PROJECT NO: Y-64-49
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

123 CLIFF CAVE ROAD
SAINT LOUIS, MO., 63129

PHONE: TILDEN 6-2540

Certificate of Analysis

June 13th, 1964

SUBJECT - AROCLOR

Toxicological Investigation Of: MCS - 295 (THERM. NOL FR-O)

Monsanto Sample Number 57

Monsanto Project Number Y-64-49

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 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.

GBRN002919

EXHIBIT
K-55

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits)

The undiluted compound was applied to the clipped, intact skin of albino 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)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino 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)

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 150-milliliters of the compound contained in a 300-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 six 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 and, since there were no deaths, all were held for ten days observation.

The data are shown in Table V.

SUMMARY -

MCS - 295

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 3740 to 4700 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 501 milligrams per kilogram and less than 794 milligrams per kilogram.

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

SUMMARY - (Continued)

C) Skin Irritation (Rabbits)

The compound was classed as a moderate skin irritant when applied undiluted to intact rabbit skin.

The average maximum score was 4.3 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits)

The compound was classed as a moderate eye irritant.

The average maximum score was 41.6 out of a possible 110 in twenty-four hours.

E) Vapor Inhalation (Male Rats)

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

Fred M. Younger

BY: FRED M. YOUNGER

TABLE I

THE ORAL LD_{50} OF 'MCS-295' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	210	3160	Survived
2- Female	225	3160	Survived
3- Male	230	3160	Survived
4- Male	215	3160	Survived
5- Female	220	3160	Survived
6- Female	230	3980	Died
7- Male	245	3980	Survived
8- Male	235	3980	Survived
9- Female	225	3980	Died
10- Female	220	3980	Survived
11- Male	250	5010	Died
12- Male	240	5010	Died
13- Female	215	5010	Died
14- Female	230	5010	Died
15- Male	245	5010	Died
16- Male	240	6310	Died
17- Female	230	6310	Died
18- Female	245	6310	Died
19- Male	250	6310	Died
20- Male	255	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 3740 to 4700 milligrams per kilogram.

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

Survival time was one to four days with most deaths occurring in three to four days.

Toxic symptoms included severe diarrhea, increasing weakness, tremors, and collapse.

At autopsy there was renal and liver hyperemia as well as inflammation of the gastric mucosa by macroscopic examination.

TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS-295'
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	3.1	501	0.0	Survived
2 - Female	2.6	794	- 0.2	Died -- 6 Days
3 - Male	3.2	1260	- 0.3	Died -- 7 Days
4 - Female	2.9	2000	-----	Died -- 4 Days
5 - Male	3.4	3160	- 0.3	Died -- 5 Days
6 - Female	2.8	5010	-----	Died -- 4 Days
7 - Male	3.1	7940	-----	Died -- 3 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 501 milligrams per kilogram and less than 794 milligrams per kilogram.

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

Survival time was three to seven days.

Aside from reduced appetite and moderate lethargy there was little show of toxicity until approximately twenty-four hours preceding death. Increasing weakness, tremors, and dyspnea appeared at this time.

Autopsy findings included liver with yellowish coloration and renal hyperemia.

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-295'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	1	4	3	2	1	0
2	1	4	2	2	0	0
3	2	5	4	2	1	0
Average	1.3	4.3	3.0	2.0	0.6	0.0

DISCUSSION -

The compound was classed as a moderate skin irritant when applied undiluted to intact rabbit skin.

The average maximum score was 4.3 out of a possible 8 in twenty-four hours.

Barely perceptible to well-defined redness was present after one hour. Overnight there was moderate redness and edema for an average score of 4.3. There was no blistering. Inflammation gradually reduced following removal of the compound so that within five days only a trace of erythema remained on two animals.

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-295'

Sample (0.1 Milliliter) Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	35	47	41	30	19	6
2	28	36	29	19	8	0
3	32	42	33	22	12	0
Average	31.6	41.6	34.3	23.6	13.0	2.0

DISCUSSION -

The compound was classed as a moderate eye irritant.

The average maximum score was 41.6 out of a possible 110 in twenty-four hours.

Discomfort was moderate immediately following application.

Mild redness and edema, moderate lacrimation, and mild dullness of the corneal area developed within one hour. Congestion increased somewhat in twenty-four hours at which time the average score was 41.6. Discharge had ceased and edema was still mild but iris details were not as clear compared to the one hour reading. Within seven days two animals were free of inflammation. Slight redness of the conjunctivae was still present on the third animal.

TABLE V

INHALATION OF 'MCS-295' VAPORS BY RATS

Average Temperature Inside Chamber ..... 75° F.

Average Relative Humidity Inside Chamber ..... 49 %

Amount Of Sample -- To Start ..... 150 cc
Recovered ..... 149 cc
Vaporized or left in apparatus ..... 1 cc (0.6%)

Animal No. - Sex	Fate	Observations During Exposure
1- Male	Survived	Normal breathing rate ...
2- Male	Survived	No pawing at the nose ...
3- Male	Survived	No nasal discharge ...
4- Male	Survived	No discomfort ...
5- Male	Survived	No weakness.
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.

The animals appeared unaffected by the vapors. They showed no discomfort during exposure. No inflammation of the ocular or nasal mucosae was detected when the animals were removed from the chamber.

The ten day observation period was uneventful.

PROJECT NO. Y-64-77
REPORT FILE

45

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

July 20th, 1964

SUBJECT -

Toxicological Investigation Of: FH - 159

Monsanto Sample Number 87

Monsanto Project Number Y-64-77

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 a modification of the method of Th 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.

GBRN002927

EXHIBIT
K-56

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 2 [illegible]

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits)

The undiluted compound was applied to the clipped, intact skin of albino 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)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino 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)

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 150 milliliters of the compound contained in a 250-milliliter tall form gas washing bottle with fritted disc. Vapors from the bottle passed into a one liter bottle to remove droplets and then into the chamber.

Air flow through the sample was 7 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 and, since there were no deaths, all were held for ten days observation.

The data are shown in Table V.

SUMMARY -

FR-159

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

The Oral LD_{50} for male and female rats was placed at 8900 milligrams per kilogram with lower and upper limits of 7850 to 10,145 milligrams per kilogram.

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

GBRN002928

Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 3 (7/20/64) - Y-64-77

SUMMARY - (Continued)

E) Skin Absorption MLD (Rabbits, Mixed Sex)

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1580 milligrams per kilogram and less than 2510 milligrams per kilogram.

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

C) Skin Irritation (Rabbits)

The compound was classed as a moderate skin irritant when applied undiluted to intact rabbit skin.

The average maximum score was 4.3 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits)

The compound was classed as a moderate eye irritant.

The average maximum score was 27.3 out of a possible 110 in one hour.

E) Vapor Inhalation (Male Rats)

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

BY: FRED M. YOUNGER

The material in this report is to be used in development of [illegible] meet in St. Louis for [illegible]

— Monsanto Chemical Co., U.S.A.

GBRN002929

TABLE I

THE ORAL LD_{50} OF 'FE-159' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Rate
1- Female	210	6,510	Survived
2- Female	215	6,510	Survived
3- Male	230	6,510	Survived
4- Male	220	6,510	Survived
5- Female	210	6,510	Survived
6- Female	205	7,940	Died
7- Male	235	7,940	Survived
8- Male	240	7,940	Survived
9- Female	220	7,940	Died
10- Female	215	7,940	Survived
11- Male	245	10,000	Survived
12- Male	250	10,000	Died
13- Female	225	10,000	Died
14- Female	215	10,000	Died
15- Male	240	10,000	Survived
16- Male	260	12,600	Died
17- Female	215	12,600	Died
18- Female	220	12,600	Died
19- Male	235	12,600	Died
20- Male	250	12,600	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 8,900 milligrams per kilogram with lower and upper limits of 7,850 to 10,145 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 with most deaths occurring in two to three days.

Toxic symptoms included severe diarrhea, increasing weakness, collapse, and coma of four to eight hours duration.

At autopsy there was inflammation of the gastric mucosa and renal hyperemia.

GBRN002930

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page [illegible] ([illegible]/54) - [illegible]

TABLE II

THE MINIMUM LETHAL DOSE OF 'FM-15?'

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	2.3	631	+ 0.2	Survived
2 - Male	2.5	1000	+ 0.2	Survived
3 - Female	2.2	1580	0.0	Survived
4 - Male	2.7	2510	-----	Died -- 2 Days
5 - Female	2.5	2510	-----	Died -- 3 Days
6 - Male	2.8	3980	-----	Died - Overnight

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1580 milligrams per kilogram and less than 2510 milligrams per kilogram.

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

Survival time was several hours to three days.

Toxic symptoms included increasing weakness, tremors, salivation, and collapse.

At autopsy there was pulmonary hyperemia and liver discoloration.

GBRN002931

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'FE - 159'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	2	4	[illegible]	2	1	0
2	[illegible]	[illegible]	[illegible]	2	2	0
3	2	4	2	2	1	0
Average	2.3	4.3	2.6	2.0	1.3	0.0

DISCUSSION -

The compound was classed as a moderate skin irritant when applied undiluted to intact rabbit skin.

The average maximum score was 4.3 out of a possible 8 in twenty-four hours.

After one hour there was well-defined redness with one instance of very slight edema. In twenty-four hours moderate redness and slight swelling increased the initial average score of 2.3 to 4.3. Inflammation gradually reduced following removal of the application. Barely perceptible to slight erythema present after five days disappeared within seven days.

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'FH-159'

Sample (0.1 Milliliter) Applied Undiluted

Animal Number	Numerical evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	1.0 Hours	168 Hours
1	23	18	11	6	0	0
2	31	21	17	12	4	0
3	28	21	15	9	4	0
Average	27.3	20.0	14.3	9.0	2.6	0.0

DISCUSSION -

The compound was classed as a moderate eye irritant.

The average maximum score was 27.3 out of a possible 110 in one hour.

Discomfort was moderate immediately following application.

Slight swelling and lacrimation, moderate redness of the conjunctivae, and mild iris congestion were noted in one hour. Discharge ceased overnight and iris clarity improved. A slight degree of redness that remained on two animals after five days disappeared within seven days.

TABLE V

INHALATION OF "FE-15" VAPORS BY RATS

Average Temperature Inside Chamber ..... 80° F.

Average Relative Humidity inside Chamber ..... 18 %

Amount of Sample -- To Start ..... 150 cc
Recovered ..... 145 cc
Vaporized or Left In Equipment .. 5 cc (3%.

Animal No. - Sex	Fate	Observations During Exposure
1- Male	Survived	No nasal discharge ...
2- Male	Survived	No blinking ...
3- Male	Survived	Normal breathing ...
4- Male	Survived	Some activity ...
5- Male	Survived	Slight discomfort after four hours.
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.

The vapors had little or no effect upon the animals insofar as outward appearances revealed. Ocular and nasal mucosae were not inflamed when the animals were removed from the chamber and respiration was normal.

Activity and appetite returned quickly.

The ten day observation period was uneventful.

YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

August 11th, 1964

SUBJECT -

Toxicological Investigation Of: Hydraul 280

Monsanto Sample Number 102

Monsanto Project Number Y-64-91

Y-64-91
8/11/64

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 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.

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits)

The undiluted compound was applied to the clipped, intact skin of albino 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 Draise, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Rabbits)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino 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 - 350° F. (Male Rats)

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 150-milliliters of the compound contained in a 300-milliliter Erlenmeyer flask placed in a sand bath on a hot plate and the contents maintained at a temperature of 350° F.

Vapors from the flask passed into a train of two one-liter bottles to remove droplets and then into the chamber.

Air flow through the sample was five 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 and, since there were no deaths, all were held for ten days observation.

The data are shown in Table V.

SUMMARY -

Pydraul 280

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

The Oral LD_{50} for male and female rats was placed at 11,750 milligrams per kilogram with lower and upper limits of 9,570 to 14,390 milligrams per kilogram.

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

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 3 (8/11/64) - Y-64-91

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)

The compound was classed as a moderate skin irritant.

The average maximum score was 3.3 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits)

The compound was classed as a moderate eye irritant.

The average maximum score was 31.3 out of a possible 110 in twenty-four hours.

E) Vapor Inhalation - 350° F. (Male Rats)

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

It was concluded that the vapors were mildly toxic under conditions of the test.

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 [illegible] may [illegible] ment in St. Louis [illegible] toxicity are to be referred as before to the Medical Department in St. Louis for reply.

Monsanto Chemical Company

GBRN002937

LEXOLDMON002334

T A B L E 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	7,940	Survived
2- Female	230	7,940	Survived
3- Male	245	7,940	Survived
4- Male	235	7,940	Died
5- Female	225	7,940	Survived
6- Female	230	10,000	Survived
7- Male	250	10,000	Survived
8- Male	245	10,000	Survived
9- Female	215	10,000	Survived
10- Female	235	10,000	Died
11- Male	250	12,600	Survived
12- Male	260	12,600	Died
13- Female	225	12,600	Died
14- Female	210	12,600	Died
15- Male	240	12,600	Survived
16- Male	235	15,800	Died
17- Female	220	15,800	Died
18- Female	225	15,800	Died
19- Male	240	15,800	Survived
20- Male	250	15,800	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 11,750 milligrams per kilogram with lower and upper limits of 9,570 to 14,390 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 six days with most deaths occurring in three to four days.

Toxic symptoms included loss of appetite, severe diarrhea, increasing weakness, and collapse.

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

T A B L E II

THE MINIMUM LETHAL DOSE OF 'Pydraul 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	2.7	1,260	- 0.1	Survived
2 - Female	2.3	2,000	- 0.2	Died -- 8 Days
3 - Male	3.0	3,160	- 0.4	Died -- 7 Days
4 - Female	2.4	5,010	- 0.3	Died -- 8 Days
5 - Male	2.6	7,940	- 0.4	Died -- 5 Days
6 - Female	2.8	12,600	- 0.5	Died -- 7 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 eight days.

Toxic symptoms included reduced appetite, weakness in two to three days, and muscular impairment particularly noticeable in the neck muscles causing the head to droop.

At autopsy there was liver discoloration and pulmonary hyperemia macroscopically.

T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'Pydraul 280'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	1	3	2	2	0	0
2	1	3	3	2	1	0
3	2	4	3	2	1	0
Average	1.3	3.3	2.6	2.0	0.6	0.0

DISCUSSION -

The compound was classed as a moderate skin irritant.

The average maximum score was 3.3 out of a possible 8 in twenty-four hours.

After one hour there was barely perceptible to well-defined redness with no edema. Well-defined to moderate erythema with very slight edema in twenty-four hours produced an average score of 3.3. Following removal of the compound the average score reduced to 0.6 in five days at which time barely perceptible erythema was still present on two animals.

T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'Pydraul 280'

Sample (0.1 Milliliter) Applied Undiluted

Animal Number	Numerical Evaluation At The End Of					
	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	35	29	21	15	9	4
2	33	25	18	11	4	2
3	26	19	12	8	4	0
Average	31.3	24.3	17.0	11.3	5.6	2.0

DISCUSSION -

The compound was classed as a moderate eye irritant.

The average maximum score was 31.3 out of a possible 110 in twenty-four hours.

Considerable discomfort developed following administration.

Slight edema and discharge, moderate erythema of the palpebral conjunctivae, and mild iris congestion and corneal dullness were noted within an hour. Edema and discharge disappeared overnight. Improvement continued following irrigation leading to an average score of 2.0 in seven days.

TABLE V

INHALATION OF 'Pydraul 280' VAPORS BY RATS
(350° F.)

Average Temperature Inside Chamber ..... 79° F.

Average Relative Humidity Inside Chamber ..... 53 %

Amount Of Sample -- To Start ..... 150.0 cc
Recovered ..... 132.0 cc
Vaporized or left in apparatus ..... 7.5 cc (5%)

Condensate in 1st liter bottle ..... 10.5 cc
Condensate in 2nd liter bottle ..... 0.0 cc

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Moderate discomfort in thirty minutes ..
2 - Male	Survived	
3 - Male	Survived	Occasional irregular breathing ..
4 - Male	Survived	Moderate nasal discharge ...
5 - Male	Survived	
6 - Male	Survived	Some weakness but no danger of collapse.

DISCUSSION -

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

It was concluded that the vapors were mildly toxic under conditions of the test.

A temperature of 350° F. was reached in approximately twenty minutes. The blue color changed to pale green and gradually turned to light brown in four hours. A moderate degree of haze was present in the chamber throughout the test. Discomfort increased with time. Moderately severe inflammation of nasal and ocular mucosae was noted when the animals were removed. All had a mild degree of bronchial rales. There was no gasping but breathing was somewhat difficult.

Inflammation reduced in twenty-four hours and within three to four days breathing was nearly normal. The animals appeared in good condition at the end of the ten day observation period.

PROJECT NO. Y-64-133
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

November 12th, 1964

SUBJECT - PYDRAUL 312

Toxicological Investigation Of: MCS 312

Monsanto Sample Number 146

Monsanto Project Number Y-64-133

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 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.

GBRN002943

EXHIBIT
K-58

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits)

The undiluted compound was applied to the clipped, intact skin of albino 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)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino 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)

Four 150-gram male rats were placed in a glass desiccator, 250 mm in diameter, and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 100 milliliters of the compound contained in a 250-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 five 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 and, since there were no deaths, all were held for ten days observation.

The data are shown in Table V.

SUMMARY -

MCS 312

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

The Oral LD_{50} for male and female rats was placed at 6500 milligrams per kilogram with lower and upper limits of 5460 to 7735 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.

SUMMARY - (Continued)

C) Skin Irritation (Rabbits)

The compound was classed as a slight skin irritant when applied undiluted to intact rabbit skins.

The average maximum score was 1.3 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits)

The compound was classed as a slight eye irritant.

The average maximum score was 13.0 out of a possible 110 in twenty-four hours.

E) Vapor Inhalation (Male Rats)

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

Fred M. Younger

BY: FRED M. YOUNGER

TABLE I

THE ORAL LD_{50} OF 'MCS 312' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Rate
1- Female	195	5,010	Survived
2- Female	210	5,010	Died
3- Male	230	5,010	Survived
4- Male	225	5,010	Survived
5- Female	220	5,010	Survived
6- Female	210	6,310	Died
7- Male	240	6,310	Survived
8- Male	230	6,310	Survived
9- Female	205	6,310	Died
10- Female	215	6,310	Survived
11- Male	250	7,940	Survived
12- Male	230	7,940	Died
13- Female	215	7,940	Died
14- Female	225	7,940	Died
15- Male	245	7,940	Survived
16- Male	230	10,000	Died
17- Female	210	10,000	Died
18- Female	225	10,000	Died
19- Male	240	10,000	Died
20- Male	250	10,000	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 6500 milligrams per kilogram with lower and upper limits of 5460 to 7735 Milligrams per kilogram.

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

Survival time was one to four days with most deaths occurring in two days.

Toxic symptoms included severe diarrhea, tremors, dyspnea, and collapse.

At autopsy there was inflammation of the gastric mucosa and renal hyperemia macroscopically.

TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS 312' 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	2.7	794	+ 0.1	Survived
2 - Female	3.1	1260	- 0.1	Survived
3 - Male	2.8	2000	- 0.3	Survived
4 - Female	2.7	3160	- 0.4	Died -- 6 Days
5 - Male	2.6	5010	- 0.4	Died -- 6 Days
6 - Female	2.8	7940	-----	Died -- 4 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 four to six days.

Toxic symptoms included gradual loss of appetite, increasing weakness, and tremors. Violent convulsions and squealing were noted approximately twenty-four hours before death.

At autopsy there were hemorrhagic areas in the lungs as well as liver discoloration and renal congestion macroscopically.

T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS 312'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1	0	1	1	0	0
2	0	2	1	1	0
3	0	1	0	0	0
Average	0.0	1.3	0.6	0.3	0.0

DISCUSSION -

The compound was classed as a slight skin irritant when applied undiluted to intact rabbit skin.

The average maximum score was 1.3 out of a possible 8 in twenty-four hours.

No skin changes were noted in one hour. Overnight there was barely perceptible redness on two animals and well-defined redness on the third animal for an average score of 1.3. No edema developed. Within seventy-two hours two animals were free of color and all received a score of zero in five days.

TABLE V

INHALATION OF 'MCB 312' VAPORS BY RATS

Average Temperature Inside Chamber ..... 78° F.

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

Amount Of Sample -- To Start ..... 100.0 cc
Recovered ..... 99.5 cc
Vaporized ..... 0.5 cc (0.5%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No nasal discharge ...
2 - Male	Survived	No dyspnea ...
3 - Male	Survived	Mild lethargy ...
4 - Male	Survived	No weakness or discomfort ...
		Animals appear unaffected.

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.

As mentioned in the table, the animals appeared to be unaffected by the six hour exposure. Discomfort was at a minimum and the only change in behavior was mild lethargy after approximately one hour.

The ten day observation period was uneventful.

PROJECT NO. Y-65-213
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

January 10th, 1966

SUBJECT - PYDRAUL 135

Toxicological Investigation Of: MCS 395

Monsanto Sample Number 244

Monsanto Project Number Y-65-213

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 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) Oral MLD (Rabbits, Mixed Sex)

The undiluted compound was fed in increasing doses at increments of 0.2 fractional log intervals by stomach tube to New Zealand white male and female rabbits.

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

The data are shown in Table II.

EXHIBIT
K-59

GBRN002951

EXPERIMENTAL PROCEDURE - (Continued)

C) 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 III.

D) Skin Irritation (Rabbits, Mixed Sex)

The undiluted compound was applied to the clipped, intact skin of male and female albino 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 IV.

E) Eye Irritation (Rabbits, Mixed Sex)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of three albino 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 V.

F) Vapor Inhalation (Male Rats)

Four 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 100 milliliters of the compound contained in a 300 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 five 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 and, since there were no deaths, all were held for ten days observation.

The data are shown in Table VI.

SUMMARY -

MCS 395

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

The Oral LD_{50} for male and female rats was placed at 4615 milligrams per kilogram with lower and upper limits of 4060 to 5260 milligrams per kilogram.

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

B) Oral MLD (Rabbits, Mixed Sex)

The Minimum Lethal Oral Dose for male and female rabbits was found to be greater than 1580 milligrams per kilogram and less than 2510 milligrams per kilogram.

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

C) Skin Absorption MLD (Rabbits, Mixed Sex)

The Minimum Lethal Dose by skin absorption in male and female rabbits was found to be greater than 2510 milligrams per kilogram and less than 3980 milligrams per kilogram.

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

D) Skin Irritation (Rabbits, Mixed Sex)

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

E) Eye Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 8.3 out of a possible 110 in one hour.

F) Vapor Inhalation (Male Rats)

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

Fred M. Younger

BY: FRED M. YOUNGER

GBRN002953

TABLE I

THE ORAL LD_{50} OF 'MCS 395' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	225	3160	Survived
2- Male	240	3160	Survived
3- Female	220	3160	Survived
4- Male	255	3160	Survived
5- Female	235	3160	Survived
6- Male	260	3980	Survived
7- Female	230	3980	Died
8- Male	270	3980	Survived
9- Female	235	3980	Survived
10- Male	255	3980	Survived
11- Female	230	5010	Died
12- Male	255	5010	Survived
13- Female	225	5010	Died
14- Male	265	5010	Survived
15- Female	235	5010	Died
16- Male	280	6310	Died
17- Female	225	6310	Died
18- Male	245	6310	Died
19- Female	240	6310	Died
20- Male	265	6310	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 4615 milligrams per kilogram with lower and upper limits of 4060 to 5260 milligrams per kilogram.

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

Survival time was several hours to three days with most deaths occurring overnight. Toxic symptoms included severe diarrhea, increasing weakness, tremors, and collapse.

At autopsy there was inflammation of the gastric mucosa and renal hyperemia macroscopically.

TABLE II

THE MINIMUM LETHAL ORAL DOSE OF 'MCS 395' FOR RABBITS

Sample Fed Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.6	631	0.0	Survived
2 - Male	3.0	1000	+ 0.1	Survived
3 - Female	2.7	1580	- 0.1	Survived
4 - Male	3.1	2510	- 0.4	Died -- 8 Days
5 - Female	2.7	3980	- 0.3	Died -- 5 Days
6 - Male	2.9	6310	-----	Died -- 2 Days

DISCUSSION -

The Minimum Lethal Oral Dose for male and female rabbits was found to be greater than 1580 milligrams per kilogram and less than 2510 milligrams per kilogram.

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

Survival time was two to eight days.

Toxic symptoms in animals #4 and #5 included poor appetite in two to three days, weight loss, increasing weakness, tremors, and collapse.

At autopsy there was evidence of liver dysfunction and renal hyperemia.

T A B L E III

THE MINIMUM LETHAL DOSE OF 'M C S 395' 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	3.0	631	+ 0.2	Survived
2 - Female	2.5	1000	+ 0.1	Survived
3 - Male	2.8	1580	+ 0.1	Survived
4 - Female	2.4	2510	- 0.1	Survived
5 - Male	2.5	3980	- 0.3	Died - 7 Days
6 - Female	3.1	6310	- 0.2	Died - 9 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 2510 milligrams per kilogram and less than 3980 milligrams per kilogram.

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

Survival time was seven to nine days.

Toxic symptoms in animals #5 and #6 included reduced appetite and activity in three to four days with increasing weakness, dyspnea, and paralysis.

At autopsy the lungs were hemorrhagic and there was liver discoloration macroscopically.

T A B L E IV

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'M C S 395'

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1 - Female	0	0	0	0	0
2 - Male	0	0	0	0	0
3 - Female	0	0	0	0	0

DISCUSSION -

The compound was classed as non-irritating to intact rabbit skin when applied undiluted.

No edema or erythema developed on any of the animals as a result of a twenty-four hour exposure to the undiluted compound.

All animals received a score of zero throughout the observation period.

TABLE V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS 395'

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
1 - Female	7	4	2	0	0
2 - Male	7	4	4	0	0
3 - Female	11	6	4	2	0
Average	8.3	4.6	3.3	0.6	0.0

DISCUSSION -

The compound was classed as a slight eye irritant in male and female rabbits. The average maximum score was 8.3 out of a possible 110 in one hour.

Little discomfort was shown immediately following application.

After one hour there was slight discharge and redness, practically no edema, and very slight corneal dullness. Iris and cornea were clear in twenty-four hours and within three days only a trace of redness of the palpebral conjunctivae remained on one animal.

T A B L E VI

INHALATION OF 'M C S 395' VAPORS BY RATS

Average Temperature Inside Chamber ..... 76° F.

Average Relative Humidity Inside Chamber ..... 43 %

Amount of Sample -- To Start ..... 100.0 cc
Recovered ..... 99.7 cc
Vaporized or left in equipment ..... 0.3 cc (0.3%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No immediate reaction ...
2 - Male	Survived	Normal breathing rate ...
3 - Male	Survived	No discomfort or nasal discharge ...
4 - Male	Survived	No weakness ...
		Moderate lethargy after two hours.

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.

The animals appeared to be unaffected by the exposure. Nasal and ocular mucosae were normal when the animals were removed from the chamber.
The ten day observation period was uneventful.

PROJECT NO: Y-66-151
REPORT FILE

741

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

October 17th, 1966

SUBJECT -

Toxicological Investigation Of: MCS 90

Monsanto Sample Number 176

Monsanto Project Number Y-66-151

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 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.

GBRN002960

EXHIBIT K-60

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)

Four 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 100 milliliters of the compound contained in a 250-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 and since there were no deaths, all were held for ten days observation.

The data are shown in Table V.

SUMMARY -

MCS 90

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

The Oral LD_{50} for male and female rats was placed at 3260 milligrams per kilogram with lower and upper limits of 2740 to 3880 milligrams per kilogram.

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

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 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.

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 1.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 28.0 out of a possible 110 in one hour.

E) Vapor Inhalation (Male Rats)

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

BY: FRED M. YOUNGER

TABLE I

THE ORAL LD_{50} OF 'MCS 90' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	215	2510	Survived
2- Male	245	2510	Survived
3- Female	230	2510	Died
4- Male	255	2510	Survived
5- Female	210	2510	Survived
6- Male	255	3160	Survived
7- Female	220	3160	Died
8- Male	245	3160	Survived
9- Female	225	3160	Died
10- Male	265	3160	Survived
11- Female	215	3980	Survived
12- Male	250	3980	Died
13- Female	230	3980	Died
14- Male	245	3980	Survived
15- Female	220	3980	Died
16- Male	240	5010	Died
17- Female	235	5010	Died
18- Male	255	5010	Died
19- Female	225	5010	Died
20- Male	260	5010	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 3260 milligrams per kilogram with lower and upper limits of 2740 to 3880 milligrams per kilogram.

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

Survival time was several hours to four days with most deaths occurring in two days.

Toxic symptoms included weakness in two to three hours followed by tremors, dyspnea, and coma lasting for several hours.

At autopsy there were hemorrhagic areas in the lungs and renal congestion macroscopically.

T A B L E II

THE MINIMUM LETHAL DOSE OF 'M C S 90'
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	2.3	794	+ 0.2	Survived
3 - Male	2.9	1260	0.0	Survived
4 - Female	2.5	2000	- 0.2	Survived
5 - Male	2.8	3160	- 0.4	Died -- 6 Days
6 - Female	2.6	5010	-----	Died -- 2 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 two to six days.

Toxic symptoms included weakness in twenty-four to forty-eight hours, loss of appetite, and tremors.

At autopsy there was pulmonary congestion; otherwise no visceral changes of consequence were noted macroscopically.

T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'M C S 90'

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1 - Male	0	1	1	0	0
2 - Female	0	2	1	1	0
3 - Male	0	2	2	1	0
Average	0.0	1.6	1.3	0.6	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 1.6 out of a possible 8 in twenty-four hours.

No skin changes were noted at the end of one hour. Slight redness on all animals and two instances of slight edema were recorded in twenty-four hours. One animal was given a score of zero in three days and all were free of inflammation within five days.

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 7 (10/17/66) - Y-66-151

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS 90'

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	29	20	13	9	4	0
2 - Female	24	17	9	4	0	0
3 - Male	31	24	15	9	4	0
Average	28.0	20.3	12.3	7.3	2.6	0.0

DISCUSSION -

The compound was classed as a moderate eye irritant in male and female rabbits. The average maximum score was 28.0 out of a possible 110 in one hour.

There was blinking but no pawing at the eyes following application.

Moderate erythema, edema with mild eversion of the lids, copious lacrimation, and moderate corneal cloudiness developed within one hour. Discharge nearly ceased overnight and iris clarity improved. Edema disappeared within three days and only slight erythema remained on two animals after five days.

TABLE V

Average Temperature Inside Chamber . . . . . 77° F.
Average Relative Humidity Inside Chamber . . . . . 51 %

Amount of Sample -- To start ..... 100.0 cc
Recovered ..... 99.9 cc
Vaporized or left
in equipment ..... 0.1 cc (0.1%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No initial effect ...
2 - Male	Survived	Normal respiration ...
3 - Male	Survived	No discomfort ...
4 - Male	Survived	No nasal or ocular inflammation ... Moderate lethargy.

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.

The animals appeared to be relatively unaffected during exposure. The eyes remained open and respiration was normal. Nasal mucosae were free of inflammation when examined upon removal of the animals from the chamber.

No respiratory complications developed during the ten day observation period.

YOUNGER LABORATORIES

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128 CLIFF CAVE ROAD
SAINT LOUIS, MO., 63129

PHONE: TILDEN 6-2540

Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: PYDRAUL F-9

Monsanto Sample Number 184

Monsanto Project Number Y-66-159

11/9/66 Y-66-159

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 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.

GBRN002968

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 2 (11/9/66) - Y-66-159

SUMMARY -

PYDRAUL F-9

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

The Oral LD_{50} for male and female rats was placed at 11,200 milligrams per kilogram with lower and upper limits of 9,855 to 12,770 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 501 milligrams per kilogram and less than 794 milligrams per kilogram.

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

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

TABLE I

THE ORAL LD_{50} OF 'HYDRAUL F-9' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	215	7,940	Survived
2- Male	260	7,940	Survived
3- Female	225	7,940	Survived
4- Male	240	7,940	Survived
5- Female	230	7,940	Survived
6- Male	245	10,000	Survived
7- Female	220	10,000	Died
8- Male	255	10,000	Survived
9- Female	215	10,000	Died
10- Male	250	10,000	Survived
11- Female	230	12,600	Died
12- Male	245	12,600	Died
13- Female	220	12,600	Survived
14- Male	260	12,600	Survived
15- Female	225	12,600	Died
16- Male	270	15,800	Died
17- Female	230	15,800	Died
18- Male	245	15,800	Died
19- Female	225	15,800	Died
20- Male	240	15,800	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 11,200 milligrams per kilogram with lower and upper limits of 9,855 to 12,770 milligrams per kilogram.

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

Survival time was two to five days.

Toxic symptoms included weakness after several hours, diarrhea, loss of appetite, tremors, and dyspnea.

At autopsy there was renal and liver hyperemia by macroscopic examination.

T A B L E II

THE MINIMUM LETHAL DOSE OF 'HYDRAUL F-9'
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	2.3	316	0.0	Survived
2 - Male	2.6	501	- 0.2	Survived
3 - Female	2.4	794	- 0.3	Died -- 7 Days
4 - Male	2.8	1260	- 0.3	Died -- 7 Days
5 - Female	2.4	2000	- 0.2	Died -- 6 Days
6 - Male	2.6	3160	- 0.4	Died -- 5 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 501 milligrams per kilogram and less than 794 milligrams per kilogram.

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

Survival time was five to seven days.

Toxic symptoms included loss of appetite, lethargy, and noticeable weakness in two to three days.

At autopsy there was pulmonary hyperemia; otherwise no visceral changes of consequence were noted macroscopically.

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123 CLIFF CAVE ROAD
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Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: HYDRAUL 280

Monsanto Sample Number 186

Monsanto Project Number Y-66-161

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 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.

GBRN002980

EXHIBIT
K-64

SUMMARY -

HYDRAUL 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 10,360 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

T A B L E I

THE ORAL LD_{50} OF 'HYDRAUL 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 kilogra 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 hyperem

T A B L E II

THE MINIMUM LETHAL DOSE OF 'PYDRAUL 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.

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Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: HYDRAUL 135
Monsanto Sample Number 185
Monsanto Project Number Y-66-160

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 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.

GBRN002984

EXHIBIT
K-65

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

TABLE I

THE ORAL LD_{50} OF 'PYDRAUL 135' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
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	3930	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 r

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.

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Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: HYDRAUL A C

Monsanto Sample Number 183

Monsanto Project Number Y-66-158

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 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.

SUMMARY -

PYDRAUL A C

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

The Oral LD_{50} for male and female rats was placed at 18,920 milligrams per kilogram with lower and upper limits of 16,270 to 21,950 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 794 milligrams per kilogram and less than 1260 milligrams per kilogram.

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

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

TABLE I

THE ORAL LD_{50} OF 'HYDRAUL AC' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	215	12,600	Survived
2- Male	250	12,600	Survived
3- Female	225	12,600	Survived
4- Male	260	12,600	Survived
5- Female	220	12,600	Survived
6- Male	250	15,800	Survived
7- Female	235	15,800	Survived
8- Male	255	15,800	Survived
9- Female	215	15,800	Died
10 - Male	260	15,800	Survived
11- Female	225	20,000	Died
12- Male	245	20,000	Survived
13- Female	220	20,000	Died
14- Male	260	20,000	Survived
15- Female	210	20,000	Survived
16- Male	235	25,100	Died
17- Female	220	25,100	Died
18- Male	250	25,100	Died
19- Female	230	25,100	Died
20- Male	265	25,100	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 18,920 milligrams per kilogram with lower and upper limits of 16,270 to 21,950 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 nine days with most deaths occurring in three to five days.

Toxic symptoms included severe diarrhea, loss of appetite, tremors, and increasing weakness.

At autopsy the gastrointestinal tract was gaseous and inflamed. Liver discoloration and renal congestion were also noted.

T A B L E II

THE MINIMUM LETHAL DOSE OF 'HYDRAUL A C'
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	0.0	Survived
3 - Male	3.1	1260	- 0.2	Died — 9 Days
4 - Female	2.6	2000	- 0.3	Died - 10 Days
5 - Male	2.8	3160	- 0.4	Died — 5 Days
6 - Female	2.5	5010	- 0.2	Died — 6 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 794 milligrams per kilogram and less than 1260 milligrams per kilogram.

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

Survival time was five to ten days.

Toxic symptoms included reduced activity and weakness in two to three days followed by paralysis in animals #3 through #6 inclusive.

At autopsy there were hemorrhagic areas in the lungs and liver hyperemia.