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Via Certified Mail
December 19, 2008

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

RECEIVED
EPA/CBI/C
2008 DEC 29 AM 10:28

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

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 an ongoing study with Dimethylsilanediol (CAS Number: 1066-42-8). 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.

Chemical Substance

1066-42-8 Dimethylsilanediol



Ongoing Study

Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test for Dimethylsilanediol in Sprague-Dawley Rats via Inhalation Exposure. Dow Corning Study Number: 10872-102.

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.

CONTAINS NO CBI
Contains No CBI

Summary

Preliminary results from a repeated-dose, subacute toxicity study with reproductive/developmental screening endpoints conducted with dimethylsilanediol in Sprague-Dawley rats show test article-related liver effects that include centrilobular hypertrophy (males and females at 500 mg/kg/day) and hepatic porphyria¹ (males at 500 mg/kg/day, not present in females). To date a histopathological evaluation was only conducted for the control and high dose groups.

Details

Study Design

In a combined repeated-dose toxicity study with reproductive/developmental screening endpoints conducted with dimethylsilanediol, male and female Sprague-Dawley rats were administered the test article in corn oil at 0, 50, 250 or 500 mg/kg/day. The study animals were divided into three groups. Group 1 (male toxicity group) consisted of 10 male rats per dose level. Rats in this group were exposed for 29 consecutive days and then sacrificed for assessment of toxicity. Group 2 (female toxicity group) consisted of 10 female rats per dose level. Rats in this group were exposed for 28 consecutive days and then sacrificed for assessment of toxicity. Group 3 (female reproductive group) consisted of 10 female rats per dose level. Rats in this group were exposed for 15 days prior to the mating period, during the mating period and through post-partum day 3. Males were paired with females from the reproductive group from the same dose level beginning on study day 15. Pairing ended when there was positive evidence of copulation or 14 days had elapsed. This study design is based on the USEPA OPPTS 870.3650 and OECD 422 test guidelines that includes a neurotoxicity screening assessment. A histopathology evaluation was performed on tissues collected from male and female toxicity group rats.

Preliminary Results

Liver weight and liver-to-body weight ratios showed statistically significant increases from control values in male and female rats administered 250 and 500 mg/kg/day. In addition, in male animals, adrenal weights and ratios (500 mg/kg/day), thymus weights and ratios (500 mg/kg/day), and testes weights and ratios (500 mg/kg) showed a statistically significance decrease from control values.

Histopathologically, there were findings observed in the liver and thyroid gland. To date only the control and high dose groups have been evaluated. In the liver, findings included centrilobular hypertrophy, hepatic porphyria and periportal vacuolization. The former finding may be an adaptive change and was observed in males and females at 500 mg/kg/day. The second liver finding, hepatic porphyria, was observed only in males (9/10) at 500 mg/kg/day. It was characterized by accumulations of brown pigment in and around bile ducts. Under polarized light the material is birefringent, with a highly distinctive pathognomonic appearance that identifies it as protoporphyrin: it appears bright red with dark Maltese crosses in each globule. Pigment accumulation was accompanied by bile duct proliferation and chronic inflammation. Periportal vacuolization, consistent with increased hepatocellular lipid was observed in both sexes, but was more frequent and severe in females at 500 mg/kg/day.

¹ Also referred to as *protoporphyrinosis*. *Porphyria (or protoporphyrinosis)* refers to disorders characterized by the buildup of precursors of heme (*i.e.*, porphyrins and protoporphyrins).

There was also minimal thyroid follicular cell hypertrophy in 1/10 control males and minimal to mild hypertrophy in 9/10 males at 500 mg/kg/day. In females only 1/10 high dose group animals was minimally affected.

Developmental endpoints, reproductive parameters, clinical chemistry, hematology and prothrombin times have been submitted for statistical analyses and the results are not available at this time. Statistical analyses of motor activity and functional observational battery indicated only one pair-wise difference between the control and the high dose group regarding an increase in defecation in the treated group.

Action

SEHSC will provide U.S. EPA with a copy of the final report for this study when it is available.

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

Sincerely,

A handwritten signature in black ink, appearing to read 'K. Thomas', with a stylized flourish at the end.

Karluss Thomas
Executive Director