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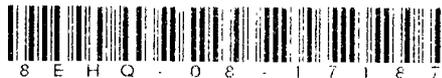
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Via Certified Mail
December 14, 2008



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



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

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 Triethoxyoctylsilane (CAS No. 2943-75-1). 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

2943-75-1 Triethoxyoctylsilane

Ongoing Study

Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test for Triethoxyoctylsilane in Sprague-Dawley Rats via Oral Gavage, HES Study Number: 10709-102.

Summary

Preliminary results from an on-going repeated-dose toxicity study with reproductive/developmental screening endpoints conducted with triethoxyoctylsilane in Sprague-Dawley rats were reported to EPA by SEHSC on June 9, 2008. 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 the triethoxyoctylsilane 422 study (10709-102) was recently completed. This evaluation included the toxicity group males and females

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.

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and the reproductive group females. Standard tissues outlined in the protocol were examined for the toxicity group animals. The same tissues were examined in the reproductive group females, and in addition the hind leg skeletal muscle (adductor and gastrocnemius) and the tibial nerve were also examined. Histopathological findings have identified several target tissues, including the liver, urinary bladder, kidneys, brain, spinal cord, peripheral nerves and skeletal muscle (examined for reproductive females only). Spleen and thymus were also identified as targets in the reproductive group females but not in the toxicity groups. 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.

Details

Study Design

In a combined repeated-dose subchronic toxicity study with reproductive/developmental screening endpoints conducted with triethoxyoctylsilane, male and female Sprague-Dawley rats were exposed by oral gavage to dose levels of 0, 100, 300, 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 dose. 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. 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. Rats in this group were exposed for 34 – 42 consecutive days. This exposure period included a two-week pre-mating phase, a 1 – 14-day mating phase, and 19 days of gestation. Beginning on study day 15, males from group 1 were paired with females of group 3 from the same dose 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. A histopathology evaluation was performed on tissues collected for rats in groups 1 and 2, and, based on clinical findings, selected tissues from the reproductive group females.

Preliminary Results

At this time complete statistical analyses are not available, and this notification is based on a subjective assessment of triethoxyoctylsilane-treated animals as compared to control group animals. A summary of the findings to date follows.

1. Liver

- a. Toxicology groups: The liver exhibited minimal to mild centrilobular hypertrophy in all high dose animals of both sexes. The finding was not observed in controls. Mean absolute and relative (liver weight/body weight ratio) liver weights were also statistically increased in the 300 and 1000 mg/kg dose group males (approximately 13% and 16%, respectively) and in the 1000 mg/kg dose group (toxicity) females (14% absolute, 28% relative).
- b. Reproductive group: Minimal to mild centrilobular hypertrophy was observed in 10/10 high dose reproductive group females. The finding was not observed in controls. Liver weight was not determined in reproductive group females.

2. Urinary Tract

- a. Toxicology groups: In the urinary bladder there was minimal to mild diffuse epithelial hyperplasia in 7/10 high dose males but not in the control males. In toxicology group females the effect was more subtle; the finding was graded as minimal in 6/10 high dose animals and 3/10 control animals. There were potentially related findings in the kidneys of 2/10 high dose males with minimal or moderate bilateral epithelial hyperplasia in the renal pelvis. The kidney finding was

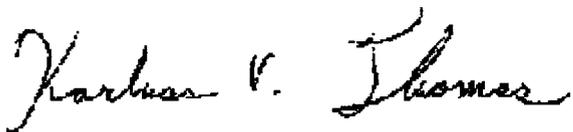
not observed in male controls or in any females. The kidney hyperplasia was not associated with any statistical increases in mean absolute or relative kidney weights.

- b. Reproductive group: The urinary bladder lesion was observed in 7/10 high dose female animals and not in controls.
3. Lymphoreticular system
- a. Reproductive group: Mild to moderate atrophy of the spleen and thymus was identified in 5/10 high dose female animals only. Spleen and thymus weights were not collected.
4. Neurologic tissues
- a. Toxicity group: In toxicology group females there was minimal white matter vacuolation in the brain, notably in the cerebellum and medulla, in 4/10 high dose animals and 1/10 controls. In the spinal cord of females there was degeneration (vacuolation) in 6/10 high dose and no control animals. The brain and spinal cord findings were not seen in males. In females, there was minimal to mild sciatic nerve degeneration in 3/10 high dose animals and no controls. Minimal sciatic nerve degeneration was also observed in 2/10 high dose males and 1/10 controls.
 - b. Reproductive group: Following the previously reported clinical findings of hindquarter weakness or paralysis in the dams, there were gross findings of muscle atrophy in many of these rats at necropsy. In the brain of reproductive group females there was minimal to marked demyelination in 8/10 high dose rats and no controls. In the spinal cord there was minimal to marked demyelination in 9/10 high dose animals and no controls. In the sciatic and tibial nerves minimal to severe demyelination or degeneration was observed in 8/10 or 9/9 high dose animals and no controls.
5. Reproductive/Developmental Toxicity
- a. Though total litter size was not different from control at the high dose level, there was a statistically significant decrease in pup viability (45% decrease) due to an increase in number of pup deaths on postnatal day 0 compared to controls.
 - b. On postnatal day 4 there remained a statistically significant reduction in pup viability. In addition, average pup and litter weights were decreased and gestation length was increased at the high dose level compared to controls by postnatal day 4.

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