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SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL of North America



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TSCA Document Control Center (7407)
Office of Pollution Prevention and Toxics
US 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

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 Statement of Interpretation and Enforcement Policy (40 FR 11110; 16 March 1975) and other Agency guidance, the Silicones Environmental, Health and Safety Council (SEHSC) submits, on behalf of its member companies, information concerning an ongoing study with hexamethylcyclotrisiloxane (CAS No. 541-05-9).

SEHSC is a not-for-profit trade association whose mission is to promote the safe use and stewardship of silicones. The Council is comprised of North American silicone chemical producers and importers. SEHSC's members represent over 95 percent of silicone chemical manufacturing capacity in North America and include: Clariant LSM (Florida), Inc.; Degussa Corporation; Dow Corning Corporation; General Electric Silicones; OSi Specialties, a Crompton business; Rhodia Inc.; Shin-Etsu Silicones of America; and Wacker Silicones, A Division of Wacker Chemical Corporation.

Chemical Substances

541-05-9 Hexamethylcyclotrisiloxane



88020000142

Ongoing Study

Combined Repeated Dose Toxicity Study with Reproductive/Developmental Toxicity Screening Test for Hexamethylcyclotrisiloxane (D₃) in Sprague-Dawley Rats. Dow Corning Study No. 9658.

Summary

Preliminary results from a repeated-dose, subacute toxicity study with reproductive/developmental screening endpoints conducted with hexamethylcyclotrisiloxane (D₃) in Sprague-Dawley rats show test article-related effects that include decreased litter size and implantation sites, and organ weight changes (decreased epididymal, seminal vesicle, and prostate weights at 2500 ppm). Additional

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findings include increased liver weight in male (2500 ppm) and female (500 and 2500 ppm) rats and decreased locomotor activity. Decreased locomotor activity was observed at 2500 ppm for both male and female rats and a slight decrease in reactivity to handling was observed for the females at 2500 ppm. The number of pups per litter and the number of implantation sites per dam were reduced at the 2500 ppm D₃ exposure concentration.

Details

Study Design

In a combined repeated-dose subacute toxicity study with reproductive/developmental screening endpoints conducted with D₃, male and female Sprague-Dawley rats were exposed to vapor concentrations of 0, 100, 500, or 2500 ppm D₃ for 6 hr/day for 28 to 39 consecutive days. The study animals were divided into three groups. Group 1 (male toxicity group) consisted of 10 male rats per exposure concentration. Rats in this group were exposed for 28 consecutive days and then sacrificed for assessment of toxicity. Group 2 (female toxicity group) consisted of 10 female rats per exposure concentration. Rats in this group were exposed for 29 consecutive days and then sacrificed for assessment of toxicity. Group 3 (female reproductive toxicity group) consisted of 10 female rats per exposure concentration. Rats in this group were exposed for 34 – 39 consecutive days. This exposure period included a two-week pre-mating phase, a 1 – 5-day mating phase, and 19 days of gestation. Males from group 1 were paired with females of group 3 from the same exposure concentration beginning on study day 14 after each daily exposure period. Pairing ended when there was positive evidence of copulation. This study design is based on the USEPA OPPTS 870.3650 and OECD 422 test guidelines that includes a neurotoxicity screening assessment. A limited histopathology evaluation will be performed on tissues collected for rats in groups 1 and 2.

Preliminary Results

Male rats (group 1) exposed to 2500 ppm D₃ for 28 days were found to have decreased epididymal (10% and 4%), seminal vesicle (30% and 27%), and prostate (21% and 16%) weights relative to controls (absolute and relative to body weight, respectively). These organ weight changes appear limited to the highest exposure concentration. A histopathology assessment of these organs has not yet been conducted.

Litter size (number of pups born per litter) and the number of implantation sites per dam was decreased for group 3 rats in the 2500 ppm D₃ exposure concentration. Mean litter sizes were 15.3, 15.4, 15.0, and 10.3 pups/litter for exposure concentrations of 0, 100, 500, or 2500 ppm D₃, respectively. Mean implantation sites per dam were 16.5, 15.9, 15.2, and 11.1 for exposure concentrations of 0, 100, 500, or 2500 ppm D₃, respectively.

Additional findings include an increase in mean absolute and/or relative liver weight observed in male rats exposed to 2500 ppm D₃ and in female rats exposed to 500 and 2500 ppm D₃. The absolute and relative liver weight increase in male rats was approximately 22% and 31%, respectively. Absolute and relative liver weight increase in female rats at the 2500 ppm exposure concentration was approximately 32% and 41%, respectively. At the 500 ppm

exposure concentration, the increase in relative liver weight in female rats was 6% with no apparent increase in absolute liver weight.

A statistically significant decrease in locomotor activity was observed for group 1 and group 2 rats at the 2500 ppm exposure concentration during the fourth week of exposure. In group 1, there was a 45% decrease in total counts; in group 2, there was a 30% decrease in total counts.

Reactivity to handling demonstrated a treatment-related response in the functional observational battery (FOB). Specifically, the mean grade for group 2 control rats was 3 (moderate struggling with little or no vocalization); whereas, the group 2 rats in the 2500-ppm exposure concentration had a mean grade of 2 (minimal struggling). This effect was limited to the highest exposure concentration and was not observed for male rats in group 1.

Actions

SEHSC will notify EPA of any further relevant information that may be developed concerning this material. SEHSC also will provide EPA with the final copy of the report for this study when it is available.

If you have any questions concerning these studies, please contact me at (703) 904-4322, rmanning@sehsc.com, or at the address provided herein.

Sincerely,



Reo Menning
Executive Director