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March 31, 2008

**Via Federal Express**

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Attention: 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
1201 Constitution Ave., NW  
Washington, DC 20004

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Dear 8(e) Coordinator:

8EHQ-08-17079

Sepiolite – Hydrated Magnesium Silicate CAS # 63800-37-3  
Sepiolite Nanoclay – Organically Modified Hydrated Magnesium Silicate

This letter is a supplement to our letter of February 14, 2008 with additional results (the 3-month post-exposure observation period) of a pulmonary bioassay screening study in rats with the above-identified test substances. Both test substances were supplied to submitter by another company. The study is now complete.

Cell differential analyses of cytocentrifuge preparations from lavaged rats revealed the presence of multinucleated macrophage giant cells recovered from the lungs with both test substances, although the percentages of giant cells were reduced from the 5-week postexposure time period.

Following the bronchoalveolar lavage procedure, the lungs of selected rats were then infused with formaldehyde fixative. Lung tissues from the PBS control (3 rats), the positive control quartz (3 – high dose rats), the negative control ultrafine TiO<sub>2</sub> (3 – high dose rats), and low and high dose (5 rats from each) for each of the two test substances were then processed for lung tissue histopathology analyses. Sagittal sections from the left lobe, right upper lobe, and right lower lobe were prepared for histology. Following tissue processing, the lung sections were evaluated by light microscopy.

The histopathology results indicated that quartz particles produced foamy alveolar macrophage accumulation and patchy evidence of alveolar tissue thickening, indicating incipient phases of lung fibrosis. Exposures to the ultrafine TiO<sub>2</sub> particles resulted in accumulation of phagocytic alveolar macrophages but no tissue thickening. Exposures to the two test substances produced evidence of multinucleated giant cells in airspaces (most of the giant cells had been washed out of the lungs following bronchoalveolar lavage) and patchy evidence of minimal septal tissue thickening, suggesting the development of early phase lung fibrosis. The severity and frequency of tissue thickening with the two test substances appeared to be dose related.

Sincerely,



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