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8EHQ - 0298 - 14130

DuPont Haskell Laboratory

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February 11, 1998

Via Federal Express

Document Processing Center (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street SW
Washington, D.C. 20460-0001

8EHQ-98-14130

Contains No CBI

Dear 8(e) Coordinator:

1,1,3,3-Tetramethylurea
CAS # 632-22-4

88980000059

This letter is to inform you of the preliminary results of recently conducted inhalation toxicity studies with the above referenced test material.

Acute Inhalation Range Finding Study: In preparation for a two-week inhalation study, four groups of three to six rats each were exposed (whole-body) by inhalation to vapor atmospheres of the test substance. Exposure duration ranged from a single, four-hour exposure period to a series (two to three consecutive days) of four- to six-hour exposure periods. The estimated mean atmospheric concentration of the test substance for the four exposures were 110 ppm (two, four- to six-hour exposures), 170 ppm (three five- to six-hour exposures), 260 ppm (two, six-hour exposures), and 360 ppm (one, four-hour exposure). Rats had slight to moderate body weight losses following exposures but no deaths occurred at any of the concentration levels. No clinical signs of toxicity were observed.

Subchronic Inhalation: For the two-week inhalation study, three groups of ten male rats each were exposed (whole-body) by inhalation for six hours/day for a total of nine exposures to vapor atmospheres of the substance at concentrations of approximately 2, 20, or 100 ppm. A procedural control group of ten male rats was exposed simultaneously to air only. Rats were weighed and observed daily for clinical signs of toxicity during the exposure period. At the end of the exposure period, five rats/group had blood and urine samples collected for clinical pathology evaluation and were then sacrificed for pathology examination. Following a 18-day recovery period, all surviving rats were given the same clinical pathology and pathology examinations.

Rats exposed to 100 ppm had statistically significant decreased mean body weights throughout the exposure period. No clinical signs of toxicity were observed. Preliminary results for microscopic evaluation of the tissues showed that all rats exposed to 100 ppm had degeneration/necrosis of the olfactory epithelium immediately following the exposure period. Although this effect was still observed in rats at this concentration following the recovery period, repair (metaplasia) was also evident and with sufficient recovery time it is reasonable to expect complete repair of the lesion. No other compound related microscopic findings were noted.

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Pilot Developmental Study (rat): Groups of 8, assumed pregnant, rats were exposed by inhalation to daily atmospheric concentrations of 0, 2, 20, or 100 ppm of the test substance over days 7-21 of gestation (days 7-21G). On day 22G, all dams were sacrificed and were examined grossly. The uterine contents were examined and the fetuses were weighed, sexed, and examined externally.

No clinical signs of toxicity were observed. Maternal toxicity was seen at 100 ppm. There were significant reductions in mean maternal body weight, weight change, and food consumption. Mean maternal weight change was significantly reduced over days 7-9G and was reduced (not statistically significant) when averaged over the entire dosing period, days 7-22G (using either absolute or adjusted final body weight). Developmental toxicity was evident at 100 ppm as a significant reduction in mean fetal weight. There was no evidence of either maternal or developmental toxicity at 20 or 2 ppm.

Concurrent with these studies, we reviewed our files and became aware of several pre-1977 studies with this material (1966; 1970). In all cases, the purity of the sample tested was unspecified. The findings are as follows:

Acute Oral Toxicity: LD50 794 mg/kg; clinical signs included depression, mild tremors, loss of righting reflex, ataxia, and salivation (1966).

Acute Dermal Toxicity: LD50 Rabbits 3,160 mg/kg; clinical signs included tremors prior to death (1966). Approximate Lethal Dose in rabbits was 5,000 mg/kg; clinical signs included fasciculations, incoordination, salivation, and weakness (1970).

Acute Inhalation Toxicity: Approximate Lethal Concentration (rats; 1-hour) 19,202 ppm; clinical signs included depression (1966). Approximate Lethal Concentration (rats; 4-hours) 312 ppm; clinical signs included unresponsive to sound and incoordination (1970).

The findings described above appear to be reportable, based upon EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,

A. Michael Kaplan

A. Michael Kaplan, Ph.D.
Manager-Regulatory Affairs

AMK/SMM:jat
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