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TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

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COMMENTS:

DOES NOT CONTAIN CBI

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May 14, 2010

8EHQ-0510-17952A

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



DCN: 88100000281

Re: TSCA Section 8(e) Notification: Octamethyltrisiloxane

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 octamethyltrisiloxane (CAS No. 107-51-7). 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

Octamethyltrisiloxane (CAS No.: 107-51-7)

Study Title

28-Day Oral (Gavage) Toxicity Study in the Sprague-Dawley Rat with Octamethyltrisiloxane

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

Summary

This study was conducted in accordance with OECD 407 test guidelines (Repeated Dose 28-Day Oral Toxicity Study in Rodents). Groups were comprised of five Sprague-Dawley rats per sex and were sacrificed after 28 days of repeated dose treatment. Daily doses of octamethyltrisiloxane (L3) were administered via oral gavage at levels of 0, 5, 25, 250, and 1000 mg/kg bw in corn oil vehicle. An additional five animals/sex/group were included in the 0 and 1000 mg/kg bw dose groups as satellite recovery groups. These animals were treated for 28 days and then allowed a 14-day treatment-free recovery period after which they were sacrificed.

Preliminary results from a 28-day repeated-dose toxicity study conducted with L3 in Sprague-Dawley rats show test article-related decreases in body weight gain in males at 1000 mg/kg bw and a dose-response related increase in liver weights in males at 25, 250 and 1000 mg/kg and females at 250 and 1000 mg/kg bw. The test article-related liver effects included hepatocellular hypertrophy and presence of the brownish pigment in intrahepatic bile duct with associated bile duct proliferation and periportal chronic inflammation in males at the top two dose levels and in females at the top dose only. The serum biochemistry was consistent with the liver effects. In addition, hematological parameters for high dose males showed an increased red blood cell (RBC) count with a reduction in the fraction associated with immature RBCs, decrease in mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). After the 14-day recovery period, hepatocellular hypertrophy showed complete regression while brownish pigment accumulation and periportal chronic inflammation was still present in both sexes at 1000 mg/kg bw. Bile duct proliferation persisted only in high dose males. There were additional findings that consisted of increased incidence and severity of hyaline droplets in males at 25, 250, and 1000 mg/kg bw, and incidence of thyroid gland follicular cell hypertrophy (minimal severity) in both sexes at 1000 mg/kg bw. Hyaline deposits of the male kidneys and follicular cell hypertrophy of the thyroid gland showed complete regression after the 14-day recovery period. The study data are currently under review and the study report has not yet been finalized.

Details

Study Design

In this repeated dose toxicity study, octamethyltrisiloxane (L3) was administered daily by oral gavage to Sprague-Dawley rats of both sexes at dose levels of 5, 25, 250 and 1000 mg/kg/day for 28 consecutive days. A control group was treated similarly with the vehicle, dried and deacidified corn oil.

The groups, comprised of five animals per sex, were sacrificed the day after the last dose. An additional five rats/sex /group were dosed at the 0 and 1000 mg/kg dose levels. These animals were treated for 28 days and then allowed a 14-day treatment-free recovery period after which they were sacrificed.

Clinical signs, outside cage observation, food consumption and body weights were recorded periodically during the treatment and recovery periods. Functional observational battery, locomotor activity and grip strength were performed during week 4.

At the end of the dosing and the treatment-free recovery period, blood samples were drawn for hematology and clinical chemistry analysis. Urine samples were collected for urinalyses. All animals were killed, necropsied and examined post-mortem. Histological examinations were performed on

organs and tissues from all control and high dose animals. Liver (both sexes), thyroid gland (both sexes) and kidney (males) were identified as potential target organs and these tissues from the intermediate dose groups were submitted for evaluation.

Preliminary Results

All animals survived until their scheduled necropsy date. There were no test article effects of toxicological relevance on food consumption and clinical observations/functional observational battery, including grip strength.

At the end of the treatment, body weight in high dose males was reduced due to decrease in body weight gain.

Dose response related increases in liver weights were seen in males treated with 25, 250 and 1000 mg/kg bw and in females at 250 and 1000 mg/kg bw. In males, relative liver weight was increased in 25 ($p<0.05$), 250 ($p<0.01$) and 1000 mg/kg bw ($p<0.01$) dose groups, and absolute liver weight was increased ($p<0.01$) at 250 and 1000 mg/kg bw. In females, relative liver weight was increased at 250 ($p<0.05$) and 1000 mg/kg bw ($p<0.01$) and absolute liver weight was increased ($p<0.01$) at the top dose. The increase in absolute liver weights was reversible in both sexes after 14-day recovery period, while the relative liver weights were still increased ($p<0.01$) in males and in females compared to the controls. Increased relative kidney weight in males at 1000 mg/kg bw was reversible after the two-week recovery period.

Macroscopically, dark or black brown discoloration of the liver was noted in all males treated with 250 and 1000 mg/kg bw and in 2 of 5 females treated with 1000 mg/kg bw. The enlargement of the liver was noted in all males treated with 250 mg/kg bw, in 4 of 5 males treated with 1000mg/kg and in 2 of 5 females at the top dose. After the 14-day recovery period, discoloration of the liver was recorded in all males at 1000 mg/kg bw.

Microscopic evaluation of tissues collected from the main study and recovery group animals revealed the following treatment-related pathology findings in the liver, kidney and thyroid gland (presented as incidence, mean severity grade):

Brownish pigment in intrahepatic bile ducts was recorded in males at the 250 (5/5, 2.8) and 1000 mg/kg (5/5, 3.0), bile duct proliferation at 250 (4/5, 1.8) and 1000 mg/kg (5/5, 1.8), chronic inflammation at 250 (5/5, 1.2) and 1000 mg/kg (5/5, 1.0) and hepatocellular hypertrophy at 250 (2/5, 1.0) and 1000 mg/kg (3/5, 1.0). After the 14-day recovery period, brownish pigment (5/5, 3.0), bile duct proliferation (5/5, 2.0) and chronic inflammation (5/5, 1.0) were still present in the high dose males. In females, brownish pigment in intrahepatic bile ducts (2/5, 2.0), bile duct proliferation (1/5, 1.0), chronic inflammation (2/5, 1.0) and hepatocellular hypertrophy (3/5, 1.0) was recorded in the 1000 mg/kg bw dose group. After the 14-day recovery period, brownish pigment (4/5, 1.5) and chronic inflammation (2/5, 1.0) persisted in females at 1000 mg/kg bw.

In the kidney of male rats, hyaline droplet nephropathy that was observed at 25 (2/5, 1.0), 250 (5/5, 1.6) and 1000 mg/kg bw (5/5, 1.8) was reversible after the 14-day recovery period.

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The incidence of thyroid gland follicular hypertrophy (minimal severity 1.0) was present in 2/5 males and 1/5 females at 1000 mg/kg/day at the end of the treatment. The same finding was not seen in the control or recovery males or females.

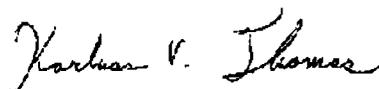
There were additional findings that consisted of increased serum levels of cholesterol (males \geq 250, females at 1000 mg/kg), increase in phospholipids (males \geq 250, females at 1000 mg/kg), increased levels of bilirubin (males \geq 250) and increased triglyceride (females at 1000 mg/kg). Serum biochemistry in males treated with 1000 mg/kg was consistent with liver effects. In males treated with 1000 mg/kg hematological findings consisted of increased red blood cell count with a reduction in the fraction associated with immature RBCs, decrease in MCV and MCH. In the differential white blood cell count, the relative and absolute number of eosinophils was below the control level.

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 this submission, please contact me at (703) 788-6570, kthomas@sehsc.com, or at the address provided herein.

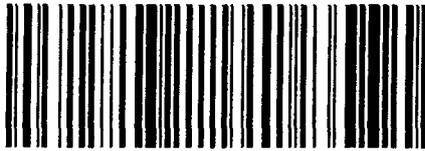
Sincerely,



Karluss Thomas
Executive Director

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CERTIFIED MAIL



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