YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

5620 TELEGRAPH ROAD
ST. LOUIS 29, MISSOURI
PHONE: TILDEN 6-2540

Certificate of Analysis

July 9th, 1962

C+25AM

SUBJECT -

Toxicological Investigation Of: Aroclor 1268

Monsanto Sample Number 44
Monsanto Project Number Y-62-42

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

COPY

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats)

The diluted compound was fed by stomach tube to Sprague-Dawley strain albino 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 D. J. de Beer.

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

The data, together with the dilution at which the compound was fed, are shown in Table I.

B) Skin Absorption MLD (Rabbits)

The diluted compound was applied in increasing doses at increments of 0.1 fractional log intervals to the closely clipped, intact skin of New Zealand white female rabbits.

The treated areas were covered with plastic strips and the animals placed in wooden stocks for periods up to twentyfour hours, after which time they were assigned to individual cages.

Observations were made for toxic symptoms and since there were no deaths, no autopsies were performed.

The data, together with the dilution at which the compound was applied, are shown in Table II.

GBRN002788

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EXHIBIT
K-34

SUMMARY -

Aroclor 1268

A) Oral LD_{50} (Rats)

The Oral LD_{50} for male and female rats was placed at 10,900 milligrams per kilogram with lower and upper limits of 9,590 to 12,320 milligrams per kilogram.

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

B) Skin Absorption MLD (Rabbits)

The highest application of 2510 milligrams per kilogram was found to be non-lethal by skin absorption in female rabbits.

No higher dose was applied due to poor solubility of the compound in corn oil.

The compound was classed as not more than slightly toxic by skin absorption in female rabbits.

YOUNGER LABORATORIES

Fred M. Younger

BY: FRED M. YOUNGER

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— Monsanto Chemical Company

TABLE I

THE ORAL LD_{50} OF 'Aroclor 1268' FOR RATS

Sample Fed As A 50.0% Solution-Suspension In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	195	7,940	Survived
2- Female	205	7,940	Survived
3- Female	215	7,940	Died
4- Male	230	7,940	Survived
5- Male	220	7,940	Survived
6- Male	245	10,000	Died
7- Female	200	10,000	Survived
8- Female	210	10,000	Survived
9- Female	210	10,000	Died
10- Male	235	10,000	Survived
11- Male	255	12,600	Died
12- Male	220	12,600	Survived
13- Female	210	12,600	Died
14- Female	215	12,600	Died
15- Female	195	12,600	Died
16- Male	240	15,800	Died
17- Male	235	15,800	Died
18- Male	220	15,800	Died
19- Female	210	15,800	Died
20- Male	230	15,800	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 10,900 milligrams per kilogram with lower and upper limits of 9,590 to 12,320 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 with most deaths occurring in two days.

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

At autopsy there was inflammation of the gastric mucosa, liver discoloration, and pulmonary hyperemia macroscopically.

LEXOLDMON002187

T A B L E II

THE MINIMUM LETHAL DOSE OF 'Aroclor 1268' BY SKIN ABSORPTION IN RABBITS

Sample Applied as a 10.0% Solution-Suspension In Corn Oil

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 4 Days Later Kg.	Fate
1 - Female	2.5	794	0.0	Survived
2 - Female	2.3	1000	+ 0.1	Survived
3 - Female	2.6	1260	0.0	Survived
4 - Female	2.4	1580	- 0.1	Survived
5 - Female	2.5	2000	- 0.2	Survived
6 - Female	2.4	2510	- 0.2	Survived

Note: The compound was applied to animals #4, #5, and #6 over a period of three days to avoid run-off.

DISCUSSION -

The highest application of 2510 milligrams per kilogram was found to be non-lethal by skin absorption in female rabbits.

The compound was classed as not more than slightly toxic by skin absorption in female rabbits.

No higher dose was applied due to poor solubility of the compound in corn oil.

There was lethargy and reduced appetite for several days at the higher dosage levels but no real symptoms of systemic toxicity were observed.

LEXOLDMON002188

PROJECT NO. Y-62-43
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

5620 TELEGRAPH ROAD
ST. LOUIS 29, MISSOURI

PHONE: TILDEN 6-2340

Certificate of Analysis

July 17th, 1962

SUBJECT -

Toxicological Investigation Of: Aroclor 2565

Monsanto Sample Number 45
Monsanto Project Number Y-62-43

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats)

The diluted compound was fed by stomach tube to Sprague-Dawley strain albino 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, together with the dilution at which the compound was fed, are shown in Table I.

B) Skin Absorption MLD (Rabbits)

The diluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white 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, together with the dilution at which the compound was applied, are shown in Table II.

GBRN002792

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EXHIBIT
K-35

SUMMARY -

Aroclor 2565

A) Oral LD_{50} (Rats)

The Oral LD_{50} for male and female rats was placed at 6310 milligrams per kilogram with lower and upper limits of 5,360 to 7,420 milligrams per kilogram.

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

B) Skin Absorption MLD (Rabbits)

The Minimum Lethal Dose by Skin Absorption in 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 female rabbits.

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

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— Monsanto Chemical Company

TABLE I

THE ORAL LD_{50} OF 'Aroclor 2565' FOR RATS

Sample Fed As A 20.0% Solution In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	195	5,010	Survived
2- Female	210	5,010	Died
3- Female	215	5,010	Survived
4- Male	230	5,010	Survived
5- Male	220	5,010	Survived
6- Male	240	6,310	Survived
7- Female	215	6,310	Died
8- Female	230	6,310	Survived
9- Female	210	6,310	Survived
10- Male	240	6,310	Died
11- Male	225	7,940	Died
12- Male	250	7,940	Survived
13- Female	210	7,940	Died
14- Female	215	7,940	Died
15- Female	225	7,940	Died
16- Male	235	10,000	Died
17- Male	240	10,000	Died
18- Male	230	10,000	Died
19- Female	230	10,000	Died
20- Female	215	10,000	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 6310 milligrams per kilogram with lower and upper limits of 5360 to 7420 milligrams per kilogram.

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

Survival time was two to six days with most deaths occurring in three days.

Toxic symptoms included weight loss, increasing weakness, dyspnea, and salivation.

At autopsy there was inflammation of the gastric mucosa and liver congestion macroscopically.

GBRN002794

LEXOLDMON002191

T A B L E II

THE MINIMUM LETHAL DOSE OF 'Aroclor 2565' BY SKIN ABSORPTION IN RABBITS

Sample Applied As A 20.0% Solution In Corn Oil

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.3	794	0.0	Survived
2 - Female	2.1	1260	0.0	Survived
3 - Female	2.5	2000	- 0.2	Survived
4 - Female	2.3	2000	- 0.1	Survived
5 - Female	2.5	3160	- 0.2	Died - 14 Days
6 - Female	2.4	5010	- 0.3	Died - 8 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in 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 female rabbits.

Survival time was eight to fourteen days.

Toxic symptoms included weakness in animals #5 and #6 after several days, reduced appetite, lethargy, and weight loss.

At autopsy there was liver discoloration and pulmonary hyperemia macroscopically.

LEXOLDMON002192

PROJECT NO. Y-63-12
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

123 CLIFF CAVE ROAD
ST. LOUIS 29, MISSOURI

PHONE: TILDEN 6-2540

Certificate of Analysis

March 4th, 1963

SUBJECT - AROCLOR

Toxicological Investigation Of: Inerteen PPO

Monsanto Sample Number 22

Monsanto Project Number Y-63-12

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats)

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino 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)

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 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.

EXHIBIT
K-36

GBRN002796

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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.

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 (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 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 6 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 -

Inerteen PFO

A) Oral LD_{50} (Rats)

The Oral LD_{50} for male and female rats was placed at 2370 milligrams per kilogram with lower and upper limits of 2095 to 2690 milligrams per kilogram.

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

B) Skin Absorption MLD (Rabbits)

The Minimum Lethal Dose by Skin Absorption in female rabbits was found to be greater than 3160 milligrams per kilogram and less than 5010 milligrams per kilogram.

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

LEXOLDMON002194

SUMMARY - (Continued)

C) Skin Irritation (Rabbits)

The compound was classed as a moderate skin irritant.

The average maximum score was 4.6 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 35.6 out of a possible 110 in one hour.

E) Vapor Inhalation (Rats)

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

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

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

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= Monsanto Chemical Company

LEXOLDMON002195

TABLE I

THE ORAL LD_{50} OF 'Inerteen PPO' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	220	1580	Survived
2- Female	210	1580	Survived
3- Male	235	1580	Survived
4- Male	240	1580	Survived
5- Female	215	1580	Survived
6- Female	225	2000	Survived
7- Male	245	2000	Survived
8- Male	240	2000	Died
9- Female	210	2000	Died
10- Female	220	2000	Survived
11- Male	235	2510	Died
12- Male	245	2510	Survived
13- Female	205	2510	Died
14- Female	215	2510	Died
15- Male	250	2510	Survived
16- Male	235	3160	Died
17- Female	210	3160	Died
18- Female	220	3160	Died
19- Male	235	3160	Survived
20- Male	245	3160	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 2370 milligrams per kilogram with lower and upper limits of 2095 to 2690 milligrams per kilogram.

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

Survival time was approximately twenty-four hours to six days with most deaths occurring in three to five days.

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

At autopsy there was marked liver and renal hyperemia as well as pulmonary congestion.

LEXOLDMON002196

T A B L E II

THE MINIMUM LETHAL DOSE OF 'Inerteen PPO' 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	794	+ 0.2	Survived
2 - Female	2.1	1260	0.0	Survived
3 - Female	2.4	2000	0.0	Survived
4 - Female	2.3	3160	- 0.1	Survived
5 - Female	2.5	5010	- 0.4	Died -- 5 Days
6 - Female	2.7	7940	- 0.6	Died -- 6 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in female rabbits was found to be greater than 3160 milligrams per kilogram and less than 5010 milligrams per kilogram.

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

Survival time was five to six days.

The animals that succumbed lost appetite and wasted away. Movement reduced as the animals weakened but no definite paralytic symptoms were observed.

At autopsy the liver had a jaundiced-like appearance and there was pulmonary hyperemia macroscopically.

LEXOLDMON002197

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'Inerteen PPO'

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	4	3	2	1
2	3	5	4	2	2	1
3	3	5	5	4	2	1
Average	2.6	4.6	4.3	3.0	2.0	1.0

DISCUSSION -

The compound was classed as a moderate skin irritant.

The average maximum score was 4.6 out of a possible 8 in twenty-four hours.

After one hour there was well-defined erythema with barely perceptible swelling for an average score of 2.6 out of a possible 8. Inflammation increased overnight at which time the average score was 4.6 based upon moderate redness and slight edema. Daily improvement was noted after the application was removed. Irritation reduced to barely perceptible erythema on all animals within seven days.

LEXOLDMON002198

T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'Inerteen PPO'

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	37	30	21	15	8	4
2	29	21	15	9	4	0
3	41	30	19	12	6	0
Average	35.6	27.0	18.3	12.0	6.0	1.3

DISCUSSION -

The compound was classed as a moderate eye irritant.

The average maximum score was 35.6 out of a possible 110 in one hour.

Moderate discomfort was shown following application.

Within one hour there was mild edema, copious discharge, mild to moderate redness of the conjunctivae, and slight iris congestion and corneal dullness for an average score of 35.6 out of a possible 110. Discharge and cloudiness decreased overnight. Iris clarity was normal within five days and within seven days two of three animals were free of inflammation.

LEXOLDMON002199

TABLE V

INHALATION OF 'Inerteen PPO' VAPORS BY RATS

Average Temperature Inside Chamber	76° F.
Average Relative Humidity Inside Chamber	47 %

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Mild eye and nasal irritation after twenty to thirty minutes ...
2 - Male	Survived	Moderate discomfort ...
3 - Male	Survived	Lethargy ...
4 - Male	Survived	Occasional moderate dyspnea ...
		No serious weakness ...
		Slight nasal discharge.

DISCUSSION -

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

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

Mild inflammation of the nasal musoca was evident when the animals were removed from the chamber. Breathing was slightly irregular but no rasping sound was detected and the animals were only mildly weakened. Animal behavior was practically normal, in forty-eight hours. No respiratory complications developed during the ten day observation period.

LEXOLDMON002200

Scientific Associates

1474 S. Vandeventer Ave. - St. Louis 10, Mo.

February 19, 1951

CERTIFICATE OF ANALYSIS

SUBJECT -

The Minimum Lethal Dose of Pydraul F-9 when fed orally to New Zealand White Rabbits.

Monsanto Project No. M-28

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

EXPERIMENTAL PROCEDURE -

The Minimum Lethal Dose (M.L.D.) of Pydraul F-9 was found by the introduction of measured single doses of the undiluted compound into the stomachs of healthy mature New Zealand white rabbits by means of a rubber catheter.

The animals were observed occasionally for outward signs of toxicity and those receiving a lethal dose were autopsied and the internal organs examined macroscopically.

The data are given in Table I.

RESULTS -

The Minimum Lethal Dose of Pydraul F-9, when fed orally to New Zealand white rabbits, was between 0.45 and 0.67 milliliters per kilogram of body weight.

SCIENTIFIC ASSOCIATES

Fred M Younger

BY: FRED M. YOUNGER

EXHIBIT K-37

GBRN002804

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To: Monsanto Chemical Company, St. Louis, Mo.
Scientific Associates Certificate of Analysis (2-19-51)

TABLE I

THE MINIMUM LETHAL DOSE OF "PYDRAUL F-9" WHEN FED ORALLY TO NEW ZEALAND WHITE RABBITS

Animal Number	Animal Weight Kg.	Dose/Kg. of Body Weight Ml.	Fate -- Length of Survival
1	2.3	9.1	Died -- 4th Day
2	2.0	7.7	Died -- 3rd Day
3	2.4	6.5	Died -- 5th Day
4	2.1	4.8	Died -- 3rd Day
5	1.7	3.5	Died -- 3rd Day
6	1.9	2.4	Died -- 5th Day
7	2.0	1.4	Died -- 4th Day
8	1.8	1.0	Died -- 5th Day
9	2.1	0.67	Died -- 8th Day, 15.0% Weight Loss
10	1.6	0.45	Survived -- 8.5% Weight Loss, later regained.
11	2.2	0.33	Survived -- 6.0% Weight Loss, later regained.
12	1.9	0.20	Survived -- 7.5% Weight Loss, later regained.

DISCUSSION -

Pydraul F-9 was relatively slow acting on rabbits when the M.L.D. of 0.45 to 0.67 milliliters per kilogram of body weight is considered. Animals receiving a lethal dose ate and acted normally for the first 48 hours but developed mild lethargy and loss of appetite after this time. There was some diarrhea at feeding levels above 2.4 milliliters per kilogram of body weight.

Rabbit No. 9, which died on the 8th day, suffered a 15% weight loss as a result of lowered food consumption. The survivors, Rabbits No. 10, 11, and 12, also temporarily lost weight for the same reason.

Macroscopic examination of the internal organs of those animals fed a lethal dose showed a mottled effect on the livers in two rabbits. Otherwise, there were no specific abnormalities noted.

GBRN002805

LEXOLDMON002202

Scientific Associates

1474 S. Vandeventer Ave. - St. Louis 10, Mo.

April 17, 1951

CERTIFICATE OF ANALYSIS

SUBJECT -

The Minimum Lethal Dose of Pydraul F-9 when fed orally to laboratory rats.

Monsanto Project No. M-23

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

EXPERIMENTAL PROCEDURE -

The Minimum Lethal Dose of Pydraul F-9 was found by the introduction of measured single doses of the undiluted product into the stomachs of mature laboratory rats by means of a rubber catheter.

The animals were observed occasionally for outward signs of toxicity. Those receiving a lethal dose were autopsied and the internal organs examined macroscopically. The data are given in Table I.

RESULTS -

The Minimum Lethal Dose of Pydraul F-9 when fed orally to mature laboratory rats was 8.4 -12.5 milliliters per kilogram of body weight. By contrast, our report of 2-19-51 showed an M.L.D. of 0.45 -0.67 milliliters per kilogram of body weight for New Zealand white rabbits.

SCIENTIFIC ASSOCIATES

Fred M. Younger

BY: FRED M. YOUNGER

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GBRN002806

EXHIBIT K-38

LEXOLDMON002203

TABLE -I

THE MINIMUM LETHAL DOSE OF "PYDRAUL F-9" WHEN FED ORALLY TO MATURE LABORATORY RATS

Animal No. - Sex	Animal Weight Kg.	Dose Ml./Kg. Body Weight	Fate
1 - Male	0.28	0.55	Survived - No loss in weight
2 - Male	0.31	1.06	Survived - Maximum Weight Loss 6%
3 - Female	0.26	2.80	Survived - Maximum Weight Loss 5%
4 - Male	0.29	3.40	Survived - Maximum Weight Loss 9%
5 - Female	0.24	5.30	Survived - Maximum Weight Loss 18%
6 - Female	0.22	6.66	Survived - Maximum Weight Loss 15%
7 - Female	0.20	8.40	Survived - Maximum Weight Loss 21%
8 - Male	0.30	10.15	Died (27 Days) - Wt. Loss at Death 19%
9 - Male	0.32	12.25	Survived - Maximum Weight Loss 26%
10 - Female	0.23	12.50	Died (41 Days) - Wt. Loss at Death 20%
11 - Female	0.25	13.62	Died (38 Days) - Wt. Loss at Death 29%
12 - Male	0.32	15.10	Died (33 Days) - Wt. Loss at Death 42%
13 - Male	0.29	16.03	Died (30 Days) - Wt. Loss at Death 40%
14 - Male	0.31	18.32	Died (11 Days) - Wt. Loss at Death 26%
15 - Male	0.33	20.07	Died (8 Days) - Wt. Loss at Death 22%

DISCUSSION -

As the table indicates, animals receiving a lethal dose of Pydraul F-9 survived for as long as 41 days. The weight losses ranged up to 42% and in all cases there was a general pattern of loss of appetite and severe jaundice.

At autopsy, the surface of the liver appeared normal but the skin was yellow all the way through and the coat had also taken on a yellowish tinge.

Animals receiving doses of 3.4 milliliters per kilogram of body weight and over assumed a kangaroo-like posture a few days after dosing. The underside of the animal as well as the area around the eyes became red and nearly all the hair was lost from these spots. The redness persisted as long as the animal survived.

The M.L.D. level is probably 8.4 - 12.5 milliliters per kilogram of body weight. The reason for the wide range is because one animal died at 10.15 milliliters per kilogram while another lived at 12.25 milliliters per kilogram, showing that the kill point of a slow acting compound such as Pydraul F-9 is not always sharply defined.

GBRN002807

LEXOLDMON002204

Scientific Associates

1424 S. Vandeventer Ave. · St. Louis 10, Mo.

January 13, 1954

CERTIFICATE OF ANALYSIS

SUBJECT -

(A) The Acute Oral Toxicity (LD_{50}) of Functional Fluid CS-54 Per Rats
(B) Inhalation of CS-54 Fumes By Rabbits Over Period of Three Days
(C) Ocular Irritation Produced By CS-54

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

Monsanto Project No.: 54-20

EXPERIMENTAL PROCEDURE -

(A) The LD_{50} was determined by the introduction of measured single doses of undiluted CS-54 into the stomachs of Sprague Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe. Rats with a weight range of 175-245 grams were used in the test.

After the approximate Minimum Lethal Dose was found, groups of animals were fed at levels designed to bracket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to a modification of the method of Bliss (Quart. J. of Pharm. and Pharmacol. 11, 1938).

Selected animals from those receiving a lethal dose were autopsied and macroscopic examination made of the viscera. The data are found in Table I.

(B) The inhalation studies were conducted in a metal chamber approximately 3 feet long and 2 feet in diameter with a clear plastic door for observation. Four New Zealand white rabbits were placed inside the chamber and exposed to CS-54 that was atomized at room temperature by forcing compressed air through a container of the fluid. A great deal of frothing took place with only a light cloud of CS-54 particles appearing in the chamber. Air pressure of 10-12 pounds per square inch was used.

The rabbits were exposed to this atmosphere for four hours with no outward show of discomfort. Since the concentration of atomized CS-54 inside the chamber was only 0.3 milligram per liter, it was decided to place a chrome steel straight type heater inside the drum and drop the fluid from a burette onto a shallow copper dish attached to the heater which in turn was attached to a Powerstat variable transformer.

The CS-54 was volatilized at a temperature of 260°-280° C. with air intake at a rate of 1.0 liter per minute. Under these conditions a dense, whitish-gray fog was produced that obscured the animals excepting when they were near the transparent

GBRN002808

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EXHIBIT K-39

LEXOLDMON002205

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Scientific Services Certificate of Analysis -- Page 2 (1-13-54)

door. The rabbits were exposed daily for three consecutive days for a total exposure time of 20 hours. The survivors were held 7 days for observation after completion of the exposure. Six young mature albino rats were also placed in the drum alongside the rabbits the last day of exposure.

The concentration of vapors was found by passing a measured volume of chamber fumes through a train of three absorption flasks containing acetone and the optical density read on a Beckman Spectrophotometer at a wave length setting of 250 millimicrons. The acetone was first slowly evaporated off and the residue taken up in ethyl alcohol. The concentration per liter of air was found by comparison with a curve prepared from known amounts of CS-54 dissolved in ethyl alcohol. The data are given in Tables II and III.

(C) The degree of ocular irritation produced by CS-54 was found by using the technique developed by Draize, Woodard and Calvery (J. Pharmacology and Experimental Therapeutics, Vol. 82, No. 4, 1944). Briefly, it consisted of dropping 0.1 milliliter of the fluid into the conjunctival sac of the right eye of six albino rabbits and observing the effect over a period of several days. The left eye served as a control. The scores are given in Table IV.

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Scientific Associates Certificate of Analysis — Page 3 (1-13-54)

TABLE I

THE ACUTE ORAL TOXICITY (LD_{50}) OF
FUNCTIONAL FLUID OS-54 FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Fate
1- Male	235	9.07	Survived
2- Male	220		Died
3- Female	190		Survived
4- Female	175		Survived
5- Male	240		Survived
6- Male	230		Died
7- Male	245		Survived
8- Female	200		Survived
9- Female	185		Survived
10- Female	205		Survived
11- Male	220		Survived
12- Male	240	12.10	Died
13- Male	210		Died
14- Male	225		Survived
15- Female	180		Survived
16- Female	195		Survived
17- Female	175		Died
18- Male	220		Survived
19- Male	240		Survived
20- Female	200		Survived
21- Female	190		Died
22- Female	230		Survived
23- Female	210		Survived
24- Male	245	15.10	Died
25- Male	225		Died
26- Male	230		Died
27- Female	185		Survived
28- Female	195		Died
29- Male	230		Survived
30- Male	215		Died
31- Male	225		Died
32- Male	240		Died
33- Male	240		Survived
34- Female	180		Died
35- Female	200	18.15	Died
36- Female	185		Died
37- Female	195		Survived
38- Male	225		Survived
39- Male	220		Died
40- Male	210		Died
41- Male	235		Survived
42- Male	235		Died
43- Female	200		Died
44- Female	185		Died

GBRN002810

LEXOLDMON002207

DISCUSSION -

The LD_{50} of Functional Fluid CS-54 was calculated to be 13.50 grams per kilogram with lower and upper limits of 12.69-14.43 grams per kilogram. Survival time for these animals receiving a lethal dose varied from 36 hours to 8 days. There was moderate to severe diarrhea in all animals dosed at the levels shown in the table. Survivors lost part of the hair on the underside of their bodies. However, the hair grew back after several weeks.

At autopsy of animals receiving a lethal dose, the intestinal tract was gaseous and irritated, and both the liver and spleen were abnormally dark.

TABLE II

FATE AND WEIGHT CHANGES OF RABBITS EXPOSED TO CS-54 VAPORS

Animal No.- Sex	Initial Weight Kilograms	Weight Change 7 Days After Exposure Expressed As % of Initial Weight	Fate
1- Male	2.0	---	Died--2nd Day
2- Male	1.8	0.0	Survived
3- Male	2.1	---	Died--2nd Day
4- Male	2.2	---	Died--3rd Day

TABLE III

AVERAGE DAILY CONCENTRATION OF CS-54 VAPORS IN CHAMBER

Day	Concentration Of CS-54 Vapors Mg./Liter	Average Temperature Inside Chamber °F.	Average Relative Humidity Inside Chamber %
First	2.80	84.0	62.0
Second	2.58	82.5	56.8
Third	2.71	87.3	60.5
Average	2.69	84.6	59.8

GBRN002811

LEXOLDMON002208

DISCUSSION -

The four rabbits survived the first day's exposure although they were rather exhausted when taken out of the chamber. The fumes produced moderately severe nasal irritation that caused the animals to search every corner of the drum in an effort to escape them. During the second day when two of the animals died, a nasal discharge, consisting of thick yellowish mucus, appeared. At the end of the second day, bronchial rales were evident in the two survivors. Both recovered reasonably well overnight but one died during the third day's exposure. The survivor regained its normal appetite within a few days and at the end of the 7 days observation period appeared to be in satisfactory condition.

The fumes caused moderate ocular erythema with mild edema. Lacrimation was moderate but cleared up soon after the animals were taken out of the drum each day.

The six rats exposed for approximately seven hours to the vapors survived without incident although the degree of nasal and ocular irritation was comparable to that for the rabbits.

The average concentration of OS-54 fumes was 2.69 milligrams per liter of air at an average temperature of 84.6° F. and relative humidity of 59.8%. Approximately 20% of the fluid was volatilized under the conditions of the test.

Macroscopic examination at autopsy of rabbits dying in the chamber revealed severe pulmonary congestion with numerous hemorrhagic areas present.

TABLE IV

SCORES REPRESENTING THE SEVERITY OF
OCULAR IRRITATION PRODUCED BY
FUNCTIONAL FLUID OS-54

	NUMERICAL EVALUATION AT THE END OF				
Animal No.	1 Hour	4 Hours	24 Hours	48 Hours	72 Hours
1	24	26	18	8	0
2	18	22	16	8	0
3	28	24	18	10	0
4	22	22	16	10	0
5	24	28	22	10	0
6	20	20	12	6	0
Average	22.7	23.7	17.0	8.6	0.0

GBRN002812

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DISCUSSION -

Ocular irritation consisted of moderate erythema with slight to moderate edema developing within the first hour for an average score of 22.7 out of a possible score of 110. The iris and cornea were only slightly affected although they were somewhat dull for several hours because of the coating of fluid. Edema was confined principally to the eyelids. The count had lowered to 17.0 after 24 hours and all signs of irritation had disappeared within 72 hours.

SUMMARY -

(A) The Acute Oral Toxicity of Functional Fluid CS-54 for rats was found to be 13.50 grams per kilogram with fiducial limits of 12.69-14.43 grams per kilogram.

(B) Four rabbits survived one day's exposure to CS-54 fumes at a concentration of 2.80 milligrams per liter of air. Two of the animals died during the second day's exposure while a third died during the third day. The fumes were rather dense in the chamber.

A group of rats exposed for one day under the same conditions survived without incident.

It was concluded that CS-54 fumes are reasonably toxic in heavy concentrations over an extended period of exposure.

(C) CS-54 was mild to moderately irritating to the eyes of rabbits. An average maximum score of 23.7 out of a possible 110 was recorded 4 hours after the fluid was placed in the eyes.

SCIENTIFIC ASSOCIATES

Fred M. Younger

BY: FRED M. YOUNGER

GBRN002813

LEXOLDMON002210

Scientific Associates

1474 S. Vandeventer Ave. · St. Louis 10, Mo.

September 13, 1954

CERTIFICATE OF ANALYSIS

SUBJECT -

The Toxicological Investigation of Fluid OS-57 Hydraul 150

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.
Monsanto Project No.: SA-77

EXPERIMENTAL PROCEDURE -

(A) Acute Oral Toxicity

Measured single doses of undiluted Fluid OS-57 were introduced into the stomachs of Sprague Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe. The material was found to be non-lethal at the highest dose fed which was 28.5 grams per kilogram. The animals were held for seven days observation following treatment, but no autopsies were performed in view of the results. The data are given in Table I.

(B) Toxicity By Skin Absorption

Fluid OS-57 was applied in varying amounts to the closely clipped intact skin of albino rabbits in an effort to find the Minimum Lethal Dose. The treated areas were covered with plastic shields to retard evaporation. The data are shown in Table II.

(C) Skin Irritation In Rabbits

The degree of skin irritation was determined according to the method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, Dec. 1944). Observations made over a period of several days on the intact skin of three rabbits treated with Fluid OS-57 are scored in Table III.

(D) Ocular Irritation

0.1 ml. of Fluid OS-57 was placed in the conjunctival sac of the right eye of each of three albino rabbits and the amount of inflammation resulting was scored according to the method of Draize, Woodard and Calvery. The results are shown in Table IV.

(E) Vapor Inhalation In Rats

Four mature male rats were placed in a small metal chamber and exposed for six hours to a saturated atmosphere of atomized Fluid OS-57 produced by passing a stream of compressed air at a rate of three liters per minute

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LEXOLDMON002211

through a container of the liquid placed inside the chamber. The animals, all of which survived, were held for seven days observation following exposure. The data are found in Table V.

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TABLE I

THE ACUTE ORAL TOXICITY OF
FLUID OS-57 FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	220	0.3	+ 4.5	Survived
2- Male	210	0.8	+ 6.0	Survived
3- Female	195	1.1	+ 8.0	Survived
4- Female	175	2.0	+ 4.0	Survived
5- Female	230	3.3	+ 7.0	Survived
6- Male	245	5.2	+ 3.0	Survived
7- Male	215	7.0	+ 4.0	Survived
8- Female	200	8.9	0.0	Survived
9- Female	185	11.3	0.0	Survived
10- Male	235	16.0	- 2.0	Survived
11- Male	250	21.7	- 6.0	Survived
12- Male	240	24.0	- 5.5	Survived
13- Female	180	28.5	- 10.0	Survived
14- Male	190	28.5	- 6.5	Survived

DISCUSSION -

All animals survived even when the dose reached 28.5 grams per kilogram which was the largest amount fed. There was severe diarrhea at levels above 7.0 grams per kilogram and in all probability much of the Fluid OS-57 was excreted unchanged. Appetite of the animals was affected for the duration of the diarrhea which was 2 to 3 days. Otherwise, there were no outward signs of toxicity.

T A B L E II

THE TOXICITY OF FLUID OS-57
BY SKIN ABSORPTION IN RABBITS

Animal No.- Sex	Weight Kilograms	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	1.8	1.8	+ 4.0	Survived
2- Male	2.1	3.3	+ 2.0	Survived
3- Male	1.9	5.2	+ 3.0	Survived
4- Male	1.8	7.0	0.0	Survived
5- Male	2.2	8.8	0.0	Survived
6- Male	1.7	9.5	0.0	Survived

DISCUSSION -

The maximum dose of 9.5 grams per kilogram was non-lethal by skin absorption. The activity of the animals was not markedly affected by the treatment. There appeared to be some discomfort and partial loss of appetite for 2 to 3 days, but evidently the Fluid OS-57 had little or no systemic effect.

T A B L E III

SKIN IRRITATION OF
FLUID OS-57 IN RABBITS

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 2 Hours	24 Hours	48 Hours	72 Hours
1- Male	1	1	1	0
2- Male	1	2	1	0
3- Male	1	1	1	1
Average	1.0	1.3	1.0	0.3

DISCUSSION -

Slight erythema with no edema was present on the skin in two hours. The condition remained about the same for two days and had cleared completely in two of the rabbits by the third day. There was no evidence of subcutaneous damage. Fluid OS-57 was considered to be a very mild to mild skin irritant.

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T A B L E IV

OCULAR IRRITATION OF
FLUID OS-57 IN RABBITS

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 1 Hour	24 Hours	48 Hours	72 Hours
1- Male	8	6	2	0
2- Male	6	4	0	0
3- Male	10	5	2	0
Average	8.0	5.0	1.3	0.0

DISCUSSION -

Eye irritation consisted of mild conjunctival redness, slight swelling of the eyelids and slight, temporary corneal dullness. This added up to an average score of 8.0 out of a possible maximum of 110 after one hour. The score dropped to 5.0 in 24 hours and the inflammation had disappeared in one rabbit after 48 hours and had all but disappeared in the other two animals. There was no damage of a permanent nature.

T A B L E V

VAPOR INHALATION TOXICITY OF
FLUID OS-57 FOR RATS

Animal No.	Fate	Concentration Of Fumes Inside Chamber	Average Temperature Inside Chamber °F.	Average Relative Humidity Inside Chamber %
1	Survived	Saturated Atmosphere	81.8	73.5
2	Survived			
3	Survived			
4	Survived			

DISCUSSION -

The animals survived the six hours exposure as well as the following seven days observation period. A moderately dense cloud of atomized Fluid OS-57 resulted from the operation. Eye and nasal irritation were mild to moderate and ocular irritation had practically disappeared after twenty-four hours. There was a trace of bronchial rales in two of the animals for 3 to 4 days. The rats were moderately lethargic during the exposure, but regained normal activity rapidly when removed from the chamber.

SUMMARY -

Fluid OS-57 was non-lethal when given orally to rats in doses as high as 28.5 grams per kilogram. Much of the material was apparently excreted unchanged.

A maximum dose of 9.5 grams per kilogram placed on intact rabbit skin was not fatal.

Skin irritation amounted to slight erythema with no edema for a maximum average score of 1.3 out of a possible 8.0.

Eye irritation consisted of mild erythema with slight swelling of the eyelids for an average maximum score of 8.0 out of a possible 110.

Exposure to a saturated atmosphere for six hours of atomized Fluid OS-57 was not fatal to four mature rats.

SCIENTIFIC ASSOCIATES

Fred M. Younger

BY: FRED M. YOUNGER

Scientific Associates
1474 S. Vandeventer Ave. · St. Louis 10, Mo.

February 1, 1955

CERTIFICATE OF ANALYSIS

SUBJECT:

Toxicological Investigation of Pydraul F-9 (FH-103)

TESTS CONDUCTED FOR:

Monsanto Chemical Company, St. Louis, Missouri.
Monsanto Project No. SA-90

EXPERIMENTAL PROCEDURE:

A) Acute Oral Toxicity
The oral LD_{50} was found by the introduction of measured single doses of undiluted compound into the stomachs of Sprague-Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe.
After the approximate Minimum Lethal Dose was determined, groups of rats were fed at levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50}.
Selected animals from those succumbing were autopsied and macroscopic examination made of the viscera.
The data are shown in Table I.

B) Toxicity By Skin Absorption
Undiluted Pydraul F-9 (FH-103) was applied to the closely clipped intact skin of albino rabbits in varying amounts in order to find the Minimum Lethal Dose. The treated area was covered with a plastic shield to retard evaporation and the animals were placed in special cages to prevent them from licking off the sample.
The results are found in Table II.

C) Skin Irritation In Rabbits
The scoring method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944) was used in evaluating Pydraul F-9 (FH-103) as a skin irritant when placed on intact rabbit skin.
Observations made over a period of several days are scored in Table III.

D) Eye Irritation In Rabbits
Undiluted compound in the amount of 0.1 ml. was placed in the conjunctival sac of the right eye of each of three albino rabbits and the degree of irritation scored according to Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944).
The results are given in Table IV.

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To: Monsanto Chemical Company,
St. Louis, Missouri.
Scientific Associates Certificate of Analysis - Page 2, 2-1-55

EXPERIMENTAL PROCEDURE: (Continued)

E) Vapor Inhalation
Four mature male rats were placed in a small metal drum and exposed for six hours to a saturated atmosphere of Pydraul F-9 fumes by passing a stream of compressed air through a container of the fluid placed inside the chamber. Air pressure was 16 pounds per square inch. The animals were checked for symptoms of toxicity and all were held for seven days observation following exposure.
The data are shown in Table V.

SUMMARY:

The Oral LD_{50} of Pydraul F-9 (FH-103) for rats was found to be 24.0 grams per kilogram.

The Minimum Lethal Dose by skin absorption in rabbits was 2.0 - 2.8 grams per kilogram.

Slight redness with a trace of edema for an average score of 2.3 resulted from skin application.

Eye irritation amounted to moderate redness with slight edema for an average maximum score of 12.3 in 30 minutes. The iris and cornea were hardly affected.

No deaths resulted when rats were exposed to a saturated atmosphere of Pydraul F-9 for six hours.

SCIENTIFIC ASSOCIATES

Fred M. Younger

BY: FRED M. YOUNGER

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[illegible] material [illegible] without the approval of [illegible] Louis. Customer [illegible] toxicity are to be referred as before to the [illegible] ment in St. Louis for reply.
— Monsanto Chemical [illegible]

GBRN002821

To: Monsanto Chemical [illegible]pany,
St. Lou s, Missouri.
Scientific Associates Certificate of Analysis - Page 3, 2-1-55

TABLE I

THE ORAL LD_{50} OF PYRENUL P-9 (FH-1[illegible]3) FOR LABORATORY RATS

Animal No. - Sex	Weight Gm.	Dose Gm. / Kg.	Fate
1- Male	260	18.0	Survived
2- Male	275	18.0	Survived
3- Female	215	18.0	Survived
4- Male	240	18.0	Died
5- Male	230	18.0	Survived
6- Female	220	21.0	Died
7- Female	245	21.0	Survived
8- Male	250	21.0	Died
9- Female	195	21.0	Survived
10- Male	220	21.0	Survived
11- Male	250	24.0	Survived
12- Male	230	24.0	Died
13- Female	210	24.0	Died
14- Female	195	24.0	Survived
15- Female	235	24.0	Survived
16- Male	245	24.0	Died
17- Male	210	27.5	Died
18- Male	259	27.5	Died
19- Male	245	27.5	Died
20- Male	230	27.5	Survived
21- Male	265	27.5	Died

DISCUSSION:

The Oral LD_{50} was placed at 24.0 grams per kilogram. Survival time was one to eight days with severe diarrhea present in all animals. In all probability, part of the dose was excreted relatively unchanged due to the combination of diarrhea and high dosage. Appetite was affected but aside from the gastro-intestinal disturbances no other symptoms of toxicity were observed.

At autopsy the viscera appeared normal except for irritation of the digestive tract.

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T A B L E II

THE MINIMUM LETHAL DOSE OF HYDRAL F-9 (FH-103)

BY SKIN ABSORPTION

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 5 Days After Dosing %	Fate
1 - Male	2.1	0.8	0.0	Survived
2 - Male	1.8	1.4	- 7.5	Survived
3 - Female	1.7	2.0	- 6.[illegible]	Survived
4- Female	1.8	2.8	-[illegible].0	Died -- 8 Days
5 - Male	1.9	3.6	-[illegible].0	Died -- 5 Days
6 - Male	2.[illegible]	4.8	-15.[illegible]	Died -- 7 Days

DISCUSSION:

The Minimum Lethal Dose was found to be 2.0 to 2.8 grams per kilogram. Survival time was five to eight days. The animals became lethargic and lost appetite and weight before succumbing. They also developed multiple neuritis with partial paralysis of the hind quarters.

At autopsy the viscera appeared normal excepting for slight liver discoloration.

COPY

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF PYDRAUL F-9 (FH-103)

Animal No. - Sex	Numerical Evaluation At The End Of 30 Min.	24 Hours	48 Hours	72 Hours
1 - Female	2	3	3	2
2 - Male	1	2	1	1
3 - Female	2	2	2	2
Average	1.6	2.3	2.0	1.6

DISCUSSION:
Slight redness with practically no edema was present within 30 minutes for an average score of 1.6 out of a possible 8.0. The score was 2.3 after 24 hours and was due to a slight increase in redness with a trace of edema. By the third day the sample had nearly disappeared from the surface of the skin and the average score had reduced to 1.6.
Pydraul F-9 (FH-103) was considered to be a mild skin irritant.

- - - -

TABLE V

VAPOR INHALATION OF PYDRAUL F-9 (FH-103) BY RATS

Animal No. - Sex	Fate	Concentration Of Pydraul F-9 Vapors In Chamber	Average Temperature Inside Chamber	Average Relative Humidity Inside Chamber
1 - Male	Survived	Saturated Atmosphere	76.5°F.	30.0%
2 - Male	Survived			
3 - Male	Survived			
4 - Male	Survived			

DISCUSSION:

The vaporized Pydraul F-9 settled quite rapidly on the fur of the animals and the chamber walls. Ocular and nasal irritation was moderate. Breathing became fairly heavy and irregular. Lethargy developed to a moderate extent shortly after exposure began.

The animals were quite exhausted when taken out of the chamber but all had regained normal activity and appetite within 48 hours following exposure. There were no deaths either during or following exposure.

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Scientific Associates

1474 S. Vandeventer Ave. · St. Louis 10, Mo.

February 3, 1955

CERTIFICATE OF ANALYSIS

SUBJECT -

Toxicological Investigation of Fluid CS-43

TESTS CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.
Monsanto Project No. SA-91

EXPERIMENTAL PROCEDURE -

A) Acute Oral Toxicity
The Oral LD_{50} was found by the introduction of measured single doses of undiluted compound into the stomachs of Sprague-Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe.
After the approximate Minimum Lethal Dose was determined, groups of rats were fed at levels designed to bracket the toxicity range thereby supplying data for calculation of the LD_{50}.
Selected animals from those succumbing were biopsied and macroscopic examination made of the viscera.
The data are shown in Table I.

B) Toxicity By Skin Absorption
Undiluted Fluid CS-43 was applied in varying amounts to the closely clipped intact skin of albino rabbits in order to find the Minimum Lethal Dose. The treated areas were covered with plastic shields to retard evaporation and the animals were placed in special cages to prevent them from licking off the sample.
The results are found in Table II.

C) Skin Irritation In Rabbits
The scoring method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944) was used in evaluating Fluid CS-43 as a skin irritant.
Observations made over a period of several days, after the compound was placed on intact rabbit skin, are scored in Table III.

D) Eye Irritation In Rabbits
Undiluted compound in the amount of 0.1 ml. was placed in the conjunctival sac of the right eye of each of three albino rabbits and the degree of irritation scored according to Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944).
The results are given in Table IV.

EXHIBIT
K-42

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EXPERIMENTAL PROCEDURE - (Continued)

E) Vapor Inhalation
Four mature male rats were placed in a small metal drum and exposed for six hours to a saturated atmosphere of Fluid 38-63 by passing a stream of compressed air at a pressure of 15 pounds per square inch through a container of Fluid placed inside the chamber. The animals were checked for symptoms of toxicity and all were held for seven days observation following exposure.
The data are shown in Table V.

SUMMARY -

The Oral LD_{50} of Fluid 38-63 for rats was found to be 17.0 grams per kilogram.

The Minimum Lethal Dose by skin absorption in rabbits was 2.4 to 3.0 grams per kilogram.

Skin irritation amounted to mild erythema with practically no edema for an average maximum score of 2.0 out of a possible 8.0.

The average maximum score for eye irritation was 13.0 out of a possible 110. There was slight to moderate redness of the eyelids with mild edema.

A six hour exposure to a saturated atmosphere of Fluid 38-63 was non-lethal for rats.

SCIENTIFIC ASSOCIATES

By: FRED M. YOUNGE

COPY

The [illegible] in this report is to be used in development [illegible] toxicity [illegible] to the Medical Department in St. Louis for reply.

— Monsanto Chemical Company

LEXOLDMON002224

To: Monsanto Chemical Company,
St. Louis, Missouri.
Scientific Associates Certificate of Analysis - Page 3 (4/3/55)

TABLE I

[illegible]

Animal No. - Sex	Weight Gm.	Dose Gm. / Kg.	Rate
1- Female	135	15.0	Survived
2- Female	220	15.0	Survived
3- Male	240	15.0	Survived
4- Male	230	15.0	Died
5- Female	215	15.0	Survived
6- Male	250	18.0	Died
7- Male	210	18.0	Died
8- Female	195	18.0	Survived
9- Female	225	18.0	Died
10- Female	190	18.0	Survived
11- Male	210	21.0	Died
12- Male	235	21.0	Died
13- Female	220	21.0	Died
14- Female	195	21.0	Survived
15- Female	240	21.0	Died
16- Male	260	24.0	Died
17- Male	245	24.0	Died
18- Male	230	24.0	Survived
19- Male	250	24.0	Died
20- Female	215	24.0	Died

DISCUSSION -

The Oral LD_{50} was found to be about 17.0 grams per kilogram. Survival time was two to seven days. Severe diarrhea developed causing weight losses up to 25 % in some rats. It is likely that part of the dose was excreted before complete digestion took place. Loss of appetite and muscular incoordination developed in 24 to 48 hours.

At autopsy there was evidence of liver dysfunction in addition to severe gastro-intestinal irritation.

COPY

TABLE II

THE MINIMUM LETHAL DOSE OF FIELD CS-63

BY SKIN ABSORPTION

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	1.8	1.2	- 5.0%	Survived
2 - Female	2.0	2.4	- 7.0%	Survived
3 - Male	2.1	3.0	- 14.0%	Died — 6 Days
4 - Male	1.7	3.6	- 25.0%	Died — 8 Days
5 - Female	1.8	4.8	- 30.0%	Died — 14 Days
6 - Female	1.7	6.1	—	Died — 3 Days

DISCUSSION -

The Minimum Lethal Dose by skin absorption was 2.4 to 3.0 grams per kilogram. All animals dosed lost weight and those succumbing lost as much as 30%. There was a gradual wasting away with partial paralysis of the hind quarters and a convulsive-like movement of the head as outward symptoms of toxicity. Survival time was three to fourteen days.

At autopsy there were no specific abnormalities observed by macroscopic examination. The compound apparently affects the nerve tissue.

COPY

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF FLUID 38-63

Animal No. - Sex	Numerical Evaluation At The End Of 30 Min.	24 Hrs.	48 Hrs.	72 Hrs.
1 - Female	2	2	1	1
2 - Female	2	3	2	0
3 - Female	2	2	2	1
Average	2.0	2.3	1.6	0.6

Discussion -
Skin irritation consisted of mild erythema with practically no edema for an average score of 2.0 after one hour. There was no appreciable change until the third day when the average score dropped to 0.6. At this time one animal was free of inflammation and only a trace of redness remained on the other two rabbits.

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF FLUID 38-63

Animal No. - Sex	Numerical Evaluation At The End Of 30 Min.	24 Hrs.	48 Hrs.	72 Hrs.
1 - Male	14	8	2	0
2 - Female	19	4	0	0
3 - Female	12	8	4	0
Average	13.0	6.6	3.0	0.0

DISCUSSION -
Slight to moderate redness of the eyelids with mild edema developed for an average score of 13.0 after thirty minutes. The corneal area remained unaffected excepting for a slight dullness due to the coating of Fluid 38-63. After 24 hours the score dropped to 6.6. At this time the iris and cornea were clear and only a slight amount of redness remained. The animal was free of irritation in 48 hours and all eyes appeared to be normal in three days.

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TABLE V

INHALATION OF FLUID E-63 VAPORS BY RATS

Animal No. - Sex	Date	Concentration Of Fluid E-63 Vapors Inside Chamber	Average Temperature Inside Chamber	Average Relative Humidity Inside Chamber
1 - Male	Survived	Saturated Atmosphere	79.0°F.	72.0 %
2 - Male	Survived			
3 - Male	Survived			
4 - Male	Survived			

DISCUSSION -

The Fluid E-63 fumes were non-lethal over a six hour exposure. Ocular and nasal irritation was moderate. The animals gradually became lethargic and developed irregular breathing but none collapsed during exposure. The fog produced settled quite rapidly on the chamber walls.

COPY

LEXOLDMON002228

Scientific Associates
3755 FOREST PARK BOULEVARD
ST. LOUIS 8, MISSOURI • JEFFERSON 1-5922

July 13, 1955

CERTIFICATE OF ANALYSIS

SUBJECT -

Toxicological Investigation of Pydraul 600.

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.
Monsanto Project No.: SA-55-43
Monsanto Sample No.: 56, Lot 107

EXPERIMENTAL PROCEDURE -

(A) Oral LD_{50} In Rats

The acute oral toxicity was found by the introduction of measured single doses of undiluted Pydraul 600 into the stomachs of Sprague Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe. After the approximate Minimum Lethal Dose was determined, groups of rats were fed at levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50}.

Selected animals from those succumbing were autopsied and macroscopic examination made of the viscera. The data are shown in Table I.

(B) Toxicity By Skin Absorption In Rabbits

The Minimum Lethal Dose was found by the application of increasing single doses of undiluted Pydraul 600 to the closely clipped intact skin of New Zealand white rabbits. The treated areas were covered with plastic shields and the animals were placed in special cages to prevent them from licking off the sample. Observations were made for outward signs of toxicity and the vital organs of selected animals from those succumbing were examined macroscopically. The data are given in Table II.

(C) Skin Irritation In Rabbits

The scoring method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, December 1944) was used in evaluating Pydraul 600 as a skin irritant. Observations made over a period of several days following application of the undiluted liquid to intact rabbit skin are scored in Table III.

(D) Eye Irritation In Rabbits

0.1 ml. of undiluted Pydraul 600 was placed in the conjunctival sac of the right eye of each of three albino rabbits and the resulting irritation scored according to Draize, et al. The results, based on several days observation, are shown in Table IV.

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EXHIBIT K-43

(E) Vapor Inhalation In Rats

Four mature male rats were placed in a metal chamber of approximately 30 liters capacity and exposed for six hours to a concentrated atmosphere of atomized Pydraul 600 obtained by passing a stream of compressed air through a container of fluid inside the chamber. Air pressure was 22 pounds per square inch.

The animals were observed through the clear plastic top and, inasmuch as there were no deaths, all animals were held for seven days observation. The data are shown in Table V.

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— Monsanto Chemical Company

TABLE I

THE ORAL LD_{50} OF PYDRAUL 600 FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Fate
1- Male	275	22.7	Survived
2- Female	215		Survived
3- Female	230		Survived
4- Female	195		Survived
5- Male	240		Survived
6- Male	220	26.0	Survived
7- Female	210		Survived
8- Female	235		Died
9- Male	250		Survived
10- Male	245		Survived
11- Male	220	29.2	Died
12- Male	260		Survived
13- Female	225		Survived
14- Female	240		Survived
15- Female	215		Died
16- Male	240		Survived
17- Male	250	32.5	Died
18- Male	245		Died
19- Female	210		Died
20- Female	200		Died
21- Female	190		Died

DISCUSSION -

The oral LD_{50} was placed at 30.5 grams per kilogram. Survival time was 2 to 6 days. Severe diarrhea developed in all animals dosed at the above levels as might be expected. There was loss of appetite and considerable lethargy present.

At autopsy no specific abnormalities were observed by macroscopic examination with the exception of moderately severe gastrointestinal inflammation and a gaseous condition in the stomach.

LEXOLDMON002231

TABLE II

THE MINIMUM LETHAL DOSE OF PYDRAUL 600
BY SKIN ABSORPTION IN RABBITS

Animal No.- Sex	Weight Kilograms	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	1.8	0.7	+ 6.0	Survived
2- Male	2.1	1.3	+ 5.0	Survived
3- Male	1.8	2.6	0.0	Survived
4- Male	1.6	3.9	- 4.0	Survived
5- Male	2.3	5.2	- 8.0	Died--8 Days
6- Male	2.0	6.5	- 5.0	Died--5 Days
7- Male	1.8	7.8	-11.0	Died--7 Days

DISCUSSION -

The Minimum Lethal Dose was found to be 3.9 to 5.2 grams per kilogram. Survival time was 5 to 8 days. The animals gradually became less active and lost appetite. This resulted in a weight loss for all rabbits dosed at levels above 2.6 grams per kilogram. Moderate weakness of the hind quarters with some unsteadiness developed.

At autopsy no definite changes were noted in the viscera by macroscopic examination.

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T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF PYDRAUL 600

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 2 Hours	24 Hours	48 Hours	72 Hours	120 Hours
1- Male	2	2	1	1	0
2- Female	2	3	2	2	0
3- Female	2	2	2	2	0
Average	2.0	2.3	1.6	1.6	0.0

DISCUSSION -

The average score after 2 hours was 2.0 out of a possible 8.0. There was slight to moderate redness with no observable edema. The average score stayed within the range of 2.3 to 1.6 for three days with slight differences in the degree of erythema being the only changes noted. Within five days the inflammation had disappeared.

T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF PYDRAUL 600

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1- Female	18	10	6	2	0
2- Female	20	12	8	3	0
3- Female	14	10	4	0	0
Average	17.3	10.6	6.0	1.6	0.0

DISCUSSION -

There was little immediate reaction on the part of the animals. The average score after 1 hour was 17.3 out of a possible 110. Moderate erythema and lacrimation with slight edema developed. The iris and cornea were not actually affected excepting for the temporary film of Pydraul 600 that gave the corneal area the appearance of dullness. This film cleared within a few hours. Overnite the average score reduced to 10.6 and continued to decrease until no irritation was observed on the fifth day.

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T A B L E V

VAPOR INHALATION OF PYDRAUL 600 BY RATS

Animal No.- Sex	Fate	Concentration Of Atomized Pydraul 600 Inside Chamber	Average Temperature Inside Charber °F.	Average Relative Humidity Inside Chamber %
1- Male	Survived	Concentrated	81.0	69.5
2- Male	Survived	Atmosphere		
3- Male	Survived			
4- Male	Survived			

DISCUSSION -

No deaths resulted from the six hour exposure nor during the following seven day observation period. A fairly dense fog developed although the atmosphere was probably less than saturated. The nature of the fluid made it difficult to atomize even at 22 pounds pressure.

Ocular and nasal irritation were mild to moderate. Activity and breathing gradually slowed as exposure time increased. The animals were quite lethargic when removed from the chamber, but appeared normal the following day.

SUMMARY -

The oral LD_{50} of Pydraul 600 for rats was 30.5 grams per kilogram.

The Minimum Lethal Dose by skin absorption in rabbits was found to be 3.9 to 5.2 grams per kilogram.

Skin irritation in rabbits amounted to slight to moderate erythema for a maximum average score of 2.3 out of a possible 8.0 in 24 hours.

Eye irritation consisted of moderate erythema and lacrimation with slight edema for an average maximum score of 17.3 out of a possible 110 in 1 hour.

No deaths resulted in rats from a six hour exposure to a concentrated atmosphere of atomized Pydraul 600.

SCIENTIFIC ASSOCIATES

Fred M. Younger

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GBRN002837

LEXOLDMON002234

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September 26, 1955

CERTIFICATE OF ANALYSIS

SUBJECT -

Toxicological Investigation of Pydraul 600.

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

Monsanto Project No.: 55-43A.
Monsanto Sample No.: 56, Lot 107.

EXPERIMENTAL PROCEDURE -

(A) Acute Oral Toxicity In Rats

In our report dated 7/13/55, we found an oral LD_{50} in rats of 30.5 grams of Pydraul 600 per kilogram. The large dose produced diarrhea that persisted for days.

In order to find out what would happen if another group of rats was fed at a high level, the same sample of Pydraul 600 was given orally by stomach tube to six rats at a level of 25.0 grams per kilogram. The results are shown in Table I.

(B) The Oral LD_{50} of Pydraul 600 For Rabbits

Undiluted Pydraul 600 was introduced into the stomachs of New Zealand white rabbits by means of a rubber catheter attached to a hypodermic syringe. After the lethal dose range was found, groups of rabbits were fed at levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50}.

Selected animals from those succumbing were autopsied and macroscopic examination made of the viscera. The data are given in Table II.

The material in this report is to be used in [illegible] toxicity [illegible] referred as before to the [illegible] ment in St. Louis for reply.

— Monsanto Chemical Company

EXHIBIT
K-44

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LEXOLDMON002235

T A B L E I

THE ACUTE ORAL TOXICITY OF PYDRAUL FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Female	255	25.0	- 18.0	Died--7 Days
2- Male	240	25.0	- 21.0	Died--6 Days
3- Female	235	25.0		Died--4 Days
4- Female	255	25.0	- 12.0	Survived
5- Female	220	25.0	- 20.0	Died--6 Days
6- Male	260	25.0	- 14.0	Survived

DISCUSSION -

Four of the six rats dosed at 25.0 grams per kilogram died in 4 to 7 days. Weight losses in five days ranged from 12.0 to 21.0% for all of the animals. Severe diarrhea developed in a few hours after dosing and continued in animals 1, 2, 3, and 5 until they died. The two survivors did not recover from the condition for at least a week. Death or survival seemed to depend upon whether or not the animals were able to overcome the severe diarrhea.

At autopsy there was severe gastrointestinal inflammation with excess mucus. Both the liver and lungs were moderately congested.

LEXOLDMON002236

TABLE II

THE ORAL LD_{50} OF PYDRAUL 600 FOR RABBITS

Animal No.- Sex	Weight Kilograms	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	2.0	0.45	+ 4.0	Survived
2- Female	2.0		0.0	Survived
3- Female	1.9		- 6.5	Died--10 Days
4- Male	2.5		- 3.0	Survived
5- Female	2.3		+ 5.0	Survived
6- Female	2.5	0.67	- 7.5	Died--13 Days
7- Female	2.0		0.0	Survived
8- Male	2.2		- 8.0	Died--7 Days
9- Female	2.7		- 4.5	Survived
10- Female	2.1		0.0	Survived
11- Male	2.6	0.85	- 10.0	Died--14 Days
12- Male	2.7		- 6.0	Died--6 Days
13- Male	2.5		- 14.0	Died--15 Days
14- Female	2.3		- 5.5	Survived
15- Female	1.8		- 8.0	Died--8 Days

DISCUSSION -

The oral LD_{50} was placed at about 0.72 gram per kilogram. Survival time ranged from 6 to 15 days. The animals became lethargic, lost appetite, and gradually wasted away. Weight losses ran as high as 35% in those surviving for the longest length of time. Some of the animals developed convulsions a few hours before death. There was mild to moderate diarrhea that cleared up after several days.

At autopsy the liver was somewhat dry and discolored. The stomach was moderately shrunken from lowered food intake.

SUMMARY -

Out of six rats fed Pydraul 600 orally at a level of 25.0 grams per kilogram, four died and two survived. In a previous study with a different group of rats, we found an oral LD_{50} of 30.5 grams of Pydraul 600 per kilogram. The same sample was used in both tests.

The oral LD_{50} of Pydraul 600 for rabbits was 0.72 gram per kilogram. The compound proved to be much more toxic for rabbits than for rats.

SCIENTIFIC ASSOCIATES

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