



8EHQ-0102-1347

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**DuPont Chemical Solutions Enterprise**

January 23, 2002

**By United Parcel Service**

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Attention: TSCA Section 8(e)  
U.S. Environmental Protection Agency  
ICC Building  
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Washington, DC 20460

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Dear 8(e) Coordinator:

8EHQ-0991-1347

Referencing earlier communications on the subject topic dated (variously) September 6, 2001, November 7, 2001 and November 27, 2001, following are findings believed to be TSCA §8(e) reportable that are described in the preliminary pathology report just issued by the testing laboratory.

Groups of 10 male and 10 female Crl:CD(SD) IGS BR rats per dose group were administered the test compound through the diet. Test concentrations were 0, 10, 50 and 150 mg/kg body weight/day. The test was conducted in accordance with OECD Protocol 408. In-life phase evaluations included clinical observations, detailed physical examinations, sensory reactivity and grip strength, motor activity, body weight changes, food and water consumption and ophthalmic, hematologic and biochemical examinations. Macroscopic pathology was conducted on a variety of organ tissues from all the test animals. Histology was performed on all the animals that died or were killed prematurely, on all terminal animals in the control and high dose groups and on abnormal tissues from animals in the low and intermediate dose groups.

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Microscopic pathology of terminal and decedent animals revealed the following treatment-related effects:

- ◆ In the stomach, statistically significant increased incidence and severity of epithelial hyperplasia in the limiting ridge was noted in male and female rats receiving 50 or 150 mg/kg/day.
- ◆ In the ileum, statistically significant minimal to moderate mucosal hyperplasia was observed in rats dosed at 150 mg/kg/day.



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- ◆ Increased incidence of pigmented macrophages was noted in the mesenteric lymph node of female rats receiving 150 mg/kg/day. Minimal mastocytosis was observed in male (and to a lesser extent in female) rats in this dose group.
- ◆ Tubular pigment was noted in the kidneys of males (and to a lesser extent in females) receiving 150 mg/kg/day. Special staining, however, did not yield positive results. An increased incidence and severity of cortical tubular basophilia was observed in female (and to a lesser extent in male) rats in this dose group.
- ◆ Minimal pigmented Kupffer cells were noted in the liver of male rats receiving 150 mg/kg/day when compared with controls. Perls' staining on representative tissues was positive, indicating haemosiderin.

As reported earlier, four females from the high dose group were killed on Day 7 of the study and a male in the same group was sacrificed during Week 13 for humane reasons. The animals which died during the study exhibited mucosal hyperplasia in the gut as well as in the ileum, whereas in the terminal animals mucosal hyperplasia was confined to the ileum. Gastric changes were noted in both terminal and decedent animals. However, only a few decedents showed changes in the mesenteric lymph node and the tubular pigment in the kidney. Basophilic tubules in the kidney were identified in some decedent and some terminal animals.

Decedent animals also exhibited decreased cellularity in various lymphoid tissues including the spleen, mesenteric lymph node and mandibular lymph node. Acinar cell atrophy, degranulation in the salivary gland, and involution/atrophy in the thymus were also noted. However, the histological findings observed in the decedents were not considered to be of sufficient severity to qualify as factors contributing to death.

No histological findings were observed in the testis or adrenals to explain the increased organ weights reported earlier.

In order to complete the investigation and establish relevant No Observed Adverse Effect Levels (NOAELS) track-down histopathology is underway on the stomach, ileum, mesenteric lymph node, liver and kidney of the terminal animals in the low and intermediate dose groups.

EPA is being notified of these findings under TSCA §8(e) because they are believed to be reportable based on guidance provided in the Agency's June 1991 TSCA Section 8(e) Reporting Guide.

You may contact me on 856/540-4576 if there are any questions.

Yours truly,

  
Kavsy D. Dastur

/mn  
By United Parcel Service