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## MEMORANDUM

TO: Dick Wiles, John Shipp

FROM: Lenore McKenna

DATED: 10/16/97

RE: Coker v. Johnson & Johnson  
54.2121  
Mesothelioma/Talc Medical Research

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According to the literature, most of the research done on mesothelioma closely links it to exposure to asbestos. However, mesothelioma was inducible in rats by intrapleural inoculation of nonasbestos fibrous materials such as synthetic aluminium silicate (ceramic fibers), fibrous glass and aramid. Although most patients with mesothelioma have had occupational exposure, spontaneous mesotheliomas do occur. (1) Since mesothelioma is considered to be closely related to exposure to asbestos, mortality from mesothelioma can be taken as an index of past exposure to asbestos in the population. (Lancet 1995 Mar 4;345(8949):535-9.). In fact, the incidence of mesothelioma in populations unexposed to asbestos is only 1-2 per million. (2)

Mesothelioma is usually malignant although it may be benign. Benign mesotheliomas are less frequent than malignant ones and they are not associated with asbestos exposure. (3) About 2/3 of all benign mesotheliomas occur in females. (3)

The majority of mesotheliomas are located in the pleura. (1) One study found that 72% of mesotheliomas were located in the pleura, 13% in the peritoneum and 11% in the lung. (1) This study also found that smoking was more prevalent in patients with mesothelioma of the peritoneum and lung compared with patients with mesothelioma of the pleura. (1)

Asbestos is divided into two main classes: the serpentines (chrysotile) and the amphiboles (crocidolite, amosite, anthophyllite, tremolite and actinolite). (2) The association between asbestos and both pleural and peritoneal mesothelioma has clearly been established since the 1960's. (2) Still, mesothelioma is an uncommon disease, even among asbestos-exposed populations. (2)

The carcinogenic effects of asbestos are related to the physical properties of size and shape of the fibers, and to their quantity. (2) In order for the fibers to cause mesothelioma, they must be less than 0.25 um in diameter and more than 5 um in length. (2) If the fiber is larger than 0.5 um in diameter and shorter than 5 um in length, then such fibers are not going to

produce mesotheliomas. (1) It must be remembered that there is also a natural incidence of mesotheliomas of the pleura and the peritoneum in both humans and experimental animals. (1)

Some researchers have argued that it is only in very large quantities that chrysotile causes mesothelioma, however, others have suggested that it is only the amphibole contaminant in chrysotile (such as the tremolite in Canadian chrysotile deposits) that causes mesothelioma and that chrysotile itself is relatively harmless. (2) Still others have reached different conclusions. (2) The most recent literature suggests that uncontaminated chrysotile fibers will not cause mesotheliomas (although most chrysotile is contaminated with tremolite). (1)

In all occupationally exposed studies of mesotheliomas, none have occurred in patients where amphibole asbestos has never been used or detected. (2) Chrysotile asbestos has not been directly implicated in any cases of peritoneal mesothelioma although there is good evidence from lung studies that chrysotile alone can cause mesothelioma. (2) It is generally accepted that the numbers and length of fibers are much more relevant to the development of mesothelioma than particle counts or total dust collection levels. (2)

The relationship between exposure to asbestos and incidence of mesothelioma is uncertain, but there is a positive correlation between the dose of asbestos and the probability of contracting mesothelioma. (2) However, there have been isolated, cases of mesothelioma in people whose only exposure appears to have been from buildings with asbestos insulation. (2)

Most reports of patients with mesothelioma contain a proportion of patients with no documented exposure to asbestos. However, later analysis of fiber counts in the patients' lungs showed the histories to be inaccurate. (2) Some mesotheliomas do occur in the absence of detectable fibers in the lungs and there are causes of mesothelioma other than asbestos. (2) That mesothelioma can be caused by nonoccupational exposure to mineral fibers is not in doubt and the highest documented incidence of mesothelioma in the world is in Karain in Turkey where naturally occurring erionite, a fibrous zeolite, has been used in building. (1) In addition, communities built around natural sources of tremolite have experienced incidence of the disease through nonoccupational exposure. (1) Erionite is considered the most potent mesothelioma producer followed by tremolite. (2) Although tremolite is a cause of mesothelioma, testing in animals has revealed that it was only the very fine tremolite (longer than 8.0 um and smaller than 0.25 um in diameter) that caused mesotheliomas. (1)

Mesothelioma may occur after brief or indirect exposure to asbestos. (2) Some studies have shown a longer latency period for peritoneal rather than pleural mesothelioma although others

have shown no difference. (2) In most reports, pleural mesothelioma remains the most prevalent with the pleural to peritoneal ratio at 3:1. (2) The high rate of peritoneal mesothelioma among insulation workers should be looked on as the exception. (2) An hereditary predisposition to mesothelioma has been suggested although most clustering of mesothelioma are linked to exposure to asbestos in the home. (2) Rare cases of mesothelioma may be related to therapeutic radiation or chronic pleuritis and fibrosis. (2)

Even with today's technology, there are still enormous problems in estimating actual levels of environmental exposure to asbestos.

### **Talc**

Some studies made between asbestos and other fibers such as glass fibers, calcium phosphate, talc and kaolin show that they have similar effects to asbestos, but yet are not carcinogenic in humans. (2) However, in several mesothelioma patients studied, both talc fibers and tremolite were detected. (2) In fact, the majority of asbestos bodies isolated from the lungs of women in the general population have tremolite or anthophyllite and because tremolite and anthophyllite are known contaminants of talc, this data suggests that rare cases of mesothelioma among women with no other identifiable exposure might be related to exposure to cosmetic talc. ((2) at p. 215).

### **Possible Environmental Exposure to Asbestos**

Environmental factors must be given the major consideration in the incidence of Mesothelioma. (1)

1. Cigarette manufacturers who used crocidolite for making filter-tips had extremely high cancer rates
2. Rochdale Textile Workers
3. Ontario Cement manufacturers
4. American insulations workers
5. Naval dockyard workers
6. Wittenoon crocidolite workers
7. Inhabitants of Karain, Turkey (erionite in local environment)
8. Asbestos
9. Household contact with asbestos workers
10. Living in the neighborhood of asbestos mines and factories (especially: Wittenoon, East London, Bohlig, Hain, Hamburg)
11. Areas with naturally occurring asbestos or asbestos-like deposits
12. Railroad workers
13. Manual laborers (plumbers, carpenters, electricians)
14. Vermiculite miners
15. Talc miners (tremolite asbestos is a known contaminant os some deposits of talc)
16. Mines in Turkey, Cyprus and Quebec

17. Auto mechanics (especially break repair)
18. School teachers (exposed to ceiling and pipe insulation over many years)

Some letters to the various journals also indicate that the following may be risk factors for the development of Mesothelioma:

1. Exposure to asbestos in dental practice (Lancet Vol 338, p. 696)
2. Clustering of Peritoneal Mesothelioma in the Midlands, UK (Lancet 1995 Jan 7;345:66-7)
3. Tremolite containing white-wash (Lancet 1987 Apr 25;1:965-7)
4. Diapers contaminated with asbestos (Lancet 1989 Apr 22;1:909-10)
5. Mesothelioma among sugar refinery workers (Lancet 1983 Dec 24-31;2:1503)
6. Chlorinated phenols (Lancet 1981 Jul 4;2:40)
7. Prenatal exposure to isoniazid (a medication) (Lancet 1980 Aug 16;2:362)
8. Mesothelioma among shoeworkers (Lancet 1980 Feb 2;1:259)

#### **Other Possible Causes of Mesothelioma**

1. Chronic inflammation and old pleural scars (may only be a risk for pleural mesothelioma)
2. Radiation treatment of Wilms' tumor in childhood
3. Erionite (a fibrous zeolite) used in building, especially in Karain in Turkey.(1)

#### **Signs and Symptoms and Prognosis**

Peritoneal mesothelioma usually presents late with dull pain, abdominal swelling, weight loss and ascites. (1) The outlook of malignant mesothelioma is poor with few patients living for 2 years; the time from diagnosis to death is usually about 6 months. (1) No chemotherapy has been of value and treatment remains symptomatic.(1)

1. The Mesothelial Cell and Mesothelioma, edited by Marie-Claude Jaurand, Jean Bignon, 1994
2. Malignant Mesothelioma, edited by Douglas W. Henderson, Keith B. Shilkin, Suzanne Le P. Langlois, Darrel Whitaker, 1992
3. Mesothelioma: Diagnosis and Management, edited by C. Frederick Kittle, 1987
4. Longo, D.L., Young, R.C.: Cosmetic Talc and Ovarian Cancer. Lancet 1979 Aug 18;2(8138):349-51
5. Philippe Chahinian, M.D., et al: Diffuse Malignant Mesothelioma. Ann Intern Med 1982 Jun;96(6 Pt 1):746-55

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