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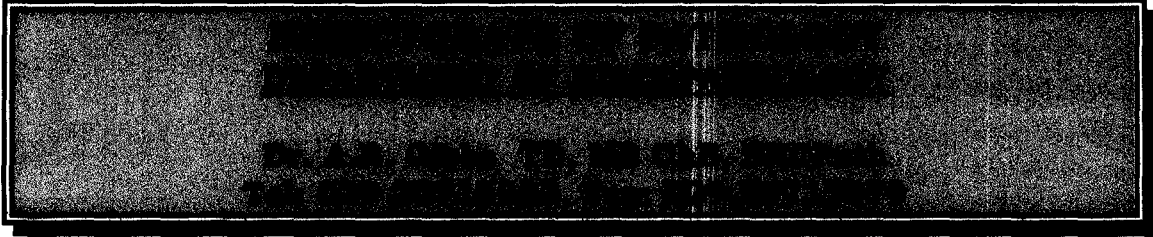
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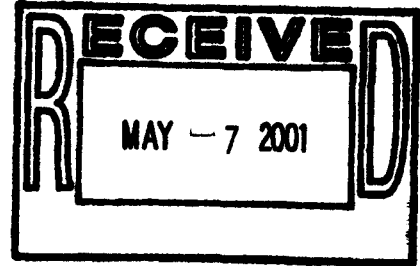
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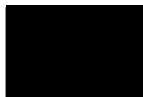


Dear Dr. Jameson

**Re: Final call for data and public comment regarding talc listing**

I enclose my comments concerning the issue of lung and pleural malignancy in association with talc exposure. This has been submitted at the request of Eurotalc.

Yours sincerely



A.R. Gibbs  
Consultant Pathologist



Awarded for excellence



## Talc and pleuropulmonary malignancy

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### Studies of miners and millers

Considerable weight has been put upon the cohort studies of the New York State miners and millers (Kleinfeld et al 1967,1974; Brown et al 1979; Dement et al 1980; Lamm et al 1988; Stille and Tabershaw 1982) with implications for carcinogenicity which the data do not justify. The talc from this area contains a high proportion of tremolite and some anthophyllite but there is considerable dispute as to whether these amphiboles are asbestiform. Many criticisms of the studies can be made which include lack of smoking data, short periods of working at the facility, excess risk confined to the 60 to 79 year age group and lack of dose response. It should be noted that no excess of lung cancer was observed in those exposed after 1965. In a case-control study based on the New York State talc workers Gamble (1993) concluded that there was no excess risk associated with talc exposure. The issue with regard to mesothelioma is even more confusing – it is not clear how many have occurred in the cohort studies, possibly four, but there may have been double reporting. There is some evidence to suggest that they may have been exposed to asbestos elsewhere and the histopathological basis for the diagnosis appears to be insecure.

Other studies of talc miners and millers, where there was no or very little exposure to tremolite or anthophyllite have not shown an excess of lung cancer or mesothelioma (Rubino et al 1976,1979; Leophonte et al 1983; Wergeland et al 1990), with the one exception of Vermont miners and millers where there was an excess of respiratory malignancies but no mesotheliomas (Selevan et al (1979). However, this only occurred in the miners and not the millers. The latter were more heavily exposed to talc, suggesting the presence of confounding factors such as radon exposure.

There has been a recent INRS report of the long term follow up of the Luzenac, France, talc workers (Wild 2000). Luzenac talc comprises a mixture of talc (59%), chlorite (39%) and dolomite with traces of pyrite and quartz. A cohort study and a nested case-control study were carried out on the workers and information characterising occupational exposures and smoking were collected. The study included all subjects active in 1945 or hired thereafter up until 1994 who were employed continuously for at least one year in the milling plant at Luzenac. The cohort comprised 1070 men and 90 women amounting to 30,805 person-years. A slight excess of lung cancer compared to the local but not the national population was found but detailed analysis did not demonstrate an occupational origin. No mesotheliomas were found.

### Mineralogical studies of human tissues

Mineralogical analysis of lung tissues from subjects exposed to substantial quantities of “talc” from different locations is a useful way of evaluating and characterising exposures to “talc” since talc sources vary considerably in mineralogical composition. Since the lung can act as a type of filter for some minerals, such as amphiboles, minerals may be identified in the lung tissues which might not have been apparent from examination of the ores or talc products themselves. A study by Gibbs et al (1992) examined lung tissues from 17 subjects with substantial exposures to talc from mining industries, secondary exposures such as rubber and pharmaceutical industries, and a domestic exposure. The study demonstrated a variety of minerals in the lung tissues including silicates other than talc, particularly in the secondary exposures. Indeed one case thought to be a talc pneumoconiosis turned out to be a mica pneumoconiosis. Tremolite fibres were found in only two cases – a worker from the Swiss ceramic industry and one Vermont miner who could have been exposed elsewhere. The findings illustrate the difficulties in assessing “talc” exposure in secondary industries where a number of other minerals are used which may confound investigations of the effects of talc on mortality and morbidity. In the two Luzenac workers who had been heavily exposed to talc the predominant minerals detected in the lung tissues were talc (70.5% and 96.2%) and chlorite (25.5% and 3.8%) with no tremolite or anthophyllite detected. These results compare well with the known composition of Luzenac talc indicating that Luzenac talc workers were unlikely to have been exposed to tremolite or anthophyllite as a result of working with talc.

### Pleurodesis

Obliteration of the pleural space by adhesions is indicated for recurrent effusions of fluid or recurrent episodes of pneumothorax and it can be accomplished by a variety of methods including intrapleural instillation of various agents (pleurodesis). Talc is one such agent and it is cheap and reliable (Kennedy & Sahn 1994; Kennedy et al 1995; Weissberg & Ben-Zeev, 1993). Pleurodesis with talc and other agents has been performed for many years (since 1935 in the UK) usually for recurrent pneumothorax. This provides a human model for studying the effects of direct inoculation of the pleura by talc comparable to animal studies with asbestos. To date pleurodesis with talc free of amphibole has not resulted in mesothelioma, apart from a single case report (Jackson & Bennett 1969). This described an adenocarcinoma of the pleura developing two years after iodised talc insufflation for spontaneous pneumothorax but in view of the short latency it was thought to be causative. In a study of 210 subjects treated by talc and kaolin pleurodesis for recurrent pneumothorax which was carried out jointly by Medical Research Council and the British Thoracic Association there was no increased incidence of lung cancer or mesothelioma found after long term follow-up (Chappell et al. 1979; Lange et al 1988). This has been confirmed in other studies (Kennedy & Sahn 1994). In my own personal experience of about three thousand mesotheliomas none has been linked with prior talc pleurodesis.

## Conclusion

There is no convincing evidence which links respiratory malignancy including mesothelioma with talc exposure.

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