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

HASKELL LABORATORY REPORT NO. 244-71 [redacted]

Material Tested: [redacted]

Material Submitted by: [redacted] Organic Chemicals Department Haskell No.: 6917
Jackson Laboratory Other Codes: [redacted]

ACUTE ORAL TEST

Procedure: The test material, as an a[illegible]ous 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.	301	12.68	4.2	None	> 11,000 mg/kg
25	7,500†	S - 14 d.	313	14.15	4.4		
25	5,000	S - 14 d.	352	15.65	4.4		
25	3,400	S - 14 d.	328	14.55	4.4		
25	2,250	S - 14 d.	312	13.79	4.4		

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

† Administered in divided dose

TEN-DOSE ORAL SUBACUTE TEST

Procedure: The test material was administered by intragastric intubation, as a 15% aqueous suspension, to a group of six young adult ChR-CD male rats, five times a week for two weeks; an additional group of six rats served as controls and was intubated with distilled water. Three control and three test 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
2250	0/6	23.0	17.8	7.8	5.6	1	-	B	B
		27.0	18.6	8.2	4.8	1	-	A+,B	B
		21.9	16.8	7.9	4.9	1	-	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,C	-

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.

No clinical signs were observed during the first week of the test phase. During the second week and the recovery period, the test animals gained weight at a rate slightly less than that of the controls.

‡ Gross and histopathologic code:

- \- = No abnormality detected
- 1 = Large and heavy
- A = Degeneration and necrosis of isolated hepatocytes
- B = Reduction in number of centrilobular cytoplasmic vesicles
- C = Focal RE cell hyperplasia
- \+ = Slight degree of change

Summary: [redacted] has low acute 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.

The repeated administration of the test compound to rats at 2250 mg/kg/day for ten doses produced heavier liver weights and larger liver/body weight ratios at the end of the test phase. These values returned to the normal range after the 14-day recovery period. The histologic effect which was present at the end of the test period and after the 14-day recovery period was characterized by a depletion of cytoplasmic vesicles, which are usually found in centrilobular hepatocytes of control male rats of this age group. Recovery from this type of liver change probably would have occurred if the recovery period had been longer.

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