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April 14, 2006

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

Re: TSCA Section 8(e) Notification of Substantial Risk: A Fourteen-Day Whole-Body Inhalation Toxicity Range-Finder Study with Methyltrimethoxysilane in Sprague-Dawley Rats

Dear TSCA Section 8(e) Coordinator:

In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (68 Federal Register 33129; June 3, 2003) and other Agency guidance, the Silicones Environmental, Health and Safety Council of North America (SEHSC)¹, on behalf of its member companies, submits the following information. 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

1185-55-3 Methyltrimethoxysilane



Ongoing Study

A Fourteen-Day Whole-Body Inhalation Toxicity Range-Finder Study with Methyltrimethoxysilane in Sprague-Dawley Rats – Dow Corning Corporation Study Number: 10079-102.



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.

Summary

Preliminary results from an ongoing study with Methyltrimethoxysilane show indications of treatment-related effects. Signs of excessive urine staining and bloody urine were present following the first or second day of exposure in animals from both the 8000-ppm and 4000-ppm exposure groups. All animals from the 8000-ppm exposure group and three animals from the 4000-ppm group were euthanized prior to scheduled terminal sacrifice. Gross pathology of these animals primarily revealed urinary bladder and kidney findings. Urinary bladder findings included dilation, calculi, as well as abnormal contents and color. Kidney findings included dilation ranging from mild to moderate in both males and females. In addition, females from the 4000-ppm exposure group also included findings of enlarged adrenal glands, small thymus, and a mild gaseous intestinal tract.

Details

Study Design

The objective of this study was to evaluate the potential toxic effects of methyltrimethoxysilane in Sprague-Dawley rats following whole-body inhalation exposure in preparation of dose level selection for a 90-day repeated dose toxicity study. This range-finding study was conducted in accordance with the Organisation for Economic Co-Operation and Development (OECD) 412 guideline for testing of chemicals and included exposures levels of 0 (control), 400, 800, 4000, and 8000 ppm methyltrimethoxysilane. Each group consisted of five male and five female Sprague-Dawley rats with exposures conducted 6 hours per day plus one 20-minute equilibration time (T_{99}), for 14 consecutive days.

Preliminary Results

Urinary Bladder Calculi

Multiple calculus, ranging from mild to moderate in size, were observed in the urinary bladders of 4/5 males and 5/5 females in the 4000-ppm exposure group as well as 2/5 males and 5/5 females in the 8000-ppm exposure group.

Liver Weight Increase

Liver weight was increased 14% ($n = 5$) and 35% ($n = 2$) in the 4000-ppm exposure group males and females respectively. These increases were not statistically significant.

Kidney Weight Increase

Kidney weight was increased 15% ($n = 5$) and 58% ($n = 2$) in the 4000-ppm exposure group males and females respectively. The increase in males was statistically significant ($p < 0.01$), however, with the small sample size and large percent standard deviation (55%), statistical significance could not be confirmed for females.

Thymus Weight Decrease

Thymus weight was decreased in a dose-related manner for males. The decreases were 3%, 13%, and 26% for 400, 800, and 4000-ppm exposure group males, respectively. These decreases were not statistically significant.

Thymus weight was decreased in a dose-related manner for females. The decreases were 4%, 17%, and 57% for the 400, 800, and 4000-ppm exposure group females, respectively. The decrease at 4000 ppm was statistically significant ($p < 0.01$).

Adrenal Gland Weight Increase

Adrenal gland weight was increased 28% ($n = 5$) and 54% ($n = 2$) in the 4000-ppm exposure group males and females respectively. The increase in females was statistically significant ($p < 0.01$).

Actions

SEHSC will notify U.S. EPA of any further relevant information that might be developed concerning this material. SEHSC also will provide U.S. EPA with the copy of the final report containing these study results when it is available. If you have any questions concerning this study, please contact me at (703) 788-6570, rmanning@sehsc.com, or at the address provided herein.

Sincerely,



Reo Menning
Executive Director