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March 28, 1994

John E. Bailey
Acting Director, Office of Cosmetics and Colors
Center for Food Safety and Applied Nutrition, FDA
200 C Street S.W.
Washington, D.C. 20204

Dear Mr. Bailey:

Subject: **Comments on IS RTP/FDA Workshop on Talc (1/31 & 2/1,
1994)**

Mr. Jean-Pierre Grange, R&D Director for Luzenac Group, was in attendance at the two day workshop on talc held last month. He requested that I respectfully forward to you the following facts and commentary regarding European study data that shows the lack of association between talc and carcinogenicity.

Mr. Grange's submission is as follows:

DATA ASSOCIATED WITH THE POTENTIAL CARCINOGENICITY OF TALC

The European Community has generated a significant amount of study data showing *the lack of an association* between talc and carcinogenicity. Specifically:

(1) Epidemiological mortality studies on talc miners and millers.

- The Val Chisone Mine and Mill (Italy) published by Rubino⁽¹⁾ in 1976 and updated in 1979^(2,3).
- The Luzenac Mill (France) published by Leophonte⁽⁴⁾ in 1983 and updated in 1991⁽⁵⁾.
- The Knarrevik Mill and Altermarkt Mine (Norway) published by Wergeland⁽⁶⁾ in 1990.

All three studies found no increase of mortality from cancer at any site and no reduction in life expectancy compared to regional or national controls. This is in spite of the fact that many of the cohort were exposed to high dust levels prior to the installation of modern

dust controls. While there were reports of pneumoconiosis resulting from these early high exposures, carcinogenicity was not a factor.

(2) In vivo intrapleural injection of rats, reported by Endo-Capron⁽⁷⁾ in 1990, confirmed the lack carcinogenesis.

(3) In vitro genotoxicity assay by Endo-Capron⁽⁸⁾ in 1993 also showed the lack of carcinogenic response. These assays were performed with three samples of talc having different crystalline sizes (Val Chisone large crystal, Luzenac medium crystal, and Spanish Respina microcrystalline talc).

Prof. J.Bignon (France) states "the talc harmlessness regarding cancer genesis has been confirmed by the fact that no cases of mesotheliomas or of lung tumor has been reported, even after the various pleurodesis done by powdering of the pleural cavity with large quantities of medicinal talc, including to some young patients with recurrent pneumothorax, for whom our follow-up exceeds 25 to 30 years."⁽⁹⁾

In total, these studies neither support the relevance to humans of the NTP observations on female rats; nor the biological plausibility of a casual association of talc and ovarian cancer.

RELEVANT LEVEL OF LUNG CLEARANCE

A progressive study of pulmonary response to occupational talc exposure has been in progress at the Luzenac mill in France for the last ten years and is intended for publication in 1994. The study is based on a very large number of dust exposure assessments by individual samplers (CIP10), as well as lung X-ray imagery and periodical lung function assessment for a cohort of 200 workers. The preliminary results show that no occurrence of talc pneumoconiosis was observed in an operating environment that complied with the French TLV for talc (same for nuisance dust) of 5mg/m³ (respirable dust). This would suggest adequate lung clearance at this level of occupational exposure.

OVARIAN CANCER ASSOCIATION PRIOR TO 1960

The observation by B.Harlow that the association between ovarian cancer and the perineal application of talc was observed for applications prior to 1960. B.Harlow suggests that asbestos contamination could have been a confounding factor. Since 1960 however, the elevated risk association between talc and ovarian cancer was not confirmed. This would suggest one of two suppositions:

- What ever might have been present in the talc prior to 1960 to confound the results was evidently no longer present after 1960.

- The whole premise that talc is associated with an elevated risk of ovarian cancer is spurious and not supported by any other plausible data.

The B.Harlow study does show 30 years of the lack of association between the perineal application of talc and ovarian cancer. Clearly, this does not support the need for new or substantive regulation on this issue.

(End of submission from Mr. J.P. Grange)

Thank you in advance for your consideration of these comments.

Sincerely,



Richard J. Zazenski
Manager Quality Assurance

cc. J.P. Grange
R&D Director - Luzenac Group

T.J Kwasizur
President - Luzenac America

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