disease (macrophage and neutrophil infiltration, bronchiolization, multinucleated giant cells) and interstitial fibrosis in the lungs. CROC and AMO caused prominent pleural fibrosis but CHRY asbestos did not. This was impressive in light of the fact that the numbers of CHRY and AMO fibers in the lung of hamsters were comparable at 12 mo (CHRY = 4.6×10^{10} and AMO = 2.6×10^{9} WHO/lung) and the number of CHRY fibers (23.9×1010^{9}) in the lungs of rats were actually ~two orders of magnitude greater than CROC (647×1010^{9}). CHRY failed to cause either pulmonary neoplasms or mesotheliomas in hamsters. In contrast, while no lung neoplasms were observed, 17 of 87 (20%) hamsters had mesotheliomas. Even though the CROC exposure in rats was for only 10 mo compared to 24 mo for CHRY and the number of CHRY fibers were much greater, the number of lung tumors and mesotheliomas were comparable: CROC = 14 of 106 (13%) and CHRY = 13 of 69 (19%).

The results of the study suggest that AMO and CROC are more carcinogenic in rodents than CHRY asbestos.

877 ESTIMATING THE MAXIMUM TOLERATED DOSE OF FIBER GLASS FOR A CHRONIC INHALATION STUDY USING SYRIAN GOLDEN HAMSTERS.

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A hamster subchronic inhalation study of fiber glass (FG) was used to estimate the MTD (maximum tolerated dose) for a hamster chronic inhalation study. Results from both the chronic and subchronic studies demonstrate that the dose chosen for the latter was the appropriate MTD. For the subchronic study, hamsters were exposed for 6 hr/d, 5 d/wk, for 13 wk to insulation FG (MMVF10) at 0, 3, 16, 30, 45, or 60 mg/m^3, then maintained for 10 wk. of recovery. Results demonstrating MTD were: mild inflammatory response with all fiber exposures; lung epithelial cell proliferation elevations with all but the lowest fiber dose; lung lavage neutrophil elevations with doses ≥16 mg/m^3 and lavage LDH and protein elevations with doses ≥30 mg/m^3; and persistent macrophage/fiber clumps in lungs exposed to 45 and 60 mg/m^3, believed to be symptomatic of lung overload. For the chronic study, hamsters were exposed for 78 weeks to MMVF10a or MMVF33 (filration FG) at 30–37 mg/m^3 (250 fibers longer than 5 µm), or to similarly-sized amosite asbestos at an equivalent dose and 2 lower doses. Results from the chronic study which demonstrate that adequate lung-dosing was achieved are as follows: Six-hr. lung depositions were equivalent for MMVF10a, MMVF33, and high dose amosite. After 13 and 26 wk. of exposure, lung burdens were similar for the 2 FGs and amosite low dose and for RCF1, which was carcinogenic in a previous study. From 52–78 wk of exposure, lung burdens of all fiber-exposed groups showed an accelerated rate of increase, suggesting impairment of clearance mechanisms resulting from lung overload. All fiber-exposed animals developed pulmonary inflammation and elevated lung lavage cells and lung cell proliferation. These findings substantiate that exposures in these studies adequately tested the toxic potential of 2 different types of FG.

878 CHRONIC INHALATION OF SHORT ASBESTOS: LUNG FIBER BURDENS AND HISTOPATHOLOGY FOR MONKEYS MAINTAINED FOR 11.5 YEARS AFTER EXPOSURE.

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In an earlier report, Platek, et al (Fundam. Appl. Toxicol. 5, 327–340, 1985) presented the results of an 18 month inhalation exposure of rats and monkeys to short chrysotile asbestos. The mean chamber exposure level was 1.0 mg/m^3 with an average of 0.79 fibers/cc > 5µm in length. Gross and histopathological examination of exposed and control rats indicated no treatment-related lesions. Asbestos bodies adjacent to the terminal bronchioles, but no fibrosis, were found in lung biopsy tissue taken from the exposed monkeys at 10 months post exposure. Fifteen monkeys (9 exposed and 6 controls) from this study were maintained for 11.5 years following exposure. Lung fiber burdens were determined by transmission electron microscopy. The mean lung burden (± std. dev.) for 59 samples from exposed monkeys was $63 \pm 30 \times 10^{6}$ fibers/g dry lung (range, 18–139 $\times 10^{6}$). The median fiber length was 3.5 µm with 35% of the fibers being > 5 µm in length. These data indicate some chrysotile fibers, particularly longer fibers, are durable *in vivo* for a significant period of time. Lungs were examined grossly and histopathologically for neoplasia, fibrosis and other lesions. Initial pathological evaluations of the lungs showed no lesions attributable to the inhalation exposure.

879 DNA DAMAGE-ASSOCIATED GENE EXPRESSION DOES NOT CORRELATE WITH TOXICITY OF NATURAL AND MANMADE INORGANIC FIBERS.

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This study was undertaken to compare the protein expression of DNA damage-associated genes (p53, p21, and Gadd 153) in A549 cells (human alveolar type II cell carcinoma) treated with a variety of natural (crocidolite, amosite, and erionite) and manmade vitreous fibers (ceramic [RCF1], rock [MMVF 21], slag, [MMVF 22], and glass [MMVF 11 and JM Code 100]) to their known toxicities following inhalation in rats. A549 cells in log-phase growth were treated with graded concentrations of fibers for 20 hr, the medium was changed, and cells were harvested 18 hr post-treatment. The cells were fixed, and proteins were stained with primary antibody, biotinylated secondary antibody, and streptavidin conjugated fluorochrome. After labeling the cells were analyzed by flow cytometry, and the number of cells with increased protein expression was determined by a cumulative subtraction method. Crocidolite readily induced all three proteins; the response was less marked with amosite, while erionite produced a very limited response. The manmade fibers showed a range of responses; slag wool was as equally responsive as crocidolite to the induction of p53; ceramic fiber induced p53 in a similar manner to amosite; and MMVF 11, 21, RCF1, and JM Code 100 were equally unresponsive as erionite to p21 induction. These results show that the known toxicity of natural fibers such as erionite does not correlate with the *in vitro* expression of genes associated with DNA damage. Research sponsored by NIH Grant ES 07665.

880 CHRONIC INHALATION TOXICITY OF TWO TYPES OF FIBROUS GLASS AND AMOSITE ASBESTOS IN SYRIAN GOLDEN HAMSTERS.

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Male Syrian golden hamsters were exposed *via* nose only inhalation to ~30mg/m^3 (~250 WHO f/cc) to two types of fibrous glass (FG); a typical type of insulation glass (MMVF 10a) and a special application glass (MMVF 33) for 6 hr/da, 5 da/wk for 18 mo and were held unexposed until ~20% survival. Three levels of amosite (AMO) asbestos [0.7 (33 WHO f/cc), 3.5 (158 WHO f/cc) and 7 mg/m^3 (255 WHO f/cc)] were used as a positive control. The lungs were examined for histopathology and fiber lung burden at various times during the studies.

Exposure to MMVF 10a resulted in a mild degree of pulmonary inflammation (macrophage infiltration and microgranulomas). MMVF 33 caused more prominent inflammation including bronchiolization and multinucleated giant cells and interstitial and pleural fibrosis. Severe pulmonary and pleural disease were induced by the mid and high exposure to AMO. While no lung neoplasms were observed with any of the fibers, 1 of 83 (1%) of the hamsters exposed to MMVF 33, 3 of 83 (4%) low dose, 22 of 85 (26%) mid dose and 17 of 87 (20%) high dose AMO exposed hamsters had mesotheliomas. The results of the study suggest that the pathogenic and carcinogenic potential of glass fibers differ significantly from asbestos.

881 PLEURAL MESOTHELIAL CELL PROLIFERATION IN RATS AND HAMSTERS FOLLOWING SUBCHRONIC INHALATION OF FIBERS.

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The Syrian Golden hamster has been shown to develop more severe pleural responses following the inhalation of fibers than does the rat, a more commonly utilized rodent model in safety assessment. The objective of the present studies was to examine and compare the pleural proliferative response in these two species following the subchronic inhalation of known rodent carcinogenic fibers (RCF1, amosite asbestos) and noncarcinogenic fibers (MMVF10a). Animals were exposed to 45 mg/m^3 MMVF10a, RCF1, or 15 mg/m^3 amosite asbestos in nose-only tubes for 4 h/d, 5 d/wk, for 12 wk with recovery groups held for an additional 12 wk period. The labeling index of mesothelial cells was assessed on the surface of lung, costal wall, and diaphragm. Basal levels

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