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8EHQ-0509-17450B

Via Certified Mail

May 7, 2009



DCN:89090000265

NO MAY 14 11:00:23

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: Supplemental TSCA Section 8(e) Notification of Substantial Risk: Dimethoxydimethylsilane
8EHQ-09-17450

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 Dimethoxydimethylsilane (CAS No. 1112-39-6). 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.

Chemical Substance

1112-39-6 Dimethoxydimethylsilane

Ongoing Study

Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test for Dimethoxydimethylsilane in Sprague-Dawley Rats via Oral Gavage.

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

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Summary

Preliminary results from an on-going repeated-dose toxicity study with reproductive/developmental screening endpoints conducted with dimethoxydimethylsilane in Sprague-Dawley rats were reported to EPA by SEHSC on March 16, 2009. As follow up to that submission, we note that the initial histopathological evaluation of the control and high dose (1000 mg/kg/day) groups of this same study was recently completed. This evaluation included the toxicity group males and females. Standard tissues outlined in the protocol were examined for the toxicity group animals. The findings presented are based on data that have been through a quality control review but have not yet been audited, and as such, are subject to change.

In comparing male tissues from controls with tissues from the high dose group of 1000 mg/kg/day, there were significant differences in organ weight and/or organ weight to body weight ratios in addition to histomorphologic findings in the adrenal glands (adrenal cortical atrophy), liver (hepatic porphyria², periportal chronic inflammation, bile duct hyperplasia, panlobular hypertrophy), kidney (minimal and mild nephropathy), epididymides (immature spermatids and mild/moderate hypospermia), testes (moderate/marked seminiferous tubule degeneration), and chronic inflammation of the splenic serosa. In female rats, statistically significant differences in organ weight and organ weight to body weight ratio for the liver were noted with histomorphological findings of periportal hepatocellular vacuolation and panlobular hypertrophy in the high dose animals as compared to controls. An increased incidence of minimal to moderate diffuse hypertrophy in the thyroid gland was observed for both high dose group males and females. Minimal pulmonary histiocytosis was observed in high dose group males and females.

Details

Study Design

In a combined repeated-dose subchronic toxicity study with reproductive/developmental screening endpoints conducted with dimethoxydimethylsilane, male and female Sprague-Dawley rats were exposed by oral gavage to doses of 0, 50, 250 or 1000 mg/kg bw/d for 28 to 42 consecutive days. The study animals were divided into three groups. Group 1 (male toxicity group) consisted of 10 male rats per exposure concentration. Rats in this group were exposed for 29 consecutive days and then euthanized the next day for assessment of toxicity. Group 2 (female toxicity group) consisted of 10 female rats per dose group. Rats in this group were exposed for 28 consecutive days and then euthanized the next day for assessment of toxicity. Group 3 (female reproductive toxicity group) consisted of 10 female rats per dose group. Rats in this group were exposed for a two-week pre-mating phase, a 1 – 14-day mating phase, and through day 3 post-partum. Beginning on study day 14, males from group 1 were paired with females of group 3 from the same dose group after each daily exposure period. Pairing ended when there was positive evidence of copulation. This study design is based on the USEPA OPPTS 870.3650 and OECD 422 test guidelines that include a neurotoxicity screening assessment.

² Also referred to as *protoporphyrinosis*. *Porphyria* (or *protoporphyrinosis*) refers to disorders characterized by the buildup of precursors of heme (*i.e.*, porphyrins and protoporphyrins).

Preliminary Results

A summary of the histopathological findings and any associated organ weight and organ weight to body weight ratios follows.

Liver

In the liver there was mild to moderate panlobular hypertrophy in all high-dose animals of both sexes. This finding was not observed in control rats and is considered an adaptive change.

Additionally, there was minimal to moderate brown pigment accumulation in and around bile ducts, with associated bile duct hyperplasia and chronic inflammation in 5/10 high-dose males. The pigment was birefringent under polarized light, appearing bright red with Maltese cross patterns, characteristic of protoporphyrin. The finding was split into three components and recorded as 1) hepatic porphyria, 2) periportal chronic inflammation, and 3) bile duct hyperplasia associated with hepatic porphyria. These findings were not observed in control or female rats.

Finally, there was minimal to mild periportal vacuolization, consistent with increased hepatocellular lipid. It was observed in all groups of both sexes, but was more frequent and severe in high dose females (8/9).

These histopathological findings were associated with statistically significant increases in liver weights and liver to body weight ratios for both males and females at ≥ 250 mg/kg. In male rats the liver weight was increased 18% at the 250 mg/kg/day dose and 60% at the 1000 mg/kg/day dose. In female rats the liver weight was increased 17% at the 250 mg/kg/day dose and 92% at the 1000 mg/kg/day dose.

Testes

There was moderate to marked seminiferous tubule degeneration observed in all high-dose male rats and in no control animals. The finding was characterized by degeneration of spermatocytes and increased incidence of meiotic spindles.

At the high dose, testes weight (31%) and organ weight to body weight ratio (23%) was statistically decreased as compared to controls.

Epididymides

All high dose male rats exhibited a mild increase in immature spermatids throughout the epididymides, however they were especially common in the head portion. Mild to moderate hypospermia was also observed, but it should be noted that this was largely confined to the head of the epididymides. Sperm numbers appeared to be near normal in the remainder of the epididymides.

Epididymide organ weight at the high dose was statistically decreased compared to controls by 16%. Statistical significance was not observed for the organ to body weight ratio of the high dose group compared to controls.

Kidneys

Minimal to mild nephropathy was observed in all high dose group male rats. Nephropathy was not present in control group males or in female rats of any group.

The kidney weight to body weight ratio was statistically increased (13%) compared to controls at the high dose. Absolute high dose group kidney weight was not statistically different from control group.

Thyroid Gland

There was minimal to moderate follicular cell hypertrophy in all high-dose group rats of both sexes. The finding occurred in 1/10 control males and no control group females.

Lung

There was a marginal increase in minimal pulmonary histiocytosis (aggregates of foamy macrophages) in rats of both sexes. Among males, 4/10 controls and 9/10 high dose animals were affected. Among females, 1/10 controls and 4/10 high dose rats were affected. There was no clear increase in severity associated with dosage.

Adrenal Glands

There was minimal adrenal cortical atrophy in 5/10 high dose male rats. The finding was not observed in control males or any female rats.

The decreases in organ weight (24%) and organ to body weight ratio (15%) were statistically significant.

Spleen

Chronic inflammation of the splenic serosa (outside capsule) was observed to be more prevalent and severe in high dose males (5/10) as compared to control males (1/10). In the more severe degrees (mild to moderate), the finding was characterized by fibrotic plaques with lymphocyte aggregates on the surface of the spleen. Chronic inflammation was not observed in high dose female animals and was observed in 1/10 animals in the control group.

The decreases in organ weight (21%) and organ to body weight ratio (18%) in high dose group females were statistically significant. Statistically significant organ weight changes were not observed in males.

Low-and mid-doses

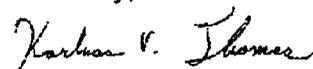
Tissue sectioning and histopathology results for the low and mid dose toxicity female and male groups are not yet available.

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