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December 12, 2008

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: 1,1,1,3,5,5,5-Heptamethyltrisiloxane

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 two toxicology studies conducted with 1,1,1,3,5,5,5-Heptamethyltrisiloxane (CAS No. 1873-88-7) that were identified during a scientific review for establishing dose levels for a repeated dose study. 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

1873-88-7 1,1,1,3,5,5,5-Heptamethyltrisiloxane

Study 1

Acute Oral Toxicity Study in the Rat (Up and Down Procedure) Conducted at RCC LtD. 16-May-2008

Summary

A limit test with female Wistar rats at a dose of 2000 mg/kg showed possible test article-related neurological signs including ruffled fur, poor coordination, hunched posture, and ventral recumbency.

Details

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Study Design

In a limit test, 5 female Wistar rats were exposed by oral gavage to the limit dose of 2000 mg/kg body weight. The test article was diluted in vehicle (corn oil) at a concentration of 0.2 g/mL and administered at a dosing volume of 10 mL/kg. The animals were examined daily during the acclimization period and mortality, viability and clinical signs were recorded. All animals were

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examined for mortality/viability and clinical signs within the first 30 minutes and approximately 1, 2, 3, and 5 hours after treatment on day 1 and once daily during test days 2-15. Body weights were recorded on the day before test article administration (prior to removal of food), on test days 1 (prior to administration) 8 and 15. All animals were necropsied and examined macroscopically. This study design is based on the USEPA OPPTS 870.1100 and OECD 425 test guidelines.

Results

All animals survived until the end of the study period.

Slight to moderate ruffled fur was noted in all animals from the 1- or 5-hour post-dose up to test day 2 or 3, with it persisting in one animal through test day 7. Slight to marked sedation was recorded in all animals from the 2-, 3-, or 5-hour observation up to 5 hours post-dose or test days 2 or 3. Two animals showed slightly poor coordination on test day 2 only, while two other animals showed slight to marked or slight to moderate poor coordination from 5-hours post-dose until test day 2. Hunched posture was observed in four animals at the 1-hour reading and persisted through the 5-hour evaluation in one animal and through test day 2 in three animals. Ventral recumbency was noted in one animal on test day 2.

Study 2

Dose Range-Finding Study for a Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test in the Han Wistar Rat. Conducted at RCC LtD. 14-October-2008. Please note that the limited nature of this study design - only 3 animals per dose group were used and no organ weights were taken following necropsy.

Summary

Results from a dose range-finding conducted with 1,1,1,3,5,5,5-heptamethyltrisiloxane in Han Wistar rats show test article-related signs in the reproductive data. Findings from this study include reduction in mean number of corpora lutea per dam (not statistically significant); statistically significant increase in pre-implantation loss; statistically significant reduced number of implantation sites; and a reduced number of embryos. These findings were observed in high dose group animals (1000 mg/kg).

Details

Study Design

In a dose range-finding study for a combined repeated dose toxicity study with the the reproductive/developmental toxicity screening test conducted with 1,1,1,3,5,5,5-heptamethyltrisiloxane, male and female Han Wistar rats (3/sex/dose group) were exposed by oral gavage to dose levels of 0, 100, 300, or 1000 mg/kg bw/d. Males were treated over a 14-day pre-pairing period and during the pairing period and up to one day before necropsy (for a total of

at least 28 days of treatment). Females were treated throughout the pre-pairing, pairing, and gestation period up to 13 days post coitum. The purpose of this study was to select suitable dose levels to be used in the subsequent combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in the Han Wistar rat.

Results

Results from a dose range-finding study with reproductive and developmental screening endpoints conducted with 1,1,1,3,5,5,5-heptamethyltrisiloxane show test article-related effects on reproductive parameters. In the high dose group females, the mean number of corpora lutea per dam was reduced without statistical significance (8.7 compared to 15.3 in the control group). Pre-implantation loss was statistically significantly increased (38.5% of the corpora lutea compared to 0 in the control group). This led to a statistically significantly reduced number of implantation sites (61.5% of the corpora lutea compared to 100% in the control group) and a reduced number of embryos (5.3 per dam compared to 14.3 in the control group).

Actions

Testing on this material was conducted by the Silicones Environmental, Health and Safety Council (SEHSC) in support of the International Council of Chemical Associations (ICCA) High Production Volume (HPV) Chemicals Program, sponsored by U.S. EPA. This material is currently undergoing additional testing including a repeated dose toxicity study with reproduction/developmental toxicity screening (OECD 422) in the Han Wistar rat. Dow Corning will submit any additional findings from this repeated dose study, when they are available.

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,

Michael E. Thelen for Kathleen P. Plotzke

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

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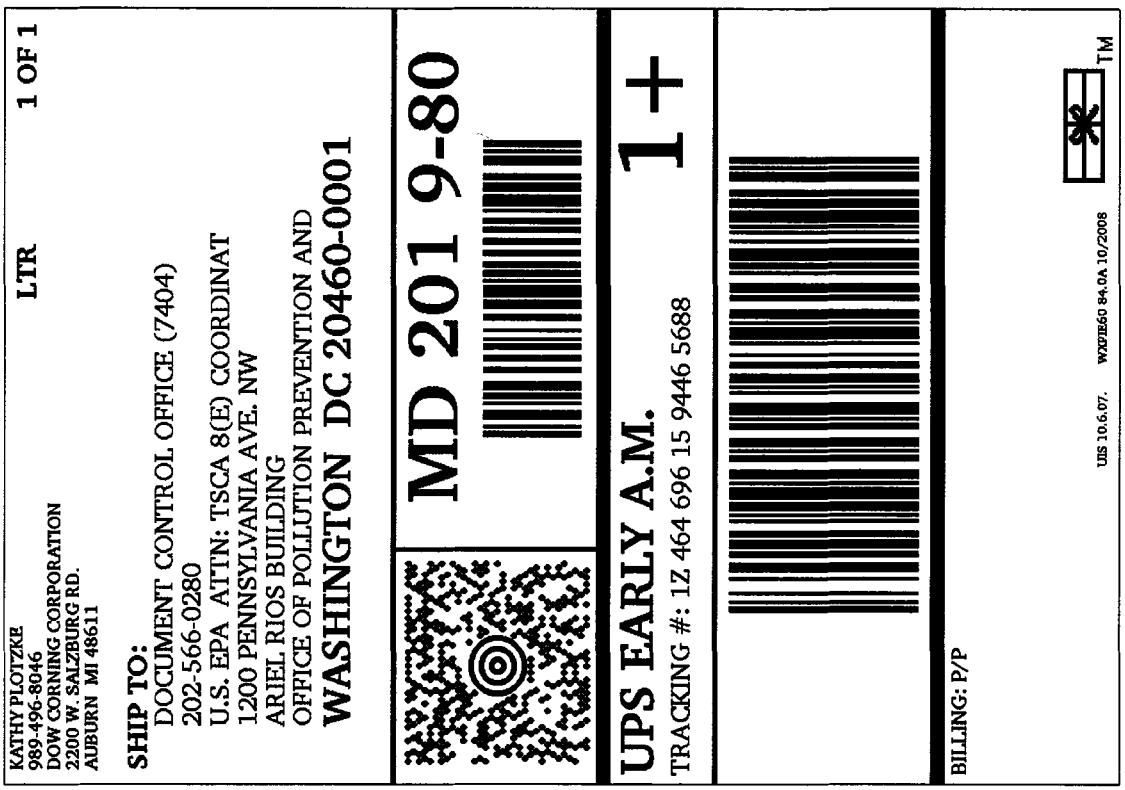
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