[redacted]

Copies to: [redacted]

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

HASKELL LABORATORY REPORT NO. 11-64 [redacted]

Material Tested: [redacted] Haskell No.: 3662

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

ACUTE ORAL TEST

Procedure: The material was administered, as received, by stomach tube to young adult ChR-CD male rats in single doses. Survivors were sacrificed 14-15 days later.

Results:

Dose* (mg/kg)	Mortality**	Toxic Signs	Weight When Killed Body (gm)	Weight When Killed Liver (gm)	Liver Wt. / Body Wt. x 100	ALD
11,000	S - 15 d.	Slight initial weight loss	345	23.2	6.7	
7,500	S - 15 d.		334	18.9	5.7	> 11,000 mg/kg
5,000	S - 14 d.		314	15.3	4.9	
2,250	S - 14 d.		305	15.7	5.1	

* Based on active ingredient, [redacted]
** S - ( ) d. = Sacrificed ( ) days after dosing

TEN-DOSE SUBACUTE ORAL TEST

Procedure: The test material, as received, was administered daily by stomach tube to each of six young adult ChR-CD male rats, five times a week for one or two weeks. Where animals survived, groups of three test rats, along with controls, were sacrificed four hours and 14 days after the last treatment.

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
5,000	6/6	Death after 3-5 doses, weight loss, diarrhea, discoloration of perineal area.								
2,250	0/6	First Week: slight weight loss	13.9	29.8	16.8	24.2	4.5	11.5	4.4	6.1
		Second Week: slightly depressed rate of weight gain.	16.6	35.2	16.6	25.0	5.0	11.6	4.3	6.9
		Recovery Period: none; weight gain parallel that of controls	17.4	30.2	18.6	23.9	5.0	11.8	4.3	6.8

* Based on active ingredient, [redacted]

Summary: [redacted] has low acute oral toxicity for the male rat, its Approximate Lethal Dose (ALD) being greater than 11,000 mg/kg of body weight, based on active ingredient. The compound produced an increase in the liver weight of the animal dosed at 11,000 mg/kg, and possibly in the animal dosed at 7,500 mg/kg.

[redacted] shows high cumulative oral toxicity. When administered to each of six rats at a dose of 5,000 mg/kg/day, all died after having received three to five doses. Two of the animals examined histologically showed kidney and terminal lung damage; in addition, their stomach contents were in the form of a firm core that was not passing along the digestive tract in a normal manner. When administered to rats at a dose of 2,250 mg/kg/day, [redacted] produced extremely heavy livers in animals sacrificed after the tenth dose, with evidence of some recovery when the animals were sacrificed after a 14-day recovery period. Microscopically, the heavy livers contained some enlarged liver cells and enlarged nuclei which had prominent nucleoli or an uneven distribution of chromatin material. The lesions observed were not those usually indicative of degenerative changes.

Because of the effect of [redacted] upon the liver of rats after high levels of oral dosing, their use as a component of food wrapping material would require (a) that studies be conducted to determine the extent, if any, to which they migrate from wrapping into foods and (b) that additional feeding studies of longer duration be initiated to determine a "no-effect" level as a preliminary to securing Food and Drug Administration approval for such use.

Report by: Henry Sherman
Henry Sherman
Toxicologist

Approved by: D. B. Hood
D. B. Hood
Chief, Toxicology Section

John A. Zapp, Jr.
John A. Zapp, Jr.
Director

HS/bjd
Date: February 3, 1964