



Date: JULY 29, 1987
To: W.R. TARR
From: G.M. RUSCH
Subject: ASBESTOS SUBSTITUTE FIBERS

At the July 1987 Toxicology Forum meeting one session was dedicated to a review of asbestos and alternate fiber toxicology. This was an excellent program and I will send a copy of the Proceedings when they become available.

Dr. Roger McCellan provided an introduction and overview of the toxicology of inhaled fibers, especially asbestos. The most biologically active fibers are those with a diameter of 1.0 to 1.5 micrometers and a length of eight micrometers or greater. Fibers are retained by the lungs by one of four mechanisms: impaction, sedimentation, diffusion and interception (potentially very important for fibers). In focussing on asbestos, it was noted that it can cause four adverse health effects: mesothelioma, lung cancer, asbestosis (fibrosis) and plural plaque formation. The increased incidence of lung cancer associated with asbestos exposure, where the normal background level for the non-smoking population is 11 per 10⁵, is about 5X, for smokers it is 10X, and for people with exposure to asbestos and smoke, it is 53X (an incidence of almost 600 per 10⁵).

In addition to asbestos, other durable fibers can also be involved in lung disease. In assessing these, one should look at:

- 1) Fiber characterization (morphology, chemistry, density, impurities or other components present)
- 2) In vitro solubility
- 3) Fiber induced cytotoxicity.

Dr. McCellan mentioned that during a lifetime study with diesel exhaust only 19% of the tumors were seen by 24 months. The remaining 81% were seen between 24 to 31 months. Thus, with these studies, we may want to consider longer observation periods.

When we look at lifetime studies with Titanium dioxide and Kevlar, it would appear that exposures above 2 mg/m³ can lead to the development of fibrosis since they exceed the normal clearance mechanism in the rat. This could then suggest a practical upper exposure limit for rodent lifetime studies of some value in this general range.

Gerry Kennedy of DuPont presented a summary of their lifetime study with Kevlar. This study was run at levels of 400, 100, 25 and 2.5 fibers/cc. The exposure at 400 had to be discontinued after one year due

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to toxicity, but the surviving animals were held for two years. Increased tumor incidences were indicated at 400 and 100 fibers/cc. Fibrosis was seen at 100 f/cc (at 6 months) and 25 f/cc (at 24 months). The 2.5 f/cc level appears to be a no-observed effect level, and 25 f/cc, a minimal effect level. Although DuPont has a permissible exposure limit of 5 fibrils/cc for Kevlar, considering these results, a lower number may be warranted, and the controls needed for Kevlar may not be that different from those suggested for asbestos. Concentrations are expressed in terms of fibers/cc not mg/m^3 as a result of fiber bulking properties since the two do not directly equate. For example:

0.10 mg/m^3 corresponds to 1.3 fibers/cc

0.52 mg/m^3 corresponds to 26 fibers/cc

3.0 mg/m^3 corresponds to 280 fibers/cc

Based on these values, 5 fibers/cc is approximately 0.2 mg/m^3 .

Dick Waritz of Hercules presented a summary of information on carbon fibers. Carbon fibers can be derived from polyacrylonitrile (PAN) or pitch sludge. These appear very different from a toxicology endpoint. The pitch derived ones show some mutagenic activity while the PAN ones were inactive. In a skin painting study, with 16 weeks of application followed by 32 weeks of observation PAN fibers showed no effect, while the pitch derived ones produced sarcomas and carcinomas.

George Levinskas presented an update on Monsanto's toxicology program with Calcium metaphosphate. While nothing new was presented regarding the toxicology, he announced that as a result of product liability concerns, Monsanto has decided not to market this product. In spite of this decision, they will complete their toxicology program.

Struthers from SOHIO presented information on the studies being conducted at Los Alamos on ceramic fibers. In a two-year study they saw a slight increase in tumor yield. While this may indicate only a very low level of activity, it was mentioned that, considering the findings with diesel exhaust, the observation period may not have been long enough.

There was an excellent presentation on an epidemiology study of men employed in the Man Made Mineral Fiber industry (glassware and rock wool). This study involved a cohort of 22,000 workers, 2,710 of whom had died. Only one case of mesothelioma was reported. However, in the rock wool industry, there was a three-fold excess of lung cancer among former workers with 20 or more years of experience. While the authors caution that the number of people in this group is small, this is also not that different from the five-fold excess of lung cancer reputed for non-smokers working with asbestos. Thus, one should handle the mineral wool fibers with care.

It was further mentioned that the IARC Monograph on Mineral Fibers classifies rock wool and slag wool as showing limited evidence of carcinogenicity (2B).

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