

RECEIVED
09 AUG 17 AM 11:07

09 AUG 17 AM 11:07

Phone: 703.788.6570
 Fax: 703.788.6545
 www.sehsc.com
 2325 Dulles Corner Boulevard
 Suite 500
 Herndon, VA 20171

Via Certified Mail

Contains No CBI

August 10, 2009

TSCA Confidential Business Information Center (7407M)
 EPA East – Room 6428
 Attn: Section 8(e)
 U.S. Environmental Protection Agency
 Ariel Rios Building
 1200 Pennsylvania Avenue, NW
 Washington, DC 20460-0001



Re: TSCA Section 8(e) Notification of Substantial Risk: Dodecamethylcyclohexasiloxane

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, the Silicones Environmental, Health and Safety Council (SEHSC)¹ submits, on behalf of its member companies, information concerning a study with dodecamethylcyclohexasiloxane (CAS No. 540-97-6). Neither SEHSC, nor any member company, has made a determination at this time that any significant risk of injury to human health or the environment is presented by these findings.

Recently, the data from this study were re-evaluated and the results of this re-examination are being presented at this time.

Chemical Substances

540-97-6 Dodecamethylcyclohexasiloxane

**Study**

Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in the Sprague-Dawley Rat

¹ SEHSC is a not-for-profit trade association whose mission is to promote the safe use of silicones through product stewardship and environmental, health, and safety research. The Council is comprised of North American silicone chemical producers and importers.

MR 321059

Summary

Results from a repeated-dose toxicity study with reproductive/developmental screening endpoints conducted with dodecamethylcyclohexasiloxane in Sprague-Dawley rats show a dose response for increased liver weight in female rats but no dose response for an increase in incidence and severity of periportal lipidosis in females. Both of these findings were statistically significantly increased over control values. In the original study report, the findings were not considered to be related to the test article due to the inconsistencies in the dose response between liver enlargement and the histopathology finding as well as the occurrence of periportal lipidosis in the controls with only a similar or slightly increased severity in the treatment groups. Upon re-evaluation, since there was a dose response associated with liver weight increase and hepatic histopathological changes in female rats, it could not be ruled out that the findings may be test article related.

Details

Study Design

In an OECD test guideline 422, rats were exposed by oral gavage to dodecamethylcyclohexasiloxane (D6, CAS # 540-97-6). Dodecamethylcyclohexasiloxane was administered in corn oil (vehicle) at dosages of 100, 330, and 1000 mg/kg bw/day, and controls received the vehicle only. Dodecamethylcyclohexasiloxane was administered to Toxicity group female and male rats for 28 and 29 days, respectively. A separate group of females were used to screen for reproductive/developmental toxicity and these animals were administered D6 for 14 days prior to pairing, through the pairing and gestation periods, and until the F1 generation reached day 4 postpartum.

Results

The key findings from the re-evaluation of data from this study were dose responsive liver weight increases and a non-dose responsive increase in the incidence and severity of periportal lipidosis in the female rat liver.

Group mean absolute liver weight for females in the 100, 330, and 1000 mg/kg bw/day dose groups was increased (9, 13, and 23%, respectively), although only the increase in the high dose group achieved statistical significance ($p < 0.01$). Mean liver-to-body weight ratios were increased for the 100, 330, and 1000 mg/kg bw/day dose group females (14, 19, 24%, respectively, $p < 0.01$), with each dose group achieving statistical significance.

Group mean absolute liver weight for males in the 100, 330, and 1000 mg/kg bw/day dose groups was increased ($p < 0.05$) 20, 20, and 18%, respectively. Group mean liver-to-body weight ratios were increased ($p < 0.01$) 15, 22, 17% for males in the 100, 330, and 1000 mg/kg bw/day dose groups.

Periportal lipidosis in the liver was observed in 4/10, 10/10, 10/10, and 9/10 females in the control, 100, 330, and 1000 mg/kg bw/day dose groups, respectively. The increased incidence in females was statistically significant for each dose group ($p < 0.05$). The finding was of minimal severity in controls and minimal to moderate severity in the treated animals.

TSCA Section 8(e) Coordinator
US Environmental Protection Agency
August 10, 2009
Page 3 of 3

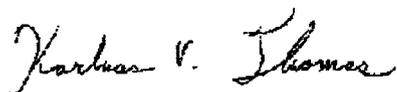
Based upon the re-evaluation, there were no other changes in organ weights or histopathology that appeared to have a dose responsive relationship and were considered related to test article treatment.

Action

SEHSC will provide U.S. EPA with a copy of the amended report.

If you have any questions concerning this submission, please contact me at (703) 788-6570, kthomas@sehsc.com, or at the address provided herein.

Sincerely,

A handwritten signature in cursive script that reads "Karluss Thomas".

Karluss Thomas
Executive Director