YOUNGER LABORATORIES
*Biochemists . . . Pharmacologists . . . Analysts*

128 CLIFF CAVE ROAD
SAINT LOUIS, MO., 63129
PHONE: TILDEN 6-2840

# *Certificate of Analysis*

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: PYDRAUL 135

Monsanto Sample Number 185

Monsanto Project Number Y-66-160

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

COPY

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 a modification of the method of E. J. de Beer.

Observations were made for toxic symptoms and the viscera of the animals that succumbed 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 placed in wooden stocks for periods up to twenty-four hours, after which time they were assigned to individual cages.

Observations were made for toxic symptoms and the viscera of the animals that succumbed were examined macroscopically.

The data are shown in Table II.

MONS 037868

This confidential report is not to be used in any form of advertising without written permission

SUMMARY -

PYDRAUL 135

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

The Oral $LD_{50}$ for male and female rats was placed at 4200 milligrams per kilogram with lower and upper limits of 3025 to 5840 milligrams per kilogram.

The compound was classed as slightly toxic by oral ingestion in male and female rats.

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.

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

The material in this report is to be used in development of the product and may be given to responsible sales contacts, but it is not to be used by them in advertising copy. The source of this material is not to be divulged until it appears in formal publications. No exceptions to the established rule may be made without the approval of the Medical Department in St. Louis. Customers' inquiries regarding matters of toxicity are to be referred as before to the Medical Department in St. Louis for reply.

— Monsanto Company

TABLE I

THE ORAL $LD_{50}$ OF 'HYDRAUL 135' FOR RATS

Sample Fed Undiluted

| Animal No. - Sex | Weight Gm. | Dose Mg./Kg. | Rats |
|---|---|---|---|
| 1- Female | 210 | 3160 | Survived |
| 2- Male | 235 | 3160 | Survived |
| 3- Female | 220 | 3160 | Died |
| 4- Male | 245 | 3160 | Survived |
| 5- Female | 215 | 3160 | Survived |
| 6- Male | 255 | 3980 | Died |
| 7- Female | 225 | 3980 | Died |
| 8- Male | 250 | 3980 | Survived |
| 9- Female | 220 | 3980 | Died |
| 10- Male | 265 | 3980 | Survived |
| 11- Female | 215 | 5010 | Survived |
| 12- Male | 240 | 5010 | Died |
| 13- Female | 230 | 5010 | Died |
| 14- Male | 265 | 5010 | Survived |
| 15- Female | 225 | 5010 | Died |
| 16- Male | 270 | 6310 | Died |
| 17- Female | 230 | 6310 | Died |
| 18- Male | 245 | 6310 | Survived |
| 19- Female | 230 | 6310 | Died |
| 20- Male | 265 | 6310 | Died |

DISCUSSION -

The Oral $LD_{50}$ for male and female rats was placed at 4200 milligrams per kilogram with lower and upper limits of 3025 to 5840 milligrams per kilogram.

The compound was classed as slightly toxic by oral ingestion in male and female rat

Survival time was several hours to three days.

Toxic symptoms included tremors in two to three hours, diarrhea, loss of appetite, and coma of six to eight hours duration.

At autopsy there was renal, liver, and pulmonary hyperemia in addition to inflammation of the gastrointestinal mucosa.

TABLE II

THE MINIMUM LETHAL DOSE OF 'PYDRAUL 135'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

| Animal No. - Sex | Weight Kg. | Dose Mg./Kg. | Weight Change 5 Days Later Kg. | Fate |
|---|---|---|---|---|
| 1 - Male | 2.8 | 501 | - 0.1 | Survived |
| 2 - Female | 2.4 | 794 | - 0.1 | Survived |
| 3 - Male | 3.0 | 1260 | - 0.2 | Survived |
| 4 - Female | 2.6 | 2000 | - 0.2 | Died - 11 Days |
| 5 - Male | 2.8 | 3160 | - 0.4 | Died — 9 Days |
| 6 - Female | 2.5 | 5010 | - 0.3 | Died — 8 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 eight to eleven days.

Toxic symptoms included reduced activity, loss of appetite, marked weakness, and collapse.

At autopsy there was liver discoloration and renal hyperemia macroscopically.