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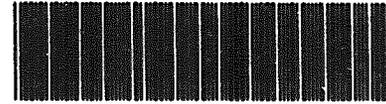
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July 26, 1996

EXPRESS MAIL-RETURN RECEIPT REQUESTED

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



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Dear 8(e) Coordinator:

1,5-Cyclooctadiene  
CAS Number 111-78-4

In February 26, 1996 DuPont informed the Agency of the results of acute inhalation toxicity studies with the above referenced test substance. This letter is to inform you of preliminary results of a two-day inhalation micronucleus study and two-week inhalation/neurotoxicity studies in rats with this test substance.

In the micronucleus study, one group of five male (control) and one group of 10 male (test) rats were exposed whole-body to 1,5-cyclooctadiene (COD) vapor for six hours/day for two days at 1500 ppm or 0 ppm. During exposures, rats in the 1500 ppm group exhibited depression or absence of an alerting response mainly during the latter half of the daily exposures, and incoordination was evident in three of 10 rats during the first exposure. Immediately after exposures, all rats in the 1500 ppm group exhibited lethargy. All test rats displayed incoordination after the first exposure, and two of 10 rats exhibited abnormal gait after the second exposure. No clinical signs of toxicity were evident the day after each exposure.

During a generation trial conducted prior to the micronucleus study, one group of six male rats was exposed whole-body to atmospheres of COD for six hours/day for two consecutive days. The concentrations for the exposures were 1000 ppm (day 1) or 1000 ppm (day 2). During exposures, rats displayed no response to an alerting stimulus and



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two of six animals exhibited incoordination. Immediately after exposures, all rats appeared lethargic. In addition, all rats exhibited incoordination after the exposure to 1300 ppm. The aforementioned clinical signs of toxicity were no longer evident 30 minutes after exposure.

In the two-week/neurotoxicity study, four groups of 20 male rats each were exposed for six hours/day for a total of nine exposures to COD at concentrations of approximately 500, 150, 50, or 0 ppm. 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 500 ppm group exhibited diminished or no response to an alerting stimulus during the latter half of the daily exposures. No clinical signs of toxicity were observed after exposures or during the recovery period. No clinical signs of toxicity were observed in rats in the 150 or 50 ppm groups.

Neurobehavioral evaluations conducted after the ninth exposure indicated rats in the 500 ppm group showed a statistically significant increase in the incidence of curled-up posture and sleeping behavior in the home cage. Rats from the 150 ppm group also showed similar incidences in these two parameters but the findings were not statistically increased over the control values. The 500 ppm rats also had an increase in the incidence of low arousal in the open field arena as compared to the controls; however, this finding was not statistically significant. No findings on the FOB or motor activity were observed after the fourth exposure.

Neuropathologic exam revealed one rat in the 500 ppm group that had a mild lesion in one dorsal root fiber. This lesion was not observed in any other rats in the two-week study. Since this lesion is known to occur spontaneously in rats\*, it is not known whether it is related to the test substance.

Under these experimental conditions, the observed findings would appear to be reportable, based upon EPA guidelines regarding the reportability of such data under EPA TSCA Section 8(e) criteria.

Sincerely,

*Charles F. Reinhardt*

Charles F. Reinhardt, M.D.  
Director

CFR/DPK:dj  
(302)366-5285

**Best Available Copy**

\* Eisenbrandt, D.L. et al. "Spontaneous Lesions in Subchronic Neurotoxicity Testing of Rats", *Toxicologic Pathology*, 18, No. 1, pp 154-164.