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November 19,2009

Document Control Office (7407)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Attn: TSCA Section 8(e) Coordinator
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20004



Re: TSCA Section 8(e) Notification of Substantial Risk:
Hexamethylcyclotrisiloxane and Hexamethyldisiloxane

Dear TSCA Section 8(e) Coordinator:

In accordance with the provisions of Section 8(e) of the Toxic Substances and Control Act (TSCA), as interpreted in the TSCA Section 8(e) Policy Statement and Guidance, Fed. Reg. 33129 (June 3,2003) and other Agency guidance, Dow Corning is submitting information from a 28-day oral toxicity (gavage) study conducted with **hexamethylcyclotrisiloxane** and hexamethyldisiloxane in Sprague-Dawley Rats that was recently identified during a scientific review of historical studies for which exposure gave rise to pigment accumulation in the liver. Dow Corning has not made a determination at this time that any significant risk of injury to human health or the environment is presented by these findings.

Chemical Substances

541-05-9 **Hexamethylcyclotrisiloxane**
107-46-0 Hexamethyldisiloxane

Study

A 28-Day Subchronic Oral Gavage Feasibility Study of Various Low Molecular Weight Silicone Oligomers in Rats.



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Summary

In recent toxicity studies in rats with several linear and cyclic methylated siloxanes brown pigmented deposits in intrahepatic bile ducts have been observed. The material appears bright red with Maltese cross patterns when viewed under polarized light. The presence of the accumulated pigment (protoporphyrin) elicits bile duct proliferation (hyperplasia) and a chronic inflammatory response. Brown pigmented material was also observed in earlier studies which prompted a review of tissues from those studies as to the nature of the brown pigment. The potential relevance of a cytotoxic mode of action for porphyrinogenic materials in liver carcinogenesis was described in Holsapple *et al.*, *Toxicol Sci* 89(1) 51-56, 2006. One of the studies reviewed was a 28-day subchronic oral gavage feasibility study of various low molecular weight silicone oligomers in rats (1990) where brown pigmented material was observed in the liver. In light of the recent liver protoporphyrinosis observed with several linear and cyclic methylated siloxanes and the published review, the tissues from the 1990 study were re-examined to allow for a more detailed characterization of the accumulated pigment. This study is the subject of this submission.

Details

Study Design

In a 28-day subchronic oral gavage study, male and female Sprague-Dawley rats were administered 1500 mg/kg bw/day of **hexamethylcyclotrisiloxane (D3)** in a sesame oil vehicle or neat hexamethyldisiloxane (HMDS) for 5 days/week.

Results

Based on a recent review of liver histopathology slides from this study, dark brown pigment was observed in bile ducts from about half (4/6, 3/6, respectively) of the male rats in groups II (HMDS) and XI (D3). The pigment under polarized light showed red birefringence and "Maltese cross" patterns and was accompanied by bile duct proliferation and chronic inflammation.

In the reported study (1990) the brown pigmented material had been observed; however, the reported histopathology observations were called bile stasis with an attendant granulomatous cholangitis. The correct diagnosis from the recent histopathology review is liver protoporphyrinosis.

Actions

Dow Corning Corporation will notify EPA of any further relevant information that may be developed concerning these materials. The final report for this study was previously submitted to EPA under the Siloxane Reporting Rule (HSDR-ITC-30) on 4/20/1994. An amended report will be sent to EPA upon completion. If you have any questions concerning this submission, please contact me at (989) 496-8046, kathy.plotzke@dowcorning.com, or at the address provided herein.

Sincerely,



Kathleen P. Plotzke, Ph.D.
Director, Health and Environmental Sciences
(989) 496-8046

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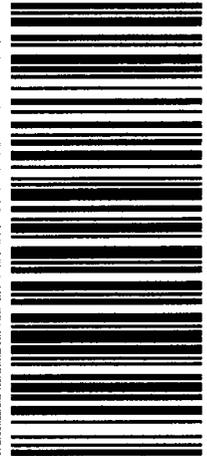
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