YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

128 CLIFF CAVE ROAD
SAINT LOUIS, MO., 63129
PHONE: TILDEN 6-2540

Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: HYDRAUL 280

Monsanto Sample Number 186

Monsanto Project Number Y-66-161

11-9-66
Y-66-161

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 M. 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 036463

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

SUMMARY -

PYDRAUL 280

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

The Oral LD_{50} for male and female rats was placed at 8,440 milligrams per kilogram with lower and upper limits of 6835 to 10,380 milligrams per kilogram.

The compound was classed as practically non-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 2000 milligrams per kilogram and less than 3160 milligrams per kilogram.

The compound was classed as slightly 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 'PYDRAUL 280' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./kg.	Fate
1- Female	220	6,310	Survived
2- Male	255	6,310	Survived
3- Female	230	6,310	Survived
4- Male	240	6,310	Survived
5- Female	215	6,310	Died
6- Male	260	7,940	Survived
7- Female	225	7,940	Died
8- Male	250	7,940	Survived
9- Female	220	7,940	Died
10- Male	270	7,940	Survived
11- Female	225	10,000	Survived
12- Male	265	10,000	Died
13- Female	230	10,000	Died
14- Male	250	10,000	Survived
15- Female	225	10,000	Survived
16- Male	260	12,600	Died
17- Female	215	12,600	Died
18- Male	255	12,600	Died
19- Female	210	12,600	Died
20- Male	240	12,600	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 8,440 milligrams per kilogram with lower and upper limits of 6,835 to 10,380 milligrams per kilogram.

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

Survival time was several hours to four days.

Toxic symptoms included tremors after two to three hours, lethargy, loss of appetite, and collapse.

At autopsy there was inflammation of the gastric mucosa as well as liver hyperemia.

TABLE II

THE MINIMUM LETHAL DOSE OF 'HYDRAUL 280' 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	2.6	794	0.0	Survived
2 - Female	2.3	1260	- 0.2	Survived
3 - Male	2.7	2000	- 0.2	Survived
4 - Female	2.5	3160	- 0.4	Died - 10 Days
5 - Male	2.7	5010	- 0.3	Died -- 7 Days
6 - Female	2.3	7940	- 0.3	Died -- 7 Days

Discussion -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 2000 milligrams per kilogram and less than 3160 milligrams per kilogram.

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

Survival time was seven to ten days.

Toxic symptoms included weakness and inactivity after two to three days followed by tremors and collapse.

At autopsy there was liver dehydration and discoloration as well as pulmonary congestion.