the asbestiform variety, i.e., chrysotile. A mixture of talc spiked with the serpentine mineral chrysotile will give the same XRD pattern as a mixture of talc spiked with the very common platy serpentine mineral antigorite. It should be obvious that an unknown talc showing a serpentine peak cannot be prejudged or branded as containing chrysotile asbestos under such circumstances. Unfortunately, the literature has articles by responsible authors who have overlooked that error in logic [5,6,7].

For research purposes only, single crystal XRD can provide information as to whether or not the specimen could be asbestos. However, due to the difficulty of handling minute specimens, single crystal XRD is inadequate for particles smaller than about 20 x 5 μm, and, of course, is also inadequate for routine monitoring procedures.

Amphiboles

Each of the five amphibole minerals, anthophyllite, cummingtonite-grunerite, riebeckite, tremolite, and actinolite has an asbestiform variety, namely anthophyllite asbestos, amosite, crocidolite, tremolite asbestos, and actinolite asbestos, respectively. Tremolite asbestos is quite rare, and actinolite asbestos is so rare that a recent NIOSH project to prepare reference standard minerals has been unable to locate a source of pure actinolite asbestos [8].

The amphiboles (named from the Greek "amphibolos," meaning ambiguous) are characterized by similar crystal structure and wide variation in chemical composition and appearance. All amphiboles have XRD patterns which are similar, and are characterized by having their (110) or (210) diffraction peaks occur within ±0.2Å of each other (Table 1, Figure 1). Reliable identification of individual amphibole species is difficult in the absence of confirming composition data.

Examination of Table 1 and Figure 1 illustrates that attempted identification of a specific amphibole on the basis of $d_{(110)}$ or $d_{(210)}$ has good potential for being in error. For example, selection of Joint Committee on Powder Diffraction Standards (JCPDS) card 13-437 as being definitive of tremolite presents serious problems. Twenty-nine additional JCPDS amphiboles have their (110) or (210) peaks within ±0.1°2θ of this tremolite (110) peak at 10.56°2θ. Identification of an amphibole as tremolite on the basis of a peak at 10.56°2θ is obviously an identification with very low reliability. In other words, a peak at that location is not necessarily the mineral tremolite since it could be one of 29 other minerals.

Table 1. Amphibole JCPDS Card No's., $d_{(110)}$ or $d_{(210)}$ peak position, and relative intensity.

JCPDS card #	Å[a]	2θ(Cu)	I	Name
23-118	8.58(1)	10.31	100	prieskaite
10-456	8.55(1)	10.35	100	richterite
20-734	8.53(1)	10.37	70	mboziite
20-378	8.52(1)	10.38	100	dashkesanite
14-633	8.51(1)	10.39	70	arfvedsonite
21-149	8.51(1)	10.39	55	hornblende
19-467	8.50(1)	10.41	100	ferropargasite, syn
20-982	8.50(1)	10.41	65	richterite, syn
23-665	8.48(1)	10.43	45	richterite, calcian, syn
23-664	8.47(1)	10.44	35	edenite, sodian, syn
23-667	8.47(1)	10.44	45	richterite, calcian, syn
23-663	8.46(1)	10.46	40	eckermanite, calcian, syn
9-434	8.45(1)	10.47	50	hornblende
13-499	8.45(1)	10.47	100	magnesioriebeckite
20-656	8.45(1)	10.47	100	magnesioriebeckite
20-470	8.44(1)	10.48	100	crossite
23-666	8.44(1)	10.48	40	tremolite, sodian, syn
20-469	8.43(1)	10.49	100	hastingsite
23-1405	8.43(1)	10.49	80	edenite
23-1406	8.43(1)	10.49	40	paragasite
20-1310	8.43(1)	10.49	40	tremolite, syn
10-428	8.42(1)	10.51	100	richterite, fluor, syn
23-603	8.42(1)	10.51	100	tirodite
10-431	8.41(1)	10.52	80	edenite, fluor, syn
19-1061	8.40(1)	10.53	100	riebeckite
20-481	8.40(1)	10.53	100	hornblende
20-1390	8.40(1)	10.53	90	winchite
23-302	8.40(1)	10.53	100	cummingtonite, mangoan
19-1063	8.39(1)	10.54	70	richterite
13-437	8.38(1)	10.56	100	tremolite
17-478	8.38(1)	10.56	65	kaersutite
23-495	8.38(1)	10.56	80	eckermanite
9-330	8.37(1)	10.57	100	tremolite, fluor, syn
17-750	8.36(1)	10.58	25	richterite, ferrian
20-386	8.35(1)	10.59	40	eckermanite, syn
22-531	8.35(1)	10.59	30	joesmithite
16-401	8.33(2)	10.62	70	anthophyllite, magnesian, syn
17-725	8.33(1)	10.62	100	grunerite
17-745	8.33(1)	10.62	100	grunerite
20-376	8.31(1)	10.65	100	crossite
17-726	8.30(1)	10.66	100	cummingtonite
20-484	8.29(1)	10.67	100	richterite
13-506	8.27(2)	10.70	80	gedrite
23-679	8.27(1)	10.70	90	glaucophane
9-455	8.26(2)	10.71	55	anthophyllite
20-453	8.26(1)	10.71	100	glaucophane
11-253	8.23(2)	10.75	100	ferrogedrite
23-310	8.20(1)	10.79	75	richterite, ferrian
13-401	8.11(2)	10.91	100	holmquistite

[a] $(110)^1$ or $(210)^2$.

Maximum $\Delta 2\theta(Cu)$ = 10.91° - 10.31° = 0.6°

Table 1 illustrates the very close proximity of the (210) or (110) XRD peak of all amphiboles, showing the inability to identify a specific amphibole on the basis of $d_{(210)}$ or $d_{(110)}$.

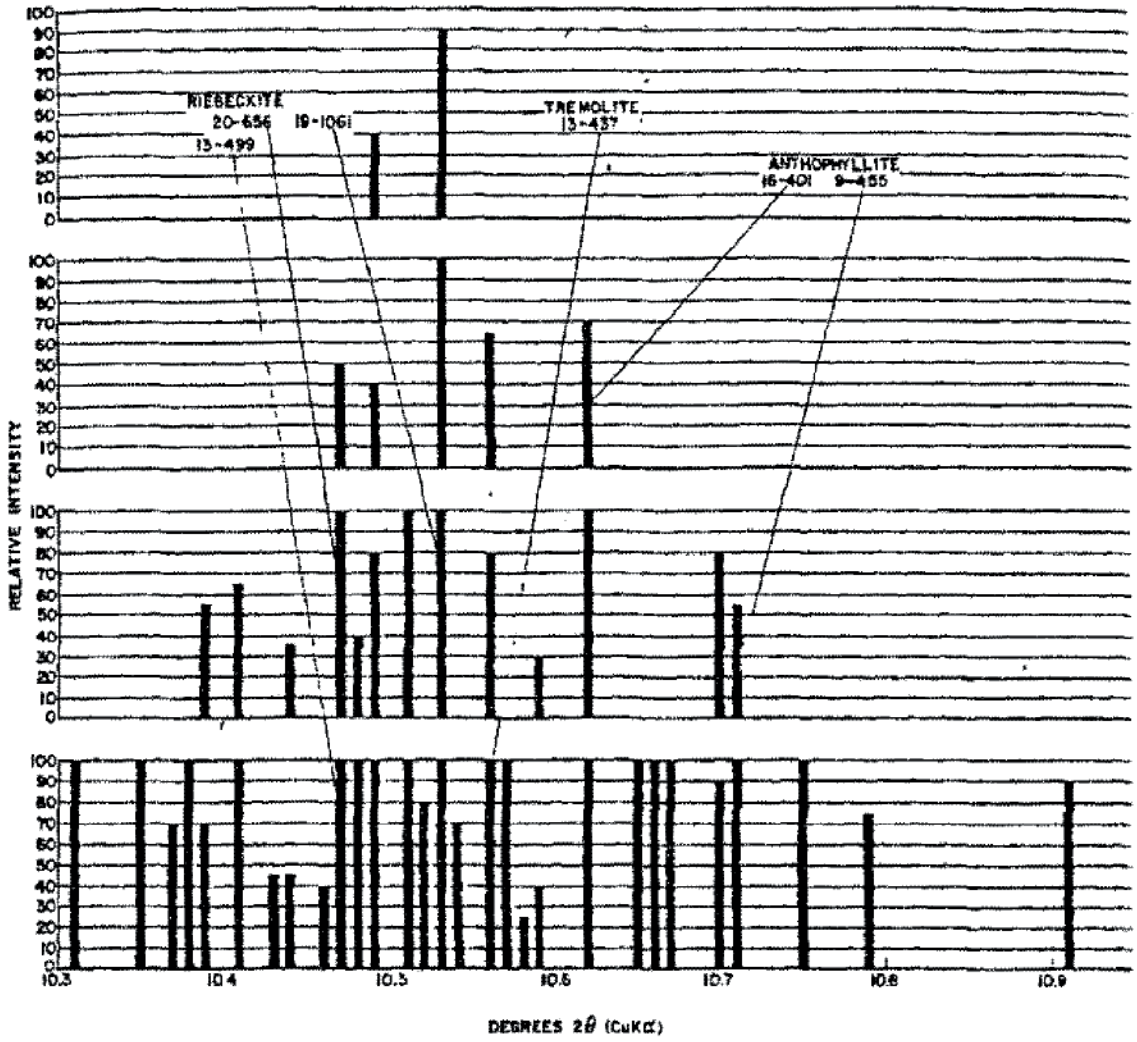

Figure 1. Amphibole $d_{(110}$ or $d_{(210)}$ – peak positions (2θ for CuK) and relative intensity.

An additional problem further affecting the reliability of identification by XRD is the effect of shift in peak position caused by slight mispositioning of the sample surface in the instrument. For example, a 100 μm mispositioning of the specimen surface will result in a shift of approximately 0.6-0.7 Å in d-spacing at low 2θ angles [9]. A slight shift in the position of the peak (from a different amphibole or mispositioning of the sample surface, for example) could go unnoticed, resulting in misidentification of an amphibole that is not even present.

In order to conclusively identify an amphibole by XRD, it is necessary to have an essentially complete diffraction pattern. In order to obtain such an XRD pattern, the sample must have a relatively high amphibole content and the pattern must be acquired with a time-consuming slow scan. Acquisition and interpretation of such patterns is time-consuming, and discourages proper application of the full procedure, especially for routine monitoring where large numbers of samples require analysis. Shortened procedures, such as single peak identification of amphiboles, provide good opportunity for misidentification. The shortened procedure of single peak identification was apparently used in a 1972 paper [7], where our examination of some of the same samples disagreed with identifications of serpentine, tremolite-actinolite anthophyllite, and anhydrite.

Chlorite is one of the most common accessory minerals found associated with talcs. The chlorite group of minerals are somewhat analogous to amphiboles in that they exhibit a wide variation in chemical composition and all have a similar crystal structure. The diagnostic chlorite basal XRD peaks (001), (002), and (004) are characteristic, and occur at about 14Å, 7Å, and 3.5Å, respectively. As in the case for the amphiboles, specific identification of a particular chlorite species by XRD is difficult. The XRD problem with chloritic talcs is that the serpentine first order basal peak overlaps the chlorite (002) peak, and the corresponding serpentine second order basal peak overlaps the chlorite (004) peak. Generally, however, the chlorite (004) and serpentine second order peaks are separate enough to allow unambiguous determination of the presence of both phases when present in adequate amounts to give definable peaks. Tables 2 and 3 and Figures 2, 3, and 4 are compilations of JCPDS data for the positions of the (004) basal peak for chlorites and (002), (004), or (0012) basal peak for serpentines, respectively.

Table 2. Chlorite JCPDS Card No's., $d_{(004)}$ peak positions, and relative intensity.

JCPDS card #	Å	2θ(Cu)	I	Name
10-183	3.60	24.73	100	penninite
20-671	3.60	24.73[a]	90	kämmererite
16-351	3.59	24.80	70	chlorite 1b
12-185	3.57	24.94	85	kotschubeite
7-160	3.58	24.87	60	kotschubeite
19-749	3.56	25.01	80	clinochlore
7-77	3.558	25.03	50	sheridanite
16-362	3.55	25.08	80	chlorite 1a
19-751	3.55	25.06	65	sudoite
22-712	3.55	25.08	45	nimite
7-165	3.545	25.12	60	grochauite
7-78	3.541	25.15	60	thuringite
7-171	3.541	25.15	80	diabantite
12-242	3.54	25.16	100	leuchtenbergite
7-76	3.537	25.18	50	ripidolite
13-29	3.53	25.23	80	thuringite
7-166	3.523	25.28	50	daphnite
12-243	3.52	25.30	92	aphrosiderite
21-1227	3.52	25.30	100	thuringite
3-67	3.49	25.52	100	thuringite

[a] $d_{(115)}$.

Table 2 illustrates variation in position of the chlorite $d_{(004)}$ XRD peak. Table 2 should be compared with Table 3 to see that the chlorite and serpentine XRD peaks overlap and interfere with each other. Identification and quantification of serpentine in the presence of chlorite is extremely difficult at best.

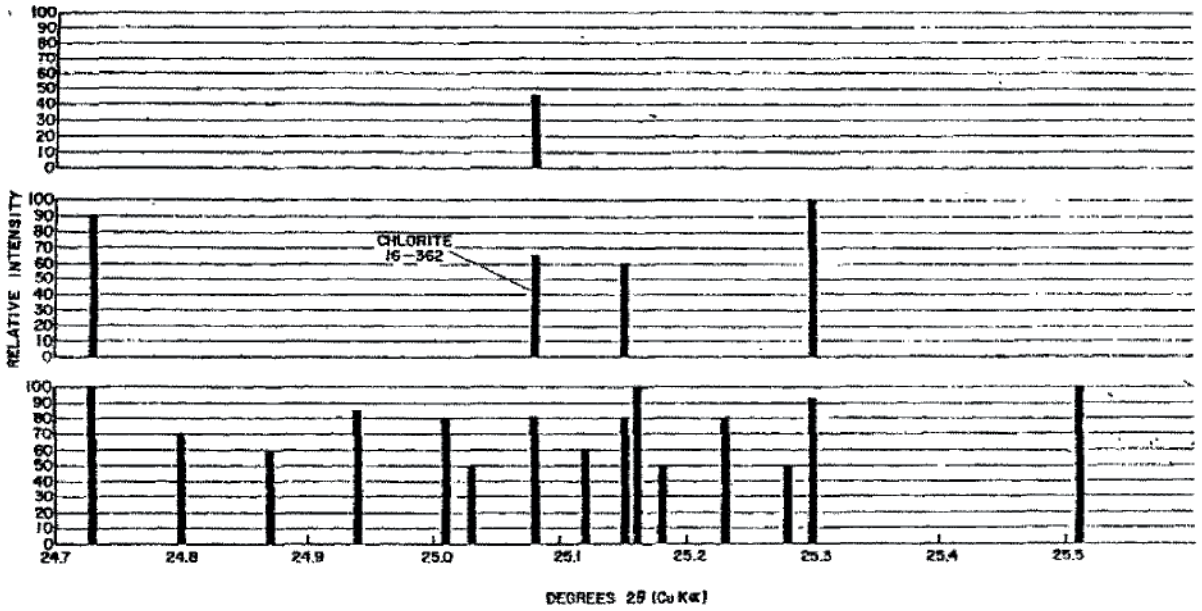

Figure 2. Chlorite $d_{(004)}$ — peak positions and relative intensity. The data of Table 2 are presented in graphical form showing the variation in position of the $d_{(004)}$ XRD peaks for different chlorites. Selection of JCPDS card 16-362 as diagnostic for chlorite can obviously result in misidentification.

Table 3. Serpentine, Kaolinite, Halloysite, and Dickite JCPDS Card Nos., peak position, miller index (hkl), and relative intensity.

JCPDS Card #	Å	2θ(Cu)	I	(hkl)	Serpentines
18-779	3.67	24.25	80	(002)	lizardite, 1M
9-444	3.66	24.32	100	(0012)	antigorite, 60
21-543	3.65	24.39	70	(004)	chrysotile, 2M
7-417	3.63	24.52	300	(102)	antigorite, 6M
11-386	3.62	24.59	60	(002)	lizardite, 10, aluminian
21-963	3.61	24.66	80	(002)	antigorite, 6M
12-583	3.56	25.01	80	(0012)	antigorite, 60, aluminian
13-4	3.56	25.01	70	(0012)	antigorite, 60, aluminian
7-339	3.55	25.08	100	(002)	berthierine
11-388	3.55	25.08	100	(0012)	antigorite, 60, syn
7-315	3.52	25.30	100	(002)	berthierine
9-493	3.52	25.30	100	(004)	amesite
					Kaolinites
6-221	3.58	24.87	100+	(002)	kaolinite, 1Md
14-164	3.579	24.88	80	(002)	kaolinite, 1T
12-447	3.56	25.01	50	(002)	kaolinite, 1T
					Halloysite
9-453	3.63	24.52	90	(002)	halloysite, dehydrated
					Dickite
10-446	3.58	24.87	100+	(004)	dickite $2M_1$

Chlorite 2θ Range: 24.73 - 25.52

Table 3 illustrates variation in position of XRD peaks of serpentine, kaolinite, halloysite, and dickite. The XRD patterns of these minerals interfere with each other and with chlorite (see Table 2).

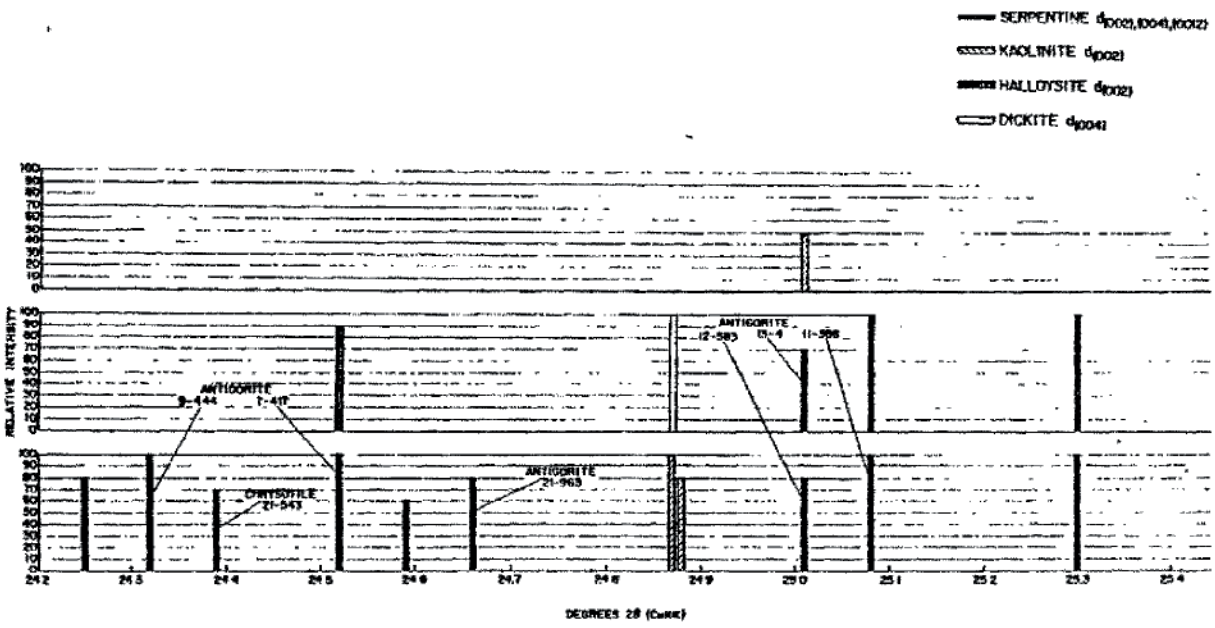

Figure 3. Peak positions and relative intensities. The data of Table 3 are presented in graphical form to illustrate the variation in position and interferring overlap of XRD peaks of serpentine, kaolinite, halloysite, and dickite.

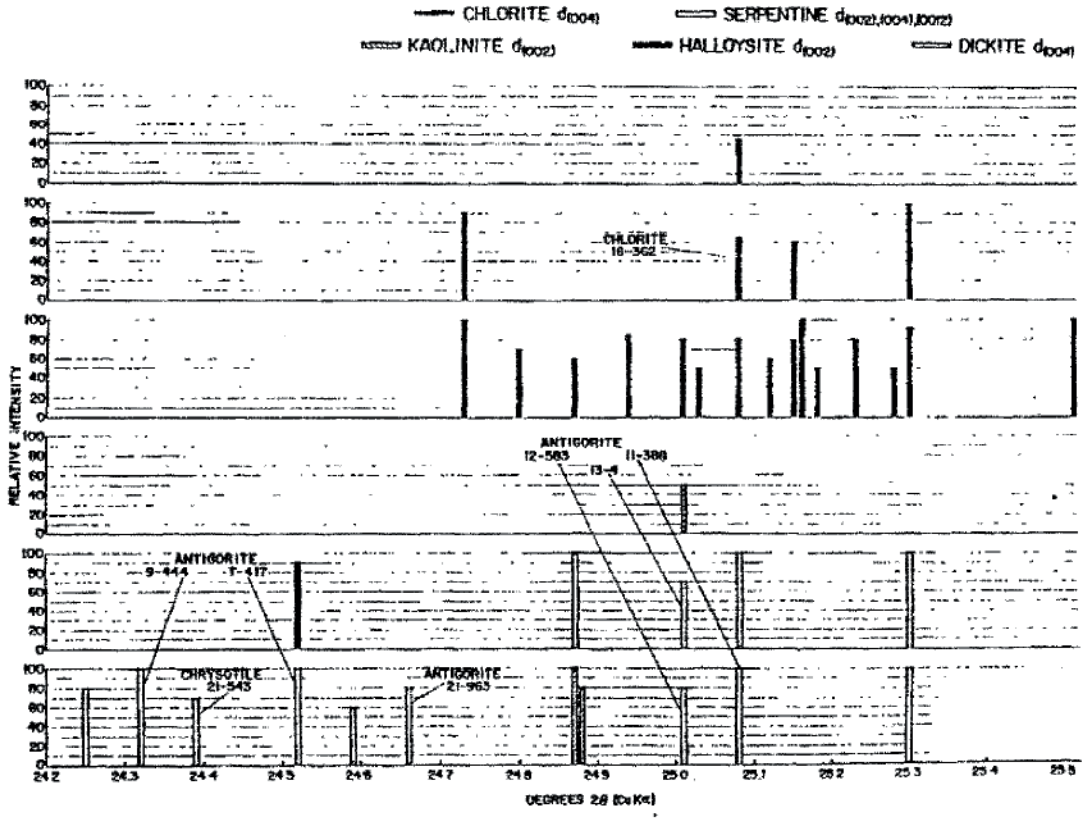

Figure 4. Peak positions and relative intensities. The data of Tables 2 and 3 are presented combined, illustrating the problems of XRD identification when chlorite and serpentine, and possibly kaolinite, halloysite, or dickite are also present.

Three essential features are demonstrated in Tables 2 and 3, and Figures 2, 3, and 4:

1. The diagnostic peaks show considerable variation in the position in which they occur ($\Delta 2\theta$=0.79° for chlorites and 1.05° for serpentines).

2. The chlorites and serpentines overlap and interfere with each other.

3. Basal peaks of the clay minerals kaolinite, halloysite, and dickite overlap the positions of the chlorite and serpentine peaks, and will interfere when present.

The significance of the chlorite-serpentine interference is increased by the fact that chlorite is a very common accessory mineral associated with talcs, whereas serpentine is much less commonly associated.

In spite of the chlorite-serpentine problem, numerous investigators have performed XRD identification and/or quantification of serpentine in chloritic talcs. It is obvious to us that they have misidentified asbestos as being present by overlooking the chlorite/serpentine interference and by misconcluding that a chlorite peak was serpentine.

Other Methods

Infrared Spectroscopy (IR)

The infrared absorption spectrum of a material results from vibrational and bending frequencies of various atomic bonds within the structure. For example, Si-O stretching frequencies produce similar IR peaks for all silicate minerals. As a result, IR spectra are not particularly useful for identifying the minerals present in a mixture, and the method certainly is not capable of determining whether or not a detected mineral is the asbestiform variety.

Differential Thermal Analysis (DTA)

The rearrangement or decomposition of mineral crystal structures due to thermal heating is a characteristic and reproducible reaction. It follows that DTA can identify specific minerals in a mixture but the method is not capable of determining morphology. Therefore, any DTA data which might point to the presence of a serpentine mineral could lead to misidenfying chrysotile asbestos in a talc when the mineral could well be a normally occurring platy antigorite having the same DTA pattern.

Electron Microscopy

Electron microscopic techniques of identification of asbestos have been amply covered in other presentations during this workshop. We do not intend to cover that subject again, but rather to point out some areas where asbestos can be misidentified.

The high magnification attainable with electron microscopy is, in itself, inadequate as the sole index of mineral identity. For example, chrysotile is often identified by the presence of a hollow central core and streaked electron diffraction spots. But the clay mineral halloysite also crystallizes in that form and will produce a similar electron diffraction pattern. Therefore, in the absence of exact chemical composition, halloysite can be misidentified as asbestos. Similar care must be exercised to avoid misidentifying other fibrous clay minerals as asbestos, e.g., attapulgite and alpha sepiolite. In addition, talc ribbons can be mistaken to be asbestos, especially when some talcs have particles which roll up into spiral tubes giving the appearance of a chrysotile particle.

Selected area electron diffraction is routinely used to identify a mineral particle as amphibole. Many investigators simply observe the electron diffraction pattern in the microscope and decide on the basis of general pattern geometry whether or not the particle is an amphibole. This can lead to misidentification, since numerous other minerals can give electron diffraction patterns with amphibole pattern geometry [10,11]. Careful measurement of an electron diffraction pattern is required in order to identify the type

of mineral which produced the pattern. Chemical composition is further required in order to have a chance at identifying the particular species when the mineral is a member of a complex group such as the amphiboles. Otherwise, misidentification will result.

Cosmetic Talc Free from Asbestos

In the United States, we have a self-regulating association known as the Cosmetic Toiletry and Fragrance Association. In certifying the purity of the talcs which they use, they are aware that no single method can identify asbestos and their most recent specification for cosmetic talc [12] combines two methods (XRD and optical microscopy) for monitoring their types of talc.

The rationale is that a talc is first examined by XRD, and if even the smallest amount of amphibole is indicated, then the test proceeds into optical microscopy using a dispersion staining technique to determine whether or not the material contains asbestiform particles in the amphibole group.

Summary

This paper has categorized the main methods which have been used for detection of asbestos in talcs. The basic principles of the various methods were categorized to explain how asbestos has been and can be misidentified in talc. Generally, misidentifications arise by jumping to a conclusion from a single mineral characteristic, when, in fact, many characteristics are required to fully identify a mineral species and/or its variety.

Both optical microscopy and XRD required a more detailed review than other methods since they have received the most attention from a monitoring point of view.

This review is presented with the hope that our guidelines will enable analysts to avoid the misidentification of asbestos in talcs.

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Discussion

A. WILEY: You said that instantaneous recognition of SAD patterns is difficult. Could you give some examples as to what kind of confusions could exist in this? Can you confuse amphibole with serpentine or amphibole with talc, or is that kind of a gross mistake possible?

J. KRAUSE: Those kinds of mistakes probably would not generally happen if you are looking at pyroxenes or olivine. Electron diffraction is not one of my areas of real expertise, but I think that you could possibly get feldspars that would give confusing patterns, depending upon their orientation in the microscope.

L. MADSEN: We are using all the methods that have been talked about today for identification for asbestos materials and do not in any way limit ourselves to fiber length and aspect ratios.

J. WAGMAN: I would like to comment that it is possible by x-ray diffraction and through a special technique to identify and measure the presence of asbestos fibers even when they are in the presence of their non-fibrous counterparts. About two years ago this was demonstrated in a study which we supported at the Naval Research Laboratory in which samples were pre-treated so that fibers were first aligned and then the x-ray diffraction intensities measured at two different orientations with respect to the x-ray beam and in this way the intensity due to the non-fibrous counterparts could be subtracted from the total diffraction intensities.

KRAUSE: You were putting the fibers in some specific preferred orientation in the sample and then looking for those orientations by XRD.

WAGMAN: That is correct, and this had the advantage of not only making possible corrections, that is correcting for the non-fibrous material present, but also it greatly enhances the detectability for the fibers themselves.

KRAUSE: Is this method being currently used?

WAGMAN: This is a method whose feasibility was demonstrated and there are two publications on this in the literature. Actually our objective was to apply this method to airborne samples, which is a much more difficult application incidently, I should think than in the case of talc. The problem here is a preparative problem in that an air sample usually has a lot of organic material, sticky material present which interferes with the ability to orient the fibers. This is a preparative problem which will have to be overcome. But I should think that in the case of talc samples you probably would not have that problem.

COLORADO SCHOOL OF MINES RESEARCH INSTITUTE
P.O. Box 112
GOLDEN, COLORADO 80401

TO W. H. Ashton

DATE June 8, 1973

FROM W. T. Caneer

PROJECT NO. C10704

SUBJECT Meeting with Bowling Green State University Geological Staff

A paper entitled "Asbestosform Impurities in Commercial Talcum Powders," published in the January 1972 issue of The Compass of Sigma Gamma Epsilon (Vol. 49, No. 2) stated that 18 commercial talcum powders examined contained from 4% to 46% asbestiform minerals. The average asbestiform content was 18%. The data in this paper has subsequently been quoted and has been a source of inquiry by interested individuals both in and outside of government agencies. The amount of asbestiform minerals reported is so large that the data could initiate costly FDA hearings on the matter. Since our general observations at the Research Institute relative to asbestiform minerals in talc are at such a large variance to those reported in the paper, an investigation of the paper was undertaken. To date we have reviewed the paper and have discussed the data with the authors. The people involved in the investigation were W. T. Caneer and Dr. Jerry Krause of the Research Institute and Dr. Maynard Slaughter of the Colorado School of Mines.

REVIEW OF THE PAPER

A review of the paper suggested that a number of errors are present. Some of these apparent errors may be illustrated by the following table which appeared in the paper:

Table I

Qualitative Mineral Analyses by X-ray Diffraction

Sample Number	Talc	Asbestosform Minerals (Serp.	Trem-Act.	Anth.)	Carbonates	Anhydrite	Clay (Mica)	Misc. Mins.*
1	x	x	x			x	x	x
2	x	x				x	x	x
3	x	x				x	x	x
4	x	x	x	x	x	x	x	x
5	x	x	x			x	x	x
6	x	x		x	x	x	x	x
7	x	x				x	x	x
8	x	x	x	x	x	x	x	x
9	x	x					x	x
10	x	x				x	x	x
11	x		x		x	x	x	x
12	x				x	x	x	x
13	x		x	x	x		x	x
14	x	x			x	x	x	x
15	x	x	x			x	x	x
16	x		x					x
17	x		x	x		x	x	x
18	x	x		x		x	x	x

*Additives and inert minerals and compounds.

According to this table, asbestiform minerals were identified by X-ray diffraction. By the method of X-ray diffraction used, one could only expect to identify mineral groups to which asbestiform minerals belong. Numerous common non-asbestiform minerals also occur in these groups.

A differentiation is shown for tremolite-actinolite and anthophyllite. It is not likely that these minerals could be differentiated by the X-ray methods used.

The mineral anhydrite ($CaSO_4$) is also reported by X-ray diffraction for all except three of the samples. We have never found anhydrite in any talc samples examined at the Research Institute. Furthermore, from the standpoint of geological occurrences and rock genesis, one would not expect to find anhydrite associated with talc. With these factors in mind, a study was made to determine how one may possibly make an identification of anhydrite in talc.

It soon became apparent that a talc k-beta diffraction peak was being interpreted as belonging to anhydrite. A filter is used to screen out k-beta radiation in X-ray diffraction analysis. However, the filter is not 100% efficient and some of the k-beta passes through the filter and can lead to erroneous interpretation.

The table also shows serpentine as one of the asbestiform minerals identified by X-ray diffraction for most of the samples. This is usually based on the occurrence of a 7-angstrom peak. However, chlorite also gives a 7-angstrom peak and chlorite is a common constituent of talc. A differentiation of the two minerals can usually be made based on other diffraction peaks. Since chlorite is a common constituent of talc and none was reported for the 18 samples, it is likely that chlorite was misidentified as serpentine.

Table II was presented in the paper and shows quantitative mineral analyses by petrographic microscopic techniques.

Table II

Quantitative Mineral Analyses by Petrographic Microscope
(Volume Percent)

Sample Number	Percent Talc Flakes	Percent Carbonate Grains	Percent Asbestosform Minerals
1	73	5	22
2	92	*trace	8
3	**79	trace	21
4	57	20	23
5	82	trace to 1	18
6	72	13	15
7	89	5	6
8	61	5	34
9	80	4	16
10	92	4	4
11	86	trace	14
12	76	20	4
13	48	6	46
14	90	4	6
15	74	4	22
16	80	trace	20
17	70	6	24
18	76	trace	24

*Less than 1 percent. **Includes muscovite.

It is perhaps significant that no anhydrite was observed by microscopic techniques even though it was reported in 15 of the 18 samples by X-ray diffraction. It is perhaps also significant that no specific asbestiform minerals were reported in Table II -- only a total percent of asbestiform minerals. This led us to suspect that any grain with a high length to thickness ratio observed under the microscope would be classified as asbestiform. This could lead to the misidentification of the edges of talc plates and of talc shards as asbestiform minerals.

DISCUSSIONS WITH THE AUTHORS

Of the three authors, two were graduate students (Snider and Pfeiffer) at the time the paper was written. J. Mancuso is on the Geology Department staff and acted as advisor for the research and the paper. Snider is presently with the Michigan Geological Survey in Mt. Pleasant, Michigan, and Pfeiffer is a geologist for Texaco in Midland, Texas. We discussed the paper with Mancuso in Bowling Green and held telephone conversations with Snider and Pfeiffer. We made it clear to these people that the data presented in their paper could lead to very serious charges against the products. They readily agreed that their data could easily have errors, and if so it would save them much possible embarrassment at a later date by correcting their errors now.

Apparently the paper was submitted for publication to fill an issue of the journal which was being devoted entirely to the Bowling Green Geology Department. Apparently a Dr. I. I. Oster (a fruit fly expert in the Biology Department) told them that he had been conducting experiments related to the injection of talc products into mice for the purpose of determining the effects of the injections upon the mice. He requested that the Geology Department make mineralogical determinations of the asbestiform minerals in the talc products. None of the three authors had had any previous experience with talc mineralogy, but they decided that it would be a suitable subject for a paper. Our discussions yielded the following significant results.

1. All three authors readily admitted that they did a "rush-job." About 2 weeks was spent in gathering data for the paper.

2. They agreed that asbestiform minerals cannot be identified by X-ray diffraction. X-ray diffraction is capable only of identification of a mineral group which contains both asbestiform and non-asbestiform minerals.

3. They admitted that they did not adequately check the "talc edge effect" which could lead to the misidentification of talc plate edges as asbestiform minerals by microscopic analysis.

4. They did not take into account the possible presence of chlorite in the talc and could have well misidentified chlorite as serpentine (which of course includes chrysotile).

5. Relative to the identification of anhydrite, they admitted that they probably misidentified a k-beta talc peak.

6. They counted only 100 grains for their quantitative microscopic analyses. Though their data is presented in terms of volume percent they neither measured the size of the grains counted nor considered the difference in the volume of a fiber as opposed to a plate. We pointed out that the statistics involved are totally unacceptable.

7. They admitted that they probably made many errors in conducting the project and seem anxious to rectify them before there is a possible accounting with the FDA or some other agency.

8. The following list identifies the talc products examined in the Bowling Green Study.

Sample No.	Brand Name	Quoted % Asbestiform Minerals
1	Mennen Talc Powder	22
2	J&J Baby Powder	8
3	Corn Silk	21
4	Estee Lauder	23
5	Cuticura (South Africa)	18
6	Coty-Muquist de Boic	15
7	April Showers (N.Y.)	6
8	Remington Shave Talc	34
9	Cashmere Bouquet	16
10	Imprevu	4
11	Avons Sachete Occur	14
12	Heaven's Scent	4
13	Excalibur Spray (Avon)	46
14	Loves Fresh Lemon	6
15	Mennens Baby Magic	22
16	Ammens Medicated Powder (ZnO)	20
17	ZBT Baby Powder	24
18	Cuticura (U.S.A.)	24

9. About a year ago Howard Jack, who was with the American Geological Institute at the time, requested and got the list of various brands of talc examined in the Bowling Green study. His motivation is unknown to us. We have determined that Jack is now apparently with some governmental agency and we are trying to determine his interest in the samples.

We asked to see their X-ray diffraction patterns and also requested splits of the samples. They could not locate the diffraction patterns and found only two samples (Nos. 8 and 13) while we were there. They are still trying to locate the others and said that they would send them to us when and if they find them.

They spent an inadequate amount of time and have admitted to making errors relative to the identification and amount of asbestiform minerals. They apparently will not stand behind the data presented in the paper if they are pressed to do so. ' I also believe that they will retract the data after we present them our data and after they have had time to do some checking on their own.

/nkr

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date June 6, 1985

From QRAC (Quantitative Risk Assessment Committee)

Subject Asbestos in Talc

To W. Gary Flamm, Ph.D.
Director, Office of Toxicological Sciences (HFF-100)

Using Linda Taylor's report [1] and other information on asbestos and talc, we conclude that the added human risk of lung cancer and mesothelioma from possible asbestos in talc is less than 10^{-8} lifetime risk and quite possibly orders of magnitude less. We have used, as our population at risk, infants that may be routinely dusted with talcum powder for an estimated period of 2 years.

Infant Dose and Worker Exposure:

Based upon one experimental 2 yr. exposure scenario for talcum powder dusting, babies would apparently inhale no more than about 6.5×10^3 asbestiform fibers per year (4.95 talc fibers/cc x 1000cc/1 x .58 1/min. breathing rate x 43.8 min/wk powdering x 52 wk/yr. x .1% asbestos in talc). The asbestiform fibers are difficult to detect, poorly defined in shape, and of a highly variable subtype. We assume .1% tremolite or anthophyllite asbestos in talc based on 1977 FDA measurements and other recent samples [1, 10, 11]. To be called asbestiform fibers, the fibrous silicates must be greater than 5 um. and have length/width ratio greater than 3. These inherent detection and geometrical measurement limitations for asbestos in talc make comparisons with worker exposure to a different type (mainly amosite, crocidolite and chrysotile) and shape of asbestos highly problematical [5]. In fact there is a

general consensus that current talc mines are virtually free of asbestos (offending mines have gradually been abandoned) and that any residual silicates in talc are so finely and smoothly ground as to represent virtually no risk to humans whatsoever even where an occasional fiber just barely satisfies the technical definition for asbestiform fibers. However, this consensus belief would require better geometric measurements than currently exist for both current commercial talc fibers and for workplace asbestos fibers during the past 50 years. Nevertheless, baby exposure in fibers per year is crudely estimated at about 0.3×10^{-6} times that of worker exposure in several well known epidemiological studies (e.g., Selikoff study: 15 f/ml in workplace x 12,000 ml/min breathing rate x 60 min/hr x 8 hr/day x 5 days/wk x 50 wks./yr. = 2.16×10^{10} f/yr. vs 6.5×10^{3} f/yr for baby) [1].

A complicating factor, however, is that human cancer risk from these studies seems to follow different time-dose response patterns for the two main cancer endpoints (lung cancer and mesothelioma). Although several human epidemiological studies exist which could be utilized for quantitative risk assessment purposes, it is most illustrative to consider the largest of these occupational studies, namely, that of Selikoff, et. al. [7,8] in which 17,800 insulation workers were exposed to a mixed variety of asbestos fibers (mainly amosite and chrysotile) for about 25 years on average. Through 1976, 2,271 deaths (12.7% of total) had occurred.

Lung Cancer:

Lung cancer rates were about 4.6 times average (486 observed/106 expected). Since this nearly 360% excess lung tumor

rate seems to apply to nonsmokers alone as well as smokers and nonsmokers combined [6], then, assuming hypothetically that one can extend excess relative risks to very low asbestos exposures, one would expect to see an excess lifetime lung tumor rate among asbestos exposed nonsmokers of about 1.8% (360% x the normal lifetime nonsmoker lung tumor rate of about .5% - integrating 1979 survival rates against Garfinkel's 1960-1972 nonsmoker age-specific lung tumor rates [12, 13]). Excess lung cancer rates appear to be proportional to dose and duration of exposure, but not to some high power of time-since-first-asbestos exposure [6]. Thus, excess lifetime lung cancer risk for talc exposed babies who will never smoke would appear to be approximately the product of 1) an excess 1.8% lifetime risk for nonsmoking asbestos exposed workers, 2) a baby/worker yearly exposure ratio of 0.3×10^{-6}, and 3) a baby/worker exposure duration ratio of 2 yrs/25 yrs. This product yields a value of $.4 \times 10^{-9}$ added lifetime risk for lung tumors. Similarly, averaging eventual smokers in with the lifelong nonsmokers assumed above, the average added lifetime lung cancer risk for the talc exposed baby will be at worst about 10 times higher or about $.4 \times 10^{-8}$. We note that current (1979) lifetime total respiratory cancer rates are about 5% and have nearly doubled since 1960, possibly reflecting rapidly changing smoking patterns during and after World War II, primarily among women. However, decreased tar levels in cigarettes and decreased per capita use of cigarettes since about 1965 should result in a gradual leveling off or decline in the total respiratory and/or lung cancer rate of the general population [14].

Mesothelima:

The estimation of lifetime risk of mesothelioma is somewhat more difficult since the mesothelioma response data appears quite nonlinear in time since first exposure. We have investigated four different methods of mathematically modelling the nonlinear mesothelioma data. They all indicate an upper bound on lifetime risk for talc powdered infants of about 10^{-8} risk and quite possibly a much lower upper bound if the conservative assumptions upon which they were based do not hold. These four methods consisted of mathematically treating mesothelioma as 1) a nonincidental tumor with no time lag between tumor initiation and death, 2) a nonincidental tumor with a 10 year time lag between tumor initiation and clinical observation, 3) an incidental tumor, and 4) treating asbestos as a first stage intervener in an Armitage-Doll multistage carcinogenic process [9].

In fact methods 1-3 yielded virtually identical risks (.5-.75 x 10^{-8} risk). While method 4 yielded a risk 2-3 times higher (1.5 x 10^{-8} risk), it could easily have yielded a risk up to several orders of magnitude lower than 10^{-8} if we had simply assumed asbestos intervenes at a later stage of the carcinogenic process in this hypothetical Armitage-Doll multistage model. There was general concurrence among these four methods, and it suffices to briefly summarize Method 1.

Method 1: based upon fitting $bt^{3.1}$ (nonincidental analysis) to a 1922-1946 cohort of the Selikoff, et. al. data.

A reasonably simple way to estimate the median life (ML) risk to median survival age 77 (in 1979) for humans exposed 2 yrs. to talcum

powder during infancy is given by the product of the following terms:

(a) (77 yrs. since first exposure for infants/37 yrs. since first exposure for 1922-46 cohort as of 1978+)$^{3.1}$ = 9.70.

(b) (2 yr. infant exposure duration/34 yrs. approx. worker exposure duration for 1922-1946 worker cohort) = .059.

(c) (infant/worker) yearly exposure ratio = 0.3×10^{-6}.

(d) 1922-1946 cohort cumulative mesothelioma response of 3.75% (180 mesotheliomas/4,800 cohort members).

This product yields a median life risk of $R_{ML} = 0.64 \times 10^{-8}$.

Tumors other than Lung and Mesothelioma: (Selikoff study)

Although significant tumor increases were observed at other sites in the workers (e.g., esophagus, stomach and colon), their risk is dominated by that of the lung (less than 10^{-9} or 10^{-8} risk, depending upon whether or not the baby becomes a smoker) and by mesothelioma risk (less than 10^{-8} risk).

Other Comments on Total Cancer Risk:

These estimates of added lifetime human cancer risk are 2 orders of magnitude below those implied in Linda Taylor's memo 1) due to the fact that the more recent detection studies suggest .1% or less asbestos in talc on average rather than the 1% assumed by Dr. Taylor: and 2) due to a 10 fold conversion error going from fibers/cc in the air to fibers inhaled/yr by the infant.

Although mothers may receive an exposure for each infant powdered, their added lifetime risk from talc should be relatively smaller than the infant's since their mouths and noses are considerably further from the densest portion of the talc cloud than is the case for the captive infant during the daily powdering period (the inverse square law for exposure may apply).

Finally, the risks implied by the Selikoff study are generally on the high side of those implied by the other smaller epidemiological studies and we see little value in repeating calculations here for those studies (see reference 6 for details).

Ovarian Talc Study:

For completeness, a discussion is presented on a human epidemiological study purporting to show an association between talc use (talcum powder used for genital dusting on the perineum or on sanitary napkins) and ovarian cancer.

The Cramer et.al. study [2], which purported to show a significantly increased relative risk for ovarian cancer associated with talc use, 1) appears to have been misinterpreted statistically, 2) was uncorrected for several likely biasing factors and 3) appears to have been strongly contradicted by another study showing a reduced relative risk as significant in the negative direction as the Cramer study was in the positive direction.

The Cramer study's most prominent analysis (Mantel-Haenszel) was adjusted for only 2 factors and gave a relative risk (RR) of around 1.92 (p less than .003) and 95% confidence limits of 1.27 to 2.89 for 215 cases (talc users for genital or sanitary napkin dusting) vs 215 controls. Cramer's more comprehensively adjusted but seemingly de-emphasized multivariate regression analysis for 9 possible simultaneously confounding variables yielded a smaller and much less significant relative risk of 1.61 (p=.03), with 95% confidence limits of 1.04-2.49. It should be noted that the crude relative risk with no adjustments whatsoever was 1.89. In any case, if the authors had limited their logistic regression analysis as they subsequently did for their Mantel-Haenszel analysis, to those 121 cases where the first chosen control did not refuse to participate

(refusal bias), then the resulting p-value can be predicted through extrapolation of the other reported analyses to be greater than .05 and perhaps greater than .1. Unfortunately, the authors did not report this analysis. Instead they selectively chose to point out only that the relative risk of those exposed to talc both as a genital dusting powder and through sanitary napkins declined from a relative risk of 3.28 (p less than .001) to 2.44 (p less than .05) when the potentially biasing control refusals were eliminated from analysis. Apparently the authors felt it unnecessary to report those p-values that were greater than .05.

Since there were twice as many singles among the cases (21%) as among the controls (11%), the life style of singles might easily have biased the original overall relative risk of 1.92 [3]. However, the multivariate logistic analysis (RR=1.61) using all of the original 215 cases and 215 controls clearly adjusted for marital status along with such variables as religion, educational level, ponderal index, age at menarche, exact parity, oral contraceptive or menopausal hormone use, and smoking. The partially adjusted Mantel-Haenszel analysis (RR=1.92) only adjusted for menopausal status and crude parity.

Furthermore, it is generally assumed that any real positive cancer effect will show an increased risk with increased dose. Cramer only reported one subanalysis where he crudely considered dose response. He divided the small group of talc-dusted diaphragm users into those using diaphragms less than 5 years and into those using diaphragms more than five years. However, rather than showing an increased relative risk with increased dose (increased length of usage), the relative risk actually decreased noticeably

though not in a "statistically significant" fashion from 1.82 to 1.23 as diaphragm use increased from less than 5 years to more than 5 years.

In addition to the above interpretations of Cramer's own results, several potentially biasing factors could not be adjusted for by the logistic analysis. First, a possible positive correlation between talc use and ovarian disease etiology due to patient-perceived hygenic or cosmetic reasons would bias the relative risk upwards [4]. Second, a recall bias among hospital cases relative to community controls is quite plausible since cases may have greater incentive as well as opportunity to recall whether they should classify themselves as talc users [3]. Talc users from the community may well be modest in either participating as controls (the refusal bias already discussed) or in subsequently admitting talc use as a control subject. The recall bias might be expected to be even greater - as was possibly observed - for estimation of the relative risk for those using talc both on sanitary napkins and as a dusting powder (RR=3.28, p less than .001; or RR=2.44, p less than 0.05, after the refusal bias is eliminated) than for those engaged in only a single type of use.

Finally a talc and ovarian cancer study by Hartge, et. al. [4], appears to strongly contradict the reportedly positive Cramer study. Overall 135 cases and 171 control women matched by age, race and hospital were questioned on talc use. The estimated relative risk of ovarian cancer by talc users was reported to be 0.7 (95% confidence interval of 0.4 to 1.1). Adjustments for race, age, and gravidity (pregnancy) had no effect upon the estimate. No subanalyses

resulted in relative risks significantly greater than 1. It would appear that no refusal bias was operative in the Hartge study since none was reported. Also it would appear that recall bias was non-existent since there appeared to be no recall bias on the use or nonuse of douching.

SUMMARY

In summary, any hypothetical systemic added lifetime cancer risk (e.g., mesothelioma and lung cancer) to humans due to asbestos fibers in talc (principally for babies subject to 2 years of talc dusting) appears to be less than 10^{-8} added lifetime risk and possibly several orders of magnitude lower risk still, depending upon assumptions and uncertainties alluded to above, especially those regarding geometrical shape of any possible asbestos fibers in talc, and limits of detection for asbestos in talc. In addition, there appears to be no association between customary human talc use per se and ovarian cancer.

Robert Brown

Robert Brown

ATTACHMENT:

Signature Page

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date May 21, 1985

From Robert Brown
BRAB, Division of Mathematics (HFF-118)

Subject Four methods of quantitating mesothelioma risk based on the Selikoff, et. al., insulation workers asbestos study. Technical support for QRAC's asbestos risk assessment.

To QRAC

In fig. 1 we have plotted on a log-log scale Selikoff's original mesothelioma incidence data vs. years since first exposure to asbestos. Incidence is defined as number of mesotheliomas/man-years exposure. The data do not seem to fit a single straight line. Uncertainties of exposure in the early part of the century and the general decline in intensity of asbestos exposure after World War II are possible sources of error. For these reasons, as well as general lack of fit of both recent data and distant past data, Peto recommended use of a more homogeneous subset of workers for quantitative purposes, namely those workers first exposed between 1922 and 1946 [8]. It can be inferred from Selikoff's report that this subset consists of about 4800 workers.

Peto reports 180 mesotheliomas (3.75%) among this subgroup out of a total of 236 mesotheliomas for all 17,800 workers followed from 1967 until about 1978 or 1979. Note that Selikoff only reported 175 mesotheliomas total; however, his reported follow-up period was also shorter (1967-1976).

Plotting Peto's homogeneous 1922-46 cohort subset, we see that $bt^{3.1}$ nicely fits the data (expressed as a straight line on log-log paper with a slope of 3.1). We also see that $b(t-10)^{2.1}$ nicely fits the data (with a different value for the constant b) and may be a reasonable

way of looking at mesotheliomas since the time lag from mesothelioma induction to death is not zero. The time of mesothelioma induction is not even a well defined concept and may be intimately entertwined with the concept of stage definition in, for example, a multistage cancer process. Nevertheless, both these model fits assume mesothelioma to be a nonincidental tumor (i.e., a life table where incidence is the ratio #tumor bearers/#survivors, re-expressed in man-years, per time interval). If we assume mesothelioma annual incidence to be better approximated by a prevalence or incidental definition, (#tumor bearers/#dead in interval), then $bt^{1.64}$ seems to be a rough though not very tight fit to the original Selikoff data. Peto's reported 1922-1946 data set does not easily allow determination of a prevalence fit. However, since the prevalence denominator is defined in terms of deaths per time interval rather than the much larger number of survivors to date, the first 2,271 deaths (12.7% of 17,800 workers) reported by Selikoff are very heavily weighted with the 1922-1946 cohort used exclusively in the two nonincidental curve fits above. Therefore comparisons of slightly different cohort subsets may still be useful. We estimate that the average time since first exposure for the Peto subset (1922-1946 first exposure) is about 37 years (Peto's 1978[+] follow-up) or 35 years (Selikoff's 1976 follow-up). This compares to 25 years average time since first exposure usually reported for all 17,800 workers. We also make the assumption that workers ceased exposure on average 3 years before death.

Method 1: based upon fitting $bt^{3.1}$ (nonincidental analysis) to a 1922-1946 cohort of the Selikoff, et. al. data.

A reasonably simple way to estimate the median life (ML) risk to median survival age 77 (in 1979) for humans exposed 2 yrs. to talcum powder during infancy is given by the product of the following terms:

(a) (77 yrs. since first exposure for infants/37 yrs. since first exposure for 1922-46 cohort as of 1978+)$^{3.1}$ = 9.70.

(b) (2 yr. infant exposure duration/34 yrs. approx. worker exposure duration for 1922-1946 worker cohort) = .059.

(c) (infant/worker) yearly exposure ratio = 0.3×10^{-6}.

(d) 1922-1946 cohort cumulative mesothelioma response of 3.75% (180 mesotheliomas/4,800 cohort members).

This product yields a median life risk of $R_{ML} = 0.64 \times 10^{-8}$.

Method 2: based upon $b(t-10)^{2.1}$ (delayed observation or time lagged nonincidental analysis).

Note that to estimate real mesothelioma incidence (time of mesothelioma induction - the last stage of the multistage cancer process) at age x, the worker must be assumed to have been autopsied or surgically inspected at some average age, say x+10. Thus, assumming the worker stops exposure 3 years before death, the component relative and absolute risk factors for incidence at age 77 now are the following:

(a) ((87 yrs.-10 yrs.)/(37 yrs.-10 yrs.)$^{2.1}$ = 9.03.

(b) (2 yr. infant exposure duration/(37-10) yr. worker exposure duration) = .074.

(c) (infant/worker) exposure rate ratio = 0.3×10^{-6}.

(d) 3.75% mesothelioma response in 1922-1946 cohort

Thus $R_{ML} = 0.75 \times 10^{-8}$.

Method 3: based upon $bt^{1.64}$ (prevalence or incidental analysis):

The relative and absolute risk product factors are:

(a) (77 yrs. since first exposure for infant/35 yrs. since first exposure for the 2,271 deaths to 1976)$^{1.64}$ = 3.64.

(b) (2 yr. infant exposure/34 yr. ave. worker exposure duration for 2,271 deaths to 1976) = .059.

(c) (infant/worker) exposure rate ratio = 0.3×10^{-6}.

(d) 7.7% mesothelioma cumulative prevalence to 1976 (175 mesotheliomas/2,271 deaths).

Thus $R_{ML} = 0.50 \times 10^{-8}$.

Method 4: based upon $bt^{3.1}$ (nonincidental analysis) and a first stage effect in a generalized multistage process.

We assume that bt^{k-1} fits the time-response data of a nonincidental tumor and is consistent with a first-stage-only effect in a generalized multistage process (with R stages), where biological time t starts at age of first exposure and continues until death [9]. Although this is not precisely true for the 1922-46 asbestos worker cohort, it appears to be approximately true. Moreover the time lag from cessation of exposure to end of followup (1976 or 1978^{+}) is assumed to be small compared to total duration of exposure (i.e., exposure duration is a large fraction of time since first exposure). However, the exposure duration for infants is very small compared to median lifespan. Thus, while we fit worker yearly incidence data to bt^{k-1} we should extrapolate yearly incidence (I) for exposed infants using the expression $I = b(t^{K-1} - (t-d)^{K-1})$ for a K stage multistage process with duration of exposure d and time since first exposure t [9].

Now K-1 = 3.1 from Fig. 1 and b can be written as the product of a constant K_m and f where f is the time adjusted yearly dose of asbestos fibers in ml-yrs. K_m is a constant dependent upon the type and dimensions of the asbestos. Since f = 3.43 f/ml-yr. (15 ave. f/ml in workplace (1922-1946) x 8 hrs./24 hrs. x 5 days/7 days x 50 wks/52 wks) for the Selikoff study, K_m can be computed from the plot of $I = K_m f\, t^{3.1}$ in Fig. 1. At t = 20 yrs, $I = 5.6 \times 10^{-4}$, implying that the $\ln K_m = \ln(5.6 \times 10^{-4}) - \ln(3.43) - 3.1(\ln 20) = -7.49 - 1.23 - 9.29 = -18.01$.

Thus $K_m = 1.51 \times 10^{-8}$ (same as Peto obtains). Continuing, $I = K_m f(t^{K-1} - (t-d)^{K-1}) = K_m f t^{K-1}(1-(1-d/t)^{K-1})$ which roughly = $K_m f t^{K-1}(d/t)(K-1)$ for d much less than t (using Taylor expansions). Thus yearly incidence is approximately $I = K_m fd(K-1)t^{K-2}$. Integrating (without correcting for decreasing survival) over a total of T years yields a cumulative incidence of about $I_c = K_m fdT^{K-1}$. If d = 2 yrs. infant exposure duration, T = 77 yrs., K-1 = 3.1, f = 3.43 f/ml-yr. for worker x 0.3×10^{-6} (infant/worker exposure ratio) = 1.03×10^{-6} f/ml-yr., and $K_m = 1.51 \times 10^{-8}$, then $I_c = 2.2 \times 10^{-8}$.

However, this figure assumes no mortality from competing causes of death and does not even adjust for the effect of previous mesothelioma related deaths. Factoring in a standard population age-specific mortality or corresponding survival function into the above integral would yield a median life risk of about 75% of 2.2×10^{-8} or $R_{ML} = 1.6 \times 10^{-8}$. This correction for survival can vary depending upon the limits of integration and what functional forms are under the integral, but for median life risk estimates the correction ranges from 1.0 down to .5 at worst. We also note that integrating I out to 100 yrs. of life with

respect to a standard mortality curve should yield approximately the same risk as cumulative incidence to median age 77 yrs. without any mortality adjustments. These approximately cancelling effects of two mathematical refinements may support the utility of using the median lifespan in simple calculations.

Comments on the 4 Mesothelioma extrapolation methods:

First and most importantly, it should be noted that the first 3 methods yield virtually identical median lifespan risks for babies exposed to talc for 2 years ($.5\text{-}.75 \times 10^{-8}$). Thus many of the debates over the "correct model" appear somewhat superfluous. In particular heated debates over whether mesothelioma rates follow given high or low powers of time appear to be superfluous since the power of time is compensatingly related to other poorly defined and difficult to measure conceptual model parameters (e.g., tumor stage initiation and consequent time lag to clinical detection or death, and context of tumor observation (incidental or nonincidental)). Furthermore, small perturbations of the rough estimates of worker exposure or the power of time (K) have only a small effect on the overall risk.

All the above models appear to be reasonable summary descriptors of the observable data and result in simple extrapolatory tools for the given problem of inferring median lifetime risk from infant exposure. One can always make method 4 computationally more difficult if one avoids use of the approximations.

A second observation is that the rough mutual agreement of the results of the 4 extrapolation methods does not necessarily imply that

the obtained excess median life risk is accurate even if the infant and worker exposure were to the same type and dimension of asbestos fiber. For example, none of the four models take into account the possibility that accumulated dose rather than yearly dose rate might more accurately reflect the biological burden of asbestos due, for example, to its ability to reside in vivo in the lung, pleural or peritoneal lining for years without being excreted (although encystment may be possible). Note also that we did not define dose on a mg/kg body weight basis. Although, we prefer such a definition for routine compounds that are ingested and metabolized, we strongly suspect that routine approach to be inappropriate for asbestos. In addition, all 4 methods assume linearity in response vs. dose at all dose levels. However, we have virtually no reliable dose response data from any of the epidemiological studies.

Furthermore, some investigators have suggested that the nonconstant accumulated asbestos dose may be as conceptually consistent with a late stage multistage carcinogenic process as the more usually defined yearly asbestos dose rate appears to be consistent with a first stage Armitage-Doll multistage process [9]. Although the theory and computations are more complicated for nonconstant exposures, it does appear that median life risks from infant exposure to asbestos affecting only a late stage in the carcinogenic process will generally result in much smaller risks than those calculated above for a first-stage-only effect in the carcinogenic process.

Our third observation which we have just hinted at is that method 4 above (the first-stage-only effect in a multistage model) may be just another way of implementing method 1, but just slightly more computationally difficult and having a slightly higher risk, partially because it substitutes a theoretical risk integration against the current (1979) U.S. population's standard survival function for the implicitly observable but poorer asbestos worker's cumulative survival of an earlier era in a more toxic environment. For example, the method 4 risk is about 2.6 times greater than the average risk of methods 1-3. There are probably other reasons for this 2.6 fold increase in risk over methods 1-3. However, since even partial intervention of asbestos fibers at later stages of the carcinogenic process in the Armitage-Doll multistage model imply lower overall risks, we prefer the simpler methods 1-3 at this moment to the more complicated multistage models whose proper application with respect to the stage or stages affected is still very much in doubt.

In general, we do not put a lot of faith in mechanical use of sophisticated but unverifiable models, but we will occasionally refer to them as in method 4 where we can suggest implicit and perhaps elucidative connections to apparently more humble and simpler procedures.

Summary:

All four mathematical methods of modelling the nonlinear mesothelioma response data from the Selikoff study indicate a lifetime added human risk to infants exposed 2 years to talc powdering of at most about 10^{-8} risk, and quite probably far less risk, if for example, asbestos intervenes in the carcinogenic process at a later stage than the first stage which was assumed in method 4 for the Armitage-Doll multistage process.

Robert N. Brown

Robert N. Brown

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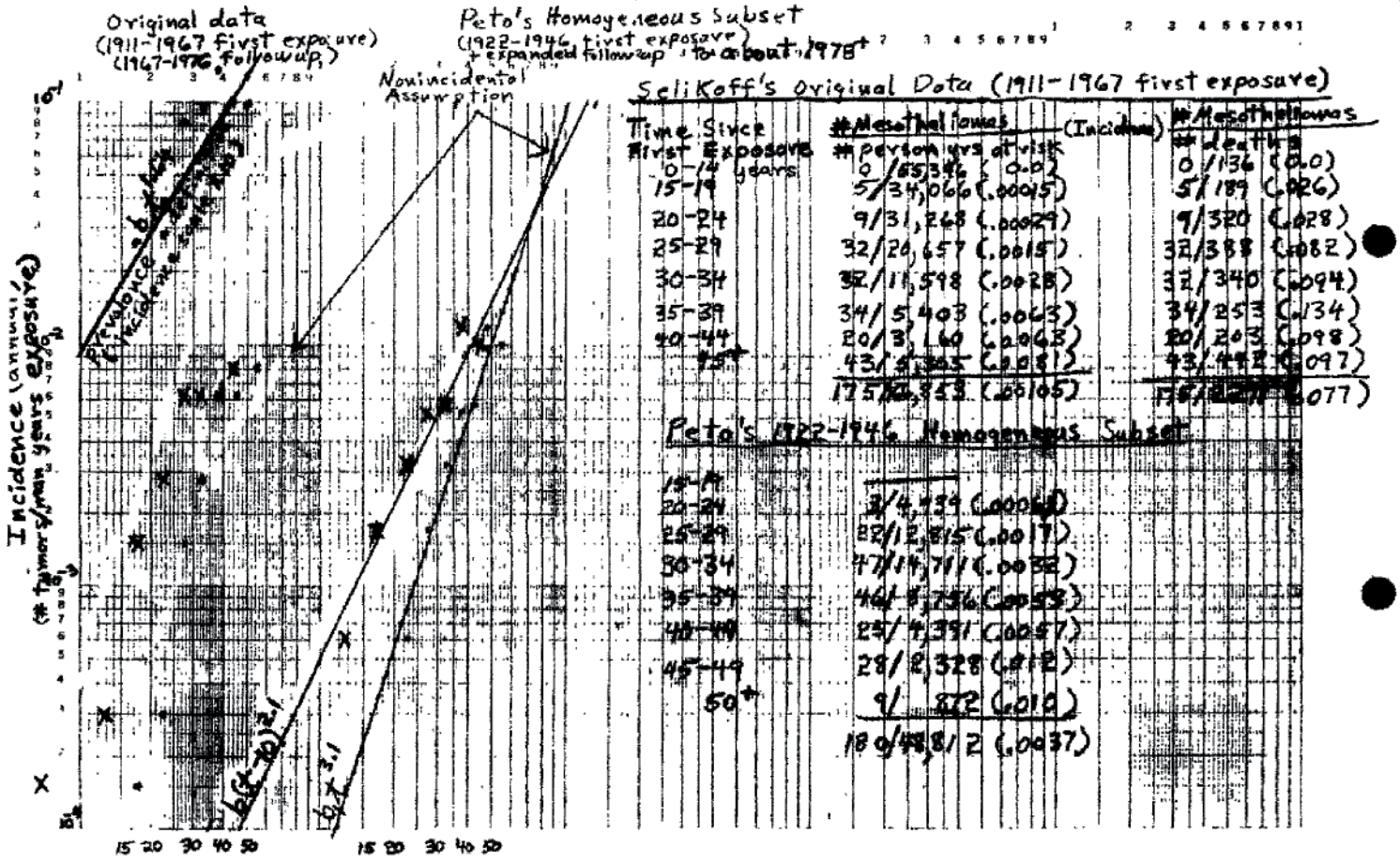
Fig 1

SeliKoff Asbestos Study (17,800 workers an asbestos union. roles as of Jan. 1, 1967)

Mesotheliomas



SeliKoff's Original Data (1911-1967 first exposure)

Time Since First Exposure	# Mesotheliomas / # person yrs at risk (Incidence)	# Mesotheliomas / # deaths
0-14 years	0 / 85,346 (0.0)	0 / 136 (0.0)
15-19	5 / 34,066 (.00015)	5 / 189 (.026)
20-24	9 / 31,248 (.00029)	9 / 320 (.028)
25-29	32 / 20,657 (.0015)	32 / 388 (.082)
30-34	32 / 11,598 (.0028)	32 / 340 (.094)
35-39	34 / 5,403 (.0063)	34 / 253 (.134)
40-44	20 / 3,160 (.0063)	20 / 203 (.098)
45+	43 / 5,285 (.0081)	43 / 442 (.097)
	175 / 199,953 (.00105)	175 / 2271 (.077)

Peto's 1922-1946 Homogeneous Subset

15-19	3 / 4,739 (.0006)
20-24	22 / 12,815 (.0017)
25-29	47 / 14,711 (.0032)
30-34	46 / 8,756 (.0053)
35-39	25 / 4,391 (.0057)
40-44	28 / 2,328 (.012)
45-49	9 / 872 (.010)
50+	
	180 / 48,812 (.0037)

November 15, 1984

Food Additives Evaluation Branch (HFF-156)

Request for Quantitative Analysis of Risk from Potential Exposure to Asbestos from Cosmetic Talc Use.

Quantitative Risk Assessment Committee
Attention: Ronald Lorentzen, Ph.D. (HFF-100)

CITIZEN'S PETITION 83P-0404

Philip Douillet
1 Holyoke Lane
Stony Brook, N.Y. 11790

Mr. Philip Douillet has submitted a petition requesting certain mandatory labeling on cosmetic talcs to warn consumers of asbestos hazards associated with such products.

BACKGROUND

Cosmetic talc is used as a face powder and body powder by both adults and children to lubricate the skin and prevent chafing and discomfort caused by moisture and heat. The normal use of cosmetic talc in infants has not been reported to be harmful[1], although the accidental aspiration of excessive amounts in infants has been reported to cause serious but reversible acute respiratory disease in some instances and death in isolated cases.[2-5]

As discussed below, talc, a hydrous magnesium silicate, occurs fairly commonly in nature. Table 1 lists the minerals that are commonly found in talc deposits.

FDA STATUS

There are no regulations concerning the use of talc as an ingredient in cosmetic products. Under current law, the burden of proof that a cosmetic may be harmful in that it contains a harmful substance rests with FDA. FDA must have data or other information demonstrating that a product contains a poisonous or deleterious substance that is harmful under customary conditions of use before any action can be taken either to restrict or prohibit the use of an ingredient or product.

TABLE I

	Mineral	Ideal formula
Carbonates	Calcite	$CaCO_3$
	Dolomite	$CaMg(CO_3)_2$
	Magnesite	$MgCO_3$
Amphiboles	Tremolite	$Ca_2Mg_5Si_8O_{22}(OH)_2$
	Anthophyllite	$(FeMg)_7Si_8O_{22}(OH)_2$
Serpentine	Antigorite	$Mg_3Si_2O_5(OH)_4$
	Chrysotile (uncommon)	$Mg_3Si_2O_5(OH)_4$
	Lizardite (uncommon)	$Mg_3Si_2O_5(OH)_4$
Others	Quartz	SiO_2
	Mica, e.g. Phlogopite	$K_2(Mg,Fe)_6[Si_6Al_2O_{20}](OH)_4$
	Chlorite, e.g. Pennanite	$(Mg,Al,Fe)_{12}[Si,Al)_8O_{20}](OH)_{16}$

IDENTITY

Talc

Talc as a pure chemical compound is defined as hydrous magnesium silicate, $Mg_3Si_4O_{10}(OH)_2$ and consists of a brucite sheet containing magnesium ions sandwiched between silica sheets that are held together by relatively weak forces. A variety of elements such as nickel and iron may be included in the talc particle lattice but are so bound within the particle that they are not free to exert any biological action[6]. Talc can be tubular, granular, fibrous, or platy, but it is usually crystalline, flexible, and soft. Talc is a member of the family of silicate minerals that have a similar atomic structure and occur widely in a large number of different varieties. These silicate minerals are derived from metamorphic alteration of mineral rocks that sometimes include the amphibole and serpentine groups of asbestos after their exposure to specific temperatures, pressures, and circulating liquid solutions. Talc may be formed also by the thermal metamorphism of silicon dolomites.

The purity and physical form of any sample of talc dust as well as the other minerals that are associated with it are, therefore, directly related to the source of the talc and to the minerals found in the ore body from which it is mined. Talc commonly contains chlorites and carbonates, the former being sheet silicate minerals containing magnesium, aluminum, and iron. The carbonate mineral components of talc are mainly magnesite, dolomite, and calcite. Quartz (free silica), iron oxides, sulphides, and various silicates can also be associated with talc.

Since serpentine is one of the minerals from which talc has evolved, it can be associated with talc and is sometimes a contaminant of talc dust. Tremolite, a member of the amphibole group of asbestos, and chrysotile or antigorite of the serpentine group, are the commonest asbestos contaminants of industrial talc dust, although (according to Pooley, F.D., 1975) chrysotile has never been reported to be present in the high-grade talc used in health and cosmetic talc. As talc dusts are obtained from different sources, the amount and specific form of talc, as well as the amount and nature of mineral contaminants, will be different for each dust.

The U.S. Department of the Interior, in a letter dated February 24, 1984,[7] indicated that, with regard to talc deposits and whether any were asbestos free, talc deposits can contain the mineral tremolite. However, even for those deposits that do contain tremolite, it was stated that it is important to understand the distinction between non-fibrous (non-asbestiform) tremolite, which may be common to some talc deposits, and fibrous, asbestiform, tremolite, which is a very rare

form for that mineral. Similarly, actinolite and anthophyllite only very rarely have fibrous forms. Therefore, the presence of tremolite, actinolite, or anthophyllite in a talc deposit does not necessarily indicate the presence of asbestos, because they usually are not fibrous. Additionally, it was stated in the letter that the minerals crocidolite and amosite do not form in the same geological environment as talc; therefore, it is extremely unlikely that they would be found in any talc deposits. However, it is possible that chrysotile might occur in rocks in or around some talc deposits, but it would probably be in only very minor amounts.

As to what percentage of talc deposits might contain 0.5% or greater of asbestos, this would have to be evaluated for individual deposits. It is also stated that asbestos cannot be formed by shearing during mining. If asbestos minerals are not present to begin with, they will not be formed by mechanical means during mining or crushing operations. This last point is disputed by others.

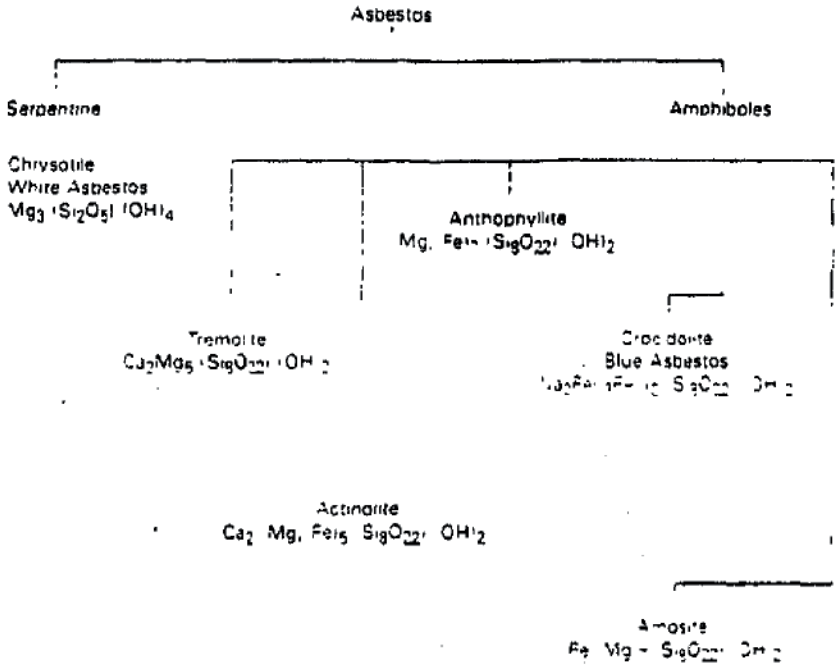
Asbestos

Asbestos is not one mineral but a generic term used to describe a family of naturally occurring fibrous hydrated silicates divided on the basis of mineralogical features into two groups: serpentines and amphiboles. The important property of asbestos as compared to non-asbestiform varieties of silicates is the presence of mineralogically long, thin fibers that can be easily separated. According to some definitions, there are as many as thirty varieties of asbestos, but only six are of commercial importance. These, together with their chemical composition, are shown in Figure 2.1.

The word "asbestos" is derived from the Greek word meaning "inextinguishable", and the origin of its name reflects one of its principle characteristics: fire resistance. But asbestos has many other qualities that enhance its commercial utility, among them tensile strength, durability, flexibility, and resistance to heat, wear, and corrosion. As an aside, because of its many uses (insulation material, as a fire retardant, linings for brakes and clutch facings, reinforcing agent in cement and pipes, as filters, etc.) and its natural occurrence, it is not surprising that asbestos is found in ambient air, in drinking water, and in foods.

The mineralogical classification of what is and what is not asbestos is complex, and as a result, many definitions of asbestos have appeared in the scientific literature. One definition of the term, asbestos, was published in the Federal Register in 1975 by the U.S. Occupational Safety and Health Administration (October 9, 1975, pp. 47652, 47760). According to this definition, asbestos is considered to include the naturally occurring minerals chrysotile, amosite, crocidolite,

Figure 2.1
Principal Varieties of Asbestos



SOURCE Dr. Eric J. Chatfield, "The Problems of Measurement of Asbestos," in Ontario, Royal Commission on Asbestos, *Proceedings of The Royal Commission on Asbestos, Second Public Meeting, Friday, December 12, 1980*, reported by Lydia Dotto (Toronto: Royal Commission on Asbestos, 1981), Appendix A, Figure 1, p. 2.

tremolite, actinolite, and anthophyllite, if the individual crystals or fragments are greater than 5 micrometers in diameter, and have a length to diameter ratio of 3 or greater.

Each of these six minerals included in OSHA's asbestos standard occurs in both an asbestiform and a non-asbestiform variety. Three of the six minerals have been given different names for each of their two forms. Chrysotile in its non-asbestiform variety is called antigorite. Crocidolite is called riebeckite. Amosite is called cummingtonite-grunerite. The other three minerals--because they occur in their asbestiform varieties so rarely in nature--are each called by only one name, regardless of their form. Tremolite, anthophyllite, and actinolite are labeled asbestos by OSHA in both their forms. According to mineralogists, this is incorrect, and it is poor science.

HEALTH EFFECTS

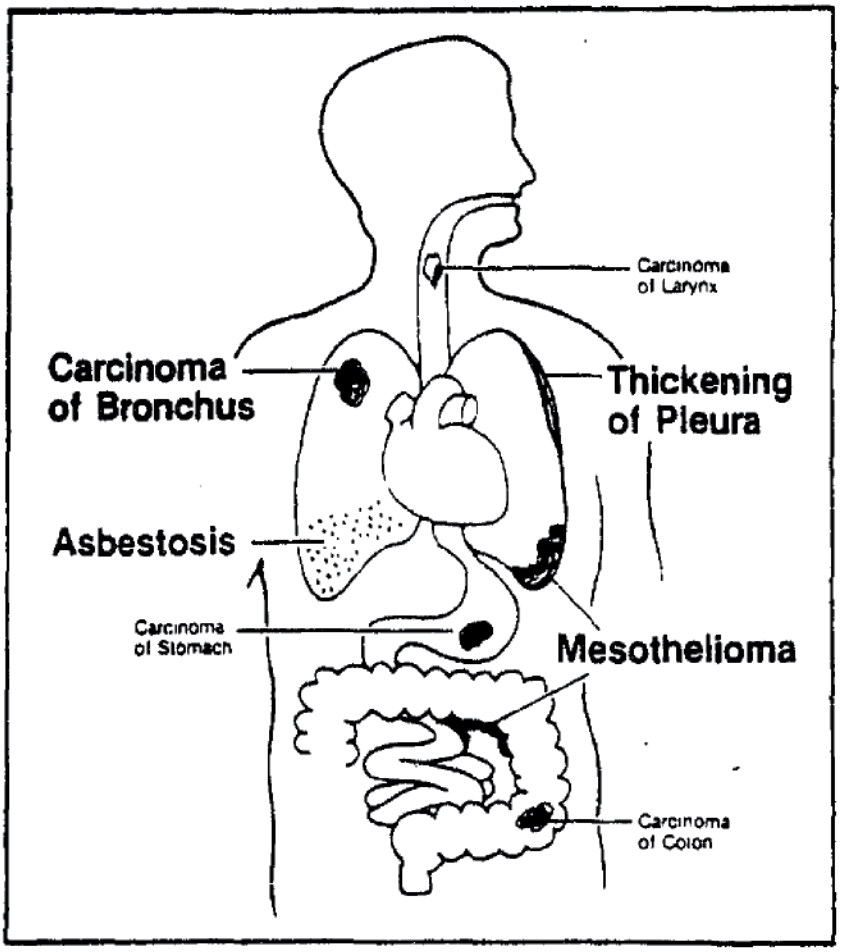
Evaluation of potential health effects from exposure to talc contaminated with asbestos and from other nonoccupational exposures to asbestiform fibers depends primarily on the results of epidemiological studies of occupational groups exposed to asbestos. Most of the data come from cohort studies (see Appendix I) of workers exposed to asbestos of various types and in a variety of industries and occupations. Much information has been obtained from these studies. However, they also suffer from limitations common to many epidemiological studies and from some additional problems related to determining dose (exposure) and response (health end point, such as death from a specific cause). Despite the limitations of individual studies, when all the studies are considered, exposure to asbestos increases the risk of developing lung cancer, mesothelioma, asbestosis, and possibly other cancers.

To quantify health risks from an exposure, it is necessary to obtain dose-response data, but exposure measurements are particularly difficult to obtain. Because of the long latency period for asbestos-associated diseases, investigators have found it necessary to try to reconstruct past exposures. Techniques of measurement vary from place to place and over time[8,9]. For example, fiber counts obtained by light microscope in various industrial settings may need to be multiplied by a factor varying from 2 to 8 to obtain a true count of fibers longer than 5 um.

Typically, a cumulative dose measurement is used. This does not take into account the time lapsed since last exposure nor does it distinguish between short exposures of high intensity and long exposures to low dust concentrations. In addition, a cumulative dose measurement does not change when exposure ceases. Variability in these exposure-related factors affects mortality responses in occupational cohorts. In some studies, exposure surrogates, such as type of job and duration of employment, are used to estimate exposure. These estimates may be less precise than actual measurements.

Figure 2.4

Principal Asbestos-Related Diseases and Conditions and Their Sites in the Human Body



SOURCE. Illustration by Mr. Jerry Farrell, Audio-Visual Centre, McMaster University, consultative assistance by Dr. David C. F. Muir, Director, Occupational Health Program, Health Sciences Centre, McMaster University, Hamilton, Ontario.

There may also be variability in reporting causes of death, ascertainment of deaths, and diagnostic accuracy of the reported cause of death. Inaccuracies are particularly likely for mesothelioma and asbestosis[10].

Methodological differences are a major source of variation in comparing studies[11]. For example, the results obtained will depend on the criteria for selecting the cohort, the choice of comparison groups, the influence of other environmental factors that may introduce competing disease risks, and the records available.

In addition, heterogeneity in the time at which onset of exposure begins can introduce additional distortion in the observed relative risks[12], especially because the types of exposure experienced by some workers in the distant past may differ from exposures experienced only more recently. Weiss also discussed how the results of lung cancer studies can be affected if persons who left a job are not included in the study cohort. He found that the exclusion of these workers could affect the relative risk by a factor of 2 to 3.

An additional difficulty is encountered when comparing dose-response results from mortality and morbidity studies, particularly if the morbidity studies are confined to active workers, which is usually the case. A bias is introduced in studies of active workers, since those with severe disease have probably already left employment. However, asbestosis generally progresses after cessation of dust exposures[13;14].

Numerous follow-up studies of asbestos-related mortality have been conducted on cohorts with varying intensity and duration of exposure, type of exposure, type of work, time and duration of follow-up periods, differences in the completeness of the cohort, completeness of mortality ascertainment, availability of smoking histories, geographic area of analysis. Because of the variations noted, it is not surprising that the standardized mortality ratios (SMRs) and dose-response results differ greatly among studies. In general, however, the same major diseases--lung cancer, mesothelioma, and asbestosis--have been observed, although not all investigators conducting these studies have reported or detected excesses of all three of these diseases.

Talc

The health effects of talc have been studied only in relation to occupational exposures[15-25]. Data available on the health hazards associated with occupational exposure to talc are not extensive. Exposure to talc itself in high concentrations has been shown to produce excess mortality, mainly due to respiratory diseases.

Workers from different geographic regions containing talc with or without fibers have been studied to determine if any adverse health effects are associated with the asbestiform fiber content of talc. Adverse effects have been found in some studies among workers exposed to talc both with and without fibers. These studies are discussed in the following paragraphs.

Epidemiological studies on workers exposed to talc containing fibers have demonstrated adverse effects on pulmonary function. In a study of 121 New York miners and millers exposed to talc containing tremolite and anthophyllite fibers, pulmonary function was found to be significantly decreased.[26] Reductions in forced vital capacity (FVC) and 1-second forced expiratory volume (FEV_1) were associated with employment duration and the amount of fiber present. Increased pleural thickening and calcification were detected in talc workers with 15 or more years of employment[26].

A mortality study of 398 New York miners exposed to talc containing fibers has demonstrated excess mortality from nonmalignant respiratory disease, excluding influenza, bronchitis, or pneumonia (5 observed/1.3 expected)[27]. An excess in lung cancer with an average latency of 20 years was also observed (9 observed/3.3 expected). Additional studies have had conflicting results. Some investigators have found no significant increases in lung cancer and nonmalignant respiratory disease[28], whereas others have reported significant increases in lung cancer, attributed to the silica content of talc.[29,30]

Morbidity and mortality studies have also been conducted on workers exposed to talc with low or undetectable levels of fibers. A study on the respiratory function of 103 Vermont talc workers indicated that there was a reduction in pulmonary function in smokers[31]. After adjusting for smoking, the effect of the exposure to talc was not statistically significant, although there was evidence of an exposure-related effect in workers with an annual dust exposure of approximately 1.5 mg/m^3. Exposure to talc dust was also associated with small opacities seen on chest radiographs.

Gamble et al.[26] conducted a cross-sectional study of 299 workers from Montana, Texas, and North Carolina who were exposed to talc containing low levels of silica and fiber. There was no significant difference in lung function, respiratory symptoms, or pneumoconiosis between workers and controls, although there was a significant increase in bilateral pleural thickening among the workers. Results of pulmonary pathology studies also have provided evidence of fibrosis in workers exposed to talc that does not contain fibers[33].

A mortality study of 392 Vermont workers exposed to talc not containing fibers showed that there were excess deaths from nonmalignant

respiratory disease, excluding influenza and pneumonia, among millers (11 observed/1.79 expected)[34]. This excess mortality was associated with small opacities seen on chest radiographs. An excess of respiratory cancer mortality among miners was also noted (5 observed/1.15 expected) but was attributed to exposures other than talc.

In a recent case-control study[37], increased risk of ovarian cancer was shown for women who regularly used talc either (or both) as a dusting powder on the perineum or on sanitary napkins compared to women who did not engage in either practice (See Table 4). No data with regard to asbestos contamination of the talc were provided. Studies of female asbestos workers are presented in Appendix I.

Table 4: Relative Risks (RR) for Common Epithelial Ovarian Cancers Associated with Talc Exposure in Perineal Hygiene

			Types of Perineal Exposure		
	No perineal exposure	Any perineal exposure	As dusting powder but not on napkins	On napkins but not as dusting powder	Both on napkins and as dusting powder
Cases (Total = 215)	123(57.2%)	92(42.8%)	43(20.0%)	17(7.9%)	32(14.9%)
Controls (Total = 215)	154(71.6%)	61(28.4%)	34(15.8%)	14(6.5%)	13(6.0%)
Crude rr	1	1.89	1.58	1.52	3.08
Adjusted RR*	-	1.92	1.55		3.28
95% confidence limits	-	(1.27-2.89)	(0.98-2.47)		(1.68-6.42)

*Adjusted for parity and menopausal status

Note: A study (reviewed in Appendix II) of mesothelioma incidence in domestic dogs concluded that there was an association between the incidence of mesothelioma and asbestos exposure; the source of exposure of the dogs was from the use of flea powders and/or the owners asbestos-related occupations (hobbies).

Additionally, an animal inhalation study (reviewed in Appendix II) with talc (Italian 00000 grade) did not indicate talc to be carcinogenic.

Asbestos

Asbestos associated diseases generally have been related to occupational exposures, such as those experienced by some miners, insulators, and factory workers (see Appendix I). Recently, however, there has been concern that exposures to asbestos and related fibers may present a health hazard to the general public.

Because asbestos and other asbestiform fibers appear to be ubiquitous, virtually everybody is exposed to some extent. During autopsy, asbestos fibers have been detected in the lungs of most urban residents studied. Reported concentrations of asbestos in urban air are shown in Table 7-6. Exposure to the general public is of concern because the population involved is large and includes unhealthy persons. Also, exposure may begin in childhood (as with baby powder application), leaving a longer time for the development of adverse effects. Additionally, asbestos may enhance the carcinogenic effects of other materials. There is little information about the health effects of most nonoccupational exposures to asbestos (see NAS report, Ref. 100). Although babies have been powdered with talc powder for many years, there is no evidence that this has resulted in an increase in asbestos-related disease.

Three principal diseases are related to exposure to one or more of the commercial asbestos minerals. These are: (1) lung cancer, which includes cancer of the trachea, bronchus, and the lung proper; (2) mesothelioma, a cancer of the pleural and peritoneal membranes that invest the lung and abdominal cavities, respectively; and (3) asbestosis, a diffuse interstitial fibrosis of the lung tissue often leading after long exposure to severe loss of lung function and respiratory failure. These diseases are not equally prevalent in the various groups of asbestos workers that have been studied; the amount and type of disease depend on the duration of exposure, on the intensity of exposure, and possibly on the type or types of asbestos to which the individual was exposed. Only lung cancer and mesothelioma will be considered here. Asbestos appears to act principally as a late stage carcinogen (promoting agent) that multiplies the underlying risk of lung cancer that occurs in the absence of asbestos exposure. The nature of the dose-response relationship for asbestos-related diseases is discussed below.

TABLE 7-6. Summary of Environmental Asbestos Exposure Samples[a]

Sample Sets	No. of Samples	Measured Concentration (ng/m^3) Median	Measured Concentration (ng/m^3) 90th Percentile	Equivalent Concentration (fibers/cm^3)[b] Median	Equivalent Concentration (fibers/cm^3)[b] 90th Percentile	Reference
1. Paris air	161	0.7	3.2	0.00002	0.00011	Sebastien et al., 1980
2. Paris (outdoor control)	19	0.7	5.2	0.00002	0.00017	Sebastien et al., 1980
3. Outdoor control samples, for U.S. schools	31	0.9	9.8	0.00003	0.00033	Constant et al., 1982
4. Air of 48 U.S. cities	187	1.6	6.8	0.00005	0.00023	Nicholson, 1971
5. Air of U.S. cities	127	2.3	7.8	0.00008	0.00026	U.S. Environmental Protection Agency, 1974
6. Air of five U.S. cities (outdoor control sample)	34	6.7	31.9	0.00022	0.00106	Nicholson et al., 1975, 1976
7. New York City air	22	13.7	42.9	0.00046	0.00143	Nicholson et al., 1971
8. Air 0.5 mile (0.8 km) from asbestos spraying	17	22.5	82.6	0.00075	0.00275	Nicholson et al., 1971
9. Air in U.S. schoolrooms without asbestos	31	16.3	72.7	0.00054	0.00242	Constant et al., 1982
10. Air in Paris buildings with asbestos surfaces	135	1.8	32.2	0.00006	0.00107	Sebastien et al., 1980
11. Air in U.S. buildings with cementitious asbestos	28	7.9	19.1	0.00026	0.00064	Nicholson et al., 1975, 1976
12. Air in U.S. buildings with friable asbestos	54	19.2	96.2	0.00064	0.00321	Nicholson et al., 1975, 1976
13. Air in U.S. schoolrooms with asbestos surfaces	54	62.5	550	0.00208	0.01833	Constant et al., 1982
14. Air in U.S. schools with damaged asbestos surfacing materials	27	121.5	465	0.00405	0.01550	Nicholson et al., 1978

[a]Adapted from Nicholson, 1983.
[b]Based on conversion factor of 30 ug/m^3 = 1 fiber/cm^3.

(1) Lung Cancer

Most epidemiological studies (reviewed in Appendix II) of asbestos workers that have demonstrated an excess lung cancer risk associated with the inhalation of asbestos have produced results consistent not only with a linear relationship between cumulative dose and mortality, but also consistent with the absence of a threshold. In all of these studies, there appears to be a progressive and proportional increase in the SMR (standard mortality ratio) for lung cancer with increasing dose and no evidence of a threshold level. This evidence cannot be accepted without some qualification, however. All of the studies have the intractable difficulty of separating out the effects of cumulative dose from duration of exposure.

Persons exposed to asbestos nonoccupationally can be at increased risk of contracting these asbestos-associated cancers. In one of the first studies linking asbestos exposure and mesothelioma, the disease was found among residents of an asbestos mining area in South Africa. These subjects had presumably inhaled the material in the surrounding air.[42] In another study, persons living in households with asbestos factory workers in New Jersey were reported to be at increased risk of asbestos-associated disease.[43]

There is debate about the carcinogenic risk at low exposure levels of asbestos because lung cancer risks at low doses over a working lifetime have not been estimated to date by observation but rather by extrapolation from observed risks at higher exposure levels.[44] Accordingly, there is no direct evidence of the existence or absence of a threshold for lung cancer. It may arguably be the case that with further inquiry and better information the scientific community will be able to demonstrate that there is a dose level for asbestos for which the body's defense mechanisms are effective, or that asbestos acts differently at lower rather than higher doses, thus demonstrating a threshold level for the induction of cancer. At the present time, that information does not appear to exist. Since a threshold dose level for asbestos-related lung cancer has not been established, many investigators conclude that it is prudent to assume that there is none and that any dose may induce lung cancer.[45] A linear non-threshold model is less likely to underestimate the risk at low doses than any other plausible model.

(2) Malignant mesotheliomas are rare cancers that appear as thick, diffuse masses inside any of the serous membranes (mesothelia) that line body cavities. Epidemiologic research has shown that exposure to asbestos can produce mesothelioma at two sites: the pleura (the serous membrane that surrounds the lungs and lines the thorax) and the peritoneum (the serous membrane that surrounds the abdominal organs and lines the abdominal and pelvic cavities).

The status of pleural and peritoneal mesothelioma as marker diseases for asbestos exposure stems from the fact that these diseases seldom occur in people who have not been exposed to asbestos in excess of normal ambient levels.

The nature of the dose-response relationship for mesothelioma has been less firmly established than that for either lung cancer or asbestosis. Indeed, it has been suggested that very trivial doses of asbestos are capable of inducing the disease and that as a result there is no dose-response relationship for mesothelioma at all.[46] That mesothelioma is associated with low levels of exposure for brief periods of time appears to be based upon isolated anecdotal case reports and upon more systematic case-series reports of mesothelioma arising from non-occupational household or neighborhood exposures.[47,48] Newhouse et al.[48] reported nine cases of mesothelioma in family contacts of asbestos workers and eleven cases among individuals whose only identified asbestos exposure was associated with living within one-half mile of an asbestos factory. In these cases of non-occupational exposure, pleural mesotheliomas predominated over peritoneal mesothelioma. The evidence is not inconsistent with the existence of a dose-response relationship for mesothelioma. Although deaths from mesothelioma have been reported after what appear to have been brief (for gas mask workers) or low (for family contact and neighborhood cases) exposures, the Ontario Commission[49] concluded that the evidence suggests that the actual exposures approached or were equivalent to corresponding occupational exposures; it further agreed with the IARC[50] conclusion that there is no evidence of risk of mesothelioma to the general population.

There is a time interval between the initial exposure to asbestos and the clinical manifestation of the diseases it causes. The latency period for cancer is thought to be long; rarely less than 10 years and often more than 20 years. Mesothelioma appears to have the widest range of latency--again, they rarely occur less than 10 years from the time of first exposure to asbestos, but they can occur as many as 40 years or more from the onset of exposure.[51] It has been suggested that the death rates from mesothelioma appear to rise at an exponential rate from the time since first exposure; death rate appears to rise at a rate between the third and fourth power of time since first exposure;[52,54] other work suggests the fifth power of time.[55] What the data demonstrate is that the incidence of mesothelioma rises rapidly the longer the time period since a person is first exposed to asbestos. As a result, the age at which a person is first exposed to asbestos becomes a very significant factor in determining the overall risk of contacting mesothelioma.

While the mesothelioma incidence rates appear to be independent of the age at which exposure first took place, the practical result is that the risk of contacting mesothelioma is greater the earlier in life one is first exposed. (This is important to keep in mind when considering baby

powder exposure.) The magnitude of the risk will still depend on the amount and duration of exposure (and, possibly, fiber type); and where that exposure is minimal, the risk, albeit greater for exposures earlier rather than later in life, will also be minimal.

The disease rate of lung cancer among persons exposed to asbestos appears to be quite unlike that of mesothelioma. Rather than being time-dependent, lung cancer rates appear to be age-dependent.[56] The majority of lung cancer deaths, both in smokers and non-smokers, occur after age 50 and over half occur after age 60, irrespective of the time of first exposure. This suggests that the risk of contracting lung cancer is much greater in older groups than in younger groups. Asbestos exposure appears to have the effect of multiplying the risk of lung cancer that exists apart from that exposure; and the risk of lung cancer contributed to by asbestos exposure appears to be virtually independent of the age when that exposure took place and will be simply proportional to cumulative dose.

The consistency of an increased cancer risk at extrathoracic sites and its magnitude are less for cancer at other sites than for lung cancer. Nevertheless, many studies document significant cancer risks at various GI sites. Cancer of the kidney has also been found to be significantly elevated. Among female workers, ovarian cancer has been found in excess (Appendix I, #16). While no other specific sites have been shown to be elevated at the 0.05 level of significance, the category of "all cancers other than lung, GI tract, or mesothelial" is significantly elevated.

Several epidemiological investigations reported in the literature provide data on exposure levels of asbestos related to mortality and specific cause of death, while most do not provide exposure data. Those with relevant data are reviewed in Appendix I (see Summary table). In these investigations, different epidemiological approaches were used, various definitions of the study groups were adopted, observations took place over different periods of time, types of controls varied, time interval from first exposure was unknown, some workers exposed to more than one type of fiber, etc.

Several studies are briefly described below:

Mining and Milling

Chrysotile. Three cohorts occupationally exposed to chrysotile asbestos during mining and milling operations had a moderately increased risk for lung cancer (SMRs from 1.0 to 2.6). In the largest investigation, McDonald et al. (1980)[57] studied all employees who had worked for at least 1 month in Quebec mines. From 1950 to 1975, 3,291 deaths occurred among the 9,850 male employees successfully traced and followed for 20 years or more after initial employment. An increase in lung cancer

mortality was observed (SMR = 1.3, 230 observed vs. 184 expected), and the risk increased with duration of employment (SMR = 1.0 for < 1 year to 1.6 for ≥ 20 years) and level of exposure (SMR = 0.9 for < 30 mppcf(yr) to 2.3 for ≥ 300 mppcf(yr). Eleven cases of mesothelioma were observed.

Anthophyllite. Male and female employees of anthophyllite asbestos mines in Finland were studied by Meurman et al. (1974, 1979),[58,59] who reported a two-fold increase in lung cancer mortality (44 observed vs. 22.4 expected) and no mesotheliomas among the 1,045 persons successfully traced. All lung cancer deaths occurred among the male employees, and the risk was associated with estimated intensity of exposure (SMR = 1.4 vs. 3.3 for low and heavy exposures, respectively). Lung cancer risk among nonsmoking asbestos-exposed employees was 1.4 compared to a relative risk of 17.0 for the asbestos-exposed employees who smoked.

Crocidolite. For exposure associated with crocidolite mining in Western Australia, there was a similar increase in risk of lung cancer (SMR = 1.6, 60 observed vs. 38.2 expected) and a strong association with mesothelioma.[60] Twenty-six cases of pleural mesothelioma were observed among the 526 deaths, and the mesothelioma risk increased with increased duration and intensity of exposure. Follow-up period was relatively short.

No increases in gastrointestinal cancer were observed for any of the mining and milling cohorts reviewed.

Manufacturing

Chrysotile. Most asbestos exposures associated with manufacturing processes involve mixed fiber types, but Dement et al. (1982, 1983a,b)[9,61,62] examined the risks associated with exposure to chrysotile asbestos in textile factory workers. They observed a marked increase in lung cancer mortality (SMR = 3.2, 35 observed/11.1 expected), and the risk was strongly correlated with exposure level. There was also one peritoneal mesothelioma. Increased risks for both lung cancer and nonmalignant respiratory disease were observed at exposure levels lower than those reported in other studies.

Amosite. Mortality due to lung cancer was increased three- to four-fold (83 observed /22.8 expected) for 820 factory workers exposed to amosite asbestos.[63] The higher risks were observed for the subgroup followed 20 years or longer after initial employment (SMR = 5.1, 52 observed/10.1 expected). This cohort is a somewhat unusual population because of its limited duration of intense work exposure (1941-1945) and long period of observation. Other excess cancers, including 14 mesotheliomas, were also reported.

Mixed. Newhouse and Berry (1979)[64] reported increased risks of lung cancer mortality for both males (SMR = 2.4, 103 observed/43.2 expected) and females (SMR = 8.4, 27 observed/3.2 expected) in a follow-up study of 4,600 male and 922 female employees of an East London asbestos factory in which crocidolite and amosite were used. Approximately 10% of all deaths resulted either from pleural or peritoneal mesothelioma.

Except for 10 cases of mesothelioma, no increased cancer mortality was observed among more than 11,000 males and females employed during 1941 or later at a British factory producing friction materials.[65,66] In a case-control study that corrected for total asbestos exposure, 5 of 6 cases had definitely worked with crocidolite, whereas 2 of 10 controls had.

A cohort of 1,345 retired asbestos products workers employed from 1941 to 1967 had increased risks for lung cancer (SMR = 2.7, 63 observed/23.3 expected) and gastrointestinal cancer mortality (SMR = 1.4, 55 observed/39.3 expected).[67] Overall mortality among the 1,075 retirees successfully traced to 1973 was 73%. The lung cancer risk was strongly associated with the amount of exposure, expressed as million particles per cubic foot multiplied by number of years of exposure (mppcf-yr), ranging from a SMR of 2.0 up to 7.8. Lung cancer risk differed by type of asbestos exposure (SMR of 2.5 for chrysotile alone vs. 5.2 for mixed chrysotile and crocidolite exposures). Five mesothelioma deaths were observed. Study results suggest that effects of asbestos exposure on lung cancer risk may continue long after the termination of exposure. Studies of a retiree cohort may result in an underestimation of actual risks, since deaths among employees under age 65 would be omitted. The Consumer Product Safety Commission (1983)[68] suggests that the risks may be understated by as much as two-fold.

No increase in lung cancer mortality or cancer of any other site, except mesothelioma, was observed in the cohort of 5,645 employees of an asbestos-cement product manufacturing facility studied by Hughes and Weill (1980).[69] In the high exposure subgroup, lung cancer risk was increased for employees exposed to crocidolite, and two mesothelioma deaths were reported. The low overall mortality, 10.6%, and the low tracing rate, approximately 75%, suggest that this study may have resulted in an underestimate of mortality risks.

Finkelstein (1983)[70] studied 328 asbestos-cement workers hired before 1960 and employed for a minimum of 9 years. Mesothelioma was strongly associated with exposure level for production workers, whereas a dose-response relationship was not observed for lung cancer. Excess lung and gastrointestinal cancers were observed.

Clemmesen and Hjalgrim-Jenson (1981)[71] studied cancer incidence among 6,372 Danish males who worked in asbestos-cement factories between 1944 and 1976. There were 55 cases of respiratory cancer compared to 33

expected, based on Danish Cancer Registry incidence rates. Three mesotheliomas were observed in addition to excess prostate, laryngeal, and stomach cancers. Cancer incidence in the unexposed employees at the same factories was not increased.

Jones et al. (1980b)[72] studied a cohort of 578 females exposed to crocidolite from western Australia during the manufacture of gas masks. The 12 cases of lung cancer (SMR = 1.9, 12 observed/6.3 expected) and the 17 mesothelioma cases (13 pleural and 4 peritoneal) were all exposed to crocidolite, whereas no cases of mesothelioma or lung cancer occurred among the 102 females exposed only to chrysotile. Overall, 10% of deaths were due to mesothelioma. Risk of mesthelioma was strongly associated with duration of exposure, although no dose-response relationship was observed for lung cancer.

Similar results were reported among 1,304 females who manufactured gas masks at three locations followed from 1951 to June 30, 1980.[8] Deaths from lung cancer (SMR = 2.0, 22 observed/11 expected) and ovarian cancer (SMR = 2.2, 17 observed/7.8 expected) were increased. Lung cancer excess was higher for those exposed predominantly to crocidolite compared to those exposed predominantly to chrysotile. Five of the six mesotheliomas occurred in those exposed predominantly to crocidolite.

All studies of occupational cohorts exposed to asbestos during manufacturing processes had an overall increased risk of lung cancer or a dose-response relationship in the exposure subgroups.[69,77] Elevated risk ratios (1.1) for gastrointestinal cancer were observed in six of the nine cohorts reviewed.[62,63,65,67,70,71]

Insulation

Mixed. All three of the cohorts involved in end product use of asbestos as insulators were exposed to mixed types of asbestos. One of the largest studies is that of Selikoff et al. (1979),[74] who studied 17,800 members of an insulator's union. Overall mortality in this cohort was 12.8%; 2,271 deaths were reported through 1976. Lung cancer risk was increased four-fold (429 observed/105.6 expected) and increases were observed for gastrointestinal cancer (SMR = 1.6, 94 observed/59.4 expected), cancer of the larynx, pharynx, buccal cavity (SMR = 1.7, 25 observed/14.8 expected), and kidney (SMR = 2.2, 18 observed/8.1 expected). Dose-response relationships were not examined because of the lack of exposure data. Mesotheliomas (63 pleural and 112 peritoneal) accounted for 7.7% of the deaths. Analysis of the relationship between smoking and lung cancer risk using data from the American Cancer Society indicated a consistent multiplicative effect, in that a 10-fold increase in risk of lung cancer was associated with smoking in both asbestos-exposed and unexposed groups. A five-fold increase in lung cancer risk was associated with asbestos exposure in both smokers and nonsmokers.[10]

Elmes and Simpson (1977)[75] reported an unusually high risk of lung cancer (SMR = 7.0, 35 observed/5 expected) and gastrointestinal cancer (SMR = 5.9, 13 observed/2.2 expected) for a cohort of 162 insulators and pipe coverers employed in Northern Ireland during 1940. Overall mortality in this cohort was 75.3% by 1975; 54% of the deaths were due to cancer. Thirteen cases of mesothelioma (eight pleural and five peritoneal) were reported. No difference in cancer risk was apparent for workers first employed before or after 1933. Ascertainment bias is unlikely to explain the magnitude of the risks reported for this cohort.

Shipyards

Mixed exposures. Rossiter and Coles (1980)[76] studied 6,076 dockyard workers employed before 1947. They reported no increase in lung cancer mortality (SMR = 0.7, 84 observed/119.7 expected) or gastrointestinal cancer (SMR = 0.8, 63 observed/83.3 expected). Mesothelioma was reported for 31 (3%) of the 1,043 deaths. However, since less than 20% of this cohort have died, excess cancers may not be fully apparent.

In a study of 2,190 Italian dockworkers, Puntoni et al. (1979)[77] observed increased risks for lung cancer (SMR = 2.2, 123 observed/54.9 expected), gastrointestinal cancer (SMR = 1.3, 74 observed/58.6 expected), laryngeal cancer (SMR = 1.9, 15 observed/7.7 expected), and kidney cancer (SMR = 2.0, 29 observed/14.7 expected).

EXPOSURE

Talc

Values between 800,000 and 960,000 tons have been reported as the amount of talc used commercially in the U.S. each year.[78,79] Talc is used in a number of industries, for a variety of purposes; e.g., the manufacture of ceramics, paints, paper, rubber, roofing, insecticides, stucco, plastics, textiles, and soaps. Pulverized talc is also used as an ingredient in such consumer products as cosmetic talcums, paper mache, and modeling compounds, in spackling, patching compounds and putties, in automotive and boat body repair fillers, and caulking compounds. The uses of talc in food products include rice coating, peanut polishing, candy molding, and salami dusting. It is also used as a filler and excipient for pharmaceutical pills, and for dusting contraceptive diaphragms. Each product carries with it a distinct and individual inhalation and/or ingestion potential of the mineral components. An estimated 30,000 tons of cosmetic-grade talc are used in cosmetic, pharmaceutical, and food products.[80]

Talc Contamination

The table below shows the principal minerals that can be combined with talc in natural deposits.[89-91]

MINERALS COMMONLY ASSOCIATED
WITH TALC IN NATURAL DEPOSITS

Carbonates:	calcite, dolomite, magnesite
Amphiboles:	tremolite, anthophyllite
Serpentines:	chrysotile, antigorite, lizardite
Others:	quartz, mica, chlorite, rutile, pyrophyllite

A 1968 study conducted by United States researchers[92] on 22 talc samples for cosmetic use showed values between 8 and 39% fibrous particles, whereas a similar study on 80 industrial talc samples conducted by N.B.S. researchers[93] indicated the presence of fibrous particles in the samples in percentages which vary from 2 to 30%. In both cases the fraction of these percentages made up of asbestos was not specified. Research conducted in Great Britain[94] on talc powders for various uses has shown that of the 27 samples examined, 3 contained tremolite. More complete and significant data are indicated for 20 talcs for cosmetic use and one talc for pharmaceutical use sampled in the New York area from 1971 to 1975: of the cosmetic products analyzed, 10 contained tremolite and anthophyllite in amounts varying from 0.1 to 14 wt.%, and showed a detectable quantity of chrysotile. (This is in conflict with Pooley who stated that no chrysotile has been found in cosmetic talc.) In an Italian article published in 1982[96], 15 samples of talc products (for industrial, cosmetic, and pharmaceutical uses) were analyzed for asbestos contamination using transmission electron microscopy and the associated analytical techniques such as electron diffraction and x-ray microanalysis. In eight of the 15 samples, the presence of asbestos was detected; in seven cases tremolite fibers were observed and in one case, chrysotile (see Table 9).

TABLE 9. PERCENTAGE OF FIBROUS PARTICLES AND ASBESTOS FIBERS IN SOME COSMETIC TALCS.

KEY: (a) % fiber in the particular matter
(b) % fiber 5 um in the particular matter
(c) % asbestos fiber in the total fiber
(d) % asbestos fiber in the particular matter, and
(e) variety of asbestos

	(a)	(b)	(c)	(d)	(e)
A	6.1±0.9	1.6±0.5	<2	<0.1	--
B	21.6±1.6	5.0±0.9	<2	<0.4	--
C	11.1±1.1	3.2±0.6	<2	<0.2	--
D	4.9±0.5	0.7±0.2	32±4.7	1.6±0.3	Tremolite
E	10.3±0.7	3.2±0.4	<2	<0.2	--
F	5.1±0.6	1.8±0.4	10±3	0.5±0.2	Tremolite

Consumer talc products marketed before 1973 were variably contaminated by asbestos. In October, 1976, the Cosmetic, Toiletry, and Fragrance Association (CTFA)[97] revised their guidelines for talc and recommended that no sample containing asbestos detectable by x-ray diffraction and optical microscopy with dispersion staining should be sold. Adherence to the revised CTFA guidelines is voluntary and monitoring of samples is left to individual manufacturers.

Samples of cosmetic talc products were analyzed in 1979 by the Division of Cosmetics Technology using x-ray diffraction (XRD). Samples found to be contaminated with tremolite or anthophyllite by XRD were also examined by optical microscopy (OM) to determine crystal morphology. In all cases, the amphiboles found (tremolite and anthophyllite) were present in the massive (non-fibrous) form. The level of detectability is approximately 0.1% for tremolite and 2% for anthophyllite. None of the samples was found to contain serpentine at a detectability limit of 1-2% (XRD). These samples were submitted for SEM analysis and, if fibers were found, the samples were to be examined by energy dispersive x-ray analysis (EDXA) to determine the nature of any fiber-like particle detected. The results of the latter (SEM and EDXA) analyses are not known to this reviewer. No analyses of cosmetic talc have been performed by FDA since 1979. As noted previously, there are non-fibrous forms of minerals with essentially the same chemical composition as the asbestos varieties. In some cases the non-fibrous form has the same name as its fibrous counterpart; e.g., tremolite. According to the U.S. Department of the Interior, non-fibrous (non-asbestiform) tremolite is the common form of this mineral, while fibrous tremolite (asbestiform) is a very rare form for this mineral.[7]

Asbestos

As stated above, asbestos bodies can be recovered from the lungs of virtually everyone in the population, on autopsy. These observations suggest that the entire population is being exposed to asbestos.

Several studies have assessed the environmental air pollution by asbestos using the transmission electron microscope (TEM) or the scanning electron microscope (SEM). European cities have shown levels as follows: 0.1-1 ng (10^{-9} gm^{-3} or ng^{-3}) of chrysotile asbestos in English cities, 10^{-2}-10^{4} asbestos fibers per cubic meter of air in Dusseldorf,[R] and 0.1-10 ng^{-3} of chrysotile asbestos in Paris. Higher concentrations (0.1-100 ng^{-3} of chrysotile asbestos) have been found in U.S. cities. The highest concentrations have been found in New York City (see Table 7-6).

Asbestos fibers have been detected in rural locations (0.01-0.1 ng m^{-3}) removed from known sources of emission suggesting the existence of background air pollution by asbestos fibers (especially chrysotile) in industrial countries.

It is to be noted that an appreciation of the extent of air contamination by asbestos depends upon which of two approaches to its measurement is adopted. If the conventional practice of counting only fibers longer than 5 um is followed, the concentrations away from immediate industrial activities are low or undetectable and even some of those in and around asbestos industries approach tolerable levels. But, if the concentration of smaller fibers is taken into account and particularly the mass concentrations revealed by electron microscopy, the situation changes. Up to 10 ng/m^3 seems to be virtually ubiquitous in urban communities.

It is to be noted also that analysis of ambient air samples for asbestos has utilized techniques different from those used in occupational circumstances because typical urban air may contain up to 100 ug/m^3 of particulate matter in which one is attempting to quantify asbestos concentrations from about 0.1 ng/m^3 to perhaps 1000 ng/m^3. Thus asbestos may constitute only 0.0001 to 1% of the particulate matter in a given sample.

It is difficult to make quantitative estimates of exposure to asbestos. A common unit of cumulative dose for occupational exposures is obtained by multiplying the average concentration of fibers in workplace air by the number of years that an individual worked there (full-time equivalent). The concentration of fibers in workplace air is expressed as fibers > 5 μm long/cm^3, as counted by the light microscope (LM) under specified conditions ((U.S. National Institute for Occupational Safety and Health, 1977); (fibers/cm^3) yr. It is to be noted that cumulative exposure measures do not take into account dose rate per unit time,

duration of exposure, and ages at exposure. These three factors, particularly the third one, could be very important in determining effects on health.

Another measure of exposure that allows comparison of different exposure situations is expressed as "lifetime fibers." This quantity is derived by integrating over time the product of fiber concentration in air (the only source of exposure considered here) and the intake rate.

When interpreting health-effects information obtained from occupational studies, it may be necessary to convert nonoccupational exposures to equivalent occupational dose expressed in (fibers/cm^3) yr. Assuming an inhalation rate of 12000ml/minute; an 8-hour work day; 5 days/week; 50 weeks/year, the amounts of inhaled fibers workers could accumulate in one year, according to work group, are shown below.

worker group	exposure level	duration	exposure per year	total life-time exposure
insulation workers (amosite, chrysotile)	15 f/ml	25 yrs	2.16×10^{10} f/yr	5.4×10^{11} f
British textile workers (chrysotile)	15-30 f/ml	20 yrs	$2.16\text{-}4.32 \times 10^{10}$ f/yr	$4.32\text{-}8.64 \times 10^{11}$ f
amosite factory workers	35 f/ml	1.46 yrs	5.04×10^{10} f/yr	7.36×10^{10} f
cement workers (chrysotile, crocidolite)	9 f/ml	12 yrs	1.296×10^{10} f/yr	1.56×10^{11} f

Similar calculations for the general population are shown below:

If ambient air concentrations are assumed to be 10 ng/m^3, using the EPA conversion factor of 30 fibers (f)/ng, the population as a whole is exposed to 3×10^{-4} f/ml. Using the further assumptions:

(1) average breathing rate - 12.72 liters/min.
(2) 24 hours per day, and
(3) 52 weeks per year as the exposure duration;

It is calculated that an individual is exposed to 2.0×10^6 f/year.

Using the assumptions and the data generated in the baby-powdering experiment[114] (concentration - 8.58 f/cc during powdering; 4.38 f/cc during settling; with 13.6% and 86.4%, respectively, of the time - with exposure time of 43.8 minutes per week; breathing rate of 05.8 1/min.), exposure of a baby from baby powder could be 6.6×10^6 f/year. It is to be noted that these calculations assume that all of the talc is asbestos. If a more realistic value of 1% asbestos is used, the number of fibers is calculated to be 6.6×10^4 f/yr.

The carcinogenic potential and the hazards of exposure to asbestos have been well documented. Also, several types of asbestos are known to be geological contaminants in talc ore. Since the accepted best index of exposure to asbestos requires counting the respirable fibers in the worker's breathing zone, a problem arises in the methodology of distinguishing asbestos fibers from talc. Characteristically, talc has a tendency to curl and stand on its edge, which may result in many erroneous counts by optical microscopy.[98]

The latest USPHS/NIOSH method for counting asbestos fibers requires phase contrast microscopy at X400-500 magnification, and arbitrarily defines a fiber as a particulate with a length to width ratio of 3:1 or greater, and a maximum width and minimum length of 5 micrometers.[99] This method is a crude determination of total fiber exposure because of the resolution limitations of optical microscopy. Most airborne asbestos fibers are less than 5 um in length, and those that are longer may have diameters too small to be resolved by phase contrast microscopy. With regard to the measurement of asbestos exposure from talc, some authors have stated that scanning electron microscopy (SEM) should be considered as an adjunct to the USPHS/NIOSH method when counting fibers in a dust environment. Phase contrast microscopy may suffice in an asbestos environment, but the resolution limitations of optical microscopy and the inability to distinguish rolled talc particles and talc "shards" from actual asbestos fibers will allow only a crude determination of the total fiber exposure.

Other than what was presented above, it is not known whether cosmetic talc (used today) is contaminated with asbestos or asbestiform minerals, what form is involved (tremolite-fibrous or nonfibrous), or what levels of asbestos, if contaminated.

In a recent (August, 1984) report[100] by the NAS Committee on Nonoccupational Health Risks of Asbestiform Fibers, who evaluated the human health risks associated with nonoccupational exposure to asbestiform fibers with emphasis on inhalation of outdoor and indoor air, it was concluded that nonoccupational exposure to asbestiform fibers in air presents a risk to human health. The Committee made a quantitative estimate of the risk of excess lung cancer and mesothelioma that might occur in persons breathing low levels of asbestos in the air. A concentration of 0.0004 fibers/cm^3 was deemed reasonable to use in

such calculations because a variety of measurements of indoor and outdoor air indicated that 0.0004 f/cm^3 is the approximate average level that may be encountered. If a person inhaled air containing asbestos at that level throughout a 73-year lifetime, the committee's best judgement is that the lifetime risk of mesothelioma would be approximately nine in a million (range 0 to 350 per million, depending on assumptions regarding the relationship of dose to risk). Risks for continuous lifetime exposures to higher or lower levels would be proportionately higher or lower. Epidemiological data and the estimates derived from them indicate that the corresponding lifetime risk for lung cancer would be about 64 in a million for male smokers (range 0 to 290), 23 in a million for female smokers (0 to 110), and 6 and 3 in a million, respectively, for male and female nonsmokers. The risk to nonsmokers appears greater for mesothelioma than for lung cancer. The Committee also emphasized the strong dependence of mesothelioma rates on time from first exposure and exposure of children to asbestos (although mainly from school exposure). (See NAS Risk Assessment - Attachment III.)

The only information available on cosmetic exposure is that of baby powder use noted above. Infants exposed to asbestos from talc could be exposed to an additional amount above background of the order of 0.04 to 0.08 f/cc for approximately 2 years. This would result in an increase of 0.05% in the cumulative lifetime exposure of 1.95×10^8f to 1.951×10^8f, with a similar increase in the lifetime risk (e.g., 9 to 9.0045 mesotheliomas per million). However this estimate is based on a linear dose response function, assuming no dose-rate effect. Cumulative exposure measures do not take into account dose rate, duration of exposure, or age at exposure. Although the cumulative amount of asbestos would appear to be of no consequence, the estimated exposure level is 100 to 200 times greater than background. Data on acute exposures of this magnitude are not available.

This memo is to request a risk assessment of the potential exposure to asbestos from use of cosmetic talc.

Linda L. Taylor, Ph.D.

APPENDIX I

Epidemiological Studies on Asbestos

1. In a follow-up study[57] of a birth cohort consisting of 10,939 men and 440 women (exposed for at least one month), dust exposure and mortality of chrysotile miners were analyzed using the "man-years" method and the "case- and multiple-control" approach.

Among men the overall excess mortality was 2% at Asbestos and 10% at Thetford Mines, which was the dustier region (see Table 2). The women, mostly employed at Asbestos, had a standardized mortality ratio (SMR) of 0.90. During the five decades, 1926-75, 4350 men died compared with 4107 expected on the basis of Quebec age- and year-specific death rates, a SMR of 1.06. There had been a net excess of 33.9 deaths at Asbestos (1.6% of the 2074.1 expected) and 208.8 at Thetford Mines (10.3% of the 2033.2 expected); SMRs of 1.02 and 1.10, respectively. Table 2 provides data on deaths of the men by age and cause of death.

Four exposure levels were used in these analyses; the mean concentrations were: low: 2.5 to 4.2; medium: 4.3 to 9.4; high: 14.4 to 23.6; very high: 46.8 to 82.6 million particles per cubic foot (mppcf). Quantitative exposure was estimated as cumulative dust exposure during the first 20 years from onset of employment. Tables 6 and 7 analyze the 3291 deaths, 20 or more years after first employment, occurring from 1951 to 1975. Comparison with Table 2 shows that, although 26.3% of all observed deaths were thus excluded from the analysis because they occurred before 1951 or within 20 years of first employment, over 90% of deaths from pneumoconiosis and from lung cancer were included, and percentages were also high for malignant neoplasms of other sites (except the larynx) and stroke.

When account is taken only of length of service (Table 6), trends of risk, as measured by the ratios of observed to expected deaths--that is, SMRs in which the standardization was by both age and era--were generally without clear trends, probably reflecting differences in selection and other factors. Exceptions were deaths attributed to pneumoconiosis and accidents: of the 42 deaths from pneumoconiosis, 36 were in men with at least 20 years' service.

TABLE 2. Deaths of [redacted], by year, age, and certified cause of death

Cause of death (ICD code*)	Age at death	Year of death					
		Before 1946	1946-55	1956-65	1966-75	Total	
All causes	<45	564	136	54	--	754	4463
	45-64	111	438	842	702	2093	
	≥65	--	--	389	1227	1616	
Pneumoconiosis (523-524)	<45	0	0	1	--	1	46
	45-64	1	6	10	13	30	
	≥65	--	--	7	8	15	
Malignant neoplasms: Lung (162-164)	<45	2	2	2	--	6	250
	45-64	0	12	51	72	135	
	≥65	--	--	20	89	109	
Oesophagus and stomach (150-151)	<45	5	2	1	--	8	154
	45-64	4	22	34	17	77	
	≥65	--	--	12	57	69	
Colon and rectum (152-154)	<45	4	1	0	--	5	88
	45-64	1	8	20	18	47	
	≥65	--	--	6	30	36	
Other abdominal (155-159)	<45	5	2	1	--	8	80
	45-64	1	6	15	14	36	
	≥65	--	--	6	30	36	
Larynx (161)	<45	0	0	0	--	0	23
	45-64	2	5	6	5	18	
	≥65	--	--	1	2	3	

Other (140-148; 160; 165-205)	45	12	4	1	--	17	276
	45-64	2	28	52	48	130	
	65	--	--	28	101	129	
Heart disease (400-443)	45	28	25	18	--	71	1543
	45-64	25	154	355	285	819	
	65	--	--	166	487	653	
Respiratory tuberculosis (001-008)	45	118	30	1	--	149	248
	45-64	20	31	27	7	85	
	65	--	--	5	9	14	
Other respiratory (470-522; 525-527)	45	60	3	0	--	63	234
	45-64	5	12	28	37	82	
	65	--	--	17	72	89	
Cerebrovascular (330-334)	45	6	2	3	--	11	268
	45-64	4	12	42	38	96	
	65	--	--	39	122	161	
Accidents (800-999)	45	170	41	17	--	228	461
	45-64	18	44	71	51	184	
	65	--	--	9	40	49	
All other known causes	45	114	23	9	--	146	669
	45-64	25	82	112	82	301	
	65	--	--	67	155	222	
Cause not known	45	40	1	0	--	41	125
	45-64	3	16	19	15	53	
	65	--	--	6	25	31	

*Code in the 7th revision of the International Classification of Diseases

TABLE 6. Deaths, by cause, in relation to duration of service

Cause of death (see table 2)	Length of gross service (yr)									
	Very short (1)		Short (1 5)		Medium (5- 20)		Long (20)		Complete cohort	
	0	SMR	0	SMR	0	SMR	0	SMR	0	SMR
All causes	885	1.07	629	1.09	679	1.15	1098	1.07	3291	1.09
Pneumoconiosis	1	1.15	3	5.00	2	3.39	36	34.62	42	13.55
Malignant neoplasms:										
Lung	47	0.97	29	0.83	50	1.37	104	1.61	230	1.25
Oesophagus and stomach	37	1.30	25	1.27	18	0.91	50	1.47	130	1.27
Colon and rectum	22	0.78	13	0.67	23	1.16	21	0.62	79	0.78
Other abdominal	20	1.98	12	0.92	14	1.04	21	0.90	67	0.98
Larynx	6	1.48	5	1.75	1	0.34	4	0.78	16	1.07
Other	67	1.12	43	1.04	48	1.13	79	1.08	237	1.09
Heart disease	370	1.06	251	1.02	287	1.15	424	0.97	1332	1.04
Respiratory tuberculosis	7	0.62	7	0.89	21	2.68	22	1.56	57	1.39
Other respiratory	29	0.66	46	1.52	22	0.71	59	1.12	156	0.99
Cerebrovascular	62	0.95	49	1.12	50	1.13	82	1.11	243	1.07
Accidents	52	1.36	38	1.32	37	1.18	56	0.96	183	1.17
All other known causes	130	1.03	94	1.07	94	1.05	132	0.85	450	0.98
Cause not known	35	--	14	--	12	--	8	--	69	--

Columns headed 0 give the numbers of deaths of men, 20 years or more after first employment, occurring during 1951-75; figures under headings SMR are ratios of deaths observed to those expected on basis of male mortality in Quebec.

TABLE 7. Deaths, by cause, in relation to dust concentration

(a) Gross service: less than one year

Cause of death (see table 2)	Accumulated dust exposure (see table 4)							
	Low		Medium		High		Very high	
	0	SMR	0	SMR	0	SMR	0	SMR
All causes	311	1.12	260	1.13	162	0.95	152	1.03
Pneumoconiosis	0	0	0	0	1	5.66	0	0
Malignant neoplasms:								
Lung	19	1.17	12	0.91	9	0.88	7	0.80
Oesophagus and stomach	12	1.24	12	1.50	9	1.54	4	0.81
Colon and rectum	5	0.52	7	0.88	6	1.03	4	0.81
Other abdominal	3	0.48	6	1.17	4	1.04	7	2.12
Larynx	2	1.45	2	1.77	1	1.19	1	1.40
Other	20	0.99	23	1.38	13	1.05	11	1.04
Heart disease	136	1.15	112	1.15	63	0.87	59	0.94
Respiratory tuberculosis	4	1.05	1	0.32	1	0.44	1	0.48
Other respiratory	11	0.74	10	0.82	3	0.33	5	0.66
Cerebrovascular	25	1.14	18	0.98	9	0.67	10	0.90
Accidents	16	1.30	19	1.86	10	1.27	7	0.90
All other known causes	45	1.06	29	0.82	26	1.00	30	1.33
Cause not known	13	--	9	--	7	--	6	--

See footnote to table 6

7(b) Gross service: one year, less than five years

Cause of death (see table 2)	Accumulated dust exposure (see table 4)							
	Low		Medium		High		Very high	
	O	SMR	O	SMR	O	SMR	O	SMR
All causes	141	1.12	246	1.09	130	1.12	112	1.04
Pneumoconiosis	0	0	3	12.80	0	0	0	0
Malignant neoplasms:								
Lung	5	0.66	13	0.95	6	0.82	5	0.78
Oesophagus and stomach	8	1.83	7	0.90	4	1.03	6	1.64
Colon and rectum	2	0.46	4	0.52	4	1.04	3	0.82
Other abdominal	2	0.70	7	1.37	2	0.75	1	0.41
Larynx	2	3.17	1	0.89	1	1.71	1	1.90
Other	14	1.53	16	0.98	9	1.08	4	0.52
Heart disease	51	0.95	99	1.03	59	1.19	42	0.92
Respiratory tuberculosis	0	0	5	1.64	1	0.61	1	0.65
Other respiratory	10	1.49	16	1.34	10	1.66	10	1.78
Cerebrovascular	18	1.83	17	0.98	10	1.19	4	0.49
Accidents	11	1.89	12	1.10	3	0.47	12	2.14
All other known causes	16	0.83	40	1.16	16	0.91	22	1.33
Cause not known	2	--	6	--	5	--	1	--

See footnote to table 6

7(c) Gross service: five years, less than 20 years

Cause of death (see table 2)	Accumulated dust exposure (see table 4)							
	Low		Medium		High		Very high	
	0	SMR	0	SMR	0	SMR	0	SMR
All causes	161	1.10	194	1.07	170	1.22	154	1.26
Pneumoconiosis	0	0	0	0	1	7.36	1	8.42
Malignant neoplasma:								
Lung	13	1.41	14	1.22	7	0.83	16	2.17
Oesophagus and stomach	6	1.21	6	0.99	5	1.07	1	0.25
Colon and rectum	4	0.81	7	1.14	9	1.92	3	0.74
Other abdominal	6	1.78	3	0.72	3	0.95	2	0.75
Larynx	0	0	0	0	1	1.44	0	0
Other	9	0.85	19	1.44	11	1.10	9	1.03
Heart disease	66	1.06	81	1.05	72	1.22	68	1.31
Respiratory tuberculosis	3	1.55	9	3.94	5	2.64	4	2.28
Other respiratory	5	0.64	5	0.51	5	0.69	7	1.12
Cerebrovascular	8	0.73	13	0.94	14	1.34	15	1.67
Accidents	8	1.07	10	1.06	10	1.33	9	1.28
All other known causes	29	1.30	21	0.77	25	1.17	19	1.01
Cause not known	4	--	6	--	2	--	0	--

See footnote to table 6

7(d) Gross service: 20 or more years

Cause of death (see table 2)	Accumulated dust exposure (see table 4)							
	Low		Medium		High		Very high	
	0	SMR	0	SMR	0	SMR	0	SMR
All causes	367	0.98	253	0.89	183	1.07	295	1.50
Pneumoconiosis	4	10.49	7	23.75	5	30.10	20	101.52
Malignant neoplasms:								
Lung	28	1.21	20	1.08	24	2.20	32	2.65
Oesophagus and stomach	17	1.36	6	0.64	8	1.44	19	2.89
Colon and rectum	7	0.56	4	0.43	1	0.18	9	1.39
Other abdominal	10	1.18	3	0.46	2	0.51	6	1.35
Larynx	2	1.07	1	0.69	0	0	1	1.03
Other	33	1.23	16	0.79	11	0.90	19	1.36
Heart disease	138	0.87	115	0.95	77	1.06	94	1.12
Respiratory tuberculosis	5	1.01	5	1.31	3	1.27	9	3.06
Other respiratory	18	0.92	10	0.68	14	1.62	17	1.74
Cerebrovascular	32	1.15	18	0.89	10	0.84	22	1.58
Accidents	16	0.82	19	1.16	9	0.85	12	1.01
All other known causes	52	0.92	29	0.68	18	0.70	33	1.10
Cause not known	5	--	0	--	1	--	2	--

See footnote to table 6

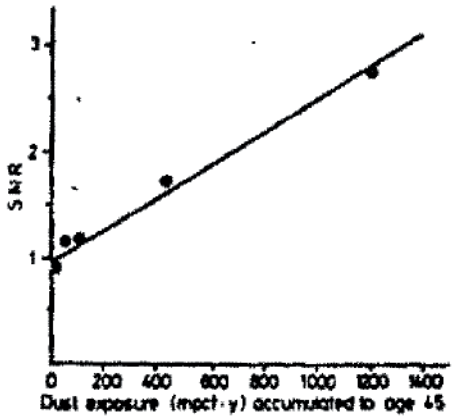
Among those in the very short and short service groups (those with gross service of less than 5 years (Tables 7(a) and (b)), careful study of differences between groups according to severity of exposure showed no consistent pattern. Table 7(c) deals with men with gross service between 5 and 20 years; their service had also been completed before the start of the study interval. There were fairly consistent trends for higher SMRs the greater the dust exposure for total mortality, for pneumoconiosis (although based on only 2 deaths), heart disease, and stroke. In addition SMRs were highest in the group with the most severe exposure, for lung cancer and "other" respiratory diseases. The authors stated that all these findings are understandable as pulmonary fibrosis could well contribute directly to cardio-pulmonary disease and, in addition, might adversely affect the probability of survival in any life-threatening condition. Table 7(d) concerns 3105 men with at least 20 years service, and an average of almost 32 years of employment. Here the most severely exposed had the highest SMR not only for total mortality but for all listed causes other than laryngeal cancer and accidents. Further, the tendency for increased risk with each augmentation in exposure was completely consistent for pneumoconiosis and for heart disease, and positive, although rather less consistent, for total mortality, lung cancer, respiratory tuberculosis, and other respiratory diseases.
The other form of a priori analysis, with exposure calculated to age 45 at which age the study interval started, is summarized in Table 8. The total number of deaths observed in this analysis was 3448 (77.3% of the deaths), with SMR = 1.07, very close to that for all causes in the complete cohort as seen in Table 6. Indeed, for each cause of death, SMRs from both methods of analysis were always close. Clear trends were found for SMRs to be higher the heavier the exposure, for total mortality, pneumoconiosis, lung cancer, cancer of the colon and rectum, respiratory tuberculosis, other respiratory diseases and stroke. The trends were most clear-cut in pneumoconiosis and lung cancer. The lung cancer trend was essentially linear as shown in the Figure below, where exposures of 30 mppcf-year or more have been broken down further, into 4 classes. The trend for respiratory tuberculosis was also consistent in the two areas, but not those for the other causes listed.

Dust exposure and mortality in chrysotile mining, 1910-75

TABLE 8. Deaths, by cause, in relation to dust exposure accumulated to age 45

Cause of death (see table 2)	Dust exposure (mpcf-y) accumulated to age 45					
	< 30		30 < 300		≥ 300	
	0	SMR	0	SMR	0	SMR
All causes	1668	1.02	1138	1.04	642	1.30
Pneumoconiosis	5	2.98	12	10.81	27	54.00
Malignant neoplasms:						
Lung	91	0.93	81	1.18	70	2.25
Oesophagus and stomach	68	1.22	42	1.14	26	1.58
Colon and rectum	34	0.62	28	0.77	18	1.11
Other abdominal	37	1.00	21	0.84	10	0.88
Larynx	9	1.11	6	1.08	2	0.81
Other	129	1.10	83	1.06	38	1.08
Heart disease	696	1.06	463	0.99	240	1.14
Respiratory tuberculosis	21	0.94	25	1.67	15	2.20
Other respiratory	71	0.84	55	0.98	40	1.62
Cerebrovascular	119	0.96	86	1.08	46	1.32
Accidents	104	1.28	60	1.00	33	1.16
All other known causes	237	0.95	154	0.92	74	0.99
Cause not known	47	--	22	--	3	--

See footnote to table 6



Lung cancer SMRs in relation to dust exposure accumulated to age 45. The line has been fitted by a modified least-squares technique.

Table 9 shows deaths from lung cancer.

TABLE 9. Deaths from lung cancer in relation to dust exposure and smoking habit

Smoking habit	Dust exposure (mpcf.y) accumulated to age 45							
	< 30		30 < 300		≥ 300		All	
	0	SMR	0	SMR	0	SMR	0	SMR
Non-smokers	5	0.18	6	0.36	8	1.24	19	0.38
Moderate smokers	73	1.14	64	1.35	52	2.31	189	1.41
Heavy smokers	13	2.12	11	2.39	10	4.50	34	2.63
All smoking habits	91	0.93	81	1.18	70	2.25	242	1.23

See footnote to table 6

Table 10 summarizes the findings from the Miettinen approach--that is, more than one control for each case, excluding those for smoking habit; the

TABLE 10: Dust exposure in deaths from pneumoconiosis and from malignant disease and in controls numbers of deaths areas table 2 (but see

	Dust exposure (mpcf.y) accumulated up to nine years before death of case				
	30	30 300	300 1000	1000	All
Pneumoconiosis					
Deaths	7	9	13	17	46
Controls(3)*	63	49	21	5	138
Relative Risk+	1	1.65	5.57	30.60	--
Lung cancer					
Deaths**	89	73	56	27	245
Controls(3)	333	243	127	32	735
Relative risk	1	1.12	1.65	3.16	--
Cancer of oesophagus and stomach					
Deaths	74	41	22	17	154
Controls(2)	143	105	53	7	308
Relative risk	1	0.75	0.90	4.69	--
Cancer of colon and rectum					
Deaths	39	29	13	7	88
Controls(2)	88	70	15	3	176
Relative risk	1	0.93	1.96	5.26	--
Other abdominal cancers					
Deaths	43	25	7	5	80
Controls(2)	83	46	26	5	160
Relative risk	1	1.05	0.52	1.93	--
Cancer of larynx					
Deaths	13	6	2	0	21
Controls(3)	36	21	5	1	63
Relative risk	1	0.79	1.11	0.00	--

*Figures in brackets are numbers of controls for each death. Method of selecting controls is described in text; those reported here were not matched for smoking habit.
+Risk calculated by method of Doll in relation to those with exposure less than 30 mpcf.y.
**Excluding five deaths coded to 162-164, but found to be due to malignant mesothelioma.

numbers of deaths are as in Table 2 (but see footnote ** in Table 10) because there were no restrictions on the start of the study interval. Four groups of dust exposure are distinguished, and the data are presented without regard to the matching. Matching was taken into account in the full analysis, however, which generally confirmed the tendencies shown in the two a priori approaches and relative risks were fairly similar at Asbestos and Thetford Mines.

Linear dose-response relations have been fitted (Berry, G., unpublished) for lung cancer (without regard to smoking habits); using the data on which Table 10 is based, but taking into account the matching of controls for each case in terms of date of birth and place of employment, the fitted line was:

$$\text{Relative risk} = 1 + 0.0014\ (\text{mppcf-y})$$

the standard error of the estimate of the slope being 0.0005. The linear fit accounted for X^2, with one degree of freedom, of 21.37, leaving only a very low value for deviations from linearity.

There were in all 11 deaths (including one women) from malignant mesothelioma observed to the end of 1975. All were of the pleura and appeared to follow a clear exposure trend.

The authors concluded that essentially linear relations have been shown between indices of exposure, based on dust concentration (mppcf) multiplied by length of service, and lung cancer, pneumoconiosis, and total number of deaths.

Because of concern regarding the risk from concentrations of asbestos dust nearer current standards, the data for the 1904 men in the cohort employed for at least 20 years in the low and medium dust exposure groups were analyzed. The concentrations to which these men were exposed (Table 4) averaged 6.6 mppcf, or perhaps 20 f/ml. The total mortality was 620 deaths, and the SMR was 0.94. The authors stated that this might be a true healthy worker effect, but not all cause-specific SMRs were below unity. There were excesses for pneumoconiosis (10.3 excess deaths, leading to X^2 on the usual basis, and with one degree of freedom, of 159.27), for lung cancer (6.4, X^2 = 0.99); cancer of esophagus and stomach (1.1, X^2 = 0.06); "other" cancers (1.7, X^2 = 0.06); respiratory tuberculosis (1.3, X^2 = 0.17); and stroke (1.8, X^2 = 0.07). Apart from pneumoconiosis, these values of X^2 are so low, even for lung cancer (where the associated p-value is 32.0%), that the observed excesses do not reach conventional levels of statistical significance. Moreover, the lung cancer SMR for the low dust exposure group (1.21) was higher than that of the medium exposure group (1.08); the authors stated that only the greatly enhanced SMRs for those with high and very high exposure allow the conclusion that there was a

response to exposure. Nevertheless, the lung cancer SMR for all 1904 men was 1.15, in close conformity with that which might be predicted from the figure (about 1.20) or the relative risk of 1.16 from the fitted line (Berry, G., unpublished).

It is noted that exposure to asbestos was presented as dust exposure in mppcf. The current trend is towards providing information in terms of fibers rather that dust counts, although there is an almost complete lack of epidemiological data based on fiber measurements. The problem with this is there is no easy conversion. The authors note that studies showed that, at relevant dust levels, the conversion factors range from about 3 to 7 fibers/ml for each mppcf; although other data point to a lower range, 1 to 5. This is a recurring problem.

CONCLUSION:

The study suggests an overall small increase in lung cancer associated with asbestos exposure. A consistent dose-response gradient was observed: SMR of 0.9 (low exposure 30 mppcf-yrs) to 2.3 for highest exposure category (300 mppcf-yrs.).

2. In this cohort study[11] of chrysotile miners and millers, only workers with at least 20 years of employment were chosen.

Dust measurements after 1969 were reviewed but no quantitative exposure data were provided. Fiber concentrations for various areas of the mills and mines ranged from 9 to 36 fibers longer than 5 micrometers/ml of air.

Table 4 shows the various causes of death observed in 130 deaths.

TABLE 4: Categorization of causes of death according to death certificate information compared with categorization following review of all available medical records and pathological material in 130 cases

Cause of Death as Ascertained (BE)*	No.	Underlying Cause of Death as Categorized on Certificate of Death, (DC)*				
		Lung Cancer	Mesothelioma	All Other Cancer	Asbestosis Including Pneumoconiosis	All Other Causes
Lung cancer	25	18		3	2	2
Mesothelioma	1		1			
All other cancer	18	1		17		
Asbestosis	24	3			14	7
All other causes	62			1	1	60
Totals	130	22	1	21	17	69

*BE - best evidence
DC - death certificate cause

The expected mortality experience was calculated using national rates of Canada (Table 5).

TABLE 5: Expected and Observed Deaths Among 544 Asbestos Miners and Millers, Thetford Mines, Quebec, Jan.-Nov., 1961 ADG, 1977*

	Total		
	Exp.	Obs.	O/E
Total deaths	159.9	178	1.11
Total cancer all sites	36.7	49	1.34
Lung cancer	11.1	28	2.52
Pleural mesothelioma	**	1	--
Cancer of the gastrointestinal tract	9.5	10	1.05
All other cancers	16.1	10	0.62
Total Noninfectious pulmonary diseases	6.7	30	4.48
Asbestosis	**	26	--
All other causes	116.5	99	0.85
Person-years		7,408	

*Expected deaths are based upon age-specific death rate data for Canadian white males.
**Death rates not available but these have been rare causes of death in the general population.

Asbestosis and lung cancer were major causes of death among these workers. Table 7 details the mortality experience according to time from onset of exposure and shows an increase in mortality between 30 and 50 years from first exposure to asbestos. There is, however, little excess mortality after 50 or more years from first exposure. The authors stated that perhaps this occurred as individuals at high risk of death (because of their particular susceptibility or because of other associated factors, as cigarette smoking) may have died preferentially in earlier years.

TABLE 7: Ratios of Observed to Expected Deaths Among 544 Asbestos Miners and Millers, Thetford Mines, Quebec, Jan.-Nov. 1961 - Aug. 1977

	Ratio of Observed to Expected Deaths (Number of Deaths in Parentheses)			
	Years from Onset of Employment			
	20-29	30-39	40-49	50 +
Total deaths	0.65 (8)	1.27 (60)	1.28 (66)	0.91 (44)
Total cancer	0.00 (0)	0.98 (11)	1.95 (24)	1.30 (14)
Lung cancer	0.00 (0)	1.94 (7)	4.19 (16)	1.67 (5)
Noninfectious pulmonary diseases (incl. asbestosis)	-- (4)	5.29 (9)	3.64 (8)	3.60 (9)
Causes other than cancer or noninfectious pulmonary diseases	0.42 (4)	1.16 (40)	0.91 (34)	0.59 (21)
	Number of deaths			
Asbestosis	3	8	8	7
Mesothelioma	0	0	1	0
Person-years of observation	1,623	3,067	1,805	914

CONCLUSION:

The study results indicate that a small increase in lung cancer risk occurs as asbestos exposure increases, but the lack of quantitative exposure data makes it difficult to evaluate this association.

3. Mortality of Italian chrysotile asbestos workers was studied[82] using two different reference groups. In the first analysis the observed number of deaths was compared with the expected number in the population of all Italy. Person-years of observation were calculated according to the method of Case and Lea[35a] and multiplied by age-specific death rates to compute the expected number of deaths. Secondly, a case control study of carcinoma of lung and larynx was undertaken. Only two exposure categories were considered, the first with cumulative exposure up to 100 fiber-years and the second, all those with a cumulative exposure greater than 100 f/yr. (The lower of the two exposures corresponds to the British standard of 2f/cc for 50 years' working life).

In Table 3 the mortality of the cohort is divided into 2 groups according to period since first employment: deaths occurring up to 19 years since first employment and deaths occurring over 20 years since first employment. The overall mortality compared to the national figures is also shown.

One death from pleural mesothelioma occurred 35 years after starting employment in a worker with 33 years exposure.

A significant excess of laryngeal cancer is seen when examining mortality over the whole period of observation. Four of these deaths occurred after 20 years since first employment. Two of the six workers dying from laryngeal cancer had less than one year of exposure. There is also a marked excess of respiratory diseases, both influenza and pneumonia and "other" respiratory diseases, consisting chiefly of chronic obstructive lung disease. Asbestosis was reported in 9 cases.

Mortality from lung cancer is shown in Table 4. No deaths were observed before 1961, nor did any deaths occur from this cause in subjects under the age of 50. However, among those of 50 years or more, the SMR rises to 111 in the quinquennium 1966-70 and reaches 226 between 1971 and 1975; for men of all ages it is 206 in the same period.

TABLE 3: Number of deaths observed and expected by period since first exposure, and cause. (Period of observation from 1946 to 1975)

Period since first exposure (yr) over	Total			Up to 19			20 and		
Person-years observation	12683			8776			21459		
Cause of death	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All causes	112	54.2	207**	220	160.2	137**	332	214.4	155**
All malignant neoplasms (140-205)	12	10.0	120	38+	37.0	103	50+	47.0	106
Lung and pleura (162-163)	1	1.7	59	10+	8.7	115	11+	10.4	106
Larynx (161)	2	0.4	500	4	1.5	267	6	1.9	316*
Gastrointestinal (151-159)	4	4.8	83	15	14.5	103	19	19.3	98
Other sites	5	3.1	161	9	12.3	73	14	15.4	91
Non-malignant respiratory diseases (470-527)	12	2.3	522**	20	11.8	169*	32	14.1	227**
Influenza and pneumonia (480-483)	8	1.6	500**	4	4.6	87	12	6.2	194*
Other respiratory diseases (470-475, 500-527)	4	0.7	571**	16	7.2	222**	20	7.9	253**
Asbestosis (523.2)	2	--	--	7	--	--	9	--	--
Tuberculosis of the lung (001-008)	13	3.9	333**	5	3.3	152	18	7.2	150**
Cardiovascular diseases (400-468)	22	14.8	149	100	67.7	148**	122	82.5	148**
Cirrhosis of the liver (581)	9	2.1	429**	22	7.8	282**	31	9.9	313**
Accidents (800-999)	30	7.8	385**	15	9.5	158	45	17.3	260**
All other causes	9	13.3	68	17	23.1	74	26	36.4	71
Unknown	5	--	--	3	--	--	8	--	--

*$p < 0.05$; **$p < 0.01$

+These numbers include one suspected case of mesothelioma of the pleura

Figures in parentheses are ICD (7th Revision) code numbers

TABLE 4: Observed and expected deaths from lung cancer (162-163) by age and calendar time

Age		Calendar years of follow-up				
		1946-60	1961-65	1966-70	1971-75	1946-75
Up to 49	Observed	0	0	0	0	0
	Expected	0.5	0.2	0.3	0.3	1.3
	SMR	--	--	--	--	--
50 and over	Observed	0	1	3	7*	11
	Expected	1.7	1.6	2.7	3.1	9.1
	SMR	--	63	111	226	121
All ages	Observed	0	1	3	7*	11
	Expected	2.2	1.8	3.0	3.4	10.4
	SMR	--	56	100	206	106

*These numbers include one suspected case of mesothelioma of the pleura

Table 5 shows the distribution of the deaths of men with lung cancer and their controls in the two exposure categories, in the upper part of the table, and the deaths from laryngeal cancer with their controls, in the lower half of the table. Ten of the deaths from lung cancer are in the higher exposure group with a relative risk of 2.89. However, tests of the significance of the association of lung cancer and high exposure gave a two-tailed P value of 0.18, thus demonstrating no statistically significant difference between the proportion of cases and controls reaching the higher exposure level. Nor is there a statistically significant excess of laryngeal cancer in the higher exposure categories (relative risk 3.33, two-tailed P value 0.28), although all but one of the deaths occurred in this group.

TABLE 5: Distribution of patients with lung and laryngeal cancer and their matched controls according to cumulative dust exposure.

Subjects	Dust exposure	
	Up to 100 fibre/yr	101 and over fibre/yr
Lung cancer	2	10+
Controls	22	38
Relative risk	1	2.89*
Laryngeal cancer	1	5
Controls	12	18
Relative risk	1	3.33**

+Including one case of lung cancer diagnosed in hospital but reported in death certificate as "cardiac failure" and one suspected case of mesothelioma of the pleura.
*two-tailed p value 0.18
**two-tailed p value 0.28

Table 7 shows the distribution of the whole cohort according to the selected exposure categories. For this analysis, workers included in the higher exposure category contributed to person-years observation in the lower category "up to 100 fibre/years" from the date of first employment to the date they reached the cumulative dust exposure of "more than 100 fibre/yr," after which they contributed to the higher category. The mean value of cumulative dust exposure in the higher category was about five times that in the lower (75 fibre/yr compared with 376 fibre/yr). About two-thirds of the cohort reached the higher exposure category. In Tables 7 and 8, man-years from 1 January 1946 only are included in the total. Thus, those who had accumulated a dose of 100 fibre/yr by 1946, immediately entered the higher exposure category.

The age-standardized death rates and the associate measure of risk for overall mortality and some selected causes of death are shown in Table 8. The relative risk for lung cancer obtained by examining the whole cohort (2.54) is similar to that calculated for the case control study (2.89, Table 5). A higher death rate for laryngeal and gastrointestinal cancer is also seen in the more highly exposed group, although comparison with the national statistics showed no

excess for gastrointestinal cancers. Non-malignant respiratory diseases, including asbestosis, tuberculosis and cardiovascular diseases, showed an increase in relative risk, whereas death rates for all other causes were almost equal in the two exposure groups.

TABLE 7: Distribution of workers according to cumulative dust exposure. Period of observation from 1946 to 1975

Dust exposure as fibre/yr	Up to 100 fibre/yr	101 and over fibre/yr	Unknown
Mean value within categories	74.7	376.2	--
Number in study	927*	611	6**
Person-years observation	8365	12976	118

*Including the 611 workers in the category "101 and over fibre/yr" before they had reached such cumulative exposure. Person-years are additive, whereas number of workers are not.
**Including 4 dead

TABLE 8: Crude and age-standardised death rates per 1000 person-years and relative risks by selected causes.

Cause of death	Cumulative dust exposure				
	Up to 100 fibre/yr		101 and over fibre		Relative risk*
	Death rate		Death rate		
	Crude	Age-standardised	Crude	Age-standardized	
All causes	11.72	13.31	17.73	16.73	1.26
Lung cancer (162-163)	0.24	0.28	0.77	0.71	2.54
Laryngeal cancer (161)	0.12	0.14	0.39	0.36	2.57
Gastrointestinal cancer (151-159)	0.48	0.57	1.16	1.09	1.91
Non-malignant respiratory diseases excluding influenza and pneumonia (470-475, 500-527)	0.48	0.46	1.39	1.28	2.21
Tuberculosis of the lung (001-008)	0.48	0.46	1.08	1.10	2.39
Cardiovascular diseases (400-468)	4.06	4.68	6.47	5.94	1.27
All other causes	5.86	6.60	6.47	6.24	0.95

*Based on age-standardised death rates

CONCLUSION:

The gradient of risk for lung cancer with time since onset of exposure (SMR 0.6 for < 20 years vs. 1.2 for > 20 years) and calendar time (SMR 0.6 for 1961-1965 vs. 2.1 for 1971-1975) was observed. Significantly higher risk was noted only for laryngeal cancer. Increased relative risk for lung cancer (2.9) and laryngeal cancer (3.3) was found when case-control groups were compared by exposure level.

4. Mortality of workers manufacturing friction materials using chrysotile was studied[65] on a population of 13460 workers. Exposure conditions are shown in Table 1.

Table 1 *Mean concentration of asbestos in air (f/ml)*

Period	*Office/ laboratory*	*Stores/ distribution*	*Grinding*	*Forming*
Pre-1931	10–20	>20	>20	>20
1932–40	<0·5	2–5	5–10	2–5
1951–69	<0·5	2–5	2–5	1–2
1970–79	<0·5	0·5–1	0·5–1	0·5–1

The observed mortality was compared with that expected, based on sex-, age-, and period-specific death rates for England and Wales, using the subject-years method. Attention was restricted to the period following 10 years exposure, and follow-up was to the end of 1979. In addition to mortality from all causes, the separate causes of death considered were cancer of lung and pleura, cancer of the gastrointestinal tract, and all other cancers. Table 7 shows the total mortality. Apart from 10 pleural mesotheliomas there was no sign of any excess mortality.

Table 7 *Observed and expected mortality after 10 years from first exposure (Number of pleural mesotheliomas included in parentheses)*

Cause of death	*No. subject-years*			
	Men		*Women*	
	Obs	*Exp*	*Obs*	*Exp*
All causes	1130	1161·9	500	525·0
Lung and pleural cancer	151 (10)	139·5	8 (2)	11·3
Gastrointestinal cancer	103	102·2	20	23·4
Other cancers	77	87·2	51	60·8
Other causes	1008	1002·4	311	329·5

When the subjects were divided into groups according to duration of exposure, there was still no sign of excess mortality nor of any trend in mortality with duration of employment. Dividing the subjects according to the period of first employment again showed no excess mortality apart from the pleural mesotheliomas. This applied even to those with 30 years' follow-up who were first employed before 1950, when dust levels were high (Table 1).

Among deaths from other cancers, there were 2 in men due to cancer of the larynx (3.6 expected). Eight of the women died of cancer of the ovary (8.1 expected), and 22 of cancer of the breast (24.4 expected). The mortality experience of workers who completed 10 years' service is shown in Table 8.

Table 8 *Observed and expected mortality after completing 10 years employment*

	Men				Women			
Follow up after 10 yrs exposure (years)	0-10		>10		0-10		>10	
No subject-years	2484 21 860		1808 10 025		627 5578		457 4277	
Cause of death	Obs	Exp	Obs	Exp	Obs	Exp	Obs	Exp
All causes	185	195.7	132	150.8	14	21.3	7[illegible]	[illegible]
Lung and pleural cancer	23	21.3	30(*)	17.4	0	0.7	2	2.2
Gastrointestinal cancer	23	16.3	25	35.8	0	1.8	9	3.5
Other cancers	7	12.6	21	28.2	3	4.5	14	11.7
Other causes	132	145.5	126	130.4	11	14.3	52	47.0

Except for deaths from mesothelioma, there was no excess in this group, even 10 years after completing 10 years' employment. A similar result was obtained when restricting attention to those who had completed 20 years' exposure.

An additional 187 deaths have occurred since the original analysis. Only one of 40 deaths in women and 12 of 147 in men were due to lung cancer. One of the men certified as dying from pleural mesothelioma was 50 and had worked at the factory for two weeks in 1960 (when aged 29) as a grinder exposed to chrysotile (only known asbestos exposure). With regard to mesothelioma, the cases observed here were analyzed in a case-control study using the method of Liddell, et al. The effect of exposure to crocidolite was examined. Four matched controls were chosen for each mesothelioma, where matching was for (1) sex, (2) year started work in factory (± 1 year), (3) year of birth (± 4 years), (4) survival up to time of death of mesothelioma, and (5) employed at factory during crocidolite period for same time as case.

Eighty percent of those dying of mesothelioma had worked on the crocidolite contract compared with only 8% of the controls. Those with mesothelioma, however, had also been exposed to higher levels of chrysotile than the controls; 90% had been exposed to more than 5 f/ml compared with 25% of the controls. The confounding effect of exposure to chrysotile was eliminated by considering only cases of mesothelioma and their controls who had been exposed to chrysotile at a level of at least 5 f/ml. This left 6 cases with 10 controls. Five of the 6 had had definite crocidolite exposure.

A case-control study of deaths due to lung cancer was carried out for males who had started work before the end of 1960 and who survived for at least 10 years after start of exposure. There were

106 deaths from lung cancer satisfying these criteria, and three controls were chosen for each case, matched for: (1) year started at factory; (2) date of birth; and (3) survival up to time of death from lung cancer. Within the restricted set of men there were 86 who had died of gastrointestinal cancer, who were also included in this study (without additional controls). Each occupational history was integrated with respect to time to give the cumulative exposure up to the date of death for the cases, and for controls up to the date of death of the corresponding case of lung cancer. The total duration was also calculated. These two measures were also evaluated up to 9 years before the above dates, on the basis that recent exposure is irrevalent to the risk of lung cancer. A fifth measure evaluated was the cumulative dose weighted by the time elapsed since the exposure occurred. This measure was evaluated up to the date of death and attaches most importance to the earliest exposure.

The distribution of duration of exposure and cumulative exposure up to death are given in Tables 13 and 14.

Table 13 *Distributions of duration of exposure up to death*

Duration of exposure (years)	*No of subjects*			*Odds-ratios*	
	Controls	*Lung cancers*	*Gastrointestinal cancers*	*Lung cancer*	*Gastrointestinal cancer*
0–0 9	74	26	16	1 00	1 00
1–4 9	86	29	24	0 96	1 29
5–9 9	25	7	9	0 81	1 39
10–19 9	37	26	26	1 03	1 56
20–115	52	18	11	0 82	0 98
Total	314*	106	86		

Table 14 *Distributions of cumulative exposure to death*

Cumulative exposure (f-s ml)	*No of subjects*			*Odds-ratios*	
	Controls	*Lung cancers*	*Gastrointestinal cancers*	*Lung cancer*	*Gastrointestinal cancer*
0–9	132	50	36	1 00	1 00
10–49	124	37	40	0 79	1 18
50–99	40	13	9	0 86	0 83
100–356	18	5	1	0 88	0 24
Total	314*	105*	86		

*For one person (6 controls, 1 lung cancer) information available on dust levels was insufficient to calculate cumulative exposure (f-s/ml = fibre-years/ml)

The odds ratio, i.e., the approximate risks of cancer, relative to the lowest exposure group, are also given.

For lung cancer there is no indication of an increased risk with either duration of exposure or cumulative exposure. For gastrointestinal cancer, there is no sign of an increased risk with cumulative exposure, and although there appears to be a trend with duration of exposure up to 20 years, this trend is not supported by

the numbers with more than 20 years' exposure and could have occurred by chance. There was also no sign of increased risk with duration of exposure or with cumulative exposure calculated to nine years before death or with the measure of exposure weighted by elapsed time (tables not given). Restricting the analysis to cases who survived for at least 15 years after first exposure also did not show any dose-response relationship.

For lung cancers, a linear relationship between relative risk and cumulative exposure was fitted using methods appropriate to matched data. The coefficient was estimated as 0.00058 per fiber-year/ml. That is, for a cumulative exposure of 100 fibers-years/ml, the relative risk was estimated as 1.06; the upper confidence limit was 1.80.

CONCLUSION:

No gradient of risk was observed with quantitative exposure level[illegible]

No evidence of excess mortality due to cancer at any site, except mesothelioma, even when examined by duration of exposure or period of initial employment.

No increased risk of lung cancer or gastrointestinal cancer was associated with either duration or cumulative exposure in the case-control analysis.

5. A report[83] on dust exposure and mortality of workers in a chrysotile asbestos friction products plant consisted of data on a cohort of 3641 men employed for at least one month. Individual exposures were estimated (in mppcf-years) from impinger measurements. Table 1 shows deaths by cause and age at death.

Table 1 *Male deaths by age and certified cause*

Cause of death (ICD code)	*Age at death (y)*			*Total*
	<45	*45–64*	*≥65*	
[illegible]causes	139	616	511	1267
[illegible]nant neoplasms				
[illegible]ng (162–63)	1	47	41	89
Oesophagus and stomach (150–51)	0	12	13	25
Colon and rectum (152–54)	3	9	20	32
Other abdominal (155–59)	4	9	12	25
Larynx (161)	0	3	1	4
Other (140–48, 160, 165–205)	11	50	40	101
Heart disease (400–443)	39	273	198	510
Respiratory tuberculosis (001–008)	3	6	2	11
Other respiratory (470–522, 525–527)	2	27	24	53
Pneumoconiosis (523–24)	0	7	5	12
Cerebrovascular (330–34)	5	30	56	91
Accidents (800–999)	35	42	15	92
Other known causes	30	87	66	183
Cause not known	6	14	18	39*

*Including one age unknown

[redacted] information is presented in Tables 2 and 3.

Table 2 *Estimated average dust concentrations (mpcf) for main processes 1930–70*

	1930–9	1940–9	1950–9	1960–9
Pulverising waste asbestos products	6	4	2	1
Sheet packings				
Fibre room	13·4	10	6	6
Mixing	2·4	2	1·5	1
Other	2·0	1·5	1	0·5
Millboard wet machines	3·1	2	2	0·5
Wire mould extruded brake lining				
Mixing	8·2	3	2	1
Other	1	1	0·5	0·2
Paper				
Autotransmission etc	—	—	0·5	0·2
Novabestos process	—	—	0·2	0·2
Grooving	—	—	0·5	0·2
Metal fabrication	—	—	1	0·5
Brake shoes	—	—	0·5	0·2
Core	—	—	0·5	0·2
Disc brake	2	1·5	1	0·5
Treat/cure	2	1·5	1	0·5
Brake finish/hot press				
Drymould mix	24	10	2·5	5
Grinding	4·3	3	2	1
Other	1·5	1·5	1	0·5
Ring finish (grinding)	5·6	4	2	1
Packing	1	1	0·5	0·1
Warehouse	2	2	0·2	0·1

Table 3 *Age at start, duration of employment, and dust exposure (men only)*

	Duration of gross service (y)				
	<1	1–<5	5–<20	≥20	Total
No	1253	918	577	747	3515
Average age at start (y)	29·62	31·96	33·95	29·64	30·95
Gross service (y)	0·38	2·53	10·58	30·59	9·05
Net service (y)	0·37	2·12	9·00	28·82	8·04
Average dust concentration (mpcf)	2·28	2·06	1·56	1·06	1·84

Table 4 summarizes the mortality experience of the cohort by duration of work. The SMR based on Connecticut rates was 108.5 (107.9 on U.S. rates). The excess was mainly due to people who had worked for less than 1 year (SMR 129.9); those who worked one or [redacted]ars had an SMR of 101.2. The lowest SMR (97.2) was for those [redacted] worked 20 or more years. SMRs were raised for the three [redacted]groups of malignant neoplasms. Again this was mainly due to high SMRs in men employed for less than one year; in none was there evidence of increasing risk with increasing duration of exposure. No mesotheliomas were observed.

Table 4 *Male deaths 20 years after first employment, by cause, in relation to duration of service*

Cause of death*	Duration of gross service (y)									
	<1		1–<5		5–<20		≥20		Complete cohort	
	0	SMR	0	SMR	0	SMR	0	SMR	0	SMR
All causes	246	129·9	189	103·0	130	104·8	238	97·2	803	108·5
Malignant neoplasms	60	144·9	50	125·7	29	114·0	63	118·3	202	126·5
Respiratory	24	180·0	19	149·4	9	122·6	21	133·4	73	148·7
Digestive	17	132·9	16	128·3	5	60·6	21	116·9	59	114·4
Other	19	120·4	25	164·9	15	190·4	21	107·2	70	115·9
Heart disease	99	125·3	79	104·9	44	83·7	100	93·1	322	102·5
Respiratory tuberculosis	0		0		0	—	4	283·3	4	145·9
Other respiratory	13	196·3	8	126·2	4	85·2	8	92·2	33	
Pneumoconiosis	(6)		(3)		(1)		(2)		(12)	
Cerebrovascular	18	137·6	14	108·4	15	142·7	20	102·4	67	119·6
Accidents	11	121·1	5	69·2	5	101·7	7	68·6	28	89·1
Other known	37	123·5	24	90·4	29	147·1	35	87·9	125	107·7

*As in table 1, except that ICD codes 160–64 are here grouped under "respiratory" malignant neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

Table 5 gives SMRs by total accumulated dust exposure. The same lack of any clear or systemic exposure-effect pattern is present. The SMR for respiratory cancer for men in the 2 highest dust groups combined (125.8) was higher than for the 2 intermediate dust groups combined (103.3) but still substantially below that for the lowest exposure category (167.4). A similar pattern of relative risk was obtained from the Mantel-Haenszel analysis (Table 6), which showed an increasing risk only if the minimal exposure group is ignored.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf y)*

	Accumulated dust exposure (mpcf y)									
	<10		10–<20		20–<40		40–<80		≥80	
	0	SMR	0	SMR	0	SMR	0	SMR	0	SMR
All causes	546	113·8	89	92·3	71	96·6	62	110·2	35	103·1
Malignant neoplasms	134	128·1	22	109·6	19	120·1	19	153·9	8	117·9
Respiratory	55	167·4	6	101·7	5	105·4	6	162·8	1	55·22
Digestive	34	102·6	9	135·1	8	153·4	5	120·2	3	126·6
Other	45	114·0	7	89·5	6	101·0	8	176·6	4	150·4
Heart disease	60	101·9	14	83·8	13	76·6	18	106·4	13	93·0
Respiratory tuberculosis	2	123·6	0	—	0	—	0	—	2	1112·9
Other respiratory	21	125·1	5	135·6	2	74·4	2	109·0	3	230·8
Pneumoconiosis	(9)		(1)		(1)		(1)		(0)	
Cerebrovascular	43	122·9	8	101·7	7	118·4	5	117·1	4	135·4
Accidents	22	101·0	3	86·5	0	—	2	86·3	1	94·2
Other known	83	109·5	15	102·9	15	128·5	10	112·2	2	43·4

The more detailed analysis for respiratory cancer in Table 8 shows that the same pattern is shared by men in the lowest accumulated dust category regardless of duration of employment.

Table 8 *Male deaths from respiratory cancer 20 years after first employment in relation to duration of service and dust exposure*

Duration of service (y)	Dust exposure (mpcf y)					
	<10		10–<40		≥40	
	0	SMR	0	SMR	0	SMR
<1	24	180·0	0	—	0	—
1–<5	17	166·3	2	83·2	0	—
≥5	14	150·0	9	109·9	7	125·4

Table 6 *Relative risks of respiratory cancer by dust exposure from (1) Mantel-Haenszel analysis and (2) SMRs*

	mpcf y					Chi-square	
	<10	10–<20	20–<40	40–<80	≥80	Difference	Linearity
Mantel-Haenszel							
Observed	54	4	5	6	1		
Expected	51·1	8·7	4·6	4·1	1·5		
Relative risk	1	0·40	0·91	1·40	1·13	4·50	0·00
From SMRs							
Relative risk	1	0·59	0·64	0·98	0·31		

The other respiratory group of diseases that included pneumoconiosis also showed little indication of an exposure response. Six of the 12 whose deaths were from pneumoconiosis (ICD 523) had worked in the plant for less than a year and only 3 of the other 12 had a total dust exposures index of 10 mppcf-yrs. or more. Table 7 shows details from death certificates given ICD code 523. In no case was asbestosis mentioned but anthracosilicosis or silicosis were given as the cause of death in all but 2 cases. It was further noted that all 12 had either been born or had died in the coal mining area of Pennsylvania.

Table 7 *Deaths attributed to pneumoconiosis (ICD 523)*

Case No	Employment			Birth place	Death		Certified cause
	Age at start (y)	Duration	Total dust (mpcf y)		Age (y)	Place	
1	36	2 months	0·1	Sandy Run, Pa	64	Freeland, Pa	Anthracosilicosis
2	26	6 months	0·2	Taylor, Pa	57	Taylor, Pa	Silicosis and emphysema
3	35	2 months	0·1	Wilkes-Barre, Pa	57	Wilkes-Barre, Pa	Anthracosilicosis
4	29	5 months	0·2	Wilmington, De	58	Wilkes-Barre, Pa	3° anthracosilicosis
5	38	10 months	0·7	Pennsylvania	68	Wilkes-Barre, Pa	Anthracosilicosis
6	22	3 months	0·1	Wyoming, Pa	53	Wyoming, Pa	Anthracosilicosis
7	50	1 y 10 m	2·0	Mexico	79	Windber, Pa	Coal workers pneumoconiosis
8	47	3 years	6·8	Scranton, Pa	75	Scranton, Pa	Anthracosilicosis
9	35	3 years	17·4	Nanticoke, Pa	58	Nanticoke, Pa	Silicosis
10	51	20 years	8·3	Scranton, Pa	72	Bridgeport, Ct	Pulmonary silicosis
11	40	16 years	21·8	Nanticoke, Pa	68	Bridgeport, Ct	Pneumoconiosis
12	31	30 years	51·4	Nanticoke, Pa	62	Bridgeport, Ct	Pneumoconiosis

CONCLUSION

The authors concluded that if it is accepted that the high mortality from all causes (including respiratory cancer) in men employed for less than 1 year was probably due to some form of selection, then the results suggest that the adverse health effects of employment in this chrysotile friction products plant were small.

6. Workers[73] in an asbestos textile factory, which were exposed to dust levels higher than current standards permit, were divided into 5 cohorts on the basis of duration and period of work in scheduled areas (Table 1).

Table 1 *Number of workers in each exposure cohort*

Cohort	Sex	Years in scheduled areas	Years in scheduled areas before 1933	Number	Person-years observation
1	Male	20 or more	10 or more	69	1656
2	Male	20 or more	Less than 10	74	1397
3	Male	20 or more	None	263	2845
4	Male	10-19	None	679*	7264
5	Female	10 or more	None	264	4388
Total				1186	16972

*Including the 263 men in cohort 3 before they had completed 20 years in scheduled areas.

The number of deaths in each group attributed to lung cancer (includes mesothelioma), other cancers, respiratory diseases and other causes are compared in Table 2 with the number expected, which is calculated from national death rates by 5-year age-groups.

Table 2 *Number of deaths observed and expected, by exposure cohort and cause*

Cause of death†	Cohort	Observed deaths‡	Expected deaths	Ratio observed/expected	Probability of observed number or more
Lung cancer and pleural mesothelioma (162, 163 and 228)	1	15 (2)	1·49	10·1	<0·001
	2	10 (1)	3·05	3·3	0·001
	3	9 (2)	5·26	1·9	0·111
	4	34 (2)	12·02	1·9	0·003
	5	3 (1)	0·92	3·3	0·066
Other cancers (140-239)	1	8	4·14	1·9	0·088
	2	3	4·29	0·7	0·691
	3	6	6·41	0·9	0·647
	4	11	17·78	0·6	0·966
	5	6	7·43	0·8	0·772
Respiratory diseases (460-519)	1	14	3·86	3·6	<0·001
	2	7	4·32	1·6	0·147
	3	8	5·93	1·3	0·246
	4	23	17·28	1·3	0·168
	5	4	1·81	2·2	0·110
Other causes	1	27	18·29	1·5	0·033
	2	23	17·89	1·3	0·139
	3	36	26·37	1·4	0·047
	4	69*	75·05	0·9	0·773
	5	11	13·34	0·8	0·776
All causes	1	64	27·78	2·3	<0·001
	2	43	29·55	1·5	0·012
	3	59	44·67	1·3	0·023
	4	127	122·94	1·0	0·369
	5	24	23·70	1·0	0·583

†Coded according to the eighth revision of the *International Classification of Diseases* (World Health Organization, 1967).
‡Deaths due to pleural mesothelioma are included in the observed number for lung cancer and also given separately in parentheses.
*Includes one case in which a pleural mesothelioma was a contributory cause of death.

Lung cancer mortality in the area of the factory was lower than the national average among men (SMR = 87) and similar for women (SMR = 104) in 1959-63.

[redacted] first exposed before 1933 (cohorts 1 and 2) suffered a [redacted] excess of lung cancer and respiratory disease, particularly those with 10 or more years' exposure prior to 1933. There is also some excess mortality from lung cancer and mesothelioma (36 observed, 19.3 expected; p 0.001) and respiratory disease (35 observed, 25 expected; p = 0.03) in those who entered after 1933 (cohorts 3, 4 and 5 combined), although the excess is very much less than in the first 2 cohorts. There were 16 deaths attributable to gastrointestinal cancers compared with 15.70 expected. No excess for any of these rubics approached statistical significance in any cohort, and no peritoneal mesothelioma was reported. In order to

distinguish between exposures of 1933 and after 1950, observed and expected deaths for those first exposed between 1933 and 1950, and those first exposed later were determined (Table 3). There is clear evidence of some excess of lung cancer and respiratory deaths among those first exposed between 1933 and 1950, although very much less than in cohorts 1 and 2. There have been few deaths among those first exposed after 1950, but there still appears to be an excess of deaths from lung cancer 15 or more years after first exposure (5 observed, 1.86 expected; p = 0.04)).

Table 3 *Number of deaths observed and expected, by date of first exposure*

Cohort	Cause	Observed deaths†	Expected deaths	Ratio observed/expected	Probability of observed number or more
Men and women first exposed 1933-1950 (n = 616)	Lung cancer	30 (5)	16·10	1·9	0·021
	Other cancers	28	27·60	0·1	0·501
	Respiratory	33	21·91	1·5	0·056
	Other causes	109*	97·04	1·1	0·348
Men and women first exposed 1951 or later (n = 347)	Lung cancer	6 (0)	3·20	1·9	0·188
	Other cancers	3	2·68	0·6	0·677
	Respiratory	2	3·11	0·6	0·817
	Other causes	13	17·01	0·8	0·808

†Deaths due to pleural mesotheliomas are included in the observed number for lung cancer and also given separately in parentheses.
*Includes one case in which a pleural mesothelioma was a contributory cause of death.

This is shown in Table 4, in which deaths from lung cancer including pleural mesotheliomas in these groups are distributed according to the time since first exposure; the relative risk increases progressively with time since first exposure in both groups.

Table 4 *Observed and expected deaths from lung cancer by date of first exposure and time since first exposure*

Cohort	Period since first entering scheduled area (years)	Observed deaths†	Expected deaths	Ratio observed/expected	Probability of observed number or more
Men and women, first exposed 1933-1950 (n = 616)	10-14	3 (0)	1·65	1·8	0·282
	15-19	4 (0)	3·69	1·1	0·572
	20 and over	23 (5)	11·16	2·1	0·031
	Total	30 (5)	16·10	1·9	0·021
Men and women first exposed 1951 or later (n = 347)	10-14	1	1·34	0·7	0·738
	15-19	3	1·34	2·2	0·188
	20 and over	2	0·52	3·8	0·004
	Total	6 (0)	3·20	1·9	0·188

†Deaths from pleural mesotheliomas are included in the observed number for lung cancer and also given separately in parentheses.

The 6 workers first exposed after 1950 who died of lung cancer were all smokers; five worked in areas where dust levels were high in 1951 and one may have had previous exposure from another job. No mesotheliomas have occurred in this group although in view of the long latency period none would be expected yet. Asbestosis was found in 3 of the 6 cases. The numbers are too small for the magnitude of the excess of lung cancer in those first employed after 1950 to be estimated with any precision. Dust levels associated with various processes are shown in Table 5.

Table 5 *Dust levels accompanying different textile processes, 1953-1974*

Process		Yearly mean dust levels				
		Casella thermal precipitator (particles per cc)		Lang running thermal precipitator or millipore membrane (fibres per cc)		
		1953	1960	1961	1968	1974
Filtering	Mixing	500	—	—	—	—
	Opening	440				
	Bag slitting	—	110	5	4	2
	Manhattan bagging	—	120	4	3	2
Carding	Fine cards	280	280	6	6	3
	Medium cards	810	480	8	8	3
	Coarse cards	1140	420	7	8	4
	Electrical silver cards	490	260	5	3	2
Spinning	Fine spinning	170	110	4	3	1
	Roving frames	340	150	5	6	3
	Intermediate frames	330	180	5	6	4
Weaving	Beaming	190	220	6	4	1
	Pirn winding	250	130	3	3	1
	Cloth weaving	180	140	3	2	1
	Lining weaving	130	110	2	1	<1
Finishing	Finishing	140	80	4	4	3

CONCLUSIONS:

Results for Groups 1 and 2 were similar to that of Doll (1955)[101] and Knox, et al. (1968)[102], in that there was a 10-fold increase in risk of lung cancer in Group 1 and a three-fold increase for Group 2.

There was approximately a 2-fold increase in lung cancer for Group 3 and no increase for cancer of other sites. A 2-fold increase in lung cancer was seen in Group 4 and a 3-fold increase in Group 5. No increase in gastrointestinal cancer was observed for all groups combined.

7. In a study[84] of asbestos textile factory workers, excess lung cancer mortality has been reported. Observed and expected deaths due to lung cancer, other cancers, respiratory disease and other causes are shown in Table 1, together with death rates for asbestosis and mesothelioma. In men first exposed before 1951 (cohort 1), there were 22 deaths due to lung cancer compared with 13.85 expected (P^1 0.05) 20 or more years after first exposure; while in later employees (cohort 2) there were 8 compared with 1.62 expected (P 0.[redacted] If it were assumed that all men not known to have died or emigrated were alive on the follow-up date, 31 December 1978, these observed/expected ratios would become 22/14.12 (cohort 1; P 0.05) and 8/1.75 (cohort 2; P 0.001), respectively.

[1] All significant levels are one-sided.

Table 1: Mortality experience of 679 male asbestos textile workers

[illegible]	[illegible]	Man-years	Lung cancer		Pleural mesothelioma		Other cancers		Asbestosis		Other respiratory disease		[illegible]	
			O	E	O	rate /10³	O	E	O	rate /10³	O			
[illegible]	15-	1034	[illegible]	1.40	0	0.0	1	2.1	0	0.0	1	[illegible]	[illegible]	[illegible]
[illegible]	15-	1460	4	2.48	0	0.0	2	3.16	0	0.0	3	[illegible]	7	[illegible]
n = 411	20-	1760	3	3.97	1	1.6	6	5.16	2	1.1	1	-	29	[illegible]
	25-	1496	10	4.54	2	1.3	6	5.38	2	1.3	9	[illegible]	24	[illegible]
	30-	537	8	3.14	2	3.4	5	4.21	2	3.4	4	[illegible]	2	[illegible]
	35-	507	1	2.20	2	3.9	4	2.93	2	3.9	5	3.46	-	-
	Total	8093	28	18.63	7	-	24	25.07	10	-	26	24.73	[illegible]	[illegible]
1951 or later	10-	1123	1	1.30	0	0.0	0	1.62	0	0.0	1	[illegible]	[illegible]	[illegible]
n = 225	15-	1022	3	1.74	0	0.0	3	2.16	0	0.0	2	1.63	[illegible]	[illegible]
	20-	556	2	1.31	0	0.0	2	1.64	0	0.0	0	[illegible]	[illegible]	[illegible]
	[illegible]	46	1	0.31	0	0.0	0	0.37	0	0.0	0	[illegible]		[illegible]
	Total	2747	12	4.65	0	-	5	5.80	0	-	3	[illegible]	-	[illegible]

The excess mortality 20 or more years after first exposure due to nonmalignant respiratory disease in men first employed before 1951 (28 observed, 18.63 expected; P 0.01) was largely accounted for by deaths specifically attributed to asbestosis. The observed incidence of mesothelioma rose steadily from 0.0006 per annum at 20-25 years after first employment to 0.004 per annum beyond 35 years among pre-1951 employees. The absence of deaths due to asbestosis or mesothelioma in later employees may be due to their relatively short period of follow-up rather than to a substantial reduction in risk. Applying the incidence rates for asbestosis and mesothelioma observed in cohort 1 in successive five-year periods to the corresponding man-years of observation of cohort 2, only 1.9 deaths due to asbestosis and 0.4 due to mesothelioma would so far have been expected, and it has been reported that 10 men in cohort 2 have already been certified as having asbestosis (Berry et al., 1979)[103]. There is no evidence of excess mortality due to any other cause of death: 14 deaths (12.60 expected) were attributed to gastrointestinal cancers (ICD nos. 151-154) in the two cohorts, including 6 (5.38 expected) 25 or more years after first exposure; and no peritoneal mesotheliomas have occurred.

Exposure data are shown in Table 2.

Table 2. Previous and revised estimates of mean dust levels in fibres/ml (weighted by the number of men at each level) in selected years

	1936	1941	1946	1951	1956	1961	1966	1971	1976
Previous estimates corresponding to early fibre counts (Peto et al., 1977)	13.3	14.5	13.2	10.8	5.3	5.2	5.4	3.4	-
Revised estimates corresponding to modern counting of static samples[a]	No measurements prior to 1951			32.4	23.9	12.2	12.7	[illegible]	[illegible]

[a] These estimates are based on preliminary data on 126 men first employed between 1951 and 1955, and should be regarded as provisional.

The authors stated that the average dust levels were in the region of 30 f/ml in 1951 and remained high until about 1974. It was further stated that levels prior to 1951 were probably not much higher than this:

The cumulative exposures of the eight men first exposed in 1951 and who later died of lung cancer 20 or more years after first exposure are compared with those of unaffected controls (Table 3). The analysis is based on cumulative exposure up to the end of 1971, and the control group consisted of 42 men born between 1901 and 1914 who entered the factory between 1951 and 1955. The eight lung cancer cases all entered the factory before 1956 and died in 1972 or later; all but one, who was born in 1925, were within the age range of the controls, and all were cigarette smokers. There is no evidence that their exposures were anomalously heavy, although this may merely reflect the inevitable inaccuracy of individual exposure estimates.

Table 3. Estimated exposures of men first exposed between 1951 and 1955

	Cumulative exposure (fibres/ml-years) to December 1971						
	0-	100-	150-	200-	300-	400+	Total
Men dying from lung cancer over 20 years after first exposure	1	1	0	4	1	1	8
Other men born 1901-1914	2	4	4	14	9	9	42

The observed relative risk for lung cancer 20 or more years after first exposure in post-1950 employees was 4.9 (8 observed, 1.62 expected; 95% confidence limits, 2.1-9.7). This is significantly higher (P = 0.01) than that observed in men entering between 1933 and 1950 (22 observed, 13.85 expected); but, as the majority of pre-1951 employees in this study were still employed in 1951, it seems likely that this apparently marked increase in risk is largely due to chance. The eventual relative risk for lung cancer among men with estimated cumulative exposures of about 200-300 fibres/ml-years (the order of magnitude of the average exposures of men first employed in 1951 or later (Table 3)) is therefore probably between 2 and 3. This is in reasonably close agreement with an earlier analysis (Peto, 1978)[109], which was based on the assumption that the relative risk would be about 2 in men who had suffered cumulative exposures of about 200 fibres/ml-years and indicated that lifelong exposure to 2 fibres/ml might eventually cause lung cancer in about 4% of men.

CONCLUSION:

The risk of lung cancer 20 years after exposure in post-1950 workers was 4.9 (8 obs. vs. 1.6 exp.), which is significantly higher than in workers initially exposed in 1933-1950 (20 obs. vs. 13.8 exp.). A relative risk of 2 to 3 for lung cancer among men with cumulative exposures of 200-300 (fibers/cm^3)(yrs.) was estimated. No clear-cut gradient in risk of lung cancer was associated with increased exposure, suggesting that exposure estimates may be imprecise.

8. Chrysotile textile workers (South Carolina)[85] were studied to investigate the risk of exposure to this asbestos-type mineral.

The mortality and exposure data were analyzed in two ways. The first followed the orthodox man-years life table approach of Hill[104] and others, whereby standardized mortality ratios (SMRs) are derived from comparison of observed numbers of deaths with numbers expected from mortality rates in a standard population. In this case age-, sex-, race (colour)-, and year-specific rates for South Carolina were used. The second approach, essentially internal and case-control in type, followed the Mantel-Haenszel (or log rank) procedure,[105] yielding relative risks from entirely intracohort comparisons. In calculating SMRs a "lag time" of 10 years before death (or end of 1977) was imposed in determining exposure, and only deaths 20 years or more from first employment were included. In the Mantel-Haenszel analysis the same exclusions were applied, controls being selected from all other members of the cohort of the same sex and colour (black or white) who met the following criteria: (1) alive at death of case, (2) same year of birth, if in or after 1900, or within five years if before 1900, (3) within five years of date of first employment, before or after 1938. The statistical significance of differences between observed and expected numbers in this analysis and for departures from linearity were calculated as X^2 values by the method of Peto and Pike.[106] Lines were fitted to exposure-response results by Liddell using the method of Hanley and Liddell (to be published).

Estimates of dust concentration in millions of particles per cubic foot (mppcf) and duration of exposure in years were established for each worker. Tables 2 and 3 give exposure estimates.

Table 2 *Estimated average prevailing dust concentrations (mpcf) in main departments, 1930–70*

	1930	*1940*	*1950*	*1960*	*1970*
Preparation	3·5	2·0		1·0	0·8
Carding	3·1	1·5		1·2	0·9
Spinning	3·5	2·0		1·6	
Winding	2·8	1·7		1·1	
Twisting	6·1	4·0		1·1	
Weaving	2·1	1·5			1·2
Finishing and inspection	1·4	1·0	0·8		0·5

*Apparent improvement usually associated with technical change

Table 3. *Age at start, duration of employment, and dust exposure (men only)*

	Length of gross service (years)				
	<1	1, <5	5, <20	≥20	Total
No	950	574	421	465	2410*
Average age at start (years)	25·6	25·9	26·5	25·2	25·77
Gross service (years)	0·39	2·43	10·50	31·86	8·71
Net service (years)	0·37	1·81	7·55	29·51	7·59
Average dust concentration (mpcf)	2·11	1·86	1·67	1·23	1·80

*Excluding five whose employment histories were incomplete

Mortality of the males of known age shown by age and cause is presented in Table 1.

Table 1 *Male deaths by age and certified cause*

Cause of death (ICD code)	Age at death			Total
	<45	45–64	≥65	
All causes	178	502	177	857
Malignant neoplasms:				
Lung (162–164)	1	47	18	66
Oesophagus and stomach (150–151)	0	13	2	15
Colon and rectum (152–154)	2	3	4	9
Other abdominal (155–159)	0	10	2	12
Larynx (161)	0	2	1	3
Other (140–48, 160, 165–205)	6	23	12	41
Heart disease (400–443)	38	189	70	297
Respiratory tuberculosis (001–008)	8	4	2	14
Other respiratory (470–522; 525–527)	10	27	11	48
Pneumoconiosis (523–4)	2	12	7	21
Cerebrovascular (330–334)	5	30	21	56
Accidents (800–999)	97	42	3	112
Other known causes	24	89	19	132
Causes not known	15	11	5	31

Table 4 summarizes the mortality experience based on the modified life table analysis. Overall, the SMR (all causes) is 27% above expectation and perhaps twice that in men employed 5 years or more.

Table 4 *Male deaths 20 years after first employment, by cause, in relation to duration of service*

Cause of death*	Length of gross service (years)								Complete cohort	
	<1		1 <5		5, <20		≥20			
	0	SMR	0	SMR	0	SMR	0	SMR	0	SMR
All causes	159	107·4	113	122·7	120	156·1	178	136·7	570	127·4
Malignant neoplasms:										
Respiratory	8	78·2	10	163·9	15	304·1	26	317·3	59	199·5
Abdominal	6	107·9	5	146·4	7	240·3	8	151·4	26	151·7
Other	12	130·2	7	124·9	9	195·9	7	146·2	35	127·5
Heart disease	69	108·9	34	87·6	45	141·7	70	120·8	218	113·7
Respiratory tuberculosis	1	231·8	1	347·8	1	307·9	1	131·5	4	222·8
Other respiratory	3	53·3	3	85·6	2	78·3	27	557·5	35	207·3
Pneumoconiosis	(0)	—	(0)	—	(0)	—	(20)	—	(20)	—
Cerebrovascular	9	83·0	14	193·0	6	107·3	9	76·2	38	107·2
Accidents	18	121·2	8	89·7	5	75·8	9	85·0	40	97·0
Other known	30	116·9	28	175·5	23	177·7	21	92·3	102	132·4
Not known	3		3		7		0		13	

*As in table 1 except that ICD codes 160–164 are here grouped under "respiratory" malignant neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

As there is (a) a 7% excess of deaths even in men employed less than one year, unexplained by any asbestos related cause of death, and (b) a 32% overall excess in deaths of "other known causes," the SMRs are probably somewhat inflated, mortality in South Carolina having presumably provided an imperfect basis for comparison. Much of the excess, however, is clearly attributable to respiratory cancer, pneumoconiosis, and gastrointestinal cancers. Table 5 shows the cohort mortality, related to dust exposure. There is a steady gradient from 115.5 to 264.4 for mortality (all causes) and a much steeper slope for respiratory cancer and also for selected other respiratory diseases (which include pneumoconiosis). No clear trend is apparent in the other diagnostic categories.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf.y) accumulated to 10 years before death*

*Cause of death**	*Dust exposure (mpcf.y)*									
	<10		*10 <20*		*20 <40*		*40 <80*		*≥80*	
	0	*SMR*	*0*	*SMR*	*0*	*SMR*	*0*	*SMR*	*0*	*SMR*
All causes	376	115·5	55	125·5	63	156·9	43	170·8	33	264·4
Malignant neoplasms:										
Respiratory	31	143·1	5	182·7	8	304·2	7	419·5	8	1035·9
Abdominal	14	114·9	4	231·6	4	247·0	4	383·6	0	—
Other	28	140·0	3	109·2	1	44·9	0	—	3	383·5
Heart disease	143	103·5	28	143·6	29	166·6	10	88·6	8	149·9
Respiratory tuberculosis	3	264·4	0	—	0	—	1	634·4	0	—
Other respiratory:	8	65·9	2	119·5	6	421·7	13	1407·8	6	1296·0
Pneumoconiosis	(0)	—	(0)	—	(3)	—	(9)	—	(8)	—
Cerebrovascular	29	115·3	2	50·0	4	124·4	2	93·4	1	99·8
Accidents	31	99·2	2	54·1	5	152·9	1	49·4	1	120·0
Other known	79	140·4	9	116·9	4	630	5	111·5	5	263·3
Not known	10		0		2		0		1	

Table 6 shows the results of the posteriori Mantel-Haenszel analysis for certain diagnostic groups only. The number of deaths included in this analysis falls short of those used in tables 4 and 5--for example, 490 compared with 570 from all causes; in the remainder no matching control could be found. There is clear confirmation of a statistically significant linear trend in lung cancer, pneumoconiosis, and deaths (all causes) but no convincing association for the abdominal cancers.

One death ascribed to mesothelioma was found--a man born in 1907 who died in 1967. He was first employed at the plant in 1925, worked as a mule spinner from 1933 to 1955 and as an oven helper until he left in 1965. The tumour was stated to be peritoneal but there was no necropsy.

Table 6 — Dust exposure in male deaths from selected causes and controls (Mantel-Haenszel analysis)

Linearity	Dust exposure (mppcf) accumulated up to 10 years before death of case					Chi square	
	<10	10-19	20-39	40-79	≥80	Difference	Linearity
Pneumoconiosis (ICD 523)							
Deaths	0	0	3	10	4	17.36	10.80
Expected	3.1	2.2	3.8	4.1	3.7		
Relative risk	—	—	—	—	—		
Lung cancer (ICD 162-4)							
Deaths	25	3	8	7	6	24.08	20.43
Expected	32.4	5.4	5.3	3.7	2.2		
Relative risk	1	0.98	2.95	4.32	15.00		
Abdominal cancer (ICD 150-9)							
Deaths	13	4	2	4	0	4.06	2.53
Expected	15.5	2.9	2.5	2.1	0		
Relative risk	1	1.64	1.30	7.63	—		
All causes							
Deaths	331	45	53	37	24	14.42	10.63
Expected	348.0	46.2	48.5	32.4	15.0		
Relative risk	1	1.05	1.43	1.51	2.17		

This study shows that the relationship of lung cancer mortality to accumulated dust exposure is virtually linear.

The pattern of mortality in this cohort of chrysotile textile workers is similar to that reported for Quebec chrysotile miners and millers, particularly those employed at Thetford Mines.[57] Overall, the SMRs for the factory workers are somewhat higher than for the miners (perhaps due in part to questions of comparability with the reference populations). There is the same scarcity of deaths attributed to mesothelioma and, in both cohorts, the relationship of lung cancer mortality to accumulated dust exposure is virtually linear. It is only when actual levels of exposure are examined that the astonishing difference between the experience of these two chrysotile-exposed cohorts is seen. This is illustrated in Fig. 1 where, to facilitate comparison, the SMRs in both cohorts are based on exposure accumulated to age 45.[57] In fact, the slope of the exposure-response line for lung cancer in the textile workers is 50 times more steep than that observed in miners and millers. This [redacted] almost exactly the findings of Dement et al.[61] in their [redacted] cohort from the same plant; the agreement is very close (see Fig. 2). The data shown in this graph are based on mortality for white men only, 15 years or more from first employment and therefore differ somewhat from the figures in Table 5.

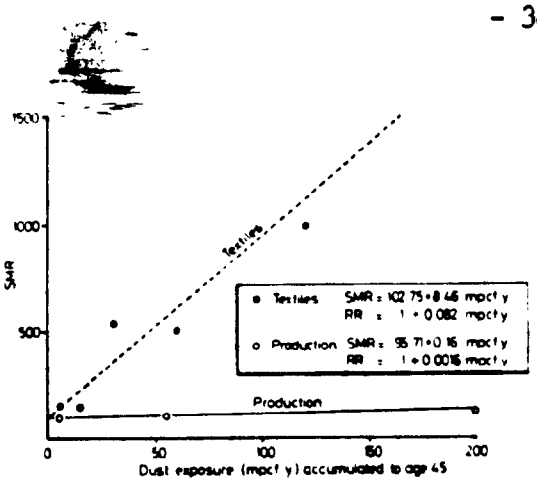


Fig 1 *Respiratory cancer SMRs in relation to dust exposure accumulated to age 45 in chrysotile production and textile manufacture*

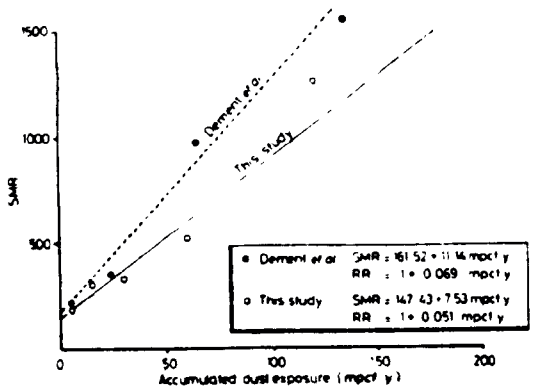


Fig 2 *Respiratory cancer SMRs in white men 15 years or more from first employment in relation to accumulated dust exposure. Comparison of this study and that of Dement et al*[9]

CONCLUSION:

Various reasons were discussed to determine whether the differences observed were due to errors in exposure estimates, etc. Assuming errors, the difference remains at least 10 fold.

9. Another cohort[86] of chrysotile asbestos factory (textile) workers in a Pennsylvania plant was studied, which included those employed during 1938-1959 for at least one month. Crocidolite and amosite were used at this plant also. Exposure data are shown in Tables 2 and 3.

Table 2 *Estimated average prevailing dust concentrations (MPCF) in main departments 1930–70*

	1930	1940	1950	1960	1970
Textile					
Preparation	15·0 * 14·6	* 3·5	* 2·0	*	1·5
Carding	12·0 * 9·3	* 3·2	* 2·0 *	1·6	
Spinning	7·0	* 2·5	* 1·8	*	1·5
Twisting	7·2	* 4·0	* 1·8	*0·5 *	1·1
Winding	3·0	* 1·5	*	0·8	
Cloth weaving	7·9 *3·4	*	0·9		
Tape weaving	7·3 *3·1	*	1·4	*	1·2
Felted tape	2·0	* 1·0	* 0·5		
Rope	4·0	* 2·5	* 1·2	*	0·5
Friction:					
Woven brakes	2·0	1·5	1·0	0·7	
Extruded brakes	2·0	1·5	1·0	0·8	
Dry [illegible]	10·0	6·0	4·0	3·8	
Cl[illegible]	2·0	1·5	1·5	1·5	
Brake finishing	2·0	1·5	1·0	0·7	
Sanding and finishing	2·0	1·5	1·0	0·7	
Finishing and shipping	0·5		0·2	0·2	
Packings, gaskets	1·3	1·3	0·6	0·7	
Maintenance, etc	0·5	0·5	0·2	0·2	

*Asterisks shown against textile processes indicate approximate date of improvements usually associated with technical change. Figures for friction and other departments are estimates for each decade

Table 3 *Age at start, duration of employment, and dust exposure (male only)*

	Length of gross service				
	<1	*1, <5*	*5, <20*	*≥20*	*Total*
No	1248	906	855	1013	4022*
Average age at start (years)	28·80	29·30	30·77	27·22	28·92
Gross service (years)	0·40	2·39	11·01	30·63	10·71
Net service (years)	0·38	1·87	8·06	27·51	9·18
Average dust concentration (mpcf)	2·60	2·40	2·73	1·58	2·32

*Excluding two whose employment histories were incomplete

Mortality was analyzed as in #8 above, using Pennsylvania death rates for reference. Mortality data by age and certified cause are presented in Table 1.

Table 1 *Male deaths by age and certified cause*

Cause of death (ICD code)	*Age at death*			*Total*
	<45	*45–64*	*≥65*	
All causes	191	667	534	1392
Malignant neoplasms:				
Lung* (162–164)	3	49	18	70
Oesophagus and stomach (150–151)	1	7	6	14
Colon and rectum (152–154)	2	21	12	35
Other abdominal* (155–159)	3	16	5	24
Larynx (161)	0	0	0	0
Other* (140–148, 160, 165–205)	16	57	40	113
Heart disease (400–443)	43	285	245	573
Respiratory tuberculosis (001–008)*	5	4	2	11
Other respiratory (470–522, 525–527)	6	17	25	48
Pneumoconiosis (523–524)	2	48	24	74
Cerebrovascular (330–334)	3	33	44	80
Accidents (800–999)	74	44	20	138
Other known causes*	23	73	80	176
Cause not known	10	13	13	36

*In 13 cases in these categories, mesothelioma was given as the cause of death, in one death ascribed to asbestosis, mesothelioma was also mentioned.

The SMR for all causes of death was 109.0. Those employed for less than 1 year had a SMR of 87.2, and those who had worked 20 or more years, 127.2. (Table 4)

Table 4 *Male deaths 20 years after first employment, by cause, in relation to length of service*

*Cause of death**	*Length of gross service years*									
	<1		*1, <5*		*5, <20*		*≥20*		*Complete cohort*	
	0	*SMR*	*0*	*SMR*	*0*	*SMR*	*0*	*SMR*	*0*	*SMR*
All causes	171	87·2	154	106·2	187	104·5	383	127·2	895	109·0
Malignant neoplasms										
Respiratory	9	69·6	3	32·9	14	128·8	27	158·9	53	105·0
Abdominal	8	72·9	11	133·7	11	105·9	24	131·3	54	112·7
Other	19	132·4	16	152·0	15	118·5	32	155·3	82	141·1
Heart disease	77	92·7	77	125·1	78	100·2	153	115·7	385	108·5
Respiratory tuberculosis	0	-	1	133·4	0	—	2	67·3	3	51·7
Other respiratory	4	54·2	2	38·1	11	161·0	50	442·4	67	215·0
Pneumoconiosis	(2)	—	(1)	—	(10)	—	(46)	—	(59)	—
Cerebrovascular	7	54·9	10	106·5	10	77·7	20	87·6	47	81·2
Accidents	13	117·5	15	181·1	8	87·2	9	60·1	45	103·5
Other known	30	75·2	15	52·4	37	103·0	62	103·1	144	87·2
Not known	4		4		3		4		15	

*As Table 1 except that ICD codes 160–164 are here grouped under "respiratory" malignnt neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

Malignant neoplasms, heart disease, and "other respiratory" disease were mainly responsible for the higher SMR in these long term workers. The other respiratory category included bronchitis and pneumonia (ICD 470-502) and pneumoconiosis (ICD 523-4) and was chosen for study because expected figures for pneumoconiosis alone were not available. Table 5 shows SMRs by cause and by accumulated dust exposure. The SMR for all causes rose steadily from 93.1 for

men with an exposure at under 10 mpcf.y to 215.2 in the highest category (80 mpcf.y). Respiratory, abdominal, and other malignant diseases and the non-malignant other respiratory group all contributed to this rising trend. On 14 death certificates a diagnosis of mesothelioma was specified: 10 were pleural tumours and four peritoneal. These deaths occurred in the period 1960-75. One (in 1960) was 16 years after first employment; the remaining 13 occurred 25-53 years after first employment. Two of the deaths from mesothelioma had been given the ICD code 199 (malignant neoplasms of other and unspecified sites); another 30 deaths 15 or more years after first employment were given the code 199. Seventeen of these 30 deaths occurred before 1965, the year after which most of the deaths from mesothelioma occurred. The diagnosis given in many of these cases was consistent with an unrecognized peritoneal mesothelioma.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf.y) accumulated 10 years before death*

*Cause of death** (See table 4)	*Dust exposure (mpcf.y)*									
	<10		*10 < 20*		*20 < 40*		*40 < 80*		*≥80*	
	O	*SMR*	*O*	*SMR*	*O*	*SMR*	*O*	*SMR*	*O*	*SMR*
All causes	470	93·1	86	82·1	130	125·6	105	174·9	104	215·2
Malignant neoplasms										
Respiratory	21	66·9	5	83·6	10	156·0	6	160·0	11	416·1
Abdominal	26	90·2	8	130·5	5	79·7	8	218·8	7	237·2
Other	47	130·4	5	68·5	11	148·6	7	164·7	12	372·8
Heart disease	221	102·7	41	89·2	60	130·6	34	130·5	29	108·5
Respiratory tuberculosis	1	34·3	0	—	—	—	1	169·7	1	163·6
Other respiratory	8	43·6	5	122·0	10	263·0	14	623·3	30	1689·2
Pneumoconiosis	(4)	—	(1)	—	(9)	—	(9)	—	(36)	—
Cerebrovascular	27	78·3	1	13·3	10	133·5	8	187·2	1	29·3
Accidents	33	120·1	3	56·2	1	18·6	6	193·9	2	91·0
Other known	74	73·3	17	80·0	23	109·7	21	172·2	9	97·8
Not known	12		1		0		0		2	

The Mantel-Haenszel (log rank) analysis[105] (table 6) bore out the exposure-response relationships observed in Table 5. There is a small shortfall (5% overall) between the numbers of cases used in this analysis and in the man-years analyses presented in Tables 4 and 5. The deficiency is explained by failure to find matching controls for every selected case.

Table 6 *Dust exposure in male deaths from selected causes and controls (Mantel-Haenszel analysis*)*

	Dust exposure (mpcf.y) accumulated up to 10 years before death of case					*Chi square Difference*	*Linearity*
	<10	*10 < 20*	*20 < 40*	*40 < 80*	*≥80*		
Pneumoconiosis (ICD 523)							
Deaths	3	4	10	11	28	39·56	39·17
Expected	14·6	8·1	10·9	8·1	14·3		
Relative risk	1	4·04	13·72	14·93	37·90		
Lung cancer (ICD 162–4)							
Deaths	20	4	10	6	11	5·77	4·98
Expected	24·4	5·2	8·0	5·6	7·7		
Relative risk	1	0·83	1·54	2·90	6·82		
Abdominal cancer (ICD 150–9):							
Deaths	26	8	5	8	7	3·22	1·09
Expected	28·8	6·8	7·0	5·3	6·1		
Relative risk	1	1·15	0·66	2·45	2·85		
All causes							
Deaths	451	81	121	100	99	34·66	26·12
Expected	476·6	104·5	118·6	80·4	72·0		
Relative risk	1	0·82	1·20	1·6	2·12		

The present cohort in the Pennsylvania plant was constituted in exactly the same way as that in the South Carolina chrysotile textile plant described elsewhere.[85]

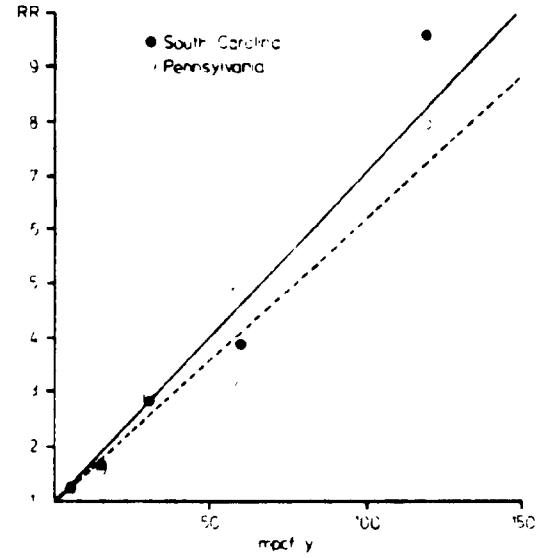
The Pennsylvania cohort was exposed to a somewhat higher average dust concentration: 2.32 mpcf compared with 1.80 mpcf in South Carolina. The mortality pattern in Pennsylvania resembled that in South Carolina in showing a rising SMR with increasing dust exposure for all causes of death, for respiratory cancer, and for pneumoconiosis. For respiratory cancer, however, the SMR for the lowest exposure group (less than 10 mpcf.y) was 115.5 in South Carolina but only 69.9 in Pennsylvania. By contrast with South Carolina, where the SMRs tended to be above 100 for causes unrelated to asbestos, and for all causes in very short-term employees,[85] the opposite was true in Pennsylvania. It seems likely that in both cohorts lack of comparability with the relevant state populations may be the explanation. Having regard for this possibility, the use of relative risks is perhaps more appropriate than SMRs for comparing the respiratory cancer mortality of the two cohorts. Table 7 shows that the relative risks of death from all causes, respiratory cancer, and pneumoconiosis in the two plants were extraordinarily similar. In both cohorts the relationships of respiratory cancer to exposure were essentially linear (figure) with slopes that were nearly identical (South Carolina, RR = 1 + 0.059 mpcf.y; Pennsylvania, RR = 1 + 0.051 mpcf.y).

Table 7 *Relative risks based on SMRs by cumulative exposure in two plants*

	mpcf.y				
	<10	*10 < 20*	*20 < 40*	*40 < 80*	*≥80*
All causes:					
South Carolina plant	1·0	1·09	1 36	1·48	2·29
Pennsylvania plant	1·0	0·88	1·35	1·88	2·31
Respiratory cancer					
South Carolina plant	1·0	1·28	2·13	2·93	7·21
	(1·32)	*(1·68)*	*(2·80)*	*(3·86)*	*(9·49)*
Pennsylvania plant	1·0	1·25	2·33	2·39	6·22
	(1·26)	*(1·58)*	*(2·94)*	*(3·03)*	*(7·87)*
Bronchitis, pneumonia, and pneumoconiosis.					
South Carolina plant	1·0	1·81	6·40	21·36	19·67
Pennsylvania plant	1·0	2 79	6·03	14·29	38·74

Figures in italics are relative risks calculated from SMRs at zero exposure derived from fitted line.

Similar proportions of all deaths in the two cohorts were from malignant disease (17% in South Carolina and 18% in Pennsylvania), but the types of malignancy differed. In South Carolina respiratory cancer accounted for 47%, abdominal 25%, and other types 28% whereas in the Pennsylvania plant the corresponding proportions were reversed, 27%, 29%, and 44%. Moreover, in South Carolina no systemic relationship with exposure was seen for abdominal or other types of malignant disease whereas in Pennsylvania there was evidence of such a relationship.



Relative risk of respiratory cancer and accumulated dust exposure in two mainly textile plants. (Lines fitted by LDK Liddell using the methods of Hanley and Liddell.)

[redacted]creased risk of mesothelioma in the Pennsylvania plant (14 cases in 1392 male deaths (1%) compared with one case in 867 (0.1%) in South Carolina) raises the question of whether the abdominal and more particularly other types of cancer included undiagnosed cases of mesothelioma. There is some support for this idea in the substantial number coded to ICD 199 (malignant disease of other and unspecified sites) and the fact that 17 of these deaths occurred before 1964 when malignant mesothelioma started to become more generally recognized. Once again there is evidence in this study of the special risk of mesothelioma associated with exposure to even quite small proportions of amphibole, in this case predominantly amosite.

CONCLUSION

The very similar exposure-response relationships for respiratory cancer and asbestosis observed in this and the South Carolina plant support the previous conclusion that the risks of these diseases in chrysotile production (mining and milling) and in textile manufacture are quite different. In the third plant studied, a friction materials plant in Connecticut, there was little or no excess risk of respiratory cancer or asbestosis.[85] This was also true in a friction materials plant in the United Kingdom.[66] Possible reasons for the striking epidemiological differences--fibre size distributions in particular--have been discussed elsewhere.[85, 107]

10. Mortality was studied[70] among asbestos-cement workers who had been hired prior to 1960 and who had been employed for a minimum of 9 years.

Table 1 gives the mortality rates for each of the three exposure groups of production workers, for the interval 20-33 years from first exposure.

Table 1 *Mortality rates in the interval 20–33 years from first exposure and estimated dust exposure of three groups of workers [redacted] (number of deaths in parentheses)*

[redacted]	Exposure group			
	Group A	*Group B*	*Group C*	*Ontario men†*
	*Rates (per 1000 man-years)**			
Mesothelioma	1·9 (1)	3·9 (2)	11·9 (6)	—
Lung cancer	13·6 (5)	26·1 (7)	11·9 (6)	1·6
Gastrointestinal cancer	0 (0)	2·5 (1)	6·0 (3)	0·6
All malignancies	17·3 (7)	35·9 (11)	31·8 (16)	4·7
Mesothelioma crude rates	2·5 (1)	4·6 (2)	11·9 (6)	—
Estimated exposure range (f-y ml)	8–69	69–121	122–420	
Estimated mean exposure (f-y ml)	44	92	180	
Standard deviation	19·4	15·8	57	

*Standardised to age distribution of group C
†Based on Ontario vital statistics 1970–4

The mean exposure levels (in f-y/ml) were: Group A-44; Group B-92; and Group C-180.

The mortality observed among the employees was compared with the mortality predicted from Ontario population rates (Table 2). To increase the man-years of observation in each cell, the second group, listed as P + M in the table combines the experience of the production and maintenance employees, all of whom were exposed to asbestos.

Table 2 *Mortality among the factory workers compared with the population of Ontario*

Cause	*Group*	*Years since first exposure*											
		15–19			*20–24*			*25–33*			*Total: 20–33*		
		Obs	*Exp*	*O/E*	*Obs*	*Exp*	*O/E*	*Obs*	*Exp*	*O/E*	*Obs*	*Exp*	*O/E*
All causes	P	8	8·9	1	16	11·8	1·4	34	11 6	2 9	50	23 4	2 1
	P + M	11	11·9	1	22	15·5	1 4	39	15 1	2 6	61	30·6	2·0
	C	7	5·0	1·4	7	5·9	1·2	7	7 4	1	14	13·3	[redacted]
All malignancies ICD. 140–209	P	2	1·9	1	9	2·8	3·2	20	2 9	6 9	29	5 7	[redacted]
	P + M	2	2 5	1	11	3 7	3·0	23	3·7	6 2	34	7·4	[redacted]
	C	3	1·1	2 7	3	1·4	2·1	1	1 8	1	4	3 2	[redacted]
Lung cancer ICD 162	P	1	0·6	1	6	1 0	6·0	11	1 0	11·0	17	2 0	8·5
	P + M	1	0·8	1	7	1 2	5·8	12	1 3	9 2	19	2 5	7 6
	C	0	0·3	0	0	0·5	0	1	0·6	1	1	1 1	1
Mesothelioma ICD 163, 158, 228	P	1	-	-	2	-	-	4	-	-	6	-	-
Gastrointestinal cancer ICD. 150–154	P	0	0·5	0	1	0 7	1	2	0·7	2 9	3	1 4	2 1
	P + M	0	0·7	0	1	0·9	1	3	0·9	3 3	4	1·8	2 2
	C	1	0 3	1	1	0 3	1	0	0·4	0	1	0·7	1
Non-malignant respiratory disease ICD. 460–519	P	1	0·4	1	1	0·7	1	3	0 8	3 8	4	1 5	2·7
	P + M	1	0·6	1	3	0·9	3 3	4	1 0	4·0	7	1 9	3 7
	C	0	0·3	0	0	0·4	0	1	0 5	1	1	0·9	1
Ischaemic heart disease ICD 410–414	P	4	3·9	1	2	4 7	0 4	5	4 6	1	7	9·3	0·8
	P + M	7	4·9	1 4	3	6·2	0 5	6	6·0	1	9	12 2	0·7
	C	3	2·1	1	1	2·4	0·4	2	2 9	1	3	5 3	0·6

P = Production workers M = Maintenance workers C = Unexposed workers

There were 10 deaths from malignant mesothelioma (5 pleural, 5 peritoneal) among the 58 deaths occurring in the production [redacted]--a proportional mortality of 17% (table 3). In addition, [redacted] the maintenance workers died of a pleural mesothelioma. All of these men had been exposed to both chrysotile and crocidolite in the pipe plant. The mean age at death of these 10 men was 51 years and none was over 60 (table 4).

Table 3 *Mortality rates from mesothelioma and lung cancer among the production workers (based on best evidence)*

Time since first exposure (years)		*Age*				
		35–44	*45–54*	*55–64*	*65–75*	*75 or more*
Mesothelioma	No of cases	2	5	3	0	0
15–33	Man-years	413	865	694	244	21·5
	Rate (per 1000 man-years)	4·8	5·8	4·3	0	0
20–33	No of cases	1	5	3	0	0
	Man-years	124	493	485	213	21·5
	Rate (per 1000 man-years)	8·0	10·1	6·2	0	0
Lung cancer	No of cases	0	0	13	6	1
15–33	Man-years	413	865	694	244	21·5
	Rate (per 1000 man-years)	0	0	18·7	24·6	46·5
20–33	No of cases	0	0	11	6	1
	Man-years	124	493	485	213	21·5
	Rate (per 1000 man-years)	0	0	22·7	28·2	46·5
	Ontario rates (based on vital statistics 1970–4) (per 1000 man-years)	0·1	0·5	1·7	3·5	3·8

The mortality rates for mesothelioma among the production workers are displayed in table 3 as a function of age. Table 5 gives the crude incidence rates for mesothelioma among all the asbestos-exposed employees, as related to the time interval since first exposure. Peto et al.[33] have suggested that the incidence of mesothelioma follows a power function relationship with time. The data are consistent with this suggestion, with an exponent value of between three and four.

There were 20 deaths from lung cancer among the 58 deaths in the production workers--a proportional mortality of 34%. Pathological information about 17 of these 20 cases indicates four were adenocarcinomas, eight were squamous, four were small cell undifferentiated, and one was a large cell undifferentiated tumor. As a group, these men were first exposed to asbestos in this plant at an older age, and they died later in life than the men dying of mesothelioma (table 4).

Table 4 *Some characteristics of the cases of mesothelioma and lung cancer (Classified according to best evidence)*

	Mean	*Range*	*Standard deviation*
Mesothelioma (n = 10)			
Age at first exposure	25	19–32	4·3
Age at death	51	42–57	5·4
Latency (years)*	25	17–30	3·8
Lung cancers (n = 20)			
Age at first exposure	39	31–52	6·4
Age at death	64	55–78	5·9
Latency (years)*	25	17–29	3·6

*Latency is the interval from first exposure to death

Table 5 *Incidence rates of mesothelioma among the production and maintenance workers exposed to asbestos*

	Time since first exposure (years)			
	15–19	*20–24*	*25–29*	*30–34*
No of cases	1	4	5	1
Man-years of risk	1182	1061	555	104
Incidence rate (per 1000 man-years)	0·8	3·7	9·0	9·6

CONCLUSION

Workers at this asbestos-cement factory exposed to historical dust conditions have experienced increased mortality rates from respiratory and malignant diseases. The lung cancer mortality rates

did not increase steadily with increasing estimates of cumulative exposure; in fact, the men in Group C experienced the lowest cancer rates of all. This may have been due to the small numbers involved, to differences in smoking habits, etc. Rates of death from mesothelioma were related to the magnitude of the cumulative exposure.

The cumulative exposure among production workers was estimated (to within a factor or 3 to 5) to have been about 100 f-y/ml, and the SMR for the period after 20 years was 850. The authors concluded that the lung cancer rates, at a cumulative exposure of 100-f-y/ml, may be raised several-fold.

11. Table 1 presents observed deaths and standardized mortality ratios (SMRs) for selected causes of death for the cohort[67] of production and maintenance-service workers (1075 men) for the intervals 1941-69 and 1970-3, which correspond to the original follow-up and the update periods, and for the total follow-up period 1941-73. For the period 1941-73, this cohort had an overall mortality rate 20.4% higher than that of all United States white males. This excess is due almost entirely to cancer and diseases of the respiratory system. For cancer, the greatest excess is in cancer of the respiratory system but with some excess also in cancer of the digestive system and all other cancers. For respiratory disease, the excess is due entirely to pneumoconiosis and pulmonary fibrosis, 19 cases of which were due to asbestosis (ISC 523.2). The pattern of deaths was similar during both of the follow-up periods, although overall mortality and cancer rates were somewhat higher during 1970-3. The increase in overall mortality for 1970-3 was primarily due to a large increase in death rates for stroke. Whether this increase is in any way related to occupational exposures is unknown.

TABLE 1

OBSERVED DEATHS AND SMRS FOR SELECTED CAUSES OF DEATH BY PERIOD OF FOLLOW-UP, 1075 MEN RETIRING FROM A UNITED STATES ASBESTOS COMPANY 1941-67 AND FOLLOWED THROUGH 1973

Cause of Death	1941-73		1941-69		1970-3	
	Observed Deaths	SMR	Observed Deaths	SMR	Observed Deaths	SMR
All causes	781	120 4	616	115 8	165	141 6
Cancer (140-205)	173	159 0	138	154.5	35	179 5
Digestive (150-159)	55	137 8	46	136.1	9	147 5
Respiratory (162 163)	63	270 4	49	270 7	14	269 2
All other cancers	55	120 6	43	115.0	12	146.3
Stroke (330-334)	74	96 4	48	76.7	26	183 1
Heart disease (400-443)	321	106 5	269	108.4	52	97 7
Respiratory disease (470-527)	68	173 0	54	178.2	14	155 6
Pneumoconiosis and pulmonary fibrosis (523 525)	31	-	25	—	6	—
Asbestosis (523 2)	19	-	16	—	3	—
All other causes	113	92 5	96	94.6	17	82.5
Death certificates not located	32	-	11	—	21	—

[redacted]Estimates of exposure were based on midget impinger counts expressed in million particles per cubic foot (mppcf). Five classifications were used. These were:

no exposure (0), less than 5 mppcf (2.5), 5-10 mppcf (7.5), 10-30 mppcf (20.0), 30-50 mppcf (40.0), 50 or more mppcf (62.5).

To compute cumulative dust exposure for each man, the dust level at each job and time period was multiplied by years at that job and summed across all jobs during his working lifetime. This total cumulative exposure can be thought of as mppcf-years.

TABLE 2

OBSERVED DEATHS AND SMRS FOR RESPIRATORY CANCER BY TOTAL DUST EXPOSURE AND PERIOD OF FOLLOW-UP, 1075 MEN RETIRING 1941-67 AND FOLLOWED THROUGH 1973

Total Dust Exposure (mppcf-years)	Number of Men	Mean Exposure (mppcf-years)	1941-73		1941-69		1970-73	
			Deaths	SMR	Deaths	SMR	Deaths	SMR
Under 125	437	62	19	197.9	15	200.0	4	190.5
125-249	224	182	9	180.0	8	200.0	1	100.0
250-499	265	352	19	327.6	13	309.5	6	375.0
500-749	105	606	9	450.0	8	470.6	1	333.3
750+	44	976	7	777.8	5	714.3	2	1000.0

Table 2 shows the relationship between total dose expressed as mppcf-years and mortality from respiratory cancer. For each dose interval, actual means are shown. These data, plotted on arithemetic paper, are also shown in Figure 1.*

[redacted]

*The relationship shown is not simply the result of time and the consequent fulfilling of latent period requirements. As noted in a previous paper, the dose rate makes an important contribution.[110]

There were 5 mesothelioma deaths observed in this cohort, of which 3 occurred during 1970-1973.

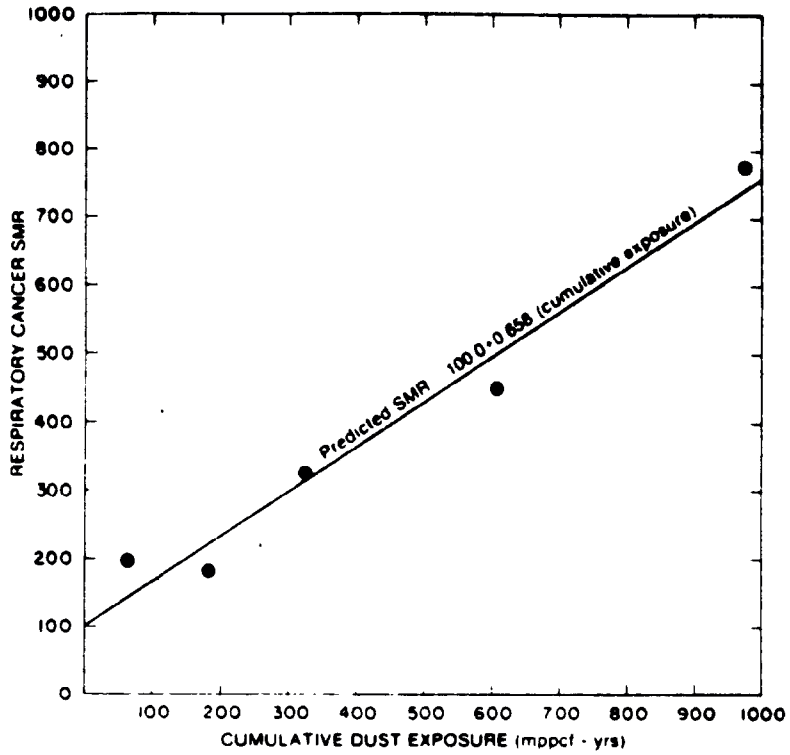


FIGURE 1 Total asbestos dust exposure and respiratory cancer mortality.

In an earlier report, it was speculated that the mathematical form of the dose-response relationship was the cumulative normal. The theoretical basis for this conjecture was the response curve in bioassay experiments. Schneiderman[108] has fitted a different curve to these data, while Peto[109] believes it is best described by a simple linear relationship. It does appear that omitting the Canadian data and adding 4 more years of follow-up change the relationship and make a linear relationship more likely. By use of the five data points from Table 1, this relationship can be expressed by the equation: predicted SMR - 100.0 + 0.658 (cumulative exposure).

The correlation between cumulative exposure and respiratory cancer SMR is 0.982. This prediction line is superimposed in Figure 1.

CONCLUSION

Respiratory cancer risk increased as the quantitative exposure level increased. The SMR for the lowest level was 2.0; for the highest level, 7.8.

The effects of asbestos exposure with respect to lung cancer risk continued well past the termination of exposure.

The study population of retirees are "survivors," and mortality experience may not reflect actual risks associated with asbestos exposure. Most likely, risks were underestimated.

12. Mortality of asbestos factory workers exposed to crocidolite, chrysotile, and/or amosite in the production of textiles or insulation materials has been reported.[64] The levels of exposure were reported as follows:

    (1) before 1945 the dust levels in certain jobs were said to average 20 fibers/ml or higher;

    (2) jobs classified as "low-moderate" were probably 5-10 f/ml;

    (3) in non-production jobs and some departments the levels were below 5 f/ml;

    (4) after 1955, many areas were probably above 2 f/ml.

    Laggers were considered separately.

    The male cohort consisted of 4600 men and 922 women. There have been 775 deaths among the male workers. An analysis of the 545 deaths that occurred among workers, excluding laggers, who had been followed for 10 years or longer is presented in Table 1. Asbestos-related disease is rarely if ever manifest in those dying within 10 years of first exposure. In the Tables, the deaths from mesothelial tumors are given in parentheses but are included in the total number of observed deaths in any particular diagnostic category.

TABLE 1
MORTALITY EXPERIENCES OF MALE FACTORY WORKERS

Cause of Death	Exposure Category							
	Low to Moderate				Severe			
	<2 Years (884)		>2 Years (554)		<2 Years (937)		>2 Years (512)	
	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected
All causes	118(4)	118 0	89 (7)	95 3	162*(16)	122.2	176*(19)	102.5
Cancers of lung and pleura (ICD 162, 163)	17(3)	11.01	16†(1)	9.0	31*(6)	12.8	56*(7)	10.4
Gastrointestinal cancer (ICD 150–158)	10	9 0	9 (4)	7 3	20‡(6)	9 5	19‡(8)	8.2
Other cancers	6	7.4	8 (1)	5.8	16‡(3)	7 9	16*(4)	6.3
Chronic respiratory disease	19	17 5	16	14 7	20 (1)	17.6	28‡	15 9

*p <0.001
†p <0.05
‡p <0.01.

There were 46 deaths from mesothelial tumors, 19 pleural and 27 peritoneal. All have been validated by histologic examination. Nearly all of the pleural tumors were identified among the intrathoracic tumors (carcinoma of the lung and pleura, ICD 162, 163). The peritoneal tumors were included with gastrointestinal tumors if certified as a peritoneal mesothelioma (ICD 158) or if confused with carcinoma of the bowel or pancreas. They were included with "other cancers" if certified as carcinomatosis (ICD 199) or as sarcoma or other tumors. Two deaths from mesothelial tumors were identified among causes of death not shown in the Tables. There were, apart from pleural mesothelioma, 103 deaths from carcinoma of the lung, which remains the most common tumor of asbestos workers.

Statistically significant excess mortality from chronic respiratory disease is seen only among those with long and severe exposure. Asbestosis was given as the cause of death in 13 instances but as the underlying cause of death in 34 of the deaths from lung cancer and in 27 of the deaths from either pleural or peritoneal mesothelioma. In four instances, coronary thrombosis was the actual cause of death. In the majority of the above cases, exposure had been long and severe.

Table 2 shows the mortality experiences of the laggers. The majority of these men were first employed after 1955. It is the custom, however, for laggers to work on contract for various employers, and some may have had previous exposure, so the authors are not entirely sure of their durations of exposure. Only approximately 2% of the entire group has been followed for 30 years or longer, but to date their experience is not dissimilar from that of other severely exposed male workers.

TABLE 2

LAGGERS AND MATES (1368 MALES)

	Observed	Expected
All causes	83*(10)	57.2
Cancers of lung and pleura (ICD 162,163)	25*(4)	5.6
Gastrointestinal cancer (ICD 150-158)	8 (5)	4.3
Other cancers	8	4.1
Chronic respiratory disease	12	7.4

*$p < 0.001$.

Mortality experience was also examined according to the length of follow-up, and an analysis of the standardized mortality ratios (SMRs) for cancers of the lung and pleura is presented in Table 3. In general, the SMR increases with increased length of follow-up and with increasing exposure, but for those with long exposure, the SMRs are higher in the group with follow-ups between 20 and 30 years. Only 20% of these workers have been followed up for 30 years or

longer, and currently about half of the deaths from mesothelial tumors occurred between 20 and 30 years after their first employment. However, as has been demonstrated previously,[111] the number of deaths from mesothelial tumors will continue to rise for some time.

TABLE 3

CANCERS OF THE LUNG AND PLEURA IN MALES (SMRs)

Length of Follow-up (years)	Low to Moderate Exposure		Severe Exposure	
	< 2 Years	>2 Years	< 2 Years	>2 Years
10-20	104	112	255	463
20-30	159	261	218	675
30+	278	184	265	446

In Table 4, a finer subdivision of job categories and of periods of employment in the factory are presented. It is noteworthy that in categories 1 and 2, ground workers, canteen workers, and production workers with very little and short exposures to dust, the SMR was 176, and there were three deaths from mesothelial tumors. Up to 1955, the estimated level of asbestos in the air was 2-5 fibers/ml.

TABLE 4

CANCERS OF LUNG AND PLEURA (SMRs)

Exposure Category	Duration of Exposure		
	>2 Years	2-5 Years	5 or More Years
Low to moderate			
1, 2	176	0	216
3	126	351	152
Severe			
4	247	227	714
5	238	236	567

However, looking at the death rates for mesothelial tumors graded by exposure category (Table 5), it is found that the rates reveal a very definite relationship to length and severity of exposure.

TABLE 5

MESOTHELIOMA DEATH RATES

Exposure Category and Duration (years)	Pleura	Peritoneum	S years	Rate per 100,000 S years
Males				
Low to moderate				
<2	3	1	12,031	33
>2	3	4	7,500	93
Severe				
<2	6	10	15,428	104
>2	7	12	7,827	243
Laggers				
<2	3	2	7,893	63
>2	1	4	2,690	186
Females				
Low to moderate	1	0	2,066	48
Severe				
<2	8	5	9,538	136
>2	4	3	4,388	360

Over 400 women were employed in the traditionally female jobs of carding, spinning, and doubling; 100 were employed in mattress making. Crocidolite was used heavily in textile departments, exposure was generally estimated to be very high, and women were also employed in other production departments, as well as in offices, canteens, and other low-exposure departments. The same pattern of analyses has been adopted, and Table 6 shows the observed versus the expected mortality in the general population, for groups with 10 years or more of followup.

TABLE 6

MORTALITY EXPERIENCES OF FEMALE FACTORY WORKERS

	Exposure Category					
			Severe			
	Low to Moderate (98)		<2 Years (396)		>2 Years (199)	
Cause of Death	Observed	Expected	Observed	Expected	Observed	Expected
All causes	34*(1)	22.0	88†(13)	65 6	78‡(7)	30 4
Cancers of lung and pleura (ICD 162.163)	3*(1)	0.5	15‡(7)	1.9	21‡(4)	0.8
Gastrointestinal cancer (ICD 150-158)	3	1.9	14†(4)	5.7	9†(2)	2.6
Other cancers	4	3 2	16 (2)	11.9	16‡(1)	5.3
Chronic respiratory disease	3	2.3	6	6 8	10†	3.2

*p < 0.05
†p < 0.01.
‡p < 0.001

In the low-moderate exposure group, there was one death from a mesothelial-pleural tumor. In all, there were 13 pleural-mesothelial tumors identified and eight peritoneal tumors, approximately the same proportion of all deaths (10%) as among the males. Among the severely exposed women with long exposures, there was a greater excess of lung cancer than among males with similar exposure. Also, apart from peritoneal mesotheliomas, there was an excess of deaths from gastrointestinal tumors and other cancers. Cancers of the ovary, uterus, and breast were analyzed separately. In the group of severely exposed women with long periods of employment, statistically significant excesses of cancer of the breast (obs., 6; exp., 2.1; p 0.05) and ovary (obs., 3; exp., 0.74; p 0.05) were noted. Not too much reliance can be placed on a single set of figures from one comparatively small cohort of women, and other factors related to marital status and parity that may operate in industrially employed women may be of importance. As in the males, the mesothelioma death rate (Table 5) relates clearly to the degree and length of exposure.

CONCLUSION

In the male cohort, SMR of 5.4 for lung cancer was observed in the severely exposed workers (20 f/cc) with 2 years of exposure (54/10.4) and 2.4 for those in the low to moderately exposed group (5-10 fibers/cc) (31/12.8). Risk increased with duration of follow-up and severity of exposure. Nineteen pleural and 27 peritoneal mesotheliomas were observed.

In the female cohort, the SMR of 6.0 (3/0.5) for lung cancer was observed in low to moderately exposed group; 7.9 (15/1.9) and 26.3 (21/0.8) in the severely exposed groups with 2 years and 2 years of employment, respectively. An apparent excess of breast (6/2.1) and ovarian (3/0.7) cancer was observed in the severely exposed group. Thirteen pleural and 7 peritoneal mesotheliomas were observed.

13. The experience of insulation workers in the U.S. has been reported by Selikoff, et al.[74] With regard to exposure data, reconstruction of work situations and extrapolation to the past suggests that these workers would have been exposed to dust levels of 4-12 fibers/ml (as time weighted averages). While there might have been periods of little or no exposure, there could also have been times of peak exposures much higher than the calculated averages.

TABLE 2

EXPECTED AND OBSERVED DEATHS AMONG 623 ASBESTOS INSULATION WORKERS NEW YORK-NEW JERSEY, 20 OR MORE YEARS AFTER ONSET OF WORK JANUARY 1, 1943-DECEMBER 31, 1962 (8545 Man-years of Observation)

Underlying Cause of Death	Expected*	Observed
Total deaths-all causes	195 4	253
Total cancer-all sites	32.1	95
Cancer of lung	6 0	42
Pleural mesothelioma	†	3
Peritoneal mesothelioma	†	4
Cancer of esophagus, stomach, colon-rectum	9 7	29
Cancer of larynx, pharynx, buccal cavity	1 7	2
Cancer of kidney	0.7	0
All other cancer	14 0	15
Noninfectious pulmonary diseases, total	4.0	14
Asbestosis	†	12
All other causes	159 3	144

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1962. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

Table 2 shows the mortality rates for workers with 20 + years of exposure followed to 1962. The authors point out that while deaths related to asbestos exposure seen in insulation workers may sometimes occur in less than 20 years from first exposure (lung cancer, asbestosis, and occasionally, mesothelioma), these are not common and, therefore, data on experience beyond the 20-year point was thought to more clearly define the influence of exposure. Observation of survivors was extended to 1976 (Table 3). The same overall pattern of causes of death continued, although distribution of deaths by cause changed somewhat, reflecting a number of epidemiological influences. Thus, pleural and peritoneal mesothelioma, which tend to occur somewhat later than bronchogenic

carcinoma, became proportionately more common. Thus change also reflects the smaller proportions of older men who ever smoked cigarettes, and also a "survivor effect." Since the smokers in the original group had increased mortality risk (especially from lung cancer and cardiovascular disease) there would likely have been comparatively fewer of these and still fewer who continued smoking at least the same amount, among the cohort survivors, as the years went by. Except as influenced by other factors associated with advancing lapsed time since onset of exposure, this would make for fewer deaths of lung cancer, with more men at risk of dying of other asbestos-associated disease.

TABLE 3

EXPECTED AND OBSERVED DEATHS AMONG 632 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS JANUARY 1, 1943–DECEMBER 31, 1976

(13,925 Man-years of Observation)

Underlying Cause of Death	Expected*	Observed
Total deaths, all causes	328.9	478
Total cancer, all sites	57.0	210
Cancer of lung	13.3	93
Pleural mesothelioma	†	11
Peritoneal mesothelioma	†	27
Cancer of esophagus	1.4	1
Cancer of stomach	5.4	19
Cancer of colon-rectum	8.3	23
Cancer of larynx, pharynx, buccal cavity	2.8	6
Cancer of kidney	1.3	2
All other cancer	24.5	28
Noninfectious pulmonary diseases, total	9.3	45
Asbestosis	†	41
All other causes	262.6	223

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S National Center for Health Statistics, 1949–1976. Rates for specific cause of death for 1943–1948 were extrapolated from rates for 1949–1955.

†Rates are not available, but these have been rare causes of death in the general population.

Lung cancer remained the most important cause of excess deaths, with 93 observed, 13.3 expected. Gastrointestinal cancer was also increased as seen in the original report (43 observed, 15.1 expected). Seventy-six percent of the original cohort enrolled in 1943 had died by 1976.

Variations in distribution of deaths by cause over time are shown in Table 4.

TABLE 4

EXPECTED AND OBSERVED DEATHS AMONG 632 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS JANUARY 1, 1943-DECEMBER 31, 1976

Number of Men Attaining Category Man-years of Observation	Less than 20 Years 325 1970		20-34 Years 561 6263		35 or More Years 698 5692	
Underlying Cause of Death	Expected*	Observed	Expected*	Observed	Expected	Observed
Total deaths, all causes	9.0	9	80.4	119	239.5	358
Total cancer, all sites	1.1	2	13.5	53	42.4	155
Cancer of lung	0.2	0	3.0	26	10.1	67
Pleural mesothelioma	†	0	†	4	†	7
Peritoneal mesothelioma	†	0	†	3	†	24
Cancer of esophagus	0.02	0	0.4	0	1.0	1
Cancer of stomach	0.1	0	1.5	6	3.8	13
Cancer of colon-rectum	0.2	0	1.9	7	6.2	16
Cancer of larynx, pharynx, buccal cavity	0.05	2	0.8	2	1.9	2
Cancer of kidney	0.03	0	0.4	0	0.9	2
All other cancer	0.5	0	5.5	5	18.5	23
Nonmalignant pulmonary diseases, total	0.1	0	1.6	4	7.6	41
Asbestosis	†	0	†	3	†	38
All other causes	7.8	7	65.3	62	189.5	154

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1976. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

The experience of workers exposed after 1943 (reflecting postwar "cleaner" conditions) has also been reported. In the 15,520 man-years of observation during the less than 20-year period (Table 6), there was no unusual mortality experience. Altogether there were fewer deaths than expected, and there was no increase in cancer deaths.

TABLE 6

EXPECTED AND OBSERVED DEATHS AMONG 833 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS FIRST EMPLOYED JANUARY 1, 1943-DECEMBER 31, 1962, AND OBSERVED FROM FIRST EMPLOYMENT-DECEMBER 31, 1976
(Duration from Onset of Employment)

Number of Men Attaining Category Man-years of Observation	Less than 20 Years 833 15,520		20-34 Years 523 3281	
Underlying Cause of Death	Expected*	Observed	Expected*	Observed
Total deaths, all causes	39.8	23	24.8	39
Total cancer, all sites	5.1	5	5.0	15
Cancer of lung	1.1	2	1.8	8
Pleural mesothelioma	†	0	†	2
Peritoneal mesothelioma	†	0	†	1
Cancer of esophagus, stomach, colon-rectum	0.7	1	0.8	2
Cancer of larynx, pharynx, buccal cavity	0.2	1	0.3	1
Cancer of kidney	0.1	0	0.1	1
All other cancer	3.0	1	2.0	0
Nonmalignant pulmonary diseases, total	0.5	0	0.6	7
Asbestosis	†	0	†	6
All other causes	34.2	18	19.2	17

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1976. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

In the 3281 man-years of observation 20-34 years from onset of exposure, there were 3 times as many cancer deaths as expected, primarily due to lung cancer.

CONCLUSION

No dose-response inference is possible because of the lack of exposure data.

14. Observations on 17,800 asbestos insulation workers in the U.S. and Canada followed from 1967 to 1976 is discussed below.[64] During the decade of observation 2271 deaths occurred (Table 12), whereas only 1658.9 deaths were expected. The excess deaths were primarily the result of an increased number of instances of cancer at several sites.

TABLE 12

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967 DECEMBER 31, 1976

NUMBER OF MEN 17,800

MAN-YEARS OF OBSERVATION 166,853

Underlying Cause of Death	Expected*	Observed (BE)	Observed (DC)	Ratio o/e (BE)	Ratio o/e (DC)
Total deaths, all causes	1658 9	2271	2271	1.37	1 37
Total cancer, all sites	319 7	995	922	3.11	2 88
Cancer of lung	105.6	486	429	4.60	4 06
Pleural mesothelioma	†	63	25	—	—
Peritoneal mesothelioma	†	112	24	—	—
Mesothelioma, n.o.s.	†	0	55	—	—
Cancer of esophagus	7.1	18	18	2.53	2.53
Cancer of stomach	14 2	22	18	1.54	1.26
Cancer of colon-rectum	38 1	59	58	1.55	1 52
Cancer of larynx	4.7	11	9	2.34	1 91
Cancer of pharynx, buccal	10.1	21	16	2.08	1 59
Cancer of kidney	8.1	19	18	2.36	2.23
All other cancer	131.8	184	252	1.40	1.91
Nonmalignant pulmonary diseases, total	59 0	212	188	3.59	3 19
Asbestosis	†	168	78	—	—
All other causes	1280 2	1064	1161	0 83	0 91

*Expected deaths are based upon white male age-specific U.S death rates of the U.S. National Center for Health Statistics, 1967-1976.

†Rates are not available, but these have been rare causes of death in the general population

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC). Number of deaths as recorded from death certificate information only.

Apart from lung cancer, mesothelioma, gastrointestinal cancer, cancer of the larynx, pharynx and oral cavity and cancer of the kidney, there was still an excess of cancer of other sites, with 184 observed, 131.8 expected (Table 13).

TABLE 13

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967-DECEMBER 31, 1976
NUMBER OF MEN 17,800
MAN-YEARS OF OBSERVATION 166,853

Underlying Cause of Death	Expected*	Observed (BE)	Observed (DC)	Ratio o/e (BE)	Ratio o/e (DC)
Total deaths, all causes	1658.9	2271	2271	1.37	1.37
Cancer, all sites	319.7	995	922	3.11	2.88
Deaths of less common malignant neoplasms					
Pancreas	17.5	23	49	1.32	2.81
Liver, biliary passages	7.2	5	19	0.70	2.65
Bladder	9.1	9	7	0.99	0.77
Testes	1.9	2	1	—	—
Prostate	20.4	30	28	1.47	1.37
Leukemias	13.1	15	15	1.15	1.15
Lymphomas	20.1	19	16	0.95	0.80
Skin	6.6	12	8	1.82	1.22
Brain	10.4	14	17	1.35	1.63

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976.
(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).
(DC): Number of deaths as recorded from death certificate information only.

From a purely statistical point of view, in view of the increased incidence of cancer of several sites among asbestos insulation workers, it was expected that a proportion of these men would suffer multiple cancers simultaneously, even beyond the tendency of such findings to be made among individuals with cancer, in general.[12] Again, this would not be reflected in tabulations of causes of death by single underlying cause, as is the usual practice. Analysis demonstrated one hundred malignant neoplasms present but not causing death (Table 14). Sometimes these additional neoplasms were

TABLE 14

MORTALITY EXPERIENCE AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA 1967 1976 OBSERVATIONS IN 2271 CONSECUTIVE DEATHS

Malignant Neoplasms Present, but not Causing Death* Site	Number
Lung	24
Pleural mesothelioma	2
Peritoneal mesothelioma	1
Esophagus	0
Stomach	1
Colon	19
Oropharynx	3
Larynx	5
Kidney	3
Other	42†
	100‡

*Twenty-one of these neoplasms were mentioned on the death certificate (but were not categorized as underlying cause of death).
†Including leukemia 5, lymphoma 3, bladder 5, prostate 13, thyroid, etc.
‡In 92 individuals; total includes multiple cancers in eight cases.

mentioned on the death certificate but as an "other significant condition," not in the section on the underlying cause of death. Forty were present among the 1064 cases where death was due to causes other than cancer or asbestosis (Table 15). Among the 168 deaths of asbestosis, cancer was also present in 7, 6 of these being bronchogenic carcinoma. Analysis of the circumstances leading to death, however, indicated that the underlying cause was asbestotic pulmonary insufficiency, and that the lung cancers were present but with no decisive influence at the time of death. Nineteen other cancers were present among the 486 deaths of lung cancer and 10 other cancers accompanied the 175 deaths of mesothelioma. There were 9 "incidental" neoplasms among the 99 deaths of gastrointestinal cancer. Although experiences are so far limited, it may not be wholly unexpected that there were proportionately more incidental neoplasms accompanying deaths of colon-rectum cancer, compared to those of lung cancer (8.5% vs. 3.9%). One may speculate that this could be due to the longer

TABLE 15

MORTALITY EXPERIENCE AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA 1967-1976: OBSERVATIONS IN 2271 CONSECUTIVE DEATHS NUMBER OF INCIDENTAL MALIGNANT NEOPLASMS (NOT CAUSING DEATH) IN RELATION TO UNDERLYING CAUSE OF DEATH AS ESTABLISHED BY BEST EVIDENCE (BE)

Underlying Cause of Death	Number of Deaths of Underlying Cause	Incidental Malignant Neoplasms	
		No. of Deaths	Total Cancers
Cancer all sites	995	45	50
Cancer of lung	486	17	19
Pleural mesothelioma	63	4	4
Peritoneal mesothelioma	112	5	6
Cancer of esophagus	18	1	1
Cancer of stomach	22	3	3
Cancer of colon-rectum	59	5	5
Cancer of larynx	11	0	0
Cancer of pharynx, buccal cavity	21	2	3
Cancer of kidney	19	0	0
All other cancers	184	8	9
Nonmalignant pulmonary diseases, total	212	10	10*
Asbestosis	168	7	7*
All other causes	1064	37	40
Total	2271	92	100

*Six of these were lung cancer.

clinical course of many patients with colon-rectum cancer, compared to lung cancer, with greater opportunity, simply in terms of time, to develop additional disease.

Multiple cancers were present, overall, in 2.1% of deaths among these asbestos insulation workers (48 of 2271). It is perhaps to be expected that this was more likely to be the case among those for whom cancer was the primary cause of death (4.5%), while only 3 of the 1276 other deaths had this finding.

It is now well appreciated that most asbestos associated disease is first seen after considerable periods from onset of exposure in both occupational and environmental circumstances. This is true both for the presence and extent of parenchymal fibrosis and pleural fibrosis and/or calcification,[3,13] and for asbestos-associated neoplasms.[14]

Some limited excess disease was observed in less than 20 years from onset of exposure (Table 16). Among 12,683 men with such experience, covering 89,462 man-years of observation, the number of cancer deaths was about doubled, with 42.6 deaths expected and 83 observed. There were no excess deaths of gastrointestinal cancer and only 5 deaths of mesothelioma, with these in the 15-19 years from onset category. Age, year and sex specific mortality data of the U.S. National Cancer for Health Statistics indicated that 11.9 deaths of lung cancer were to be expected. Thirty-six occurred. There were 8 deaths from asbestosis.

TABLE 16

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967–DECEMBER 31, 1976. ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

Total Men	Before 20 Years from Onset 12,683					20 or More Years from Onset 12,851				
Man-years of Observation	89,462					77,391				
		Observed		Ratio o/e			Observed		Ratio o/e	
Underlying Cause of Death	Expected*	(BE)	(DC)	(BE)	(DC)	Expected*	(BE)	(DC)	(BE)	(DC)
Total deaths, all causes	282.9	325	325	1.15	1.15	1376.0	1946	1946	1.41	1.41
Cancer, all sites	42.6	83	77	1.95	1.81	277.1	912	845	3.29	3.05
Cancer of lung	11.9	36	32	3.03	2.69	93.7	450	397	4.80	4.24
Pleural mesothelioma	†	2	2	—	—	†	61	23	—	—
Peritoneal mesothelioma	†	3	0	—	—	†	109	24	—	—
Mesothelioma, n.o.s.	†	0	1	—	—	†	0	54	—	—
Cancer of esophagus	0.6	1	1	—	—	6.5	17	17	2.64	2.64
Cancer of stomach	1.5	1	0	—	—	12.7	21	18	1.65	1.42
Cancer of colon-rectum	4.1	4	4	—	—	34.0	55	54	1.62	1.59
Cancer of larynx	0.4	2	2	—	—	4.3	9	7	2.09	1.63
Cancer of pharynx, buccal	1.3	3	2	—	—	8.8	18	14	2.05	1.59
Cancer of kidney	1.1	3	3	—	—	7.0	16	15	2.29	2.14
All other cancer	21.7	28	30	1.29	1.38	110.1	156	222	1.42	2.02
Noninfectious pulmonary diseases, total	5.2	8	11	1.54	2.12	53.8	204	177	3.78	3.28
Asbestosis	†	8	2	—	—	†	160	76	—	—
All other causes	235.1	234	237	1.00	1.01	1045.1	830	924	0.79	0.88

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967–1976.
†Rates are not available, but these have been rare causes of death in the general population.
(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).
(DC): Number of deaths as recorded from death certificate information only.

On the other hand, extensive disease was seen among the 12,051 men who had reached 20 or more years from onset during the decade of study. Here, 1376.0 deaths were anticipated; 1946 occurred. There were 160 deaths of asbestosis and 912 of cancer. It was at this time that bronchogenic carcinoma made its heaviest contribution, with 93.7 such deaths expected and 450 observed. One hundred and seventy deaths of mesothelioma were then seen and the increase in gastrointestinal cancer found. Table 17 depicts these data in some detail, in five-year periods from onset of employment. Lung cancer data are given as both expected and observed numbers of death. This practice cannot be followed for mesothelioma, where expected deaths cannot be computed for the general population. Instead, both the number of deaths of pleural and peritoneal mesothelioma, as well as the number of deaths of these causes per thousand persons years at risk are provided. The latter does not take into account variations in achieved age, but this may have less influence than achieved duration from onset of employment. It will be seen that very major increases in numbers of deaths of lung cancer are first seen at 15-24 years from onset of work, with continued further increases. The extraordinary increase in deaths of mesothelioma, both of the pleura and the peritoneum, is not observed until somewhat later, reaching 2.78 deaths per thousand person-years at risk for pleural mesothelioma at 35-39 years from onset of work, and 5.47 deaths of peritoneal mesothelioma per thousand person-years at 45 + years from onset.

TABLE 17

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN UNITED STATES AND CANADA, JANUARY 1, 1967-DECEMBER 31, 1976
ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

Duration from Onset (Years)	Number of Men	Person-years of Observation	Lung Cancer					Pleural Mesothelioma			Peritoneal Mesothelioma		
			Exp.*	Observed (BE)	Observed (DC)	Ratio o/e (BE)	Ratio o/e (DC)	Number (BE)	Number (DC)	No./1000 Person-years (BE)	Number (BE)	Number (DC)	No./1000 Person-years (BE)
- 10	8,190	26,393	0.7	0	0	—	—	0	0	0	0	0	0
10-14	9,083	29,003	2.7	7	5	2.55	1.82	0	0	0	0	0	0
15-19	9,948	34,066	8.5	29	27	3.40	3.17	2	2	0.06	3	0	0.09
20-24	8,887	31,268	17.0	59	57	3.48	3.36	6	4	0.19	3	2	0.10
25-29	6,596	20,657	21.0	105	96	5.00	4.58	13	5	0.63	19	3	0.92
30-34	3,547	11,598	18.4	112	103	6.08	5.59	9	3	0.78	23	6	1.98
35-39	2,020	5,403	11.5	65	57	5.68	4.98	15	4	2.78	19	5	3.52
40-44	1,108	3,160	8.1	40	131	4.93	3.82	4	3	1.27	16	3	5.06
45 +	1,448	5,305	17.8	69	53	3.89	2.98	14	4	2.64	29	5	5.47

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976. Smoking habits not taken into account.

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

In another reflection of the clinical concerns among these workers, Table 18 indicates that approximately one-third of all deaths were due to lung cancer at 30-34 years from onset, while mesothelioma accounted for 13% of all deaths at 35-39 years.

Altogether, lung cancer was responsible for 21% of all deaths observed in this cohort and mesothelioma for 8%.

TABLE 18

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA, JANUARY 1, 1967 DECEMBER 31, 1976.
ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

Years from Onset of Employment	Total Deaths	Percent of All Deaths							
		Lung Cancer		Mesothelioma					
				Pleural		Peritoneal		Total	
		(BE)	(DC)	(BE)	(DC)	(BE)	(DC)	(BE)	(DC)
<10	51	0	0	0	0	0	0	0	0
10-14	85	8 2	5.9	0	0	0	0	0	0
15-19	189	15.3	14.3	1.1	1.1	1.6	0	2.7	1.6
20-24	320	18.4	17.8	1.9	1.3	0 9	0.6	2.8	2.5
25-29	388	27.1	24.7	3 4	1 3	4.9	0.8	8.3	5.2
30-34	340	32.9	30.3	2 7	0.9	6.8	1.8	9.4	6.5
35-39	253	25.7	22.5	5 9	1.6	7 5	2.0	13.4	7.9
40-44	203	19.7	15.3	2.0	1.5	7 9	1.5	9.9	6.4
45+	442	15.6	12.0	3.2	0.9	6.6	1.1	9.7	4.1
Total	2271	21.4	18.9	2.8	1 1	4 9	1.1	7.7	4.6

*Total includes mesothelioma not specified as either pleural or peritoneal.
(BE). Best evidence Number of death categorized after review of best available information (autopsy, surgical, clinical).
(DC) Number of deaths as recorded from death certificate information only.

CONCLUSION

The study results indicate a high increase in risk of lung cancer associated with asbestos exposure, but the lack of exposure data makes it difficult to show a dose-response relationship.

15. Asbestos cement building materials plant workers have been studied[87] to determine the risk of respiratory malignancy in relation to duration, degree, and fiber type of exposure to asbestos. Subjects were classified into 5 total dust categories for which mean length of follow-up and mean age at initial exposure are comparable. (Table 1)

TABLE 1

COHORT BY FOLLOW-UP WITHIN EXPOSURE CATEGORIES

Total Dust within 20 Yr of Initial Exposure (mppcf-yr*)	No	Mean Follow-Up (yr.)	Mean Age at Initial Exposure (yr)
≤ 10	3,037	26.7	27.6
11-50	1,303	27.3	27.4
51-100	383	28.1	27.6
101-200	344	27.3	27.7
> 200	878	28.7	28.6

*Million particles per cubic foot-yr.

[redacted] the standard man-yr approach, expected numbers of deaths for each exposure category were calculated on the basis of race-age-cause-specific rates for both the U.S. and Louisianna male populations for 1950, 1960, and 1970.

Cause-specific standard mortality ratios, SMR (100 x observed number of deaths/expected number), were obtained for various causes for each of the 5 exposure categories (Table 2). SMR for all causes combined remain generally low, but increase slightly with degree of exposure: 60, 64, 75, 80, and 94. SMR for respiratory system neoplasms remain low for the 3 lowest exposure groups, but exceed 100 in the 2 highest categories: 77, 70, 26, 290, and 226. The very low SMR in the middle dust category is probably a chance occurrence; with only 3.8 respiratory neoplasm deaths expected, the probability (assuming a Poisson distribution) of observing one or fewer is 0.11.

TABLE 2

STANDARD MORTALITY RATIOS BY CAUSE WITHIN EXPOSURE CATEGORIES

	Total Dust Within 20 Yr of Initial Exposure (mppcf-yr*)									
	≤ 10 (n = 2,037)		11-60 (n = 1,369)		61-100 (n = 363)		101-200 (n = 344)		> 200 (n = 578)	
Cause of Death	O/E†	SMR‡	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR
All causes	260/433.7	60	141/216.9	64	66/76.1	78	42/52.2	80	109/116.1	94
All malignant neoplasms (140-209)	54/77.3	70	27/37.1	73	7/12.9	54	14/9.6	147	18/19.8	91
Digestive system (150-159)	10/24.6	41	10/11.9	84	3/4.2	71	0/3.0	-	2/6.4	31
Respiratory system (160-163)	19/24.7	77	8/11.4	70	1/3.8	26	8/3.1	260§	14/6.2	226§
Other (residual)	25/28.0	89	9/13.8	65	3/4.9	61	6/3.4	147	2/7.2	28
Major cardiovascular diseases (390-448)	129/215.7	60	78/113.9	68	33/40.1	82	14/26.5	53	61/57.4	106
All other causes	76/140.7	54	26/47.8	54	12/16.2	74	6/11.6	78	26/23.8	84

* Millions of particles per cubic foot-yr

† Ratio of observed to expected deaths.

‡ Standard mortality ratio

§ $P < 0.01$ (number of observed deaths compared to the number expected, assuming a Poisson distribution).

In the 3 lowest exposure categories, the SMR for over-all mortality and respiratory neoplasms are comparable, as demonstrated graphically (figure 1) by the extensive overlap of their respective 95 per cent confidence intervals (based on a Poisson distribution). On the contrary, there was no overlap in either of the 2 highest exposure groups. Assuming no association between trace and cause of death, the close agreement of the over-all and respiratory malignancy SMR in the low exposure groups is additional evidence that, although some underestimation might have occurred because of those lost to view, there are no excess respiratory neoplasms in these categories.

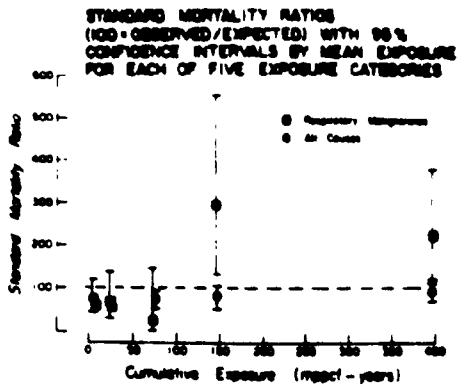


Fig 1 Standard mortality ratios with 95 per cent confidence intervals by mean exposure for each of 5 exposure categories.

No excess mortality occurred in any exposure group for any cause other than respiratory neoplasms.

The analysis was also performed with the number of deaths expected on the basis of Louisiana death rates. Because lung cancer rates are higher in Louisiana than in most states, the expected numbers of respiratory neoplasms are greater than with the U.S. rates, thus resulting in lower SMR. The patterns observed for the 5 exposure categories were the same as with the U.S. rates; over-all mortality SMR were 56, 64, 71, 73, and 83; respiratory neoplasm SMR were 64, 59, 23, 225, and 187. As with U.S. rates, no excess mortality other than for respiratory neoplasms were observed.

Two pleural mesotheliomas were diagnosed in the total study population: one person was employed for 10 months (with known exposure only to chrysotile), the other for 14 yr (with most of his employment in the pipe plant, which resulted in exposure to both chrysotile and crocidolite). Because these men died 18 and 19 yr after initial employment, respectively, neither fulfilled the cohort criterion of a minimum of 20 yr of follow-up and therefore are not included in this analysis. It was considered possible that this tumor was underdiagnosed in this population.

The results of Newhouse[112] suggest that the latent period for the development of asbestos-related neoplasms may be less than 20 yr, as with the 2 mesotheliomas found here. Using Newhouse's methodology, the effect of latency on the mortality experience of this population was assessed by performing the analysis by 5-yr periods after initial employment. In each analysis, persons with follow-up of less than the prescribed minimum are excluded; an individual person's exposure is calculated at the start of the particular time period. Because each period is only 5 yr in length, it was necessary to condense the original 5 exposure categories into three, although the expected numbers of deaths remain very small.

Results for the 2 lowest exposure categories (representing the original 3 lowest groups) indicate no discernible pattern for respiratory neoplasm SMR as time since initial exposure increases; those for the highest exposure category exhibit an increasing trend as long as 30 yr. since initial exposure (Table 3).

TABLE 3

RESPIRATORY MALIGNANCY STANDARD MORTALITY RATIOS BY 5-YR FOLLOW-UP AND TOTAL DUST AT START OF PERIOD

Yr since Initial Exposure	No.	Total Dust at Start of 5-Yr Period (mppcf-yr)					
		< 10		10–100		> 100	
		O/E	SMR	O/E	SMR	O/E	SMR
10–15	6,328	7/4.4	159	1/2.4	42	1/1.3	77
15–20	6,144	6/6.5	94	5/4.3	116	3/2.4	126
20–25	5,648	10/12.1	83	5/6.4	78	6/3.9	154
25–30	4,367	6/10.1	59	3/5.4	56	7/3.0	233*
30–35	1,220	3/1.8	167	1/2.2	45	5/1.5	333*
> 35	313	0/0.6	0	0/1.0	0	4/1.3	308*

For definitions of abbreviations, see table 2.

*P < 0.05 (number of deaths observed compared to number of deaths expected, assuming a Poisson distribution).

To compare the preceding results with those which would have been obtained with a different study design[115], an alternate method of analysis was performed for this cohort (men with at least 20 yr of follow-up) by considering 4 control subjects for each case of lung cancer. These control subjects were selected at random from among men in the cohort who were born in the same year as the cancer patient, were of the same race, had survived at least into the year following that in which the patient died, and if they subsequently died, did not die of a malignancy.

The mean total dust exposure (accumulated within 20 yr. after initial employment) was 164.1 mppcf-yr. for the cancer patients and 77.8 for the control subjects. A 2-way analysis of variance (the matched sets acting as a blocking factor), with Scheffe's multiple comparisons, found that there were no differences among the exposure means of the 4 sequences of control subjects, but that the mean dust exposure for the patients was significantly greater than that of the control subjects (P 0.005).

The distributions of the cancer patients and the control subjects by total exposure to dust are presented in Table 4. The odds ratio, an estimate of relative risk, was calculated for each category relative to the lowest degree of exposure.

TABLE 4

LUNG CANCER CASES AND MATCHED CONTROLS (4 PER CASE): TOTAL DUST EXPOSURE AND ODDS RATIOS

Total Dust within 20 Yr of Initial Exposure (mppcf-yr*)	No. Cases	No. Controls	Odds Ratio† (Relative to Lowest Category)
< 10	17	87	1.00
10–99	7	26	1.14
99–199	1	11	0.62
199–299	8	16	2.08‡
> 299	14	29	2.78‡
Total	47§	169	

*Million particles per cubic foot-yr.

†Usual estimate of relative risk.

‡$P < 0.05$, based on a χ^2 (1) distribution.

§The total of 51 respiratory malignancy deaths in table 2 resulted from random allocation of deaths without certification.

The over-all pattern of the odds ratio is similar to that of the respiratory malignancy SMR: the risk in the second exposure category is comparable to that in the lowest, an unexplained dip occurs in the third category (doubtless the same chance occurrence), and a significantly greater risk is observed at the 2 highest exposure categories.

Because information had already been collected on the entire cohort, the case-control approach, using only a subset of the population, does not make full use of the data available. Moreover, although this alternate approach provides estimation of the risk for each exposure category relative to the lowest category, no assessment of the risk experienced in the lowest category is possible. Despite these limitations, the observed pattern of risk across exposure categories was similar to that obtained with man-yr., prospective design, and analysis.

The preceding analysis was based on cumulative dust exposure, which has 2 components: (1) duration of exposure, and (2) average dust concentration. To assess the contribution of each, the population was divided into 9 duration-by-average-concentration categories. For these groups, the mean values of each variable within a fixed category were comparable across the categories of the other, and mean follow-up times were homogeneous (Table 5).

TABLE 5

COHORT BY DURATION AND CONCENTRATION OF EXPOSURE

Average Dust Concentration (mppcf)*	Duration of Employment (yr)		
	< 2	2–10	> 10
< 5	n = 1,223	n = 204	n = 108
	4.6†	4.2	3.2
	0.5‡	4.7	21.6
	26.8§	27.5	28.3
5–20	n = 1,691	n = 361	n = 269
	17.9	13.6	12.9
	0.5	4.6	21.7
	27.9	28.2	27.6
> 20	n = 764	n = 288	n = 174
	34.6	29.4	26.7
	0.7	4.4	22.0
	27.1	28.7	28.7

*Million particles per cubic foot.
†Mean average dust concentration (mppcf).
‡Mean length of employment (yr).
§Mean length of follow-up (yr).

The SMR for respiratory malignancy for these groups (Table 6) generally indicate increasing risk with duration of employment, which is concentration dependent, and increasing risk with average concentration, which is duration dependent. These results are consistent with others,[88] which indicate that it is not sufficient to equate total exposure with either duration or average concentration; each constitutes an important component of risk, and each exhibits degrees with no apparent excess hazard.

TABLE 6

STANDARD MORTALITY RATIOS FOR RESPIRATORY MALIGNANCY BY DURATION OF EMPLOYMENT AND AVERAGE DUST CONCENTRATION

Average Dust Concentration (mppcf)*	Duration of Employment (yr)			
	< 2	2–10	> 10	All Durations
< 5	7/10.0†	2/3.2	1/1.0	10/14.1
	70	91	98	71
5–20	12/17.1	1/2.8	12/5.2	25/25.1
	70	36	231‡	100
> 20	5/5.3	3/2.5	7/2.2	15/10.0
	94	120	318‡	150
All dust concentrations	24/32.4	6/7.5	20/8.3	
	74	80	216‡	

*Million particles per cubic foot.
†Ratio of observed deaths to expected deaths.
‡P < 0.01 (based on a Poisson distribution).

In assessing the possible influence of fiber type exposure on risk of respiratory malignancy, workers with exposure to chrysotile only (n = 4,201) were compared with 2 groups of workers exposed to crocidolite: those with steady employment in the pipe plant (n = 1,004) and those with intermittent exposure to crocidolite through occasional maintenance work in that area (n = 235). Persons with exposure to amosite (n = 205) were excluded from this analysis. All follow-up times were similar, and total fiber exposures were comparable among the fiber type groups within each category of exposure (Table 7).

TABLE 7

COHORT BY TYPE AND LEVEL OF FIBER EXPOSURE*

Exposure	Total Fiber Exposure within 20 Yr of Initial Employment (mppcf-mos†)		
	< 20	20–200	> 200
No crocidolite exposure	n = 2,503 6.0‡ 26.9§	n = 1,337 64.8 28.2	n = 361 663.8 29.8
Intermittent exposure to crocidolite in pipe plant	n = 44 6.2 25.4	n = 86 69.7 27.2	n = 105 663.6 28.6
Steady employment in pipe plant with crocidolite exposure	n = 221 10.5 25.6	n = 363 77.0 26.9	n = 420 666.2 27.2

*Subjects with exposure to amosite are excluded (n = 205).
†Millions of particles per cubic foot-months.
‡Mean total fiber exposure (mppcf-mos).
§Mean length of follow-up (yr).

The pattern that emerges from the SMR (Table 8) suggests that the addition of crocidolite to chrysotile enhances the risk for respiratory malignancy, particularly for those workers exposed intermittently in maintenance jobs. The exposure history of this latter group is characterized by exposure to high concentrations of dust for short periods of time.

TABLE 8

STANDARD MORTALITY RATIOS FOR RESPIRATORY MALIGNANCY BY FIBER TYPE

	Total Fiber Exposure within 20 Yr of Initial Employment (mppcf-mos*)			
	< 20	20–200	> 200	Total
No crocidolite exposure	12/21.4 56	10/13.0 77	6/4.4 182	30/38.8 77
Intermittent exposure to crocidolite in pipe plant	2/0.2 1,000†	0/0.7 0	5/1.4 357†	7/2.3 304†
Steady employment in pipe plant with crocidolite exposure	1/1.0 100	1/1.9 53	7/2.9 241†	9/5.8 155

*Million particles per cubic foot months.
†$P < 0.05$

CONCLUSION

The risk increased more steeply with increased quantitative exposure than with increased duration of employment. Excess mortality for lung cancer was observed only for groups with moderate and high cumulative exposure (SMR 2.9 and 2.3).

There was no detectable excess risk of lung cancer in persons employed for less than 2 years or with low exposure. The risk appears high for two subgroups exposed to crocidolite, but only in the high exposure group (200 mppcf-yr.). There was no increased risk observed for gastrointestinal cancer in any subgroup.

There were 2 pleural mesotheliomas observed (one employed less than 1 year and one for 14 years).

There was no increased risk of respiratory cancer for exposures below 10 mppcf-yrs.

There was a low (75%) tracing rate.

16. In a study of female asbestos workers[35], compared with national rates there was an excess overall mortality among those who worked in jobs with low to moderate exposure (Table 2), which was partly accounted for by deaths from cancer.

Table 2

Mortality of Women with Low to Moderate Asbestos Exposure

Registered cause of death	All periods of employment (126 women)	
	Obs.	Exp.
All causes	29[1]	18.1
Cancer of lung and pleura	2[1]	0.3
Other cancer	8	4.4
Respiratory disease excluding cancer	2	2.2
Other disease	17	11.2

[1] $P < 0.05$

In the group with severe exposure who had worked for less than two years (Table 3), there was an excess of cancer of the lung and pleura.

Table 3

Mortality of Women with Severe Exposure

Registered cause of death	Duration of employment: Less than 2 yrs (557 women) Obs.	Exp.	More than 2 yrs (239 women) Obs.	Exp.
All causes	55	49.9	56[3]	24.5
Cancer of lung and pleura	6[3]	1.0	14[3]	0.5
Other cancer	16	12.4	17[8]	6.1
Respiratory disease excluding cancer	10	7.4	11[2]	3.6
Other disease	23	29.1	14	14.3

[2] P 0.01
[3] P 0.001

However, the most marked increased mortality was in those with severe exposure who had worked for more than two years in the asbestos factory; in this group there were excess deaths from cancer of the lung and pleura, from other cancers, and from respiratory diseases. Three deaths registered as cancer of the pleura were identified as pleural mesotheliol tumors; in all there were 11 mesotheliomas, six of pleural and five of peritoneal origin.

In this study the results were assessed by comparing the number of observed deaths with the number of expected deaths. The "expected" deaths were calculated by the "man-years" method,[36] multiplying years of risk by death rates. Excess mortality has been tested by treating the observed number of deaths as a Poisson variable with expectation equal to the man-years expected number of deaths. Mortality as a function of length of time from first exposure is shown in Table 5.

Table 5

Mortality by Length of Follow-Up since First Exposure

Registered cause of death	Years since first exposure: Less than 10 (922 women)		10 to 20 (692 women)		More than 20 (655 women)	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
All causes	25	23.7	36[1]	29.3	79[3]	39.4
Cancer of lung and pleura	0	0.2	3[1]	0.6	19[3]	1.1
Other cancer	5	4.2	10	7.8	26[3]	10.8
Respiratory disease excluding cancer	9	6.1	5	3.4	9[1]	3.7
Other disease	11	13.2	18	17.5	25	23.8

[1] p 0.05
[3] p 0.001

There were four deaths in all registered as cancer of the ovary; three of these occurred among women with severe and long exposure and, compared with the expected number of 0.6 in this particular group, this was a significant finding ($p=0.0025$). The histological review suggested that at least two of the other deaths in the group that were registered as carcinomatosis were due to this cause. The possibility that ovarian cancer may be caused by exposure to certain hydrous magnesium silicates such as talc and asbestos has been raised by several researchers. Strong evidence of a link was found by Graham and Graham,[36] who injected mice, hamsters, guinea pigs, and Dutch rabbits with tremolite asbestos. The mice and hamsters showed no lesions, presumably because of a protective layer of peritoneum surrounding their ovaries, which is absent in the guinea pig and rabbit. Both of these latter species developed an atypical papillary pattern of ovarian epithelial hyperplasia, which the authors suggested was similar to early ovarian epithelial tumors in women. Additionally, birefringent bodies were observed in sections of six out of twelve ovarian tumors, and none of nine normal controls. These bodies were thought to be asbestos (but were not examined).

APPENDIX II

1. Mesothelioma in Pet Dogs Associated with Exposure of Their Owners to Asbestos. Glickman, L.T., Domanski, L.M., Maguire, T.G., Dubielzig, R.R., and Churg, A. Environ. Res., 32, 305-313 (1983)

This paper describes the findings of an epidemiological study of pet dogs and the incidence of mesothelioma and asbestos exposure. Eighteen histologically-confirmed canine mesotheliomas were diagnosed at the Veterinary Hospital of the University of Pennsylvania (VHUP), Philadelphia, from April 1977 to December 1981. An asbestos-related occupation or hobby of a household member and use of flea repellents on the dog were significantly associated with mesotheliomas. In addition, there was a trend indicating an increased risk of mesotheliomas with an urban residence. Lung tissue from three dogs with squamous cell carcinoma of the lung had higher levels of chrysotile asbestos fibers than lung tissue from control dogs. The VHUP is a major veterinary referral center for the Northeast and Middle-Atlantic regions of the U.S. Each year there are approximately 17,000 admissions and visits to the VHUP and an additional 6000 submissions of biopsy specimens to the Pathology Department (could not ascertain whether these numbers refer to all animals or to dogs only).

A cancer and noncancer control patient were selected from hospital records and matched to each mesothelioma case by age and date of diagnosis (± 1 year), sex, and breed. Excluded from the noncancer control group were dogs with any respiratory disease or suspected malignancy. Dogs with respiratory cancer were excluded from the cancer control group.

Because controls had been matched on age, sex, and breed, these characteristics for the cases were first compared to the entire canine hospital population. The odds ratio (OR), an estimate of the relative risk of disease for each category, was determined using the Mantel-Haenszel procedure.[1] Age was controlled in sex comparisons, and sex was controled in age comparisons. Odds ratios for other risk factors were determined for matched pairs using the cancer and non-cancer groups separately.[2] The control groups were then combined and odds ratios calculated for matched triplets. Using a 95% confidence interval, the null hypothesis of an odds ratio equal to one was tested with computer programs developed by Rothman and Boice.[3] Characteristics of the patients with mesothelioma and the source of asbestos exposure of their owners are listed in Table I. The distribution of mesothelioma by site was six (33%) peritoneal, five (28%) pleural, five (28%) both peritoneal and pleural, and two (11%) pericardial.

The mean age (± 1 SD) of the mesothelioma dogs was 8.0 ± 1.9 years; 17 (94%) were male and 15 (83%) were purebreeds. When compared to the entire canine hospital population, males had a relative risk for

TABLE 1

CHARACTERISTICS OF 18 CANINE PATIENTS DIAGNOSED WITH MESOTHELIOMA AT VHUP BETWEEN 1977 AND 1981, AND THEIR EXPOSURE TO ASBESTOS

Patient	Breed	Sex	Age at diagnosis (years)	Year of diagnosis	Site of mesothelioma[a]	Type of asbestos exposure		
						Owner occupation (O) hobby (H)	Household neighborhood	Other possible
1	Mixed	M	12	1978	P	Auto body repair (O)	Extensive home remodeling	None
2	German Shepherd	M	7	1978	P	Auto mechanic (H)	Change of heating system	None
3	German Shepherd	M	9	1978	P	Truck repair (O) adjacent to shipyard	None	Accompanied owner to job adjacent to shipyard
4	Doberman Pinscher	M	8	1978	P&Pl	None	None	None
5	Irish Setter	F-S[b]	8	1979	Pe	Plumbing, heating, sheet rock spackling (H)	Cement factory	None
6	Bouvier des Flandres	M	8	1979	P	None	None	Flea powder
7.	Mixed[c]	M	10	1979	P&Pl	—	—	—
8	Bouvier des Flandres	M	8	1979	Pl	None	None	None
9	German Shepherd	M	7	1979	P&Pl	Sheet rock spackling at shipyard (O)	Demolition and construction site	Flea powder
10	Boston Terrier	M	7	1979	P&Pl	None	None	None
11	Irish Setter	M	5	1980	Pl	None	Home insulation, construction site	Flea powder
12	German Shepherd	M	10	1981	P&Pl	Pipefitting at shipyard (O)	None	Flea powder
13	Bernese Mtn. Dog	M	4	1977	Pl	None	None	None
14	Old Eng. Sheepdog	M	6	1981	Pe	None	Demolition & construction sites	None
15	German Shepherd	M	8	1981	P	Auto mechanic (O)	Home insulation	None
16	German Short Hair Pointer	M	11	1981	Pl	—	—	—
17	Mixed	M	8	1981	Pl	Oil burner and furnace installation (O)	None	Flea powder
18	German Shepherd	M	6	1981	P	Auto body and used parts supply (O)	None	Accompanied owner to work

[a] P = peritoneal, Pl = pleural, Pe = pericardial

[b] Female-spayed

[c] Not included in case-control analysis. Unable to contact owner for interview.

TABLE 2

MATCHED PAIR ANALYSIS OF RISK FACTORS FOR CANINE MESOTHELIOMA

Risk factor	Noncancer controls			Cancer controls		
	Odds ratio	No. D.P.*	Confidence limits (95%)	Odds ratio	No. D.P.*	Confidence limits (95%)
Domestic and owner occupational exposures						
Home remodeling or construction	0.3	8	0.1–1.2	0.4	10	0.1–1.6
Addition of home insulation	0.5	6	0.1–2.6	0.8	7	0.2–3.3
Home in vicinity of asbestos-related industry	2.0	6	0.4–10.6	0.8	7	0.2–3.3
Occupation or hobby asbestos related	8.0	9	1.4–10.6	2.3	10	0.6–8.7
Urban (vs rural) residence of dog						
First residence	∞	5	—	1.5	9	0.4–5.3
Longest residence	4.0	5	0.5–30.3	1.2	11	0.4–3.9
Residence at diagnosis	2.0	6	0.5–10.6	1.0	10	—
Management of dog						
Source: stray vs all other	2.0	3	0.2–21.0	∞	4	—
Time outside: >50% vs <50%	5.0	6	0.7–34.5	2.5	7	0.5–12.2
Supervision: allowed to roam vs confined	2.0	9	0.5–7.8	3.0	8	0.7–13.8
Pesticides used on dog						
Flea powder	5.0	6	0.7–34.5	1.7	8	0.4–6.9
Flea spray	3.0	4	0.4–25.8	1.5	10	0.4–5.3
Flea dip	2.5	7	0.5–12.2	1.5	10	0.4–5.3
Flea collar	1.3	7	0.3–5.9	1.0	6	—
Any pesticide	11.0	5	1.5–82.1	5.0	6	0.7–35.5

* Number of Discordant Pairs

* Not able to calculate. The cases were all strays while the controls were of known origin

Not able to calculate. The cases all had an urban residence while the controls had a rural residence

TABLE 3

ASBESTOS FIBER CONTENTS IN LUNG TISSUE OF DOGS

Patient	Category	Age at Diagnosis (Years)	Fiber type (No. g dry wt.)	
			Chrysotile	Amphibole
	Mesothelioma			
12		10	3,100,000	0
14		6	7,200,000	3,300,000
18		6	22,000,000	760,000
	Lung Cancer			
A	Squamous cell carcinoma	12	8,200,000	4,800,000
B	Bronchial alveolar carcinoma	13	280,000	280,000
C	Bronchial–alveolar carcinoma	8	69,000	0
	Controls*			
D		5	325,000	81,000
E		9	700,000	0
F		6	300,000	200,000
G		6	2,900,000	720,000
H		8	1,100,000	0
I		8	0	340,000

* Non-respiratory disease and noncancer

mesothelioma of 16.6 ($CL_{95\%}$ 6.4-97.3). When dogs 1 to 4 years of age were assigned a relative risk of 1.0 the greatest risk was observed in dogs 5 to 9 years of age (OR = 16.9, $CL_{95\%}$ 3.4-84.3). The risk for purebreed dogs when compared to dogs of mixed breeding was 1.7 but this difference was not statistically significant ($CL_{95\%}$ 0.51-5.9). The relative risk for individual purebreeds represented by more than one dog with mesothelioma was Bouvier des Flandres (OR = 124.3, $CL_{95\%}$ 62.6-246.7), Irish Setter (OR = 5.3, $CL_{95\%}$ 1.4-9.6), and German Shepherd (OR = 3.3, $CL_{95\%}$ 1.3-8.2).

The cancer and noncancer control patients represented a wide variety of diseases and conditions; not more than two dogs had the same diagnosis. Owners of 16 of the 18 mesothelioma patients were contacted and interviewed. The OR for suspected risk factors for canine mesothelioma are shown in Table 2. The findings were similar when mesothelioma patients were compared to either the cancer or noncancer control group. However, for 11 of the 14 risk factors studied, a stronger association with mesothelioma was noted in the analysis using the noncancer controls. Exposure of the owner to asbestos at work or through a hobby was found to be significantly associated with mesothelioma in the analysis using noncancer controls, (OR = 8.0, $CL_{95\%}$ 1.4-45.9); when cancer controls were used the odds ratio was 2.3, but was not significant (CL_{95} 0.6-8.7). The relative risk for mesothelioma with both control groups combined was 3.5 ($CL_{95\%}$ 1.1-11.0).

Information on the use of pesticides and insect repellents was obtained because talc may be contaminated with asbestos and other mineral fibers.[4] The relative risk for all forms of pesticides was elevated and was significant when any pesticide use was considered in comparison to noncancer controls (OR=11.0, $CL_{95\%}$ 1.5-82.1). The risk associated with any pesticide use when the control groups were combined was also significant (OR= 7.6, $CL_{95\%}$ 1.2-49.0). Preliminary microscopic observations of seven commercially available pet flea powders and sprays revealed large amounts of quartz, silicates, and silica, and small amounts of antigonite, a fiber closely related to chrysotile asbestos. While asbestos fibers were not specifically identified, exposure of humans to other mineral fibers has been associated with pulmonary disease (e.g., silicosis). Results of the lung tissue fiber analysis are presented in Table 3. The three dogs with mesothelioma had the highest levels of chrysotile fibers. The amphibole consisted of tremolite and actinolite, except in the case of control dog 1, where it was commercial amphibole in the form of amosite and crocidolite. The authors stated that the tremolite and actinolite were probably contaminants of the chrysotile.

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2. An Animal Model for Inhalation Exposure to Talc; performed by Wagner, J.C., Berry, G., Hill, R.J., and Skidmore, J.W., In: Dust and Disease, ed. Lemen, R. and Dement, M.J., Pathotox. Publ. Inc., pp. 389-392 (1979)

Methods: Ninety-six male and 96 female (barrier protected caesarian derived; Wistar strain) 6-8 week old rats were randomly allocated to one of the following groups:

(a) talc - Italian 00000 grade (92% talc mineral, 3% chlorite and 1% carbonate minerals; quartz was found in the powder at 0.5-1.0% level); no asbestos minerals of either tremolite or chrysotile varieties were detected;

(b) super fine chrysotile asbestos (SFA chrysotile);

(c) controls - no exposure to either material.

The animals were housed four to a cage except when in inhalation chambers (in a separate room) when there were 6 to a cage. Rats were fed on a proprietary brand of autoclaved cubes and water ad libitum; home cages were supplied with filtered air. There were sacrifices ten days after the end of each exposure period and at one year. The remaining animals were allowed to live until they died or appeared to be distressed. A full necropsy examination was carried out on all animals.

The dust clouds were generated for 7½ hours a day, 5 days a week. After 6 months' exposure half of the rats were removed and transferred to ordinary cages and were replaced by another 24 animals per dust. These rats were in turn removed and replaced after 3 months' exposure, and all exposure ceased after another 3 months (48 rats were exposed for 3 months, 24 for 6 months, and 24 for 12 months). The dosage was calculated as the product of concentration and time. The mean respirable dust concentration was 10.8 mg/m^3 for each dust and the cumulative doses, i.e., the product of concentration and time, were approximately 4100, 8200, and 16400 mg/m^3 hrs. for the 3-, 6-, and 12-month exposures.

Results: Survival data were not presented. The amount of dust in the lungs was determined for the sacrificed rats. For talc, the mean amounts of dust in the lungs were 2.8, 4.5, and 12.3 mg per rat at the end of exposures of 3, 6, and 12 months, respectively. In contrast, the amount of SFA crysotile was close to the detection limit of the method and was estimated as only 0.6 mg/rat after 12 months' exposure.

An assessment was made of the severity of fibrosis in the lungs of rats sacrificed at the end of exposure and one year later (see Table 1 below).

TABLE 1. Inhalation Experiment - Mean Fibrosis at End of Exposure and One Year Later (Number of Rats)

Material	Time	Length of exposure: 3 months	6 months	12 months
Italian talc	End of exposure	2 2 (8)	2 7 (6)	3 4 (6)
	1 year later	2 4 (8)	3 4 (4)	4 6 (4)
SFA chrysotile	End of exposure	2 8 (8)	3 0 (6)	3 2 (6)
	1 year later	2 2 (8)	3 2 (4)	4 2 (4)
Controls	End of exposure	1 8 (8)	1 9 (6)	1 3 (6)
	1 year later	1 6 (8)	1 5 (3)	1 9 (3)

The main features are that both Italian talc and SFA chrysotile produced fibrosis to a similar extent, and that there was some evidence of progression after exposure was discontinued in the longer exposed animals.

The number of rats with lung tumors are shown in Table 2. One adenoma occurred in the control group, two adenomata were observed in the rats exposed to talc, and 13 lung tumors, including one mesothelioma and 3 adenocarcinomata were observed in the SFA chrysotile group.

TABLE 2. Inhalation Experiment - Lung Tumors

Material	Exposure	Number at risk[1]	Number of lung tumors: Adenomas	Adenomatosis	Adenocarcinomas	Mesotheliomas
Italian Talc	3 months	39	0	0	0	0
	6 months	18	0	0	0	0
	12 months	24	2	0	0	0
SFA Chrysotile	3 months	40	0	0	0	1
	6 months	18	1	2	1	0
	12 months	22	3	3	2	0
Controls		71	1	0	0	0

[1]Number surviving at least 300 days from start of exposure

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Study No.	Type of Activity	Fiber Type	Exposure (how measured*)	No. in Cohort	Total Deaths (O/E) SMR	No. mesothel-iomas	Lung Cancer Obs exp. SMR	Slope	Gastrointestinal Cancer obs exp SMR RR	Time since first exposure	Duration of Exposure	Type of Control	Analysis method
57	mining	chrysotile	mppcf low: 2.5-4.2 medium: 4.3-9.4 high: 14.4-23.6 very high: 46.8-82.6 (1)	10,939(M) 440(F)	4463(M) (1.06) 84(F) (0.9)	10(M) 1(F)	230 184 1.25	0.14 mppcf-yr	276 272.4 1.01	20+ years	At least one month	Quebec population	a,b
81	mining	chrysotile	10-36 f/ml (8)	544	178 (1.11)	1	28 11.1 2.5	mppcf-yr 0.30	10 9.5 1.05	20 yrs	20 yrs	Canadian death rates	
[redacted]	mining	chrysotile	Cumulative exposure <100 f/y 20 yrs: 1 1.7 59 ≥100 f/y 20 yrs: 10 8.7 115 (2,3)	952	332 (1.55) 20 yrs (207) 20 yrs (137)	1	11 10.4 106 20 yrs: 4 4.8 83 20 yrs: 15 14.5 103	0.17 f/ml-yr	19 19.3 98 20 yrs:	20 yrs 20 yrs	At least 30 days	National death rate (Italian)	a,c
65	friction materi-als	chrysotile chrocido-lite	Cumulative exposure (f-y/ml) (6) 0-9 10-49 50-99 100-356	13,460	M 1339 (0.9) F 299 (0.9)	8 2	M 151 139.5 1.09 F 8 11.3 0.71	f/ml-yrs 0.06	103 107 0.96 29 27 1.1		At least 10 yrs	National rates in U.K.	a,d
83	friction materi-als	chrysolite	mppcf (1) yrs level <1 2.28 1>5 2.06 5>20 1.56 ≥20 1.06 Total 1.84	3641	1267	0	73 148.7	0.16	59 114.4	20 yrs	At least 1 month	Connect-icut rates	e,f
73	textile	chrysolite crocido-lite	1951- 10.8 f/cc 1972 - 2.9 f/cc (2,3)	822 (M) 284 (F)	293 (1.3) 24 (1.0)	9 1	51 23.8 2.1 F 3 0.9 3.3		16 15.7 1.02	from 10 to greater than 20 yrs	At least 10 yrs	National death rates	

Study No.	Type of Activity	Fiber Type	Exposure (how measured*)	No. in Cohort	Total deaths (O/E)	No. mesothel-iomas	Lung Cancer			Slope	Gastrointestinal Cancer				Time since first exposure	Duration of Exposure	Type of Control	Analysis method
							Obs	Exp	SMR		Obs	Exp	SMR	RR				
	cement products	chrysotile crocido-lite	f-yr/ml (mean) (1) A - 44 B - 92 C - 180	328	125	11	37	5.6	6.6	f/ml-yr 4.82	8	5.4		1.48	20-33 yrs	at least 9 yrs	Ontario death rates	a
70			P=production workers 18 yr-112.5f-yr/ml M=maintenance workers C=unexposed workers	186	58 (1.7)	10	20	3.3	6.1	K-0.067	4	2.5		1.6		18 yrs		
67	general manufac-turing	chrysotile crocidolite amosite	mppcf (1) cumulative dust exposure <125 (62) 125-249 (182) 250-499 (352) 500-749 (606) 750 + (976)	1075	781 (1.2)	5	19 9 19 9 7 63	197.9 180.0 327.6 450.0 777.8 270.0		0.658 mppcf-yr	55	39.9		1.4	retired workers	Ave. 25 yrs (3-51)	US male population	g
64	general manufac-turing (tex-tiles insula-tion materials)	chrysotile crocidolite amosite	f/ml 2 5 5-10 ≥20	4600 (M) 922 (f)	545 (1.24) 200 (1.69)	46 21	103 27	43.2 3.2	2.4 8.4		40 20	34 10.2		118 196	from 10-30 yrs	variable	national death rates of U.K.	
74	insula-tors	chrysotile crocidolite amosite	(6) 4-12 f/ml	632	478	38	93	13.3	699		43	15.1		285	20+yrs		U.S. death	

Study No.	Type of Activity	Fiber Type	Exposure (how measured*)	No. in Cohort	Total deaths (O/E)	No. mesothel-iomas	Lung Cancer	Slope	Gastrointestinal Cancer Obs Exp SMR RR	Time since first exposure	Duration of Exposure	Type of Control	Analysis method
74	insula-tors	chrysotile amosite	4-12 f/ml (6)	17,800	2271 (1.4)	175	429 105.6 4.60	EPA .0107 1.01 (f/m/yr)	94 59.4 1.67	under 20 yrs over 20 years		U.S. death rates	
88	general manuf.	chrysotile crocidolite amosite	mppcf <125 125-249 250-400 500-749 750+	1348	754 (115)	not reported	58 21.7 267.3		53 41.8 126.8	20 yrs	ave. 25 yrs	urban popula-tion US males	
87	cement products	chrysotile crocidolite	total dust w/in 20 yrs initial exposure mppcf-yr (1) <10 11-50 51-100 101-200 >200	5645	601 (0.7)	2	<10 19 24.7 .77 11-50 8 11.4 .70 51-100 1 3.8 .26 101-200 9 3.1 2.90 >200 14 6.2 2.26 Total 51 49.2 1.0	mppcf-yr .44	10 24.6 .41 10 11.9 .84 3 4.2 .71 0 3 - 2 6.4 .31 Total 25 50.1 0.5	>20 yrs	-	US and Louisiana death rates	(a)

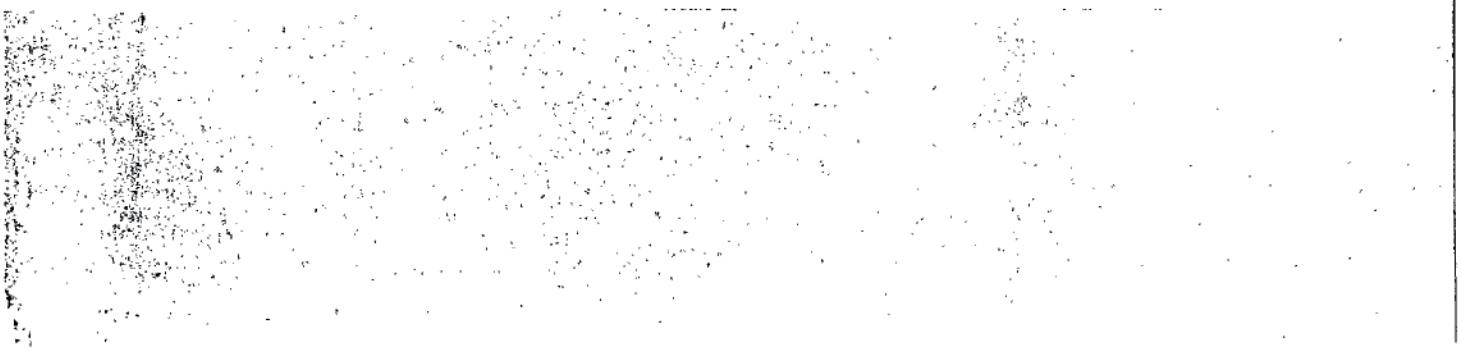
Study No.	Type of Activity	Fiber Type	Exposure (how measured*)	No. in Cohort	Total deaths (O/E)	No. mesothel-iomas	Lung Cancer			Slope	Gastrointestinal Cancer				Time since first exposure	Duration of Exposure	Type of Control	Analysis method
											Obs	Exp	SMR	RR				
84	Textile	chrysotile crocidolite	cumulative exposure(1,5) (f/ml-yrs) 100-400+	679	201	7	28	18.6	1.5	f/ml-yr 1.0	14	12.6	1.1		10-30 yrs	at least 10 yrs	national death rates	
			30f/ml (ave.)				12	4.65	2.6						10-25 yrs			
85	Textile	chrysotile crocidolite	mppcf (ave. dust conc.) yrs / level: <1 / 2.11; 1,<5 / 1.86; 5,<20 / 1.67; ≥20 / 1.23; Total (1) / 1.8	2410	857 (1.27)	1	66	(not given)		8.2	36	(not given)			at least 10 yrs	at least one month	S.Carolina rates	e,f
							59	199.5		mpcf.y 0.059	26		151.7		20 yrs			
86	Textile	chrysotile amosite crocido-lite	mppcf (ave. dust conc.) yrs / level: <1 / 2.60; 1,<5 / 2.40; 5,<20 / 2.73; ≥20 / 1.58; Total (1) / 2.32	4022	1392 (SMR= 109)	14	70			mpcf.y 0.051	73				20 yrs	at least 1 month	Penna. rates	e,f
							53	105			54		112.7					

Analysis method used

(a) man-years method-case
(b) case-Lea-multiple controls analysis
(c) McDonald & Liddell
(d) case-control - Liddell
(e) Mantel-Haenszel log-rank method
(f) man-yrs life table method - Hill
(g) modified lifetable method - Enterline

Exposure measurement procedure

(1) midget impinger
(2) membrane filter collection
(3) phase contrast microscopy
(4) thermal precipitator
(5) static membrane filter
(6) simulated conditions
(7) actual conditions
(8) NIOSH methods
(9)
(10) not stated



7
Risk Assessment

Exposure, laboratory, and epidemiological data provided earlier in this report are used in this chapter to make quantitative and qualitative (or comparative) assessments of risks from exposure to asbestiform fibers. To place the discussion in context, the chapter begins with a brief general discussion of risk assessment and a few special considerations concerning asbestos and related fibrous materials.

Various difficulties often limit the accuracy and precision with which risk to human health can be estimated. Nevertheless, when the data base is good, the risk estimates can be sufficiently informative to aid policy judgments. Some of the factors that enhance the usefulness of the data include dose-response information based on several accurately known exposure levels; knowledge of physiologic and metabolic factors that affect exposure of body tissues; an understanding of the mechanism by which the substance results in toxicity; knowledge of the extent to which experimental systems mimic the human response; and an understanding of the properties of a complex and variable substance that account for its toxicity.

Many of these issues apply in the assessment of risk from asbestiform fibers, which have varying physical and chemical properties. Some members of the class, the commonly used naturally occurring forms of asbestos, have been clearly shown to cause fibrosis of the lung and pleura as well as cancer of the lung, mesothelium, and possibly the gastrointestinal tract in humans. Some occupational data on other fibers are also available, and considerable numbers of experimental studies have been conducted. It is reasonable from a biological viewpoint to use data from occupational studies to derive estimates of risk from nonoccupational exposure. However, differences in route of exposure, type and characteristics of fiber, exposure levels, and time patterns must be considered. Moreover, because working populations are generally healthier than the public at large, the latter may contain a higher proportion of more susceptible individuals.

THE PROCESS OF RISK ASSESSMENT

The principles guiding the assessment of health risks from environmental substances were recently reviewed by a committee of the

National Research Council (1983). These principles are summarized here to provide a framework for assessing the health risks from exposure to asbestiform fibers.

The numerous terms used to describe different aspects of risk assessment include "hazard assessment," "hazard identification," "risk assessment," "qualitative risk assessment," "dose-response assessment," "comparative risk assessment," "quantitative risk assessment," and "risk characterization." The use of these terms has not been standardized.

Three concepts are generally incorporated into the risk assessment process. First is the identification of the kinds of harmful health effects, e.g., anemia, birth defects, or cancer, that can result from sufficient exposure to a substance. Second is the dose-response curve for a particular effect, i.e., the severity of damage and/or the percentage of people or animals likely to be at various exposure levels. Third is the number of people in a particular population, e.g., residents of the United States or workers in a particular industry, likely to be harmed under past, present, or projected levels and conditions of exposure.

In this report, the committee has used "risk assessment" as a broad term encompassing all three of these concepts. "Hazard identification" refers to the first concept, "dose-response" curves or relationships are used in discussions of particular sets of data, and "quantitative risk assessment" refers to the estimates of risk to humans derived by mathematical extrapolations from these data. "Population risk estimates" describe the expected frequency or incidence of a harmful effect in a specific group of humans under defined conditions of exposure.

The amount and complexity of information needed increase as we progress from hazard identification to dose-response assessment to population risk estimation, although each step builds on the preceding one. Hazard identification characterizes the nature of toxic effects that a substance is capable of causing in laboratory animals or humans. Dose-response curves based on experimental or epidemiological observations define the frequency and sometimes the severity of these toxic effects at several levels of exposure.

The dose-response information is used in quantitative risk estimation. Through mathematical modeling and application of known biological principles, attempts are often made to estimate risk for dose levels, exposure conditions, or species other than those for which dose-response data have been obtained. For example, quantitative risk assessments often rely on dose-response data from studies of laboratory animals exposed to relatively high exposure levels in order to estimate the risk to humans exposed to lower levels. Assumptions and uncertainties involved in the application of quantitative risk assessment to cancer induction have been discussed extensively (Food

Safety Council, 1980; International Regulatory Liaison Group, 1979; Office of Technology Assessment, 1981). Population risk estimates bring together quantitative risk estimates and data on exposure of a specific group of humans to identify their risk under actual or anticipated exposure conditions.

The most relevant information for categorizing the hazard or the dose-response for humans is derived from studies of exposed humans. Unfortunately, evidence from this source is often unavailable or inconclusive at times when decisions about acceptable exposure must be made. Humans are exposed to so many different substances through food, medicines, air, water, household materials, and occupational environments that sorting out the causes of harmful effects on health is often difficult. Perhaps of most importance is the fact that evidence of human health hazards from substances introduced into our environment cannot be obtained directly from observations in humans until people have been harmed.

For these reasons, evidence from laboratory animals or from other biological test systems is often used as an alternative or as a supplement to data on humans. A substantial body of evidence has demonstrated the utility of these experimental systems (Doull et al., 1980; National Research Council, 1977; Richmond et al., 1981). A variety of mathematical models have been developed for using data at high doses, usually only available from studies in animals, to estimate risks for humans at low doses (Armitage, 1982; Cornfield et al., 1978; Crump et al., 1976; Fishbein, 1980; Food Safety Council, 1980; Krewski and Van Ryzin, 1981; Van Ryzin, 1980). Because there are extensive data on the effects of asbestos and some other fibers in humans, the quantitative risk assessments in this chapter are based exclusively on data from epidemiological studies in humans, whereas the comparative risk assessments also take into consideration data from laboratory studies.

Every scientific study or technique has some lower limit to its sensitivity. A sensitive method in analytical chemistry may be capable of detecting a few molecules of a particular chemical among a billion other kinds of molecules but incapable of detecting a few among a trillion. The sensitivity of an animal test for toxicity is limited by many factors, such as the number of animals that it is practical to study, the subtlety of the effect of interest, the occurrence of similar effects in animals not exposed to the material under test, and limitations on the amounts of material that can be administered and on the methods used to administer them.

Other difficulties limit the power of epidemiological studies. For example, it is often difficult to select appropriate control groups, estimate exposure, or detect health effects from the exposures of concern, especially if the exposures are much lower than those that occur among occupational groups.

Several kinds of information are useful for estimating risks at low exposure levels on the basis of observations at higher exposures. These include the shape of the dose-response curve in the range of exposures studied, knowledge of the mechanism by which the type of toxic effect occurs, and information on dose-related changes in the uptake, distribution, chemical or physical modification, and excretion of the substance, i.e., pharmacokinetics.

Substances vary markedly both in the quantity required to produce a toxic effect and in the rapidity with which the incidence of toxic effects decreases with decreasing dose, i.e., the shape of the dose-response curve. In an experiment covering a sufficiently wide range of exposure levels, it is possible to find some levels that are toxic and some lower levels at which no toxicity is observed. The highest dose at which no toxicity is seen is often called the "no-observed-effect level," or NOEL (Klaassen and Doull, 1980). However, any experiment will have some limit in its sensitivity to small effects, and the true no-effect-level, if any, may be below the NOEL in a particular experiment.

The fundamental assumption underlying the NOEL safety factor approach is that some minimal level of a toxic substance is required to cause damage and that the substance is not toxic below that level. The NOEL type of experiment is used to find that level.

The maximum dose at which no toxicity would occur is called the "threshold" for that substance. However, several mathematical models for quantitative estimation of cancer risk assume that there is no threshold; risk diminishes with decreasing dose, but some risk is assumed to remain as long as there is any exposure.

The determination of which of these two assumptions is correct will probably depend on the nature of the toxic effect. Thus, understanding the mechanism of toxicity can provide guidance in setting acceptable exposure levels. For a substance that exerts its toxic effect by inactivating an enzyme present in abundance in each cell, it is reasonable to assume that a threshold would exist. Inactivation of a few molecules of the enzyme is unlikely to damage the cell. On the other hand, a chemical that is mutagenic or carcinogenic because it damages some critical site on a DNA molecule that starts the carcinogenic process can reasonably be assumed not to have a threshold. The likelihood that a critical site would be damaged would decrease with decreasing dose, but the possibility that this damage could occur remains at any exposure above zero.

For many effects, the severity of the toxic effect, as well as the probability that it will occur, also decreases with dose. For example, a dose that damages a high proportion of cells in the liver may be lethal; one that damages a moderate number may cause severe illness but not death; a small dose that causes damage to a few cells may not lead

to any clinical symptoms. The error in assuming a threshold if none truly existed would generally not be expected to lead to serious cases of disease in this situation.

By contrast, the severity of cancer and of mutations is not related to the dose of the substance causing them. Low dose exposure to x-rays or cigarette smoke causes fewer cancers than does high dose exposure, but the resulting cancers are just as lethal. Thus, although there may be some substances that show a threshold for cancer induction (Hoel et al., 1983), an error in assuming a threshold when none really exists would severely harm those persons who got the disease despite a low exposure.

Accurate documentation of exposure is important for determining the dose-response curves for toxicity in animals or humans and also for estimating population risks. Errors in the estimation of exposure will lead to errors in defining the dose-response curve and in making quantitative risk estimates for individuals or specific populations. The amount of a toxic substance or its active metabolite that reaches the body site that is susceptible to its effect is the exposure that accounts for toxicity, but such measures are almost never available (Hoel et al., 1983). Other measurements, such as amounts in the blood, amounts entering the body, or concentrations in the air or water of a community, are often useful surrogates, but as noted earlier in this report, they are also often unavailable.

The sensitivity of the exposed population is another consideration in the risk estimation process. Some individuals may be more sensitive than others to specific environmental insults because of nutritional deficiencies, genetic predisposition, and for children, small body size, developmental immaturity, and increased metabolic and respiratory rates (Calabrese, 1978, 1980).

With their rapid metabolic rate, children consume proportionately more food and inhale greater volumes of air than an adult for a given body weight. Thus, they would also consume or inhale proportionately more of any contaminants that are present (Babich and Davis, 1981). Human infants do not have mature hepatic detoxification systems until they reach 2 to 3 months of age (Pelkonen et al., 1973; Rane and Ackerman, 1972). Serum immunoglobulin does not attain adult levels until children are 10 to 12 years old (Calabrese, 1978). Studies in animals have also demonstrated a greater sensitivity among the young after exposure to chemicals by a variety of routes (Goldenthal, 1971). Children's lungs may also be especially sensitive to environmental pollutants. Tager et al. (1983) have observed measurable differences in lung function between children of smoking mothers and children whose mothers did not smoke.

Population risk estimation is based on all the preceding steps. First, the exposure of the study population must be known. Heterogeneity of the population with respect to level of exposure or sensitivity to the toxic material should also be considered in the calculations. Exposure, dose-response curves, distribution of sensitivity factors, and the size of the population are then used to estimate the number of people likely to suffer toxic effects from the substance of interest. If the material causes more than one type of toxic effect, each effect requires separate calculations.

Ideally, calculation of risk is an objective, scientific activity devoid of policy judgments. The latter are made separately when deciding the acceptable level of exposure. However, policy decisions can seldom be divorced completely from the process of risk assessment. The reason for this lies in the uncertainty of many of the scientific judgments required. For example, if one experimental species is more susceptible to the toxicity of a material than another and data on humans are unavailable, which species should be used for estimating human risk? Which mathematical model should be applied to the data? These and many other questions of judgment were discussed in the recent National Research Council (1983) report.

In the following sections, the committee has used epidemiological data, mostly from occupational settings, to develop a quantitative model of the relationship between fiber dose and carcinogenic response for a generalized "asbestos" exposure resulting in either lung cancer or mesothelioma. That dose-response relationship is then applied to a hypothetical, but reasonable, exposure level to show potential population risk levels in populations of arbitrary size. In the final section, the committee assesses risks for other types of fibers and, in some cases, for other diseases by qualitative comparisons with the base case of a generalized asbestos exposure.

QUANTITATIVE RISK ASSESSMENT

In the previous chapters, the committee extensively reviewed information on the health effects of asbestos and other asbestiform fibers. In preparing this section, it also reviewed several risk assessments for asbestos in the open literature and in government documents. On the basis of its evaluation of the quality and coverage of the information and the assessment techniques, the committee decided that a quantitative assessment of the risks for mesothelioma and lung cancer from nonoccupational exposures to asbestos would be meaningful. It also concluded that the information base was insufficient for useful quantitative assessments for other fiber types and diseases, but that in some cases a qualitative, comparative assessment was feasible and useful. These decisions do not mean that the asbestos assessment is without major uncertainties nor does it mean that the comparative assessments are of poor quality. In both cases, the objective is to

present information useful for evaluating the health risks of asbestiform fibers in nonoccupational settings.

First, an overview of mathematical models for carcinogenic risk assessment is presented to provide a context for the assessments for lung cancer and mesothelioma, which are of principal interest. Next, there is a review of several assessments for asbestos that were based on such models. Finally, these assessments and the committee's own analyses are applied to the information presented in earlier chapters to produce quantitative risk estimates for nonoccupational exposures to asbestos in ambient air.

Mathematical Model for Carcinogenic Risk Estimate

As explained earlier, it is not necessary to use data on asbestos exposure from animal experiments to estimate risks for humans, but it is necessary to extrapolate from the health effects observed at high occupational levels of exposure to much lower nonoccupational exposures. Occupational epidemiology makes it possible to describe the probability of dying from a particular type of cancer as a function of age at first exposure, level and duration of exposure, and current age. Mathematical extrapolation models based on the multistage theory of carcinogenesis make it possible to estimate the probability of dying from that type of cancer for different ages at first exposure, different (lower) exposure levels, and different (often longer) duration of exposure, also as a function of current age. By considering the cumulative probability throughout a lifetime, the "lifetime risk" of cancer mortality can be computed.

At any age, an individual faces some probability of reaching an end point that is related to cancer in the next year, for example, dying of lung cancer. Suppose that at a given age, a, the probability is given by p(a,d), where d is the dose of the carcinogen--in this case, asbestos. When d = 0, p(a,0) is the probability of the end point for unexposed people. If t is some age of interest, then the cumulative probability P(t,d) of reaching the end point before that age is given by the sum of the annual probabilities up to that age:

$$P(t,d) = \text{the sum of } p(a,d) \text{ over all ages, } a, \leq t. \qquad (1)$$

Reaching the end point by time t is analogous to the "failure time" for a generalized system that is no longer effective after time t. General mathematical analysis can be used to show that the probability of failure as a function of time can be written as follows:

$$P(t,d) = 1 - e^{-I(t,d)}, \qquad (2)$$

where $I(t,d)$ represents the cumulative incidence function (or cumulative hazard function) of occurrence of the observable failure prior to time t.

Armitage and Doll (1961), Peto et al. (1982), Kalbfleisch and Prentice (1980), Hartley and Sielken (1977), Hartley et al. (1981), and Kalbfleisch et al. (1983) have applied this model to carcinogenesis. If the cumulative incidence I(t,d) is small, then equation (2) may be simplified to

$$P(t,d) \doteq I(t,d), \tag{3}$$

where $\doteq$ means approximately.

In carcinogenic risk assessment, attention is usually focussed on the cumulative incidence function I(t,d) rather than on the probability function P(t,d). The Armitage-Doll (1961) multistage theory of carcinogenesis suggests that I(t,d) can be written as a product of two terms--g(d), depending only on dose, and h(t), depending only on time. That is,

$$I(t,d) = g(d)\, h(t). \tag{4}$$

If there are k dose-dependent stages in the process of carcinogenesis and the rate of transformation from one stage to the next is assumed to be a linear function of dose, the function g(d) would be a polynomial of degree k in the dose. The function h(t) depends only on time. This model and its generalization and justification have been discussed by Crump et al. (1976), Hartley et al. (1981), and Kalbfleisch et al. (1983).

To determine the values of the constants in the polynomial g(d) and the functional form for h(t), the cumulative incidence function must be fitted to data--preferably to data based on observations in human populations. The multistage model described above has been fitted successfully to many sets of cancer data, including data on asbestos, and appears at present to be a generally adequate model for assessing cancer risk. Fitting equation (4) to data involves estimating the constants in the model for some suitably determined function h(t). This model has been applied to both mesothelioma and lung cancer data on asbestos-exposed workers. The form of h(t) and the values of the constants from those studies will be discussed in the next section. The function g(d)--and thus the cumulative excess incidence function I(t,d)--can be approximated as a linear function of dose in the low-dose range that equals 0 when d = 0. This relationship can be used for extrapolating from high to low doses and has the following form:

$$I(t,d) = cdh(t). \tag{5}$$

This form assumes that there is at least one dose-dependent stage of cancer development. The argument for a linear (with respect to dose) approximation for low-dose exposures has been justified on the basis that the exposure dose d is added to a background level (Hoel, 1980; Peto, 1978). This assumption may not always be justified in application

(see Cornfield et al., 1978 and Van Ryzin, 1981), but it should lead to an appropriate upper bound for the committee's risk assessments for asbestos. Furthermore, and more importantly, ruling out a linear dose term for asbestos exposure does not seem justified by the data now available (Nicholson, 1983; Peto, 1982; Schneiderman et al., 1981). Thus, the model adopted for risk assessment in the next three sections of this chapter is based on the cancer mortality incidence calculated by equation (5).

PUBLISHED RISK ASSESSMENTS

This section reviews some published risk assessments for lung cancer and mesothelioma. These assessments helped the committee select a functional form for h(t) for the two diseases and to establish the value of the constant c in equation (5).

Lung Cancer Risk from Nonoccupational Environmental Exposures

The following summary of risk assessments for lung cancer from asbestos exposures is based on data on exposure of worker populations. These data suggest that the function I(t,d) in equation (5) becomes

$$I(t,d) = c^{*}T_{0}dI_{0}(t), \qquad (6)$$

where T_0 is the duration of exposure to asbestos at dose d, $I_0(t)$ is the cumulative mortality incidence for lung cancer up to age t for those who have not been exposed to asbestos, and c* is a constant that depends on the cohort under study, but not on dose or age. As used in equation (6) and in the remainder of this section, d is the concentration of fibers in the workplace air, usually measured in fibers/cm^3. Although d is referred to as dose, some authors would call it dose rate and would refer to the product T_0d as (cumulative) dose. Equation (6), derived by Peto (1982), is consistent with his earlier studies of chrysotile workers (Peto, 1978). This equation is also supported by four studies reviewed by Nicholson (1983), who noted that the relative risk of lung cancer deaths for asbestos workers compared to a similar population was linearly related to the accumulated dose years, i.e., fibers/cm^3 x years, or (fibers/cm^3)yr.

In equation (6), the underlying incidence rate $I_0(t)$ is considerably different for smokers and nonsmokers of each sex. Therefore, the risks for each of these groups must be assessed separately. Another consequence of equation (6) is that the relative risk of lung cancer due to asbestos exposure does not depend on age at first exposure.

Thus, lifelong risk of lung cancer resulting from exposure to asbestos can be calculated quite simply by using equation (6). As an example, consider the following calculation given by Peto (1982).

Consider the effect of 10 years of exposure at 1 fiber/cm^3. If we assume that the relative risk for lung cancer among insulation workers increased approximately fourfold [Hammond et al. (1979) reported 4.2 for nonsmokers and 3.9 for smokers] and that this risk is based on a cumulative dose of 600 fibers/cm^3 (20 years at 30 fibers/cm^3), then 10 years of exposure to 1 fiber/cm^3 will increase the relative risk by 4.0 x 10/600 = 0.067. Since approximately 15% of lifelong smokers die of lung cancer, this mortality rate will increase to 0.15 x 1.067 x 100, or 16%. Thus, the difference (1%) is the excess due to asbestos as predicted by the equation. Since only 0.5% of nonsmokers die of lung cancer, this would become 0.533% (0.005 x 1.067 x 100) for an added risk of 0.033% due to asbestos exposure.

Mesothelioma Risk from Nonoccupational Environmental Exposures

The committee reviewed two estimations of mesothelioma risk, one by Peto and his colleagues (Peto, 1982; Peto et al., 1982) and the other by Nicholson (1983). These analyses and their consequences are summarized in this section.

Using the data of Selikoff et al. (1979) on mortality among 17,800 members of the International Association of Heat and Frost Insulators and Asbestos Workers, Peto et al. (1982) showed that the mortality rate from mesothelioma in these workers was dependent on the time since first exposure, but did not depend on the age at first exposure. From this finding, and the application of the multistage theory of carcinogenesis through equation (5), the cumulative incidence function becomes:

$$I(t,d) = cd(t - t_0)^k, \qquad (7)$$

where $t - t_0$ represents time since first exposure at age t_0. For any group of workers exposed at the same dose level d, the product cd = b is a constant depending on the type of asbestos exposure. Equation (7) suggests that the risk for mesothelioma is primarily dependent on the time since first exposure ($t - t_0$). This same phenomenon was noted by Schneiderman et al. (1981) and Nicholson (1983). Fitting equation (7) with b = cd to the data of Selikoff et al. (1979) for men up to age 80 by the method of maximum likelihood estimation resulted in an estimate of k = 3.2 with a standard error of $\pm$ 0.36 and b = 4.37 x 10^{-8}. Using this calculation, Peto et al. (1982) estimated the lifelong mesothelioma risk for this worker group to be 15%, 7%, and 3% for age at first exposures of 20, 30, and 40 years, respectively. These figures have been adjusted for other competing causes of death.

Using equation (7) with k = 3.2, Peto and colleagues determined that b x 10^8 ranges in value from 2.94 to 5.15 for four other sets of data (see Table 7-1). Using k = 3.5, Peto (1982) computed a lifetime mesothelioma rate of 1 in 100,000 children exposed from age 12 to age 18

TABLE 7-1. Mesothelioma Death Rates in Various Studies and Predictions of Risk[a]

Study Population and Reference	Relative Risk ($b \times 10^8$)	Corresponding Lifetime Risk (%)[b] by Age at First Exposure (yrs)		
		20	30	40
North American insulation workers (mixed exposure) Selikoff et al., 1979	4.37	15	7	3
Factory workers (mixed exposure) Newhouse and Berry, 1976	4.95	17	8	3
Chrysotile textile factory workers Peto, 1980b	2.94	10	5	2
Australian crocidolite miners Hobbs et al., 1980	5.15	17	8	3
U.S. amosite factory workers Seidman et al., 1979	4.91	17	8	3

[a]Adapted from Peto et al. (1982). The death rate at time $t - t_0$ since first exposure at age t_0 is proportional to b, obtained by fitting equation (7) with $k = 3.2$.

[b]The calculation of "lifetime risk," i.e., the percentage of similarly exposed men who would die of mesothelioma before age 80, is based on an actuarial calculation using 1977 U.S. rates for white males for all causes of death other than mesothelioma inflated by a factor of 1.26, the observed relative risk among insulation workers (Selikoff et al., 1979).

(i.e., 6 years of school age), assuming the fiber level was 0.003 fiber/cm^3 (1/1,000 of the exposure of the insulation workers).

A second risk assessment was done by Nicholson (1983), who criticized the Peto et al. (1982) analysis for fitting equation (7) to only those men who died of mesothelioma up to age 80. By including all insulation workers, he estimated k to be 5.0.

QUANTITATIVE RISK ASSESSMENT FOR NONOCCUPATIONAL ENVIRONMENTAL EXPOSURES

As a starting point for assessing the risk from nonoccupational environmental exposure to asbestiform fibers, the committee adopted equation (6) as representing the cumulative mortality up to age t, which is appropriate for lung cancer induced by a continuous exposure of T_0 years at dose level d in fibers/cm^3. This model implies that any given total dose before time t would have the same effect on the relative risk at time t, regardless of the time at which exposure started or its duration. The model thus ignores a minimum latency period, which might cause the model to overestimate effects, but also ignores the difference between exposures at earlier and later ages, which might cause the model to underestimate effects.

Equation (7) was assumed to be a reasonable representation of the cumulative mortality from mesothelioma up to age t for continuous exposure to asbestos at dose level d in fibers/cm^3 from age t_0 until age t. In this case, latency is implicitly included in the dependence on $(t-t_0)$, because k is greater than 1, but no minimum latency is assumed. These assumptions are supported by the work of Peto (1982), Peto et al. (1982), Nicholson (1983), and Schneiderman et al. (1981), who extensively reviewed the basis for these assumptions by examining the models and their consistency for several observed worker cohorts exposed to ambient concentrations of asbestos fibers. These authors have suggested that asbestos acts as a late-stage carcinogen in producing lung cancer but acts at earlier stages in the development of mesothelioma. Using these models, the committee developed lifetime estimates of risk for lung cancer and mesothelioma mortality from continuous nonoccupational exposures to 0.0004 fibers/cm^3 and for 0.002 fibers/cm^3.

For lung cancer, the committee assessed the risk for four exposure subgroups: male smokers, female smokers, male nonsmokers, and female nonsmokers. For mesothelioma, only one calculation was made, since equation (7) and the supporting data in the papers cited above suggest that mesothelioma mortality does not depend on sex or smoking history, but does depend strongly on age at first exposure.

Lifetime Risk Estimates for Lung Cancer and Mesothelioma

Table 7-2 summarizes lifetime risk estimates for lung cancer and mesothelioma for nonoccupational environmental exposures to 0.0004 fibers/cm^3 (a median level) and 0.002 fibers/cm^3 (a high level). It is assumed this exposure is continuous from birth through a lifetime of 73 years, an approximate average lifetime in the United States. Thus, in equations (6) and (7), t = 73 years and d = 0.0004 or 0.002. In equation (6), T_0 = 73 and in equation (7), t_0 = 0 to account for continuous exposure. Because equations (6) and (7) are linear in the dose unit d, one can immediately obtain from Table 7-2 lifetime risks at other continuous (from birth) environmental exposures by multiplying by the appropriate dose factor. For example, lifetime risk estimates at 0.02 fibers/cm^3 are 10 times higher than the estimates at 0.002 fibers/cm^3.

TABLE 7-2. Estimated Individual Lifetime Risks from a Continuous Exposure to Asbestos at 0.0004 Fibers/cm^3 (a Median Dose) or 0.002 Fibers/cm^3 (a High Dose)[a]

Disease	Exposure Group	Estimated Individual Lifetime Risk x 10^6 Median Exposure (0.0004 fibers/cm^3)	Estimated Individual Lifetime Risk x 10^6 High Exposure (0.002 fibers/cm^3)
Lung cancer[b]	Male smoker	64 (0 to 290)[c]	320 (0 to 1,500)
Lung cancer	Female smoker	23 (0 to 110)	120 (0 to 530)
Lung cancer	Male nonsmoker	6 (0 to 22)	29 (0 to 130)
Lung cancer	Female nonsmoker	3 (0 to 13)	15 (0 to 66)
Mesothelioma	All	9 (0 to 350)	46 (0 to 1,700)

[a]Lifetime assumed to be 73 years; exposure occurs from birth. Lung cancer risks are calculated with c* = 1.02 or an excess risk of 2% per (fiber/cm^3)yr, estimated from nine studies with varied results. Mesothelioma risks are calculated with c = 2.53 x 10^{-8} and k = 3.2, estimated from five studies with varied results. See also explanations in text.

[b]Sex differences for lung cancer risk are due to differences in lung cancer background rates associated with smoking patterns, occupational exposures, and other factors.

[c]Range of estimates. The lower limit of 0 is always possible if linear extrapolation overestimates risk. See also text below.

The estimates in Table 7-2 were based on the following five considerations:

- Exposure levels. A mix of indoor and outdoor measured exposure levels was used to select the median value of 0.0004 fibers/cm^3 and the high value of 0.002 fibers/cm^3 as the reference levels.

- Use of the linear model. The models used by the committee all assume low-dose linearity and, as such, produce higher estimates of risk at low doses than would be obtained with other models. However, because the occupational data do not rule out low-dose linearity, the committee believes that these estimates do not unduly overstate the risks.

- Count-mass conversion. The conversion of ambient fiber mass measurements to an equivalent number of fibers was based on measurements

of mass and numbers of fibers in the workplace. The committee realized, however, that the number of fibers in ambient air would be much greater because these fibers tend to be smaller than those in the workplace (see Chapter 4). Depending on the toxicity of small fibers, the risks could be greater or less than those calculated in this chapter. If the presence of long fibers is necessary for a toxic response, risks would be lower.

- Model dependence. The results of the mesothelioma model depend very heavily on the value of k. This accounts for the large range of estimates for mesothelioma. It is assumed that this dependence on k among workers holds for the entire population throughout a lifetime. If the dependence is not as strong (i.e., a lower k value), the lower end of the range would apply. If this dependence is as strong (i.e., a higher k value), the upper bound may be more appropriate.

- Childhood exposure. The models used for extrapolation for both lung cancer and mesothelioma are based on the assumption that a unit dose of exposure (measured as fibers/cm^3 > 5 μm long) in early life is equivalent in its intrinsic carcinogenic potential to a unit dose in later life. If children are more biologically sensitive than the worker group, the risk per unit dose would be increased. Results from studies of exposure to other materials indicate that children are often more sensitive than adults to a given dose, even when expressed as dose/body weight.

The risk estimates and ranges shown in Table 7-2 are those the committee considers most reasonable. Because of the uncertain value of k and the sensitivity of equation (7) to its value, the range of estimates is much larger for mesothelioma than for lung cancer. Two conclusions can be drawn from the estimates in Table 7-2:

- For nonsmokers, the lifetime risk for mesothelioma from nonoccupational environmental exposure to asbestos is higher than for lung cancer. For smokers, however, the risks of lung cancer are substantially higher than for mesothelioma, because of the multiplicative interaction of smoking and asbestos exposures.

- Individual lifetime risk estimates for lung cancer from nonoccupational environmental exposures to 0.0004 fibers/cm^3 are much lower than the risks observed for smoking.

The basis for the calculations in Table 7-2 is discussed in detail in the following two subsections.

Calculation of the Lung Cancer Risk Estimates in Table 7-2. Calculating lifetime risk estimates from equation (6) involves the notion of relative risk up to time t, designated here as RR. From equation (6), the RR for lung cancer by age t can be shown as follows:

$$\frac{I(t,d)}{I_0(t)} \qquad (8)$$

$$= \frac{\text{cumulative lung cancer mortality by age t at dose d}}{\text{baseline cumulative lung cancer mortality by age t}}$$

$$= c^*(T_0 d),$$

where $(T_0 d)$ = total dose-years for the exposed group and c^* is a constant that depends on the cohort.

For a given study showing an increased relative risk for lung cancer,

$$c^* = (1 + P/100), \qquad (9)$$

where P is the percentage increase in lung cancer risk per unit dose [% per (fibers/cm^3)yr]. Schneiderman et al. (1981) presented the values of P for nine different worker cohorts. The results are summarized in Table 7-3.

Values for P in Table 7-3 range from 0.06 (Study 8) to 9.1 (Study 1). The higher value establishes the upper end of the range given in Table 7-2. The zero value for the lower end of the range indicates that the low-dose linear approximation in equation (5) may overstate risk.

The median value for P in the studies shown in Table 7-3 is P = 1.1 (Study 7). This value, rounded upward to 2, was used in obtaining the estimates for lifetime lung cancer risk in Table 7-2. To calculate these estimates, it was necessary to know only the baseline absolute risks for the appropriate subpopulations. The baseline cumulative incidence rates of lung cancer for the four subgroups in Table 7-2 have been estimated by Schneiderman et al. (1981) as follows: male smokers = 0.11; female smokers = 0.04; male nonsmokers = 0.01; and female nonsmokers = 0.005.

Thus, using 2% as a value for P, the lifetime risk of lung cancer for a male smoker is

$$(0.11)(1 + P/100) = (0.11)(1 + 0.02) = 0.1122. \qquad (10)$$

The increased lifetime risk attributable to asbestos exposure at 1 fiber/cm^3 for 1 year is 0.0022, i.e., 0.1122 - 0.1100. At the ambient exposure of 0.0004 fibers/cm^3 assumed in Table 7-2 and for a 73-year lifetime exposure, the increased lifetime risk of lung cancer is 6.42×10^{-5}, i.e., 0.0022 x 0.0004 x 73. Rounding to two significant figures gives the estimate in Table 7-2 for male smokers. The other calculations in that table were derived in a similar fashion.

When describing the use of the percentages given in Table 7-3, Schneiderman et al. (1981) commented that the low percentage increases in risk in Studies 3, 6, 8, and 9 probably resulted from several factors. In Study 3, for example, the subjects were retirees older than 65.

TABLE 7-3. Estimated Increase in Lung Cancer Risk per Unit of Exposure to Asbestos[a]

Study No.	Occupation of Worker Cohort	Asbestos Type	Percent Increase in Lung Cancer Risk per (fibers/cm^3)yr	Reference
1	Insulation manufacturing	Amosite	9.1	Seidman et al., 1979
2	Asbestos product manufacturing	Crocidolite, chrysotile, and amosite	1.3 males 8.4 females	Newhouse and Berry, 1979
3	Asbestos manufacturing	Amosite and chrysotile; some crocidolite	0.3	Henderson and Enterline, 1979
4	Asbestos product manufacturing	Chrysotile; some amosite and crocidolite	1.1	Nicholson et al., 1979
5	Textile production	Chrysotile	5.3	Dement et al., 1982
6	Textile production	Chrysotile	0.07 early employees[b] 0.8 later employees[b]	Peto, 1980
7	Insulation manufacturing	Chrysotile and amosite	1.7	Selikoff et al., 1979
8	Mining and milling	Chrysotile	0.06	McDonald and Liddell, 1979
9	Mining and milling	Chrysotile	0.15	Nicholson et al., 1979

[a]Adapted from Table 4 in Schneiderman et al., 1981.
[b]Early employees began work before or during 1950. Later employees began work after 1950.

Schneiderman et al. stated that the investigators may thus have missed asbestos-related deaths occurring at earlier ages. In Study 6, the disease rates for workers employed earlier were lower than those employed later who were followed for shorter periods. The discrepancy has diminished as more data have accumulated. The subjects in Studies 8 and 9 were mining and milling workers whose exposure patterns were quite different from environmental ambient air exposures. There is also some evidence that many lung cancer cases were missed in Studies 8 and 9 because of competing causes of death at earlier ages. Thus, Schneiderman et al. (1981) concluded that the range from 1.1 (Study 4) to 9.1 (Study 1) is the most representative of true values. The value of P = 2 used in the calculations in Table 7-2 falls near the bottom of this range, but is within a factor of 5 of the top of the range. If we use P = 5, which is the middle of the range, the lung cancer risk estimates in Table 7-2 would be multiplied by a factor of 2.5.

Calculation of Mesothelioma Risk Estimates. To calculate the lifetime risk with equation (7), the numbers c and k must be determined. Then the lifetime risk L at d = 0.0004 fibers/cm^3, assuming t = 73 and t_0 = 0 (continuous exposure from birth to age 73), is

$$L = c(0.0004)(73)^k. \qquad (11)$$

To apply this equation, c and k must be estimated from epidemiological studies of occupational exposures to asbestos. Each study must be stratified by duration of exposure $(t-t_0)$ to estimate these parameters. Most of the following analysis is similar to that of Peto et al. (1982).

First, let us consider the choice of k. As noted earlier, when Peto et al. (1982) fitted equation (7) to the data of Selikoff et al. (1979), they obtained the equation $I(t,d) = b(t - t_0)^{3.2}$, with b = 4.37 and k = 3.2 ± 0.36 (standard error). In equation (11), therefore, we initially use k = 3.2. Modifications using different values for k will give the range of estimates for d = 0.0004 fibers/cm^3 in Table 7-2. For d = 0.002 fibers/cm^3, we replace 0.0004 with 0.002 in equation (11). With k = 3.2, Peto et al. (1982) also fitted four other data sets to obtain four values of b in the equation $I(t,d) = b(t - t_0)^{3.2}$. The value of b is specific to each worker cohort and depends on three numbers: d (the average fiber/cm^3 exposure), ℓ (the average length of exposure), and $t - t_0$ (the average time since first exposure). These values are given in Table 7-4. In addition, Table 7-4 contains the estimates of c that are appropriate for equation (7), based on the corresponding estimate of b given by Peto et al. (1982). When exposure is not continuous from time of first exposure (t_0) to the age of observation (t) for these studies, the relationship between b and c changes from c = b/d to

$$\frac{4.56\ b/d}{1 - [1 - \ell/(t-t_0)]^{3.2}}. \qquad (12)$$

TABLE 7-4. Estimated Constants for Equations (11) and (12) for Five Studies

Study	b x 10^8	d[a]	ℓ[a]	t - t_0 [a]	c x 10^8
Selikoff et al., 1979	4.37	15	15	24	1.39
Newhouse and Berry, 1976	4.95	12.5	6	31.5	3.67
Peto, 1980a,b	2.94	16.5	14	22.5	0.85
Hobbs et al., 1980	5.15	NA[b]	NA	NA	NA
Seidman et al., 1979	4.91	35	1	35	7.22

[a]Estimated from data given in Tables 4 and 10 of Schneiderman et al. (1981), using estimated median values. The product dℓ from columns 3 and 4 above is the estimated cumulative exposure in (fiber/cm^3)yr of their Table 10.
[b]NA = not available.

The factor 4.56 adjusts from occupational exposures at about 1,920 hours per year to environmental exposures at 8,760 hours per year. Appendix G provides the mathematical basis for equation (12). Table 7-4 gives the values of the constants for each study in which Peto et al. (1982) estimated b.

To obtain the estimates for mesothelioma at the dose of 0.0004 fibers/cm^3 in Table 7-2, equation (11) is used with values for c from Table 7-4 and k = 3.2. In Table 7-2 the lifetime risk for mesothelioma at d = 0.0004 fibers/cm^3 is 9 per million. This is calculated from equation (11) with c = 2.53 x 10^{-8}, the median of the range of the c values in Table 7-4, and k = 3.2. The highest value of the range in Table 7-2 at d = 0.0004 uses equation (11) with c = 7.22 x 10^{-8}, the upper value of c in Table 7-4, and k = 3.8, obtained from 3.2 + 1.65 x 0.36. The selection of 3.8 as the value for k is based on an approximate upper 95% confidence limit for the estimate of k. The lower limit is taken as 0, which is always a possible lower limit, especially if the low-dose linear assumption in equation (5) overestimates the individual lifetime risk.

Peto (1982) recommended using a k value of 3.5 for risk assessment purposes. As an example, he estimated that the risk of mesothelioma for children exposed for a 6-year period (ages 12 to 18) at 0.003 fibers/cm^3 would be one in 100,000. Nicholson reviewed additional data, including data on older workers up to age 80, and determined that a k value would be 5. Schneiderman et al. (1981) used k = 3.0. For this study, the committee used a value of 3.2. Although neither existing data nor biological theory can provide very much guidance on the value of k, its value is very important in projecting the lifetime risks of mesothelioma from asbestos exposures. Table 7-5 shows how lifetime risk varies from the value of 9 per million for several values of k. Also shown are risk estimates for other values of c. The reader can easily calculate the results for other values of exposure.

Other authors have also estimated the risks of mesotheliomas. Enterline (1983) derived a lifetime risk of 100 per million by using current reported rates of mesothelioma, an assumption about the relative contributions of nonoccupational and occupational asbestos exposures, and other factors. This estimate clearly relates to past exposure to varying levels of asbestos. Schneiderman et al. (1981) estimated lifetime risks for mesothelioma to be between 800 and 5,000 per million for a cumulative exposure of 1 (fiber/cm^3)yr. These estimates correspond to lifetime risks of 23 to 150 per million for 0.0004 fibers/cm^3 for 73 years. As mentioned above, these investigators effectively assumed k = 3, but their equivalent c was higher than that used for the corresponding estimates in Tables 7-2 and 7-5.

TABLE 7-5. Sensitivity of Estimates for Lifetime Risks[a] of Mesothelioma to Values of k and c

	Lifetime Risk Estimates x 10^6, Using k Values from Various Studies						
	This Study (low)	Schneiderman et al., 1981	This Study (middle)	Peto et al., 1982 (middle)	This Study (high)	Peto et al., 1982 (high)	Nicholson, 1983
c \ k	2.6	3.0	3.2	3.5	3.8	4.0	5.0
0.85 x 10^{-8}	0.2	1.3	3	11	41	97	7,000
2.53 x 10^{-8}	0.7	4	9	34	120	290	21,000
7.22 x 10^{-8}	2	11	26	96	350	820	60,000

[a]All estimates are derived from equation (11), $L = c(0.0004)(73)^k$, where L = lifetime risk at a continuous exposure to 0.0004 fibers/cm^3 for a lifetime of 73 years.

Note: This table demonstrates that the risk estimates are extremely sensitive to changes in the value of k.

The Use of 0.0004 Fibers/cm^3 and 0.002 Fibers/cm^3 as the Median and High Nonoccupational Environmental Exposure Levels. The lifetime risk estimates given in Table 7-2 are based on an assumed continuous environmental ambient exposure equivalent to either 0.0004 or 0.002 fibers longer than 5 μm per cm^3 of air breathed. The committee believes that 0.0004 fibers/cm^3 is a reasonable assumption for a median population exposure level and that 0.002 fibers/cm^3 is a reasonable high exposure level (considering only exposures from breathing ambient air continuously). These assumptions are discussed below. The effects of noncontinuous high exposures are discussed later in this chapter.

Table 7-6 summarizes some environmental asbestos sampling data provided by Nicholson (1983). To convert from mass measurements (ng/m^3) of airborne exposures to fiber counts (fibers/cm^3), the committee used the conversion factor of 30 μg/m^3 for 1 fiber/cm^3. (See Chapter 4 of this report, Schneiderman et al., 1981, and Consumer Product Safety Commission, 1983 for further explanation.)

The dose-response data used in the committee's risk estimate were taken from measurements of exposures in the workplace, where the fibers tend to be longer than those in ambient environments not close to major sources of asbestos. As discussed in Chapter 4, there would typically be approximately 2,000 fibers per nanogram in workplace air; in remote areas, however, there would be approximately 70,000 ambient fibers in a nanogram. To convert mass in the workplace to ambient air, the committee used the number of fibers longer than 5 μm that would be found in the workplace when the workplace mass equaled the remote ambient fiber mass. The dose estimate in numbers of fibers would be approximately 35 times greater (70,000/2,000) if the actual sizes of fibers in ambient air were considered. If we assume that all fibers are equally potent, then the risk estimates would be correspondingly higher. On the other hand, fiber size apparently affects fiber potency, but the appropriate adjustment factors for fiber size are not known.

Table 7-6 indicates that median concentrations in outdoor air have ranged from 0.00002 to 0.00075 fibers/cm^3 in several studies (sample sets 1 to 8); their median is approximately 0.00007 fibers/cm^3. The observed median inside rooms without asbestos is 0.00054 (sample set 9). In rooms with asbestos surfaces, the median is 0.0006 fibers/cm^3 (range of medians for sample sets 10 through 14, 0.00006 to 0.00405 fibers/cm^3). If these three medians are weighted by assuming persons spend approximately one-fourth of their time outdoors, five-eighths of their time indoors in uncontaminated rooms, and one-eighth of their time in asbestos-contaminated rooms, a reasonable estimate for a median population exposure is 0.0004 fibers/cm^3.

The committee also used 0.002 fibers/cm^3 for a high value of continuous exposure in its calculations for Table 7-2. This value was obtained by using the median of the 90th percentiles in Table 7-6 for each exposure subcategory. For outdoor air, the median is 0.0003

TABLE 7-6. Summary of Environmental Asbestos Exposure Samples[a]

Sample Sets	No. of Samples	Measured Concentration (ng/m^3) Median	Measured Concentration (ng/m^3) 90th Percentile	Equivalent Concentration (fibers/cm^3)[b] Median	Equivalent Concentration (fibers/cm^3)[b] 90th Percentile	Reference
1. Paris air	161	0.7	3.2	0.00002	0.00011	Sebastien et al., 1980
2. Paris (outdoor control)	19	0.7	5.2	0.00002	0.00017	Sebastien et al., 1980
3. Outdoor control samples, for U.S. schools	31	0.9	9.8	0.00003	0.00033	Constant et al., 1982
4. Air of 48 U.S. cities	187	1.6	6.8	0.00005	0.00023	Nicholson, 1971
5. Air of U.S. cities	127	2.3	7.8	0.00008	0.00026	U.S. Environmental Protection Agency, 1974
6. Air of five U.S. cities (outdoor control sample)	34	6.7	31.9	0.00022	0.00106	Nicholson et al., 1975, 1976
7. New York City air	22	13.7	42.9	0.00046	0.00143	Nicholson et al., 1971
8. Air 0.5 mile (0.8 km) from asbestos spraying	17	22.5	82.6	0.00075	0.00275	Nicholson et al., 1971
9. Air in U.S. schoolrooms without asbestos	31	16.3	72.7	0.00054	0.00242	Constant et al., 1982
10. Air in Paris buildings with asbestos surfaces	135	1.8	32.2	0.00006	0.00107	Sebastien et al., 1980
11. Air in U.S. buildings with cementitious asbestos	28	7.9	19.1	0.00026	0.00064	Nicholson et al., 1975, 1976
12. Air in U.S. buildings with friable asbestos	54	19.2	96.2	0.00064	0.00321	Nicholson et al., 1975, 1976
13. Air in U.S. schoolrooms with asbestos surfaces	54	62.5	550	0.00208	0.01833	Constant et al., 1982
14. Air in U.S. schools with damaged asbestos surfacing materials	27	121.5	465	0.00405	0.01550	Nicholson et al., 1978

[a]Adapted from Nicholson, 1983.
[b]Based on conversion factor of 30 μg/m^3 = 1 fiber/cm^3.

fibers/cm^3; for indoor uncontaminated air, it is 0.002 fibers/cm^3; and for indoor asbestos-contaminated air, it is 0.003 fibers/cm^3. The same distribution of occupancy over time was used to arrive at the 0.002 fibers/cm^3 figure for a high exposure level.

Risk Assessments for Special Subpopulations

Table 7-2 shows lifetime risk estimates for people who are exposed throughout their lives to levels of either 0.0004 or 0.002 fibers/cm^3 in ambient air. The predominant risk is from mesothelioma, but lung cancers also contribute to the risk, especially for male smokers. For exposure patterns that are different from those assumed, lifetime risks could be higher or lower. The following are three illustrations of how lifetime risks could be derived for such special populations.

Children Exposed in Asbestos-Contaminated Schools. The committee estimated the risk for persons exposed from birth to age 73 years to environmental levels of 0.002 fibers/cm^3 (as assumed in Table 7-2) plus an additional risk from a 10-year exposure (from ages 6 to 16) in an asbestos-contaminated schoolroom for 6 hours daily, 200 days per year, to 0.02 fibers/cm^3 (550 ng/m^3, the 90th percentile in Table 7-6). The equivalent continuous daily 10-year exposure is approximately 0.003 fibers/cm^3, i.e., 0.02 x (200 x 6)/(365 x 24). Using equation (6), the lifetime risk of lung cancer for a male who eventually becomes a smoker is 0.003 x 10 x 0.0022, or 66 in a million. This risk represents an approximately 20% addition to his ambient lifetime risk of 320 in a million (0.002 x 73 x 0.0022), for a total of about 390 in a million. For such an individual, the schoolroom exposure adds relatively more to the risk of mesothelioma, as shown below. Using equations (G4) and (G5) in Appendix G for the lifetime mesothelioma risk, L, at $t = 73$ for an exposure of $\ell = 10$ years starting at age $t_0 = 6$ at the dose level d, this risk can be calculated from the formula:

$$L = cd\{1-[1-\ell/(t-t_0)]^k\}(t-t_0)^k,$$

with $d = 0.003$, $\ell = 10$, $t - t_0 = 73 - 6 = 67$, and $k = 3.2$. This lifetime mesothelioma risk becomes

$$L = c(0.003)\{1-[1-(10/67)]^{3.2}\}(67)^{3.2} = 845c.$$

If c is the median value of Table 7-4 (i.e., $c = 2.53 \times 10^{-8}$), the estimated lifetime mesothelioma risk, L, from the 10-year exposure is 21×10^{-6}.

This risk is then added to the background risk of 46×10^{-6} in Table 7-2, giving a lifetime mesothelioma risk for this subpopulation of 67×10^{-6}. If a million people had received such a pattern of exposures, about 67 might be expected to die of mesothelioma. In this example, the contribution to total risk from the schoolrooms is less than that of the lifetime exposure to the lower concentrations of asbestos estimated for the ambient air. However, if the value for k in Equation (7) were higher than 3.2, the significance of the schoolroom exposures

would increase because of the stronger dependence on time since first exposure. For example, if k = 3.8, the highest value used in Table 7-2, the lifetime mesothelioma risk would be 910 x 10^{-6}. If k were less than 3.2, the corresponding lifetime risk for mesothelioma would be less than 67 x 10^{-6}. These calculations show that childhood exposures to asbestiform fibers might contribute noticeable lifetime mesothelioma risks to those so exposed.

A Female Nonsmoker in a Relatively Asbestos-Free Environment. An example of a person in a low-risk group is a female nonsmoker exposed to an average level of 0.0001 fibers/cm^3. This exposure level would not be too unlikely for a person exposed primarily to rural indoor and outdoor air, since 0.00002 fibers/cm^3 is the lowest median value for all the outdoor city readings in Table 7-6. Then, the calculations in Table 7-2 would lead to a mesothelioma lifetime risk of 2.25 x 10^{-6} (9 x 10^{-6} divided by 4) plus a lung cancer lifetime risk of 0.73 x 10^{-6}. The lifetime individual risk for such a person would be 3 x 10^{-6} for both types of cancer.

A Male Smoker Living in an Area Contaminated with High Levels of Asbestos Who is Also Exposed to High Indoor Concentrations. As an example of a high-risk person, consider an urban male smoker exposed to 0.003 fibers/cm^3 for one-half the time and 0.018 fibers/cm^3 for the other half. This pattern is based on the assumption that the subject spends one-half of his time in indoor environments with a high asbestos concentration (see sample sets 13 and 14 of Table 7-6) and one-half either in highly contaminated outdoor environments (see sample sets 7 and 8 of Table 7-6) or in indoor environments at the high end of the distribution for rooms that are normally not contaminated with asbestos (see sample set 9 of Table 7-6). Thus, his continuous average exposure would be approximately 0.01 fibers/cm^3, i.e., 0.5(0.003) + 0.5(0.018). Therefore, multiplying the second column of Table 7-2 by a factor of 5 (0.01 = 5 x 0.002) would give the individual lifetime risks for such a person as 1.8 x 10^{-3} for the two forms of cancer taken together (230 x 10^{-6} for mesothelioma and 1,600 x 10^{-6} for lung cancer). This lifetime risk is the additional incurred risk attributable to the nonoccupational environmental exposure to asbestos and does not include the risk incurred by the smoking itself. The portion of the additional risk attributable to lung cancer is considerably higher than it would be for a nonsmoker experiencing identical asbestos exposures.

COMPARATIVE RISK ASSESSMENT

Methods

The goal of comparative risk assessments is to determine whether the fiber exposure in question presents risks--in terms of total number and severity of effects per year in the United States--that are about the same, considerably more, or considerably less than those assessed

Exhibit B

08:18:55 IN THE COURT OF COMMON PLEAS
FOURTH JUDICIAL CIRCUIT
STATE OF SOUTH CAROLINA COUNTY OF DARLINGTON

ANTOINE BOSTIC,)
Individually and as)
Personal Representative of)
the Estate of BERTILA)
DELORA BOYD-BOSTIC,) C/A No. 17-CP-16-0400
)
Plaintiffs,)
)
vs.)
)
IMERYS TALC AMERICA, INC.,)
et al.,)
)
Defendants.)

TRIAL - VOLUME 6
BEFORE THE HONORABLE JUDGE JEAN TOAL

DATE: Friday, November 9, 2018
08:47:59 TIME: 8:47 a.m.
LOCATION: Darlington County Clerk of Court
1 Public Square, B-4
Darlington, South Carolina
REPORTED BY: Marjorie Peters, RMR, CRR, NCRA-RSA

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Sarah LeBlanc, paralegal

INDEX

INDEX OF EXHIBITS

09:31:01 A. No.
09:31:02 (Exhibit D-7214 was presented.)
09:31:02 Q. Would you pull up 7214, please.
09:31:31 Do you have the cover page of that
09:31:34 document? It should say certificate on that cover
09:31:46 page. Thank you?
09:31:48 Do you recognize what that is?
09:31:49 A. Yes, I do.
09:31:50 Q. What is it?
09:31:51 A. It is a -- it's a cover page from the
09:31:55 Food and Drug Administration, which prefaces their
09:31:59 response when they were asked for that report.
09:32:04 Q. Would you go to page 4 of 102. If you
09:32:15 would please read that part of the third paragraph
09:32:17 that starts with, "In addition"?
09:32:19 A. "In addition, FDA surveillance
09:32:22 activities that were conducted in the latter portion
09:32:24 of the 1970s show that the quality of cosmetic talc
09:32:27 had significantly improved and that even when
09:32:30 asbestos was present, the levels were so low that no
09:32:33 health hazard existed. Our scientists recently
09:32:36 reviewed the data from the surveillance activities
09:32:38 and concluded that the risk for a worst case
09:32:41 estimate of exposure to asbestos from cosmetic talc
09:32:44 would be less than that -- than the risk from

09:32:47 environmental background levels of exposure to
09:32:49 asbestos from non-occupational exposure over a
09:32:53 lifetime."
09:32:54 Q. You were asked yesterday whether or not
09:32:56 there was any audits or review by the FDA. Does
09:32:59 that give you any idea of surveillance or reviews by
09:33:04 the FDA?
09:33:04 A. It indicates that they were doing
09:33:07 surveillance in the 1970s.
09:33:10 Q. What does surveillance mean to you?
09:33:12 A. They -- surveillance, you look at
09:33:15 published literature and other information you can
09:33:18 get from other national bodies to see the health of
09:33:22 the employees, and others.
09:33:24 (Exhibit D-9688 was presented.)
09:33:24 Q. I'd ask you to look at one last
09:33:31 document, 9688. Would you pull that up, please.
09:33:38 Would you read the caption.
09:33:39 A. It's captioned, "FDA authority over
09:33:42 cosmetics. How cosmetics are not FDA approved but
09:33:45 are FDA regulated."
09:33:46 Q. You were asked questions yesterday
09:33:48 whether or not the FDA was involved in the
09:33:50 regulation of cosmetic talc; correct?
09:33:53 A. I was, yes.

09:33:54 Q. Does that address that issue?
09:33:56 A. It does.
09:33:56 Q. What is your answer as to whether or not
09:33:58 the FDA is involved in the regulation of talc?
09:34:01 A. As I said yesterday, the FDA has
09:34:03 regulatory oversight over talc and other cosmetic
09:34:06 products.
09:34:07 MR. MARTIN: May I have a moment,
09:34:08 Your Honor.
09:34:23 Dr. Hopkins, thank you. Your Honor,
09:34:24 I will pass the witness.
09:34:25 THE COURT: Very good.
09:34:26 Mr. Swett. Like Mr. Martin, I told
09:34:31 you yesterday that I would allow some additional
09:34:40 opportunity for limited cross-examination, but you
09:34:42 are at about the end of the time for this witness.
09:34:45 MR. SWETT: Thank you, Your Honor.
09:34:46 May it please the court. Good morning. Good
09:34:49 morning, Ladies and Gentlemen.
09:34:50 JURY: Good morning.
09:34:54 MR. SWETT: Do we have the Elmo?
09:34:54 RECROSS-EXAMINATION
09:34:54 BY MR. SWETT:
09:35:09 Q. Good morning, Dr. Hopkins.
09:35:10 A. Good morning.

09:35:11 Q. All right. Let me show you P-157. This
09:35:19 is the Blount article that we have been discussing.
09:35:21 This came directly out of Johnson & Johnson's files;
09:35:24 right?
09:35:24 A. It has a J&J stamp on it.
09:35:26 Q. Right. Just so we're clear, when you
09:35:30 reviewed this document, you got it from Johnson &
09:35:32 Johnson's lawyers; right?
09:35:34 A. This is -- this document's in the public
09:35:38 domain. I may have read it there, or I may have
09:35:41 just read it because I can download documents from
09:35:43 the publishers. So I'm not sure -- this goes back
09:35:48 to 1991. It's a long while. I can't remember
09:35:51 whether I read it recently or back in the '90s.
09:35:55 Q. No, sir.
09:35:55 A. I certainly read it.
09:35:56 Q. This document is not in the public
09:35:58 domain.
09:35:58 A. Well, you need to show me which document
09:36:00 it is, please.
09:36:01 Q. I'm talking about the Blount article
09:36:02 with Johnson & Johnson's Bates numbers on it. This
09:36:06 document is not in the public domain, is it?
09:36:08 A. That document isn't, no, but the main
09:36:11 report --

question.

Walter Bristow was one of my mentors, and he and Jack Grimball were the kings of how they handled proffers, and they always handled them the way I'm going to suggest that they be handled, which is you just proffer it at the end, and all of the objections and proffer were taken out of the presence of the jury at one time so you didn't have to pull them in and out and in and out and in and out. That's how I would much prefer to handle this, if it can be handled that way.

With respect to any other slide shows, please exchange them, and that at least will obviate any kind of delays during courtroom time.

Now, anything further from you all?

MR. HERNS: No, Your Honor.

THE COURT: Mr. Swett.

MR. SWETT: Your Honor, just very, very briefly. Since there's some talk about proffer, our position on this issue of Dr. Longo and Sanchez is, it's that last link that's totally improper.

If he wants to say what's the proper method to test talc, this is it. But it's the next step: Well, Dr. Longo did it wrong. That's the

step that's just totally inappropriate.

THE COURT: I understand that very fully. I think I have covered that in my rulings. You may be articulating it a little more clearly than I was articulating it, but I am not preventing Dr. Sanchez from talking about his method of testing, talking about the AHERA method, the ISO method and the Blount method; but what I'm not going to allow him to do is to characterize incorrectly how Longo used those methods, implying that the method's okay, but he somehow was improper in the way he used the method.

If they want to say that, they're going to have to get much more specific about what he said about how he used those methods. That's all I'm saying.

And the reason for that is, he is an expert witness who can give opinions about matters and has that elevated status; and in order to give opinions that are legitimate to the jury, his foundation for the opinion must be stated. If that opinion is an opinion about testing that somebody else does, the platform for that opinion has to be accurate.

So I think I have made that clear

three or four times now, and that is what the ruling is.

MR. SWETT: Thank you, Your Honor.

THE COURT: All right. Anything else?

MR. EWALD: No, Your Honor.

THE COURT: All right. Court will be in recess.

MR. EWALD: Thank you.

(RECESS, 5:04 p.m.)

CERTIFICATE OF COURT REPORTER

I, MARJORIE PETERS, the officer before whom the foregoing proceeding was taken, do hereby certify that the witnesses whose testimony appears in the foregoing hearing were duly sworn; that the testimony was taken in shorthand and thereafter reduced to typewriting by me or under my direction; that this transcript is a true record of the proceedings; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this hearing was taken; and, further, that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

_____

Marjorie Peters, RMR, CRR, NCRA-RSA

Exhibit C

15 November 1972

Dr. A. J. Goudie
Johnson & Johnson
Research Center
501 George Street
New Brunswick, New Jersey 08901

Dear Dr. Goudie:

Here is our modified thinking on the baby powder samples 108T and 109T. After looking at several fresh samples on the light microscope we have not been able to substantiate the tremolite levels we originally reported.

Yours sincerely,

Ian M. Stewart
Manager, Electron Optics
Group

ajw
Ref: MA 2546
Enclosures

Exhibit D

IN THE CIRCUIT COURT OF THE STATE OF OREGON

FOR THE COUNTY OF MULTNOMAH

KYUNG LEE AND JOE LEE, Plaintiffs,	)	
v.	)	No. 23CV40369
BI-MART CORPORATION, et al., Defendants.	)	

TRANSCRIPT OF PROCEEDINGS

Volume 20, Pages 2642 - 2732

Thursday May 23rd, 2024

8:45 a.m.

Multnomah County Courthouse

Courtroom 16-C

1200 SW 1st Avenue

Portland, Oregon

BEFORE: Hon. Katharine von Ter Stegge

REPORTED BY: KELLY ANTRIM ELMORE, CSR, RPR

* * *

BY MR. STUTE: 09:18:02

Q Let me just show you this document, Dr. Kuffner, in the interest of time. Is this the document you've seen before?

A Yeah. 09:18:09

MR. ADAMS: Do you have a copy, Counsel, of what you're showing the witness?

MR. STUTE: It's an admitted exhibit, and what I'm showing is -- I don't have a copy for you because I wasn't anticipating using documents. But this is DX7214-0001. This is defendant's Exhibit 7214, for the record. 09:18:20

MR. ADAMS: Appreciate it.

MR. STUTE: Thank you for that.

BY MR. STUTE: 09:18:42

Q And Dr. Kuffner, have you seen this document before?

A Yes, I have.

Q What is it?

A This is the letter from -- from the FDA to Mr. Dulay (phonetic) in 1986 denying citizen's admission. 09:18:46

Q And that 1986 is after 1974, which is the document that plaintiffs' counsel just presented you. Correct? 09:19:04

A Correct.

Q And what is the point of that document in summary fashion so the jury can understand the point of it, Dr. Kuffner? 09:19:05

A At the end of the day, the petitioner was asking that they -- of the FDA that they add asbestos warnings on the talc-based products. And the FDA essentially said we deny your petition. We don't think asbestos warnings need to be put on products. And one of the reasons they gave is they said we understand there was some testing from the early '70s and based upon how the science was evolving at the end of the day, we discount that -- the reliability of that testing. 09:19:11 09:19:28

Q In other words, this is the FDA saying to a citizen petitioner that it does not believe there's asbestos, based on it's testing in Johnson & Johnson Baby Powder. Correct? 09:19:44

A That -- that -- that would be correct.

Q Thank you, Dr. Kuffner. I don't have any more questions for you. 09:19:56

THE COURT: All right. Thank you, Dr. Kuffner.

THE WITNESS: Thank you. Thank you.

THE COURT: And so we are ready for our 09:20:06

CERTIFICATE

I, Kelly Antrim Elmore, an CSR, RPR, do hereby certify that I reported in stenotype the testimony and proceedings had upon the hearing of this matter, previously captioned herein, before the Hon. Katharine von Ter Stegge, that I transcribed my stenotype notes through computer-aided transcription; and that the foregoing transcript constitutes a full, true and accurate record of all testimony adduced and proceedings had during the hearing of said matter, and of the whole thereof.

Witness my hand at Portland, Oregon, this 23rd day of May, 2024.

Kelly Antrim Elmore

Oregon CSR No. 21-0020

Expires 9/30/24
Registered Professional Reporter

Exhibit E

IN THE CIRCUIT COURT OF COOK COUNTY, ILLINOIS

COUNTY DEPARTMENT, LAW DIVISION

STEPHANIE SALCEDO, Individually and as Administrator of the Estate of Theresa M. Garcia, Deceased,	)	In Re: Asbestos Litigation
Plaintiff,	)	
v.	)	Calendar J1
AVON PRODUCTS, INC., et al.,	)	
Defendants.	)	Court No. 20 L 004505

DAY 5

CNTD. DX, CX, RDX EXAMINATION OF R. MARK BAILEY

REPORT OF PROCEEDINGS at the hearing of the above-entitled cause before the Honorable Patrick J. Sherlock, Judge of the said Court, on the 22nd day of March, 2024, commencing at 9:31 a.m.

Reported by:

Deborah Habian, CSR, CRR, RMR

License No. 084-02432

ribbon and a sealed copy?

A. Yes, I do.

Q. And now that you're looking at it, does this kind of refresh your memory about what you've seen before when you've read it?

A. Yes, that's true.

Q. And this is the FDA's response to the Citizens Petition, correct?

A. That's correct, yes.

MS. BUENO: And, your Honor, I'll offer into evidence now Defense Exhibit 1. It's self-authenticated domestic public document.

THE COURT: Any objection?

MR. BUHA: No objection.

THE COURT: All right. It will be admitted.

(Defendants' Exhibit 1 for ID was admitted into Evidence.)

MS. BUENO: Thank you, your Honor.

BY MS. BUENO:

Q. Before we get to exactly what is in this document, which is so important for this trial, let's see if we're on the same page about the FDA.

REPORTER CERTIFICATE

I, Deborah Habian, a Certified Shorthand Reporter within and for the State of Illinois, do hereby certify:

That the foregoing report of proceedings was reported stenographically by me, was thereafter reduced to printed transcript by me, and constitutes a true record of the testimony given and the proceedings had;

That the said report of proceedings was taken remotely before me at the time and place specified;

That I am not a relative or employee of attorney or counsel, nor a relative or employee of such attorney or counsel for any of the parties hereto, nor interested directly or indirectly in the outcome of this action.

IN WITNESS WHEREOF, I do hereunto set my hand this ____ day of _____, 20___.

_____
DEBORAH HABIAN, CSR, RMR, CRR, CLR
IL CSR NO. 084-02432
MO CCR NO. 1409