PROJECT NO. Y-71-40
REPORT FILE

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

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March 17th, 1971

Certificate of Analysis

SUBJECT -

Toxicological Investigation Of: Pydraul 230A -- Lot OR 162444
Monsanto Sample Number 40
Monsanto Project Number Y-71-40

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 four levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to 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) Acute Skin Absorption Minimal Lethal Dose (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)

0.5 Milliliter of undiluted sample was applied to the clipped, intact skin of New Zealand white male and female rabbits under a one inch by one inch square patch, two single layers thick. The patches were held in place with adhesive tape. The trunk of each animal was wrapped with plastic strips, to avoid contamination and retard evaporation, for the twenty-four hour exposure period.

Observations were made over a period of seven 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 seven 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 114.3 grams of the compound contained in a 500-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 four 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 230A -- Lot OR 162444

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

The Oral LD_{50} for male and female rats was placed at 6050 milligrams per kilogram with lower and upper limits of 5540 to 6590 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) Acute Skin Absorption Minimal Lethal Dose (Rabbits, Mixed Sex)

The Acute Skin Absorption Minimal Lethal Dose for male and female rabbits was found to be greater than 5010 milligrams per kilogram and less than 7940 milligrams per kilogram.

The compound was classed as practically non-toxic by skin absorption in male and female rabbits.

C) Skin Irritation (Rabbits, Mixed Sex)

The compound was classed as non-irritating when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 0.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 10.0 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.

BY: MELVIN D. BIRCH

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T A B L E I

THE ORAL LD_{50} OF

'Pydraul 230A -- Lot OR 162444' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	215	3980	Survived
2- Male	205	3980	Survived
3- Female	220	3980	Survived
4- Male	215	3980	Survived
5- Female	205	3980	Survived
6- Male	195	5010	Survived
7- Female	200	5010	Died
8- Male	205	5010	Survived
9- Female	205	5010	Survived
10- Male	200	5010	Survived
11- Female	235	6310	Survived
12- Male	240	6310	Survived
13- Female	220	6310	Survived
14- Male	245	6310	Died
15- Female	235	6310	Died
16- Male	205	7940	Died
17- Female	220	7940	Died
18- Male	225	7940	Died
19- Female	210	7940	Died
20- Male	240	7940	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 6050 milligrams per kilogram with lower and upper limits of 5540 to 6590 milligrams per kilogram.

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

Survival time was one to two days with most deaths occurring during the second day.

Toxic signs included reduced appetite and activity, lethargy (for one to three days in survivors), increasing weakness, collapse, and death.

At autopsy there was slight liver discoloration and acute gastrointestinal inflammation.

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

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T A B L E II

THE ACUTE SKIN ABSORPTION MINIMAL LETHAL DOSE OF
'Pydraul 230A -- Lot OR 162444' FOR RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Male	2.1	2000	- 0.1	Survived
2 - Female	2.5	3160	- 0.3	Survived
3 - Male	2.0	5010	- 0.3	Survived
4 - Female	2.0	7940	- 0.4	Died -- 7 Days
5 - Male	2.3	7940	- 0.3	Died - 11 Days

DISCUSSION -

The Acute Skin Absorption Minimal Lethal Dose for male and female rabbits was found to be greater than 5010 milligrams per kilogram and less than 7940 milligrams per kilogram.

The compound was classed as practically non-toxic by skin absorption in male and female rabbits.

Survival time was seven to eleven days.

Toxic signs included reduced appetite and activity, lethargy (lasting seven to fourteen days in survivors), increasing weakness, collapse, and death. In fourteen days animals #1 and #2 had nearly recovered starting weight; animal #3 continued to lose weight slowly.

At autopsy there was slight lung congestion, liver discoloration, enlarged gall bladder, and slight gastrointestinal inflammation.

Surviving animals were sacrificed fourteen days after dosing. Macroscopic examination revealed liver hyperemia and slight gastrointestinal inflammation in animals #1 and #2; animal #3 showed lung congestion, slight liver discoloration, and slight gastrointestinal inflammation.

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T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF
'Pydraul 230A -- Lot OR 162444'

Sample (0.5 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 - Male	0	1	0	0	0	0
2 - Female	0	1	0	0	0	0
3 - Female	0	0	0	0	0	0
Average	0.0	0.6	0.0	0.0	0.0	0.0

DISCUSSION -

The compound was classed as non-irritating when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 0.6 out of a possible 8 in twenty-four hours.

Observations following application --

1-Hour:	No skin changes; zero readings
24-Hours:	Barely perceptible erythema in two instances; no edema
48-Hours:	No erythema or edema; zero readings
72- 168-Hours:	No erythema or edema; zero readings

Note: Sample had a slight defatting effect on the skin causing the skin to flake off in ten to fourteen days. There was no injury in depth.

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T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF

'Pydraul 230A -- Lot OR 162444'

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	10	4	0	0	0	0
2 - Female	10	4	0	0	0	0
3 - Male	10	4	0	0	0	0
Average	10.0	4.0	0.0	0.0	0.0	0.0

DISCUSSION -

The compound was classed as a slight eye irritant in male and female rabbits. The average maximum score was 10.0 out of a possible 110 in one hour.

Observations following application --

Immediate:	Discomfort was slight
10-Minutes:	Moderate erythema and discharge, very slight edema
1-Hour:	Moderate erythema and discharge, very slight edema
24-Hours:	Slight erythema and discharge; no edema
48-Hours:	Eyes normal; zero readings
72- 168-Hours:	Eyes normal; zero readings

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T A B L E V

INHALATION OF

'Pydraul 230A -- Lot OR 162444' VAPORS BY RATS

Average Temperature Inside Chamber ..... 74° F.
Average Relative Humidity Inside Chamber ..... 60 %

Amount of Sample -- To start ..... 114.3 Grams
Recovered ..... 114.3 Grams
Vaporized or left in equipment ..... 0.0 Gram (0.0 %)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No nasal or ocular discharge ...
2 - Male	Survived	Normal respiration ...
3 - Male	Survived	
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 --

The animals appeared normal when removed from the chamber. There were no bronchial rales or other evidence of respiratory complications. 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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