

8EHQ-0803-15405



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August 13, 2003

Via Federal Express

Document Processing Center (Mail Code 7407M)  
Room 6428  
Attention: 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
1201 Constitution Ave., NW  
Washington, DC 20460



Contain NO CBI

Dear 8(e) Coordinator:

2,3-Dichloro-1,3-butadiene  
CAS # 1653-19-6

This letter is to inform you of the results of a pilot developmental toxicity study and a range-finding study in male rats that were recently conducted with the above referenced test substance.

In the pilot developmental toxicity study the test substance was administered by inhalation to groups of time-pregnant female CrI:CD<sup>®</sup>(SD)IGS BR rats (8 per group) on days 6-20 of gestation (G). Initial exposure levels on day 6G were 0, 50, 100, or 150 ppm. However, due to clinical signs of toxicity and weight loss on day 6G at all concentrations, the exposure concentrations for the 100 and 150 ppm groups were reduced to 10 and 25 ppm, respectively, beginning on day 7G and for the remainder of the exposure period. Clinical signs and body weights were recorded daily and food consumption was recorded on days 4, 6, 8, 10, 12, 14, 16, 18, 20, and 21G. Maternal necropsy was conducted on day 21G and the following parameters evaluated: gross pathological examination, number and status of implantation sites, and fetal assessments (viability, location, sex, fetal weight, external alterations).

Clinical signs of toxicity (lethargy, closed eyes, and salivation) were observed on the first day of exposure (day 6G) at 50, 100, and 150 ppm; reduced food consumption and body weight losses were detected in all exposed groups on day 7G. No test substance-related clinical signs of toxicity were observed in any group during the remainder of the study. Dose-related partial recovery of maternal weight gain and food consumption occurred in all groups after day 7G. There was no test substance-related maternal mortality nor were there any gross postmortem findings observed during necropsy at study termination (21G). Mean fetal body weights were significantly reduced for all exposure groups (13, 7, and 7% lower than control mean at 10, 25, and 50 ppm, respectively). With respect to controls, the mean numbers of implantation sites, resorptions, and live fetuses were not statistically significantly different across exposed groups. No test substance-related external alterations were observed at any exposure concentration.

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The maternal and developmental toxicity observed at 10 and 25 ppm may have been confounded by the initial exposures to 100 and 150 ppm, respectively, on day 6G. Thus, clear evidence of maternal and developmental toxicity could not be determined for the subsequent exposures to 10 and 25 ppm based on the results of this pilot study. However, clear evidence of maternal and developmental toxicity was observed at 50 ppm since the exposure concentration was constant throughout the exposure period.

In a concurrent range-finding study, the test substance was administered by inhalation to groups of adult Crl:CD<sup>®</sup>(SD)IGS BR male rats (6 per group) at exposure concentrations of 0, 50, 100, or 150ppm for 15 days. However, due to clinical signs of toxicity on the first day of exposure and weight loss on day 2 at all concentrations, exposure concentrations for the 100 and 150 ppm groups were reduced to 10 and 25 ppm, respectively, beginning on day 2 of exposure. Clinical signs and body weights were recorded daily and food consumption was recorded every other day. Gross necropsy was conducted on the day of sacrifice.

Clinical signs of toxicity (lethargy, partially closed eyes, and salivation) were observed on the first day of exposure at 50, 100, and 150 ppm; reduced food consumption and body weight loss were detected in all exposed groups on day 2. No test substance-related clinical signs of toxicity were observed in any group during the remainder of the study. Dose-related partial recovery of weight gain and food consumption occurred in all groups after the second day of exposure. There was no test substance-related mortality nor were there any gross postmortem findings observed at necropsy.

Under these experimental conditions, the findings described above appear to be reportable, based upon guidance given in the EPA TSCA Section 8(e) Reporting Guide (June 1991). The clinical signs observed in both studies are considered transient, as they were only observed on the first day of exposure, and were not observed throughout the remainder of the study including the 50 ppm groups, which were constant throughout both studies.

Sincerely,



A. Michael Kaplan, Ph.D.  
Director – Regulatory Affairs and Occupational Health

AMK/JML:clp  
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