## USE OF SIZE-SELECTED FIBERS TO EVALUATE THE CONTRIBUTION OF LENGTH VS CHEMISTRY IN FIBER CYTOTOXICITY.

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Studies have shown that asbestos can lead to lung disease. Therefore, substitutes have been developed that differ chemically from asbestos. However, fiber length as well as chemical composition may be an important factor in pathogenicity. The objective of this study was to investigate the role of length versus chemistry by monitoring the cellular effects of in vitro exposure to different length glass fibers (7 and 17 μm) or three types of fibers (glass, chrysotile, or ceramic) of the same length. A dielectrophoretic classifier was used to separate fibers into specified length categories. Primary rat alveolar macrophages obtained by bronchoalveolar lavage were exposed to various concentrations of fibers. Cytotoxicity and inflammatory potency were assessed by lactate dehydrogenase and tumor necrosis factor α (TNF-α) release, respectively. Data show that 7 μm glass fibers (100 μg/ml) caused 6% cell death while 17 μm glass fiber caused 31% cell death (Blake et. al., 1998). We found that long glass fibers (at a cell:fiber ratio of 1:5) were twice as potent as short glass fibers in stimulating TNF-α production. Data indicate that MAP kinases, p38 and ERK, play a role in this TNF-α production. Long glass fibers were twice as potent as short glass fibers in activating p38 and ERK. Therefore, glass fiber length is an important factor in cytotoxicity and alveolar macrophage activation. To investigate the contribution of fiber chemistry to cytotoxicity, alveolar macrophages were exposed to chrysotile, glass, and ceramic fibers of similar dielectrophoretic size cuts (17 μm target). Chrysotile appeared to exhibit the greatest cytotoxicity, i.e. 100-μg/ml chrysotile, glass, and ceramic fibers caused 30, 19, and 7% cell death, respectively. In conclusion, our results suggest that both length and chemistry play a role in cytotoxicity to alveolar macrophages. In contrast to in vivo exposures, our in vitro system failed to demonstrate the high cytotoxicity of ceramic fibers.

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**Asbestos Health Effects Conference**
**Oakland, California**
**May 24-25, 2001**