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Copies to: [redacted]

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

HASKELL LABORATORY REPORT NO. 43-64 [redacted]

Material Tested: [redacted] Haskell Nos: 3824; 3825*

Submitted by: [redacted] Organic Chemicals Department
Jackson Laboratory

Other Codes: [redacted]

[redacted]

TEN-DOSE SUBACUTE ORAL TEST (RATS)

Procedure: The test material (H-3824) was administered daily by stomach tube to each of six young adult ChR-CD male rats, five times a week for two weeks. Groups of three test rats, along with controls, were sacrificed four hours and 14 days after the last treatment.

Results:

Aqueous Susp. %	Dose (mg/kg/day)	Mortality	Toxic Signs	Individual Liver Weights (g)				Individual Liver Wt/ Body Wt X 100			
				4 Hours After 10th Dose		14 Days After 10th Dose		4 Hours After 10th Dose		14 Days After 10th Dose	
				Control	Test	Control	Test	Control	Test	Control	Test
5	220	0/6	Slight depression in rate of weight gain during test and recovery periods	17.6	15.5	19.7	16.8	5.1	5.0	4.7	4.7
				16.7	15.3	17.0	16.0	5.0	4.9	4.5	4.5
				16.1	18.8	16.3	17.8	4.8	5.7	4.2	4.8
0.5	22	0/5**	Very slight depression in rate of weight gain during test period	17.6	14.7	19.7	16.0	5.1	4.6	4.7	4.1
				16.7	14.5	17.0	16.3	5.0	4.4	4.5	4.2
				16.1	-	16.3	18.4	4.8	-	4.2	4.6

[redacted]

** One animal accidentally killed with 8th dose.

ACUTE ORAL TEST (RABBITS)

Procedure: The test material (H-3824) was administered as 33.3% aqueous suspension by intragastric intubation to male albino rabbits in single doses. Survivors were killed 10-16 days later.

Results:

Dose (mg/kg)	Mortality	Toxic Signs	Weight When Killed Body (g)	Weight When Killed Liver (g)	Liver Wt / Body Wt X 100	ALD
5000	0/1	Weight losses for 12 and 8 days, respectively, at 5000 and 3400 mg/kg; decreased food and water consumption at these doses; urine of all rabbits, first 24 hours, clear, foamy and brown	2189	135	6.2	> 5000 mg/kg
3400	0/1		2486	110	4.4	
2250	0/1		3137	170	5.4	
1500	0/1		3139	179	5.7	

ACUTE SKIN ABSORPTION TEST (RABBITS)

Procedure: The test material (H-3825), as received, was applied in single doses to the finely clipped skin of male albino rabbits and rubbed in lightly with a glass rod. The animals were restrained in wooden stocks for 24 hours, after which the skin was washed with warm water. Survivors were killed 14 days later.

Results:

Dose*** (mg/kg)	Mortality	Toxic Signs	Weight When Killed Body (g)	Weight When Killed Liver (g)	Liver Wt / Body Wt X 100	ALD
3765	0/1	None	2869	122	4.2	> 3765 mg/kg
2250	0/1		2657	167	6.3	
1500	0/1		2734	88	3.2	

TEN-DOSE SUBACUTE SKIN ABSORPTION TEST (RABBITS)

Procedure: The test material (H-3825), as received, was rubbed into the clipped skin of six male albino rabbits, five times a week for two weeks. After each exposure, which lasted six hours, the material was washed from the skin with warm water. Three test and three control rabbits were sacrificed four hours and 14 days after the last treatment.

*** Based on active ingredient.

Results:

Dose**** (mg/kg/day)	Mortality	Toxic Signs	Individual Liver Weights (g) 4 Hours After 10th Dose Control	Test	14 Days After 10th Dose Control	Test	Individual Liver Wt/Body Wt X 100 4 Hours After 10th Dose Control	Test	14 Days After 10th Dose Control	Test
1500	0/6	None	131	103	86	105	4.6	4.2	3.1	4.4
			82	110	124	180	3.6	4.6	4.2	5.9
			108	140	139	157	4.3	5.2	4.8	5.4

**** Based on active ingredient.

Summary: [redacted] exhibited low cumulative oral toxicity for the male rat when administered repeatedly at doses of 22 mg/kg/day or 220 mg/kg/day. Except for a very slight adverse effect upon weight gain, there were no clinical signs of toxicity. The livers of these test animals were gravimetrically and histologically within the range of normal. This should be contrasted with the results obtained when [redacted] was administered orally to rats at a rate of 2250 mg/kg/day; the livers of these animals were extremely heavy and histologically abnormal [redacted]

[redacted] has low acute oral toxicity and low acute dermal toxicity for the male rabbit, the Approximate Lethal Doses (ALD's) being greater than 5000 mg/kg and greater than 3765 mg/kg, respectively. [redacted] was not cumulatively toxic for the male rabbit when administered repeatedly via the dermal route at a dose of 1500 mg/kg/day. Liver weights and liver/body weight ratios were considered normal for all the rabbits examined; moreover, the livers did not exhibit any aberrations which could be attributed to the administration of the test material.

The difference between the response of the rat and that of the rabbit to acute oral doses of [redacted] with respect to liver weight suggests a species difference. Organs other than liver were not studied histologically.

Report by: Henry Sherman

Approved by: [illegible]

J. Wesley Clayton Jr.

HS/mfs
Date: May 6, 1964