

PROJECT  
REPORT

4-71-38

# YOUNGER LABORATORIES

INCORPORATED

*Consulting and Analytical Services*

CHEMICAL . . . MICROBIOLOGICAL . . . BIOLOGICAL

216

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March 17th, 1971

## *Certificate of Analysis*

SUBJECT -

Toxicological Investigation Of: Pydraul 312A -- Lot OR 162437

Monsanto Sample Number 38

Monsanto Project Number Y-71-38

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD<sub>50</sub> (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<sub>50</sub> 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.

DSW 295774

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Younger Laboratories Certificate of Analysis - Page 2 (3/17/71) - Y-71-38

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 124.0 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 312A -- Lot OR 162437

A) Oral LD<sub>50</sub> (Rats, Mixed Sex)

The Oral LD<sub>50</sub> for male and female rats was placed at 7350 milligrams per kilogram with lower and upper limits of 6720 to 8020 milligrams per kilogram.

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

DSW 295775

To: Monsanto Company

St. Louis, Missouri

Younger Laboratories Certificate of Analysis - Page 3 (3/17/71) - Y-71-38

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 a slight irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 1.0 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 9.3 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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DSW 295776

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 Younger Laboratories Certificate of Analysis - Page 4 (3/17/71) - Y-71-38

T A B L E I  
 THE ORAL LD<sub>50</sub> OF  
 'Pydraul 312A -- Lot OR 162437' FOR RATS

Sample Fed Undiluted

| Animal No. - Sex | Weight<br>Gm. | Dose<br>Mg. / Kg. | Fate     |
|------------------|---------------|-------------------|----------|
| 1- Female        | 200           | 5,010             | Survived |
| 2- Male          | 200           | 5,010             | Survived |
| 3- Female        | 215           | 5,010             | Survived |
| 4- Male          | 200           | 5,010             | Survived |
| 5- Female        | 215           | 5,010             | Survived |
| 6- Male          | 235           | 6,310             | Survived |
| 7- Female        | 210           | 6,310             | Survived |
| 8- Male          | 210           | 6,310             | Died     |
| 9- Female        | 200           | 6,310             | Survived |
| 10- Male         | 235           | 6,310             | Survived |
| 11- Female       | 235           | 7,940             | Died     |
| 12- Male         | 210           | 7,940             | Died     |
| 13- Female       | 220           | 7,940             | Survived |
| 14- Male         | 235           | 7,940             | Survived |
| 15- Female       | 225           | 7,940             | Died     |
| 16- Male         | 225           | 10,000            | Died     |
| 17- Female       | 225           | 10,000            | Died     |
| 18- Male         | 205           | 10,000            | Died     |
| 19- Female       | 200           | 10,000            | Died     |
| 20- Male         | 220           | 10,000            | Died     |

#### DISCUSSION -

The Oral LD<sub>50</sub> for male and female rats was placed at 7350 milligrams per kilogram with lower and upper limits of 6720 to 8020 milligrams per kilogram.

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

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

Toxic signs included reduced appetite and activity, lethargy (lasting two to four days in survivors), increasing weakness, collapse, and death.

At autopsy there was lung and liver hyperemia and acute gastrointestinal inflammation.

Surviving animals were sacrificed seven days after dosing. Macroscopic examination revealed slight lung congestion in some cases.

DSW 295777

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Younger Laboratories Certificate of Analysis - Page 5 (3/17/71) - Y-71-38

T A B L E II

THE ACUTE SKIN ABSORPTION MINIMAL LETHAL DOSE OF  
'Pydraul 312A -- Lot OR 162437' FOR RABBITS

Sample Applied Undiluted

| Animal No. - Sex | Weight<br>Kg. | Dose<br>Mg. / Kg. | Weight Change<br>5 Days Later<br>Kg. | Fate           |
|------------------|---------------|-------------------|--------------------------------------|----------------|
| 1 - Female       | 2.6           | 3160              | - 0.1                                | Survived       |
| 2 - Male         | 2.4           | 5010              | - 0.1                                | Survived       |
| 3 - Female       | 2.4           | 7940              | - 0.4                                | Died -- 6 Days |
| 4 - Male         | 2.1           | 7940              | - 0.1                                | Survived       |

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 six days.

Toxic signs included reduced appetite and activity and lethargy (lasting ten to fourteen days in survivors), collapse, and death. In fourteen days animals #1 and #2 began to recover weight loss; animal #4 contained slight loss of weight.

At autopsy there was lung congestion, jaundiced liver, enlarged gall bladder, and acute gastrointestinal inflammation.

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

DSW 295778

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 Younger Laboratories Certificate of Analysis - Page 6 (3/17/71) - Y-71-38

### T A B L E    I I I

#### SKIN IRRITATION IN RABBITS AFTER APPLICATION OF

'Pydraul 312A -- Lot OR 162437'

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 - Female       | 0                                  | 1        | 0        | 0        | 0         | 0         |
| 2 - Male         | 0                                  | 1        | 0        | 0        | 0         | 0         |
| 3 - Male         | 0                                  | 1        | 0        | 0        | 0         | 0         |
| Average          | 0.0                                | 1.0      | 0.0      | 0.0      | 0.0       | 0.0       |

#### DISCUSSION -

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

The average maximum score was 1.0 out of a possible 8 in twenty-four hours.

#### Observations following application --

|                |                                       |
|----------------|---------------------------------------|
| 1-Hour:        | No skin changes; zero readings        |
| 24-Hours:      | Barely perceptible erythema; 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.

DSW 295779

To: Monsanto Company  
 St. Louis, Missouri  
 Younger Laboratories Certificate of Analysis - Page 7 (3/17/71) - Y-71-38

T A B L E IV  
 E Y E IRRITATION IN RABBITS AFTER APPLICATION OF  
 'Pydraul 312A -- Lot OR 162437'

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 - Male         | 8                                  | 6        | 0        | 0        | 0         | 0         |
| 2 - Female       | 10                                 | 6        | 0        | 0        | 0         | 0         |
| 3 - Male         | 10                                 | 6        | 0        | 0        | 0         | 0         |
| Average          | 9.3                                | 6.0      | 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 9.3 out of a possible 110 in one hour.

Observations following application -

|                |                                                                       |
|----------------|-----------------------------------------------------------------------|
| Immediate:     | Discomfort was slight with eyes closed                                |
| 10-Minutes:    | Moderate erythema and discharge; very slight edema                    |
| 1-Hour:        | Slight to moderate erythema, very slight edema,<br>moderate discharge |
| 24-Hours:      | Slight erythema and discharge; very slight edema                      |
| 48-Hours:      | Eyes normal; zero readings                                            |
| 72- 168-Hours: | Eyes normal; zero readings                                            |

DSW 295780

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Younger Laboratories Certificate of Analysis - Page 8 (3/17/71) - Y-71-38

# TABLE V

## INHALATION OF

'Pydraul 312A -- Lot OR 162437' VAPORS BY RATS

Average Temperature Inside Chamber ..... 74° F.

Average Relative Humidity Inside Chamber ..... 62 %

Amount of Sample -- To start ..... 124.0 Grams  
Recovered ..... 124.0 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     |
| 5 - Male         | Survived | consequence.                     |
| 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.

DSW 295781