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E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 245-71 [redacted]

Material Tested: [redacted] Haskell No.: 6918

Material Submitted by: [redacted] Organic Chemicals Department, Jackson Laboratory Other Codes: [redacted]

## ACUTE ORAL TEST

Procedure: The test material, as an aqueous suspension, was administered by intragastric intubation to young adult ChR-CD male rats in single doses. Survivors were sacrificed 14 days later; the livers were removed for gravimetric analysis.

Results:

| Suspension (%) | Dose (mg/kg) | Mortality* | Weight When Killed (g) Body | Liver | L.W./B.W. X 100 | Clinical Signs | ALD |
|---|---|---|---|---|---|---|---|
| 25 | 11,000† | S - 14 d. | 325 | 16.20 | 5.0 | None | > 11,000 mg/kg |
| 25 | 7,500† | S - 14 d. | 330 | 16.38 | 5.0 | | |
| 25 | 5,000 | S - 14 d. | 334 | 15.27 | 4.6 | | |
| 25 | 3,400 | S - 14 d. | 343 | 16.18 | 4.7 | | |
| 15 | 2,250 | S - 14 d. | 345 | 14.62 | 4.2 | | |
| 25 | 1,500 | S - 14 d. | 318 | 13.22 | 4.2 | | |
| 25 | 1,000 | S - 14 d. | 331 | 13.65 | 4.1 | | |
| 15 | 670 | S - 14 d. | 364 | 16.00 | 4.4 | | |

* S - ( ) d. = Sacrificed ( ) days after dosing

† Administered in divided doses

## TEN-DOSE ORAL SUBACUTE TEST

Procedure: The test material was administered by intragastric intubation, as a 15% aqueous suspension, to six young adult ChR-CD male rats, five times a week for two weeks; another group of six rats served as controls and was intubated with water. Three test and three control rats from each group were sacrificed approximately four hours and 14 days after the last dose.

Results:

| Dose (mg/kg/day) | Mortality | Weight of Liver (g) Animals Killed: After 10th Dose | Weight of Liver (g) Animals Killed: 14 Days After 10th Dose | L.W./B.W. X 100 Animals Killed: After 10th Dose | L.W./B.W. X 100 Animals Killed: 14 Days After 10th Dose | Gross Pathology‡ on Liver Animals Killed: After 10th Dose | Gross Pathology‡ on Liver Animals Killed: 14 Days After 10th Dose | Histopathology‡ on Liver Animals Killed: After 10th Dose | Histopathology‡ on Liver Animals Killed: 14 Days After 10th Dose |
|---|---|---|---|---|---|---|---|---|---|
| 2200 | 0/6 | 18.2 | 14.3 | 5.9 | 3.6 | 1 | - | B | B |
| | | 19.7 | 17.6 | 6.0 | 4.8 | 1 | - | B | B |
| | | 21.2 | 18.2 | 7.2 | 5.4 | 1 | 2 | B | B |
| 0 (Control) | 0/6 | 13.0 | 17.1 | 4.2 | 4.3 | - | - | - | B |
| | | 13.9 | 13.3 | 4.2 | 4.0 | - | - | - | - |
| | | 8.4 | 18.1 | 3.6 | 4.1 | - | - | B,E | - |

In addition, the following organs were examined histologically: brain, eyes, stomach, duodenum, thymus, spleen, bone marrow, pancreas, adrenal, kidney, testis, epididymis, lung, and trachea; no compound-related histologic changes were observed in any of these organs.

‡ Gross and histopathologic code

- \- = No abnormality detected
- 1 = Large and heavy
- 2 = Slightly large and heavy
- B = Reduction of number of centrilobular cytoplasmic vesicles
- E = Focal RE cell hyperplasia

Summary: [redacted] has low toxicity when administered orally to young adult ChR-CD male rats; its Approximate Lethal Dose (ALD) is greater than 11,000 mg/kg of body weight. There was neither gross nor gravimetric evidence of liver enlargement 14 days after dosing.

Repeated administration of the test compound to rats at a rate of 2200 mg/kg/day for ten doses produced large and heavy livers at the end of the test phase, but these livers were within the normal range at the end of the 14-day recovery phase. Histologically, the compound caused a reduction of the number of centrilobular cytoplasmic vesicles after the tenth dose and after the 14-day recovery period. This type of liver change is considered reversible; this reversibility probably would have been manifest with a longer recovery period.

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