Copies to: [redacted]

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

HASKELL LABORATORY REPORT NO. 246-71 [redacted]

Material Tested: [redacted] Haskell No.: 6919

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 ~~CbR~~ GD 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	17,000†	S - 14 d.	332	17.50	5.3	None	> 17,000 mg/kg
25	11,000†	S - 14 d.	321	17.85	5.6		
25	7,500†	S - 14 d.	347	19.00	5.5		
25	5,000	S - 14 d.	346	17.40	5.0		
12	3,400	S - 14 d.	346	17.38	5.0		
12	2,250	S - 14 d.	320	15.20	4.8		
	670	S - 14 d.	349	17.00	4.9		

* 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; in addition, six rats served as controls and were intubated with corn oil. Three test and three control rats were sacrificed 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	22.2	20.6	7.4	5.2	1	1	B	B
		23.5	17.6	7.7	4.6	1	-	B	B
		25.2	21.6	8.4	5 [illegible]	1	1	B	B
0 (Control)	0/6	12.5	13.5	4.1	3.5	-	-	-	-
		14.8	14.7	4.8	4.1	-	-	-	-
		14.2	19.8	4.6	4.1	-	-	-	-

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

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‡ Gross and histopathologic code

- \- = No abnormality detected
- 1 = Large and heavy
- B = Reduction in number of centrilobular cytoplasmic vesicles

Summary: [redacted] has low acute toxicity for the male rat when administered orally in single doses, its Approximate Lethal Dose (ALD) being greater than 17,000 mg/kg of body weight; single doses of 7500 mg/kg and above caused large livers 14 days after dosing.

Given at a repeated dose rate of 2200 mg/kg/day for a total of ten days over a two-week period, the test compound caused gross and gravimetric evidence of liver enlargement; histologically, there was a reduction in the number of centrilobular cytoplasmic vesicles. These changes were apparently not reversible after the 14 day-recovery period.

An evaluation of the results reported here and i[redacted] appears to indicate that listing of the three compounds in order of increasing toxicity is as follows: [redacted]

Report by: Laurel S. Wasileski

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Approved by: John A. Zapp, Jr.

John A. Zapp, Jr.
Director

[redacted]
LSW:pgh
Date: July [illegible], 1971