PROJECT Y-70-25
REPORT

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YOUNGER LABORATORIES
INCORPORATED
Consulting and Analytical Services
CHEMICAL . . . MICROBIOLOGICAL . . . BIOLOGICAL

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Certificate of Analysis

March 27th, 1970

SUBJECT -

Toxicological Investigation Of: Pydraul 281 -- Lot QL-42

Monsanto Sample Number 28

Monsanto Project Number Y-70-25

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats, Mixed Sex)

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino male and female rats.

After the approximate Minimum Lethal Dose was determined, groups of male and female rats were fed in increasing doses at increments of 0.1 fractional log intervals at five levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to a modification of the method of E. J. de Beer.

Observations were made for toxic signs and the viscera of the test animals were examined macroscopically.

The data are shown in Table I.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits.

The treated areas were covered with plastic strips and the animals held in wooden stocks for periods up to twenty-four hours, after which time they were assigned to individual cages.

Observations were made for toxic signs and the viscera of the test animals were examined macroscopically.

The data are shown in Table II.

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EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits, Mixed Sex)

The undiluted compound was applied to the clipped, intact skin of albino male and female rabbits and removed after twenty-four hours. The application was covered with plastic strips to retard evaporation and avoid contamination.

Observations were made over a period of several days for irritation.

The data, scored according to the method of Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Rabbits, Mixed Sex)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino male and female rabbits and observations made over a period of several days for inflammation.

The eyes were rinsed with warm isotonic saline solution after twenty-four hours.

The data, scored according to the method of Draize, et al, are shown in Table IV.

E) Vapor Inhalation (Male Rats) - Ambient Temperature

Six mature male rats were placed in a metal chamber of 35-liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 179.0 grams of the compound contained in a 350-milliliter erlenmeyer flask.

Vapors from the flask passed into a one liter bottle to remove droplets and then into the chamber.

Air flow through the sample was 4.0 liters per minute as measured by a calibrated rotameter. This was sufficient to violently agitate the liquid. No supplementary air was introduced inasmuch as the above supply was ample for the animals oxygen requirements.

The animals were observed for behavior during exposure and for ten days following exposure. The viscera of the test animals were examined macroscopically.

The data are shown in Table V.

SUMMARY -

Pydraul 281 -- Lot QL-42

A) Oral LD_{50} (Rats, Mixed Sex)

The Oral LD_{50} for male and female rats was placed at 10,400 milligrams per kilogram with lower and upper limits of 9,460 to 11,440 milligrams per kilogram.

The compound was classed as practically non-toxic by oral ingestion in male and female rats.

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SUMMARY - (Continued)

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1260 milligrams per kilogram and less than 2000 milligrams per kilogram.

The compound was classed as mildly toxic by skin absorption in male and female rabbits.

C) Skin Irritation (Rabbits, Mixed Sex)

The compound was classed as a mild to moderate irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 2.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

The compound was classed as a mild eye irritant in male and female rabbits.

The average maximum score was 16.0 out of a possible 110 in one hour.

E) Vapor Inhalation (Male Rats) - Ambient Temperature

All animals survived the six hour exposure as well as the following ten day observation period.

It was concluded that the vapors were practically non-toxic under conditions of the test.

YOUNGER LABORATORIES, INC.

Melvin D. Birch

BY: MELVIN D. BIRCH

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TABLE I

THE ORAL LD_{50} OF 'Pydraul 281 — Lot QL-42' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	200	6,310	Survived
2- Male	200	6,310	Survived
3- Female	210	6,310	Survived
4- Male	220	6,310	Survived
5- Female	195	6,310	Survived
6- Male	205	7,940	Survived
7- Female	240	7,940	Survived
8- Male	200	7,940	Survived
9- Female	205	7,940	Died
10- Male	245	7,940	Survived
11- Female	240	10,000	Died
12- Male	200	10,000	Survived
13- Female	210	10,000	Died
14- Male	230	10,000	Survived
15- Female	235	10,000	Died
16- Male	210	12,600	Survived
17- Female	235	12,600	Died
18- Male	195	12,600	Survived
19- Female	215	12,600	Died
20- Male	210	12,600	Died
21- Female	220	15,800	Died
22- Male	250	15,800	Died
23- Female	235	15,800	Died
24- Male	200	15,800	Died
25- Female	225	15,800	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 10,400 milligrams per kilogram with lower and upper limits of 9,460 to 11,440 milligrams per kilogram.

The compound was classed as practically non-toxic by oral ingestion in male and female rats.

Survival time was two to seven days with most deaths occurring within three days.

Toxic signs included reduced appetite and activity, lethargy, increasing weakness, collapse, and death.

At autopsy there was lung hyperemia, liver discoloration, and gastrointestinal inflammation (acute in some cases).

Surviving animals were sacrificed ten days after dosing. The viscera appeared normal by macroscopic examination.

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TABLE II

THE MINIMUM LETHAL DOSE OF 'Pydraul 281 -- Lot QL-42'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.4	794	- 0.2	Survived
2 - Male	2.6	1260	- 0.2	Survived
3 - Female	1.9	1260	- 0.3	Survived
4 - Male	2.0	1260	- 0.4	Survived
5 - Female	2.3	2000	- 0.3	Died - 12 Days
6 - Male	2.1	2000	- 0.4	Survived
7 - Female	2.0	2000	- 0.4	Died - 13 Days
8 - Male	2.4	3160	- 0.4	Died - 10 Days
9 - Female	2.0	5010	- 0.5	Died - 5 Days
10 - Male	2.1	7940	- 0.4	Died - 5 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1260 milligrams per kilogram and less than 2000 milligrams per kilogram.

The compound was classed as mildly toxic by skin absorption in male and female rabbits.

Survival time was five to thirteen days.

Toxic signs included reduced appetite and activity, increasingweakness, tremors after four days, collapse, and death.

Note: Surviving animals sustained weight losses of 5% to 25% of initial weight after fourteen days.

At autopsy there was hemorrhagic lungs, jaundiced liver, enlarged gall bladder, discolored kidneys, and gastrointestinal inflammation.

Surviving animals were sacrificed fourteen days after dosing. Macroscopic examination revealed areas of lung congestion and slight liver discoloration.

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TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF

'Pydraul 281 — Lot QL-42'

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	0	3	2	1	0	0
2 - Female	0	2	1	1	0	0
3 - Female	0	3	1	1	0	0
Average	0.0	2.6	1.3	1.0	0.0	0.0

DISCUSSION -

The compound was classed as a mild to moderate irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 2.6 out of a possible 8 in twenty-four hours.

Observations following application --

1 Hour:	No skin changes; zero readings
24-Hours:	Barely perceptible to slight erythema, barely perceptible edema
48-Hours:	Barely perceptible erythema, barely perceptible edema in one instance
72-Hours:	Barely perceptible erythema; no edema
120-Hours:	No erythema or edema; zero readings
168-Hours:	No erythema or edema; zero readings

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TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF

'Pydraul 281 -- Lot QL-42'

Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of					
	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Female	16	6	2	2	0	0
2 - Male	16	4	0	0	0	0
3 - Female	16	4	0	0	0	0
Average	16.0	4.6	0.6	0.6	0.0	0.0

DISCUSSION -

The compound was classed as a mild eye irritant in male and female rabbits. The average maximum score was 16.0 out of a possible 110 in one hour.

Observations following application --

Immediate:	Discomfort was slight
10-Minutes:	Moderate erythema and discharge, slight edema
1-Hour:	Beefy-redness, slight edema, copious discharge There was no corneal cloudiness and iris reaction to light was normal
24-Hours:	Moderate erythema, barely perceptible edema in one instance; no discharge
48-Hours:	Barely perceptible erythema in one instance
72-Hours:	Barely perceptible erythema in one instance
120-Hours:	Eyes normal; zero readings
168-Hours:	Eyes normal; zero readings

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TABLE V

INHALATION OF 'Pydraul 281 -- Lot QL-42'

VAPORS BY RATS

Average Temperature Inside Chamber ..... 74° F.
Average Relative Humidity Inside Chamber ..... 50 %

Amount of Sample -- To start ..... 179.0 Grams
Recovered ..... 177.7 Grams
Vaporized or left in equipment ..... 1.3 Grams (0.8 %)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No immediate effect ...
2 - Male	Survived	Normal respiration ...
3 - Male	Survived	No nasal or ocular discharge ...
4 - Male	Survived	No weakness or drowsiness of consequence.
5 - Male	Survived	
6 - Male	Survived	

DISCUSSION -

All animals survived the six hour exposure as well as the following ten day observation period.

It was concluded that the vapors were practically non-toxic under conditions of the test.

Observations following exposure --

Animals appeared normal when removed from the chamber.

The ten day observation period was uneventful.

Weight gain was normal.

Surviving animals were sacrificed ten days following exposure. The viscera appeared normal by macroscopic examination.

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