



August 27, 2009

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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

me#
321294



Re: TSCA Section 8(e) Notification of Substantial Risk
Decamethyltetrasiloxane
CAS No.: 141-62-08

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 preliminary information from an ongoing 28-day oral toxicity (gavage) study conducted with decamethyltetrasiloxane (CAS No. 141-62-08) in Sprague-Dawley Rats. 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 Substance

Decamethyltetrasiloxane
CAS No.: 141-62-08



Study Title

Decamethyltetrasiloxane (L4): 28-Day Oral (Gavage) Toxicity Study in the Sprague-Dawley Rat with Decamethyltetrasiloxane

Summary

This study was conducted in accordance with OECD 407 test guideline. Groups were comprised of five animals per sex and were sacrificed after 28 days of repeated dose treatment. Daily dose levels were 0, 25, 250, and 1000 mg/kg in corn oil vehicle. An additional five animals/sex/group were included in the 0 and 1000 mg/kg dose groups as

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CONTAINS NO CBI

Contains No CBI

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.

The preliminary findings of interest include the presence of brown pigment in intrahepatic bile duct in the 250 and 1000 mg/kg dose group males. Bile duct proliferation and peribiliary chronic inflammation at 1000 mg/kg was associated with the brown pigment deposits. Though these findings persisted in high dose male rats at the end of the 14-day treatment-free recovery period the mean severity grade was decreased. Bile duct pigment accumulation and associated bile duct proliferation/chronic inflammation was not present in treated females at any dose level. Perilobular fatty change was diagnosed in treated and control female dose groups. The incidence and severity was increased in the L4 treatment groups. After the 14-day recovery period, perilobular fatty change was still present but at a reduced severity grade in the 1000 mg/kg dose group.

There was also statistically significant increases in group mean locomotor activity (early intervals and/or total session) at the 1000 mg/kg dose group males and females.

The study data is currently under review and the study report has not yet been finalized.

Details

Study Design

In this subacute toxicity study, decamethyltetrasiloxane was administered daily by oral gavage to Sprague-Dawley rats of both sexes at dose levels of 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 withdrawn 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) and thyroid gland (males) were identified as potential target organs and these tissues from the intermediate dose groups were submitted for evaluation.

Results

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

Group mean absolute and relative liver weights were elevated in males and females treated with 250 and 1000 mg/kg. Absolute liver weight in males was increased 32% ($p < 0.01$) and 23% ($p < 0.05$), and relative liver weight was increased 24% ($p < 0.01$) and 27% ($p < 0.01$) for the 250 and 1000 mg/kg dose groups, respectively. The increase in liver weights was reversible after 14-day recovery period. In females, absolute liver weight was increased 33% ($p < 0.01$) and 61% ($p < 0.01$), and relative liver weight was increased 28% ($p < 0.01$) and 60% ($p < 0.01$) for the 250 and 1000 mg/kg dose groups, respectively. The increase in liver weight was not completely reversible in females after the 14-day recovery period for 1000 mg/kg dose group showing increases in absolute and relative weight of 13% ($p < 0.01$) compared to controls. Macroscopically, accentuated lobular pattern was noted for liver in males and females treated with 250 (4/5 males and 3/5 females) and 1000 mg/kg (2/5 males and 5/5 females) but not in the control group males or females.

Microscopic evaluation of tissues collected from the main study and recovery group animals revealed the following test article related effects (presented as incidence, mean severity grade). In males there was brown pigment in intrahepatic bile ducts in the 250 (1/5, 1.0) and 1000 mg/kg (5/5, 1.8) dose groups, bile duct proliferation at 1000 mg/kg (5/5, 1.4), chronic inflammation at 1000 mg/kg (5/5, 1.4) and hepatocellular hypertrophy at 1000 mg/kg (3/5, 1.0). These microscopic findings were not present in the control group males. After the 14-day treatment-free recovery period brown pigment deposition (5/5, 1.4), bile duct proliferation (2/5, 1.0) and chronic inflammation (5/5, 1.2) were still present in the high dose males. These findings were absent in the control and treated female dose groups.

In treated females perilobular fatty change was seen with increased severity (1.2, 1.8 and 2.8 at 25, 250 and 1000 mg/kg, respectively) compared to the control group (3/5, 1.0). An increased incidence and severity of perilobular fatty change was present after the recovery period for the 1000 mg/kg dose group (4/5, 1.5) as compared to controls (2/5, 1.0).

Locomotor activity was assessed during the fourth week of exposure. Test field activity was monitored for six consecutive 10-minute periods and the data evaluated on the basis of individual periods and total of all periods. For males the activity counts during 10-20 minute period were (mean (SD)) 267(88), 279(31), 297(129), and 413(50) for the 0, 25, 250, 1000 mg/kg dose groups, respectively with the activity count for the high dose group being statistically different from control ($p < 0.01$). For males the activity counts during 20-30 minute period were (mean (SD)) 203(104), 172(85), 243(75), and 298(40) for the 0, 25, 250, 1000 mg/kg dose groups, respectively with the activity count for the high dose group being statistically different from control ($p < 0.05$). The total activity count for all periods for males were (mean (SD)) 1327(326), 1481(372), 1504(437), and 1843(220) for the 0, 25, 250, 1000 mg/kg dose groups, respectively. Total locomotor activity counts for the 60 minute measurement period was statistically significantly elevated for the 1000 mg/kg dose group males ($p < 0.01$).

Locomotor activity data for female test groups for the first 10 minutes were (mean (SD)) 462(92), 473(54), 450(66), and 611(163) for the 0, 25, 250, 1000 mg/kg dose groups, respectively. The activity count for the high dose group was statistically different from control ($p < 0.05$). The total activity count for all periods for females were (mean (SD))

1332(588), 1459(346), 1211(428), and 1345(362) for the 0, 25, 250, 1000 mg/kg dose groups, respectively. Treated groups were not statistically different from control.

Actions

The report for the subject study is not yet final. Dow Corning Corporation will notify EPA of any further relevant information that may be developed upon further review of the study data concerning this material. 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,

Paul A. Jan on behalf of Kathy Plotzke

Kathleen P. Plotzke, Ph.D.

Director, Health and Environmental Sciences

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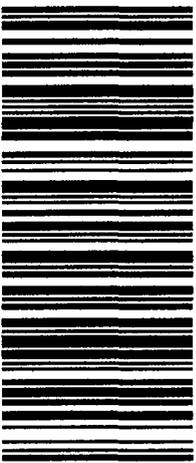
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<p style="text-align: right;">LTR</p> <p style="text-align: right;">1 OF 1</p> <p>SHELLEY WALTA 989-496-4949 DOW CORNING CORPORATION 2200 W. SALZBURG ROAD MIDLAND MI 48686</p> <p>SHIP TO: CBIC - DOCUMENT CONTROL OFFICE (202) 564-8999 EPA - OPPT DOCUMENT CONTROL OFFICER EPA EAST, MAIL: (7407), ROOM: 6248 1201 CONSTITUTION AVENUE, NW WASHINGTON DC 20460-0006</p>	<p style="font-size: 2em;">MD 201 9-80</p> 	<p style="font-size: 3em;">1+</p> <p>UPS EARLY A.M.</p> <p>TRACKING #: 1Z 464 696 15 9265 6092</p> 	<p style="text-align: center;">BILLING: P/P</p> <div style="text-align: center;">  <p style="font-size: 0.8em;">US 11.5.14. WXP260 95.0A 07/2009 TM</p> </div>
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