



DuPont Central Research
and Development

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July 26, 1996

EXPRESS MAIL-RETURN RECEIPT REQUESTED



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Document Processing Center (TS-790)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

Contains No CBI

Dear 8(e) Coordinator:

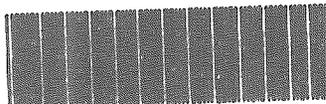
ORIGINAL

1,5,9-Cyclododecatriene
CAS Number 4904-61-4

In our April 2, 1996 letter we informed the Agency of the results of an acute inhalation toxicity study with the above referenced test substance. This letter is to inform you of the results of a two-week/neurotoxicity inhalation study and a two-day micronucleus inhalation study recently conducted in rats with this test substance.

During a generation trial conducted prior to the micronucleus study, one group of six male CrI:CD⁰BR rats was exposed nose-only to atmospheres of the test substance for six hours. The exposure was conducted at a combined aerosol/vapor concentration of 3.4 mg/L. All rats displayed no response to an alerting stimulus during exposure. Three of six rats exhibited tremors after the exposure. No clinical signs of toxicity were evident the day after exposure.

During the micronucleus study, one group of five male (control) and one group of 10 male CrI:CD⁰BR rats were exposed nose-only to the test substance at concentrations of 0 or 3.3 mg/L (aerosol/vapor) for six hours/day for two consecutive days. Rats exposed to 3.3 mg/L displayed no response to an alerting stimulus during exposure. Clinical signs of toxicity after exposure included lethargy and irregular respiration. No clinical signs of toxicity were evident prior to the next exposure or the day after the last exposure.



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During generation trials conducted prior to the two-week/neurotoxicity study, one group of six male Crl:CD[®]BR rats was exposed whole-body to atmospheres of the test substance at a combined aerosol/vapor concentration of 1.7 mg/L. Exposures were 4.5 hours/day for one day and six hours/day for two days over three consecutive days. During the exposures the rats exhibited no response to an alerting stimulus. Clinical signs of toxicity observed in all rats included periodic head bobbing during exposure and tremors and diminished alerting response following exposure. No clinical signs of toxicity were evident prior to each exposure or the day after the last exposure.

During the two-week/neurotoxicity study, four groups of 20 male Crl:CD[®]BR rats each were exposed nose-only to the test substance at concentrations of 0, 0.033 (vapor), 0.34 (vapor), or 1.6 mg/L (aerosol/vapor) six hours/day, four to five days a week for a total of nine exposures. The exposure period was followed by a 14-day recovery period. Neurobehavioral evaluations, including functional observational battery (FOB) and motor activity assessments, were performed following the fourth and ninth exposures. Rats in the 1.6 mg/L group exhibited no response to an alerting stimulus during exposure. A normal response to an alerting stimulus was observed in rats exposed at 0.34 or 0.033 mg/L. Clinical signs of toxicity following exposure included lethargy and irregular respiration in rats in the 1.6 mg/L group. No clinical signs of toxicity were evident in rats in the 0.34 or 0.033 mg/L groups. No clinical signs of toxicity were evident prior to each exposure or during the 14-day recovery period. Neurobehavioral evaluations indicated foot splay was decreased by approximately 30% in rats in the 1.6 mg/L group, compared to controls, following the fourth and ninth exposure. The significance of this effect is unknown since there was no converging evidence of neurotoxicity on the FOB, grip strength, or motor activity tests. No findings in the FOB or motor activity were evident in the 0.34 or 0.033 mg/L groups. At present, neuropathology data are being evaluated.

Under these experimental conditions, the clinical signs described above appear to be reportable, based upon EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,



Charles F. Reinhardt, M.D.
Director

CFR/JRB:dj
(302)366-5285

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