Y-56-40

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YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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Certificate of Analysis

August 3rd, 1956

SUBJECT -

Toxicological Investigation Of Hydrenal AC (OS-07).

Monsanto Sample No. 134 - Y-776
Monsanto Project No. Y-56-40

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} In Rats

Undiluted Hydrenal AC was introduced 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 found, groups of rats were fed at levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50}.

Observations were made for outward symptoms of toxicity and the viscera of selected animals from those succumbing was examined macroscopically.

The data are given in Table I.

B) The Minimum Lethal Oral Dose For Rabbits

Undiluted Hydrenal AC was fed by stomach tube in varying amounts to New Zealand white rabbits in order to find the lethal range.

Observations were made for outward symptoms of toxicity and the viscera of these animals that succumbed was examined macroscopically.

The data are shown in Table II.

C) Toxicity By Skin Absorption In Rabbits

Undiluted Hydrenal AC was applied in varying amounts to the closely clipped, intact skin of New Zealand white rabbits and the treated areas covered with plastic shields. A leather collar was placed around the neck of each rabbit to prevent them from turning their head sufficiently to get at the application.

Observations were made for outward evidence of toxicity and the viscera of all animals that succumbed was examined macroscopically.

The data are found in Table III.

EXHIBIT K-45

GBRN002841

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TOWOLDMON0001932

EXPERIMENTAL PROCEDURE - (Continued)

E) Skin Irritation In Rabbits
Undiluted Pydraul AC was applied to the closely clipped, intact skin of three albino rabbits and observations made over a period of several days for irritation.

The results, based on the scoring technique of Draize, Woodard and Calvery (J. of Pharm. & Exp. Therapeutics, Vol. 82, No. 4 (Dec., 1944), are given in Table IV.

E) Eye Irritation In Rabbits
0.1 Milliliter of undiluted Pydraul AC was placed in the conjunctival sac of the right eye of each of three albino rabbits and the resulting irritation scored according to Draize, Woodard and Calvery (J. of Pharm. & Exp. Therapeutics, Vol. 82, No. 4 (Dec.) 1944).

Data from several days observation are shown in Table V.

F) Vapor Inhalation In Rats
Four mature male rats were placed in a metal chamber of 25 liters capacity and exposed for six hours to an atmosphere of Pydraul AC vapors produced by aspirating the liquid at room temperature. The sample was poured into a three hole, round bottom flask and compressed air passed over an orifice, the lower end of which was immersed in the liquid. A glass tube led from the flask into the chamber. A glass impinger was placed in the line to break up droplets and allow, as nearly as practicable, only vapors to pass. Air pressure averaged about 4.4 pounds per square inch.

The animals were observed for toxic symptoms, and, since there were no deaths, all were held for ten days observation.

The data are shown in Table VI.

YOUNGER LABORATORIES

Fred M. Younger

BY: FRED M. YOUNGER

TOWOLDMON0001933

TABLE I

THE ORAL LD_{50} OF 'PYDRAUL AC (OS 67)'
FOR RATS

Animal No. - Sex	Weight Gm.	Dose Gm. /Kg.	Fate
1- Male	260	40.0	Survived
2- Male	245	40.0	Survived
3- Male	275	40.0	Died
4- Female	220	40.0	Survived
5- Female	210	40.0	Survived
6- Male	240	45.0	Died
7- Male	235	45.0	Survived
8- Female	225	45.0	Survived
9- Male	250	45.0	Survived
10- Female	195	45.0	Died
11- Female	210	50.0	Died
12- Female	225	50.0	Survived
13- Female	200	50.0	Survived
14- Male	260	50.0	Survived
15- Male	280	50.0	Died
16- Female	215	55.0	Died
17- Female	205	55.0	Died
18- Female	235	55.0	Survived
19- Female	245	55.0	Died
20- Male	230	55.0	Died
21- Male	240	55.0	Survived

Discussion -

The Oral LD_{50} was placed at 52.0 grams per kilogram. Survival time was overnite to four days. There was severe diarrhea in all animals as might be expected from the high feeding levels necessary to obtain kills. Weakness and lethargy of several days duration developed. There was three instances of moderate muscular incoordination in the survivors. The condition cleared in seven to ten days.

At autopsy pulmonary congestion was the only important visceral change noted macroscopically.

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TABLE II

THE MINIMUM LETHAL ORAL DOSE OF 'PYDRAUL AC (OS-67)' FOR RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm. / Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	2.8	2.0	- 4.0 %	Survived
2 - Female	2.5	3.5	-10.0 %	Survived
3 - Female	3.0	4.5	- 6.0 %	Died - 11 Days
4 - Male	[illegible].2	5.5	-14.0 %	Died - 6 Days
5 - Male	2.9	7.5	-12.0 %	Died - 11 Days
6 - Male	2.8	10.0	-10.0 %	Died - 8 Days

DISCUSSION -

The Minimum Lethal Oral Dose range was found to be 3.5 to 4.5 grams per kilogram. Survival time was six to eleven days. All animals lost weight for several days after being fed. Those succumbing continued to lose weight and became very weak before dying. There appeared to be slight paralysis.

At autopsy there was liver discoloration and moderate pulmonary hyperemia.

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TABLE III

TOXICITY OF 'PYDRAUL AC (OS-67)' BY SKIN ABSORPTION IN RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm. / Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	2.7	2.0	+ 4.0 %	Survived
2 - Male	2.4	3.0	0.0	Survived
3 - Male	2.5	4.0	- [illegible].0 %	Survived
4 - Male	2.2	5.0	- 4.0 %	Died - 21 Days
5 - Male	2.7	6.0	- 8.0 %	Died - 10 Days
6 - Male	2.8	7.5	- 5.0 %	Died - 8 Days
7 - Male	2.2	9.0	-10.0 %	Died - 12 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption was 4.0 to 5.0 grams per kilogram. Survival time was eight to twenty-one days and weight losses ran from fifteen to twenty-eight per cent. The animals gradually lost appetite and weight. This was followed by unsteadiness and some muscular incoordination, the latter becoming evident a few days before death.

At autopsy no specific abnormalities were observed macroscopically.

GBRN002844

TABLE IV

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'PYRAUL AF (OS-67)'

Animal No. - Sex	Numerical Evaluation At The End Of 2 Hours	24 Hours	48 Hours	72 Hours	120 Hours
1 - Female	0	1	1	0	0
2 - Male	1	2	1	1	0
3 - Female	0	1	1	1	0
Average	0.3	1.3	1.0	0.6	0.0

DISCUSSION -

One animal out of three showed an average score of 0.3 out of a possible 8.0. Eventually, erythema ranging from slight to fairly well defined appeared on all the animals for an average maximum score of 1.3. At this time the skin was wiped free of Pyraul AC. A slight amount of redness with no edema was still present on two of the animals after seventy-two hours. However, all received a score of zero on the fifth day. Pyraul AF was classed as a mild skin irritant.

TABLE V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'PYRAUL AC (OS-67)'

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours
1 - Male	6	2	0	0
2 - Male	8	4	2	0
3 - Female	8	4	0	0
Average	7.3	3.3	0.6	0.0

DISCUSSION -

Immediate discomfort of consequence was observed upon application. The average score after one hour was 7.3 out of a possible 110. There was moderate redness of the palpebral conjunctivae, considerable lacrimation, and slight edema. The iris and cornea were little affected. Lacrimation and edema practically disappeared eventually. The average score at this time was 3.3. Two of the animals were free of inflammation in forty-eight hours. Pyraul AC was classed as a mild eye irritant.

GBRN002845

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TABLE VI

SIX HOUR INHALATION OF
'PYRANOL 48 (CB-67)' VAPORS BY RATS

Average Relative Humidity Inside Chamber ..... 64.0 %

Average Temperature Inside Chamber ..... 76.5° F.

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Rather Mild Discomfort,
2 - Male	Survived	no paring at the nose.
3 - Male	Survived	Breathing about normal.
4 - Male	Survived	

DISCUSSION -

All animals survived the six hours exposure as well as the ten day observation period. The animals were not seriously affected by the vapors. Breathing remained regular and irritation was sufficient to produce only a slight degree of lacrimation and salivation. The nasal mucosa was slightly redder than normal when the animals were removed from the chamber but no edema was observed. Appetite seemed to be unaffected the day following exposure.

GBRN002846

TOWOLDMON0001937

SUMMARY -

The Oral LD_{50} of Pydraul AC (OS-67) for rats was found to be 52.0 grams per kilogram. Such a high figure indicates that the compound is practically innocuous when fed orally to rats.

The Minimum Lethal Oral Dose for rabbits was 3.5 to 4.5 grams per kilogram.

The Minimum Lethal Dose by Skin Absorption in rabbits was 4.0 to 5.0 grams per kilogram.

Skin Irritation in rabbits consisted of slight to well defined erythema with no edema for an average maximum score of 1.3 out of a possible 8.0. The compound was classed as a mild skin irritant.

The average maximum score for Eye Irritation was 7.5 out of a possible 110. It was also classed as a mild eye irritant.

Rats survived a six hour exposure to Pydraul AC vapors which were found to be only slightly irritating.

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— Monsanto Chemical Company

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TOWOLDMON0001938

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Certificate of Analysis

February 26th, 1957

SUBJECT -

Toxicological Investigation Of:
Hydraulic Fluid OS-81 - Monsanto Sample No. 1
Hydraulic Fluid OS-83 - Monsanto Sample No. 2

Monsanto Project No. Y-57-1

TESTS CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} In Rats
Each undiluted compound was introduced into the stomachs of Sprague-Dawley strain albino rats by means of a rubber catheter. After the approximate Minimum Lethal Dose was found, groups of rats were fed at levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50}. This was done according to a modification of the method of Bliss. Observations were made for outward symptoms of toxicity and the viscera of selected animals from those succumbing was examined macroscopically.

The data are shown in Table I and Table II.

B) The Minimum Lethal Oral Dose For Rabbits
New Zealand white rabbits were fed orally varying amounts of test compound. The viscera of animals that succumbed was examined macroscopically.

The data are found in Table III and Table IV.

C) Skin Irritation In Rabbits
Undiluted sample was applied to the closely clipped, intact skin of albino rabbits and observations made over a period of several days for irritation.

The results, based on the scoring technique of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, Dec. 1944), are shown in Table V and Table VI.

D) Eye Irritation In Rabbits
0.1 Ml. of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino rabbits and the degree of irritation scored according to the method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, Dec. 1944).

The data are found in Table VII and Table VIII.

GBRN002848

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EXHIBIT
K-46

EXPERIMENTAL PROCEDURE - (Continued)

E) Vapor Inhalation In Rats

Four mature male rats were placed in a metal chamber of approximately 50 liters capacity and exposed for six hours to an atmosphere of hydraulic fluid vapors produced by aspirating the compound at room temperature. The liquid was poured into a three hole, round bottom flask and compressed air passed over an orifice, the lower end of which was immersed in the liquid. A glass tube led from the flask into the chamber. A glass impinger was placed in the line to break up droplets and allow, as nearly as practicable, only vapors to pass.
The animals were observed for behavior and, since there were no deaths, all rats were held for two weeks additional observation.

The data are shown in Table IX and Table X.

TOWOLDMON0001940

TABLE I

THE ORAL LD_{50} OF 'HYDRAULIC FLUID OS-81' FOR RATS

Animal No. - Sex	Weight Gm.	Dose Gm./Kg.	Rate
1- Female	240	6.00	Survived
2- Female	210	6.00	Died
3- Male	235	6.00	Survived
4- Female	210	6.00	Survived
5- Male	225	6.00	Survived
6- Male	245	7.50	Died
7- Female	215	7.50	Survived
8- Female	200	7.50	Survived
9- Female	220	7.50	Survived
10- Male	250	7.50	Died
11- Male	210	7.50	Survived
12- Female	190	8.25	Died
13- Female	195	8.25	Survived
14- Female	215	8.25	Survived
15- Male	230	8.25	Survived
16- Male	255	8.25	Died
17- Female	200	8.25	Survived
18- Male	240	9.00	Died
19- Female	195	9.00	Died
20- Female	205	9.00	Survived
21- Male	235	9.00	Survived
22- Female	215	9.00	Died

DISCUSSION -

The Oral LD_{50} was found to be 8.60 grams per kilogram with fiducial limits of 8.12 to 9.03 grams per kilogram. Survival time was overnite to four days. There was diarrhea, irritability, and nervousness observed. Some survivors lost as much as 30% of their starting weight before regaining normal appetite.

At autopsy there was liver damage, moderate kidney congestion, and gastrointestinal inflammation.

GBRN002850

TOWOLDMON0001941

T A B L E II

THE ORAL LD_{50} OF 'HYDRAULIC FLUID CS-83' FOR RATS

Animal No. - Sex	Weight Gm.	Dose Gm./Kg.	Fate
1- Female	210	27.5	Survived
2- Female	220	27.5	Survived
3- Female	205	27.5	Died
4- Male	240	27.5	Survived
5- Male	210	27.5	Survived
6- Female	195	30.0	Died
7- Female	205	30.0	Survived
8- Female	215	30.0	Survived
9- Male	230	30.0	Died
10- Male	250	30.0	Survived
11- Female	190	35.0	Survived
12- Female	200	35.0	Died
13- Male	225	35.0	Died
14- Female	185	35.0	Survived
15- Female	195	35.0	Died
16- Female	215	35.0	Survived
17- Male	240	40.0	Died
18- Male	255	40.0	Survived
19- Female	230	40.0	Died
20- Female	210	40.0	Died
21- Female	205	40.0	Died

DISCUSSION -

The Oral LD_{50} was placed at 34.3 grams per kilogram with lower and upper limits of 32.6 to 38.5 grams per kilogram. Survival time was two to seven days. Severe diarrhea, trembling, irritability, and lethargy developed. Weight losses ran to 25% of starting weight.

At autopsy the stomach was gaseous and irritated. The liver was discolored and hyperemic. There was also pulmonary congestion.

TOWOLDMON0001942

TABLE III

THE MINIMUM LETHAL ORAL DOSE OF 'HYDRAULIC FLUID OS-81' FOR RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 4 Days After Dosing	Fate
1 - Male	2.8	0.25	0.0 %	Survived
2 - Female	1.9	0.35	0.0 %	Survived
3 - Male	1.9	0.50	-15.0 %	Died—4 Days
4 - Male	2.3	0.75	-10.0 %	Died—4 Days
5 - Male	2.1	1.00	-13.0 %	Died—7 Days
6 - Female	1.8	1.50	-12.0 %	Died—4 Days
7 - Female	1.8	2.00	-20.0 %	Died—5 Days
8 - Male	2.3	3.00	-18.0 %	Died—5 Days
9 - Male	2.3	5.00	-15.0 %	Died—5 Days

DISCUSSION -

The Minimum Lethal Dose was in the range of 0.35 to 0.50 gram per kilogram. Survival time was four to seven days. The animals gradually became weak from loss of appetite. There appeared to be partial paralysis after two to three days.

At autopsy liver and spleen were congested. There appeared to be blood changes.

- -

TABLE IV

THE MINIMUM LETHAL ORAL DOSE OF 'HYDRAULIC FLUID OS-83' FOR RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 4 Days After Dosing	Fate
1 - Male	2.6	2.25	0.0 %	Survived
2 - Female	2.1	3.00	+ 4.0 %	Survived
3 - Male	2.4	3.50	0.0 %	Survived
4 - Female	1.9	4.25	- 8.0 %	Survived
5 - Male	2.4	5.00	-13.0 %	Died—5 Days
6 - Male	2.2	6.50	-10.0 %	Died—6 Days

DISCUSSION -

The Minimum Lethal Dose was 4.25 to 5.00 grams per kilogram. Survival time was five to six days. Weight losses resulted from poor appetite. Animals No. 5 and No. 6 gradually became lethargic but did not appear to develop paralysis.

At autopsy kidneys, liver, and lungs were all hyperemic.

GBRN002852

TOWOLDMON0001943

T A B L E V

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'HYDRAULIC FLUID OS-81'

Animal No.	Numerical Evaluation At The End Of 2 Hours	24 Hours	48 Hours	72 Hours
1	1	1	1	0
2	0	1	0	0
3	1	1	0	0
Average	0.6	1.0	0.3	0.0

DISCUSSION -

After two hours, two rabbits showed barely perceptible redness for an average score of 0.6 out of a possible 8.0. No edema developed. Overnite very slight erythema was observed on all animals. The residue was removed from the skin after twenty-four hours. Two of the animals were given a zero score on the second day.

Hydraulic Fluid OS-81 was found to be a rather mild skin irritant.

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T A B L E VI

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'HYDRAULIC FLUID OS-83'

Animal No.	Numerical Evaluation At The End Of 2 Hours	24 Hours	48 Hours	72 Hours
1	0	1	0	0
2	1	1	1	0
3	0	1	0	0
Average	0.3	1.0	0.3	0.0

DISCUSSION -

The average score after two hours was 0.3, consisting of very slight erythema on one animal. All rabbits showed barely perceptible redness in twenty-four hours at which time the remaining compound was wiped off the skin. Two rabbits were found to be free of irritation within forty-eight hours.

Hydraulic Fluid OS-83 was classed as a rather mild skin irritant.

TOWOLDMON0001944

TABLE VII

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'HYDRAULIC FLUID OS-81'

Animal No.	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1	8	6	2	2	0
2	10	6	4	2	0
3	6	4	2	0	0
Average	8.0	5.3	2.6	1.3	0.0

DISCUSSION -

There was slight discomfort shown immediately upon application. The average score after one hour was 8.0 out of a possible 110.0. Moderate erythema and lacrimation with slight edema was observed. The iris was practically unaffected. Overnite lacrimation returned to normal and the average score reduced to 5.3. Two of the animals had a slight degree of erythema remaining after seventy-two hours.

Hydraulic Fluid OS-81 was classed as a mild eye irritant.

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TABLE VIII

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'HYDRAULIC FLUID OS-83'

Animal No.	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1	8	6	4	2	0
2	12	8	4	2	0
3	10	6	4	2	0
Average	10.0	6.6	4.0	2.0	0.0

DISCUSSION -

The degree of irritation was quite similar for both Hydraulic Fluid OS-81 and Hydraulic Fluid OS-83. Mild discomfort developed immediately upon application of Hydraulic Fluid OS-83. After one hour the average score was 10.0 out of a possible 110.0. Moderate erythema of the palpebral conjunctivae, considerable lacrimation, and mild edema developed. The iris remained clear and the cornea showed little change. All animals still showed slight redness after seventy-two hours but all were free of inflammation by the fifth day.

Hydraulic Fluid OS-83 was classed as a mild eye irritant.

GBRN002854

TOWOLDMON0001945

TABLE IX

INHALATION OF 'HYDRAULIC FLUID OS-81' VAPORS BY RATS

Average Temperature Inside Chamber ..... 75.5° F.
Average Relative Humidity Inside Chamber ..... 60.0 %

Animal No.	Fate	Observations During Exposure
1	Survived	Animals continue to move about—
2	Survived	No pawing at nose or eyes—
3	Survived	Breathing steady.
4	Survived	

DISCUSSION -

No deaths occurred during the six hours exposure nor during the subsequent two weeks observation period. Breathing and activity in general did not change materially leading to the belief that the vapors did not cause serious discomfort. Mucous membranes of the nose and throat showed only slight inflammation after exposure. Salivation was not excessive.

The fluid was agitated quite briskly at ten pounds pressure per square inch. However, little or no haze developed in the chamber atmosphere. It was possible that saturation was reached although it was apparent that the compound does not readily vaporize.

TABLE X

INHALATION OF 'HYDRAULIC FLUID CS-83' VAPORS BY RATS

Average Temperature Inside Chamber ..... 73.9° F.
Average Relative Humidity Inside Chamber ..... 57.8 %

Animal No.	Fate	Observations During Exposure
1	Survived	Animals show only slight discomfort.
2	Survived	Continue to explore cage.
3	Survived	
4	Survived	

DISCUSSION -

The animals survived the exposure without incident. The behavior pattern was very similar to Hydraulic Fluid OS-81. No excessive lacrimation or salivation was noted. Activity was not materially reduced. Inflammation of the nose and throat was very mild to mild.

Air pressure of ten to twelve pounds per square inch agitated the fluid vigorously but apparently droplets were not carried over into the chamber. The fur of the animals remained dry. As with Hydraulic Fluid CS-81 very little vapor haze accumulated in the chamber.

The vapors of both Hydraulic Fluids were considered to be only mildly irritating to rats.

GBRN002856

TOWOLDMON0001947

SUMMARY -

Toxicological Investigation Of two new Hydraulic Fluids produced the following results:

HYDRAULIC FLUID OS-81

Oral LD_{50} (Rats) — 8.60 Grams per Kilogram (Fiducial Limits 8.12 to 9.03 Gm./Kg.).

Minimum Lethal Oral Dose (Rabbits) — 0.35 to 0.50 Gram per Kilogram.

Skin Irritation (Rabbits) — Rather Mild Skin Irritant:
Average Maximum Score - 1.0 out of possible 8.0.

Eye Irritation (Rabbits) — Mild Eye Irritant:
Average Maximum Score - 8.0 out of possible 110.0.

Vapor Inhalation (Rats) — No Deaths, Mild Effect.

HYDRAULIC FLUID OS-83

Oral LD_{50} (Rats) — 34.3 Grams Per Kilogram (Fiducial Limits 32.6 to 36.5 Gm./Kg.).

Minimum Lethal Oral Dose (Rabbits) — 4.25 to 5.00 Grams Per Kilogram.

Skin Irritation (Rabbits) — Rather Mild Skin Irritant:
Average Maximum Score - 1.0 out of possible 8.0.

Eye Irritation (Rabbits) — Mild Eye Irritant.
Average Maximum Score - 10.0 out of possible 110.0.

Vapor Inhalation (Rats) — No Deaths, Mild Effect.

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

— Monsanto Chemical Company

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Certificate of Analysis

February 22nd, 1958

SUBJECT -

Toxicological Investigation Of 'OS-95.'

Monsanto Sample Number 17
Monsanto Project Number Y-58-4

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

COPY

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} In 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 rats were fed at 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 Bliss.
The viscera of the animals that succumbed was examined macroscopically.
The data are shown in Table I.

B) Skin Absorption MLF In Rabbits
The sample was applied undiluted in varying amounts to the closely clipped, intact skin of New Zealand white rabbits and the treated areas covered with plastic shields to prevent evaporation.
Observations were made for toxic symptoms and the viscera of these animals that succumbed was examined macroscopically.
The data are found in Table II.

C) Skin Irritation In Rabbits
OS-95 was applied undiluted to the clipped, intact skin of three albino rabbits and removed after twenty-four hours with soap and water.
Observations were made over a period of several days for inflammation.
Irritation was scored according to the method of Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, Dec. 1944).
The results are given in Table III.

GBRN002858

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EXHIBIT
K-47

TOWOLDMON0001949

EXPERIMENTAL PROCEDURE - (Continued)

D) Eye Irritation In Rabbits
0.1 Milliliter of sample was placed in the conjunctival sac of the right eye of three albino rabbits. The eyes were rinsed with warm isotonic saline solution after twenty-four hours.

Observations were made over a period of several days for irritation.

The data, scored according to Draize et al, are found in Table IV.

E) Vapor Inhalation In Rats
Four mature male rats were placed in a metal chamber of approximately 25 liters capacity and exposed for six hours to a concentrated atmosphere of OS-95 vapors produced by aspirating the liquid at room temperature.
The sample (250 grams) was poured into a three hole, round bottom flask and compressed air passed over an orifice, the lower end of which was immersed in the liquid. A rubber tube led from the flask into the chamber. A glass impinger was placed in the line to break up droplets and allow, as nearly as practicable, only vapors to pass.
The animals were checked for behavior and, since there were no deaths, all were held for ten days observation.
The data are shown in Table V.

SUMMARY -

The Oral LD_{50} of OS-95 was found to be 10,500 milligrams per kilogram with lower and upper limits of 9,295 to 11,865 milligrams per kilogram.

The Minimum Lethal Dose range by Skin Absorption in rabbits was 625 to 1,250 milligrams per kilogram.

OS-95 was classed as a moderate skin irritant.

OS-95 was classed as a mild eye irritant.

No deaths resulted when rats were exposed for six hours to a concentrated atmosphere of OS-95 vapors.

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

[illegible] Monsanto Chemical Company

GBRN002859

TOWOLDMON0001950

TABLE I

THE ORAL LD_{50} OF 'CS-95'
FOR RATS

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Male	270	9,000	Survived
2- Female	195	9,000	Survived
3- Female	210	9,000	Survived
4- Female	190	9,000	Survived
5- Male	230	9,000	Survived
6- Female	205	10,000	Died
7- Female	195	10,000	Survived
8- Male	215	10,000	Survived
9- Male	230	10,000	Died
10- Male	245	10,000	Survived
11- Female	185	11,000	Died
12- Female	190	11,000	Died
13- Female	210	11,000	Survived
14- Female	225	11,000	Died
15- Male	240	11,000	Survived
16- Male	220	12,500	Died
17- Female	215	12,500	Died
18- Female	200	12,500	Died
19- Female	190	12,500	Survived
20- Male	195	12,500	Died

DISCUSSION -

The Oral LD_{50} was placed at 10,500 milligrams per kilogram with lower and upper limits of 9,295 to 11,865 milligrams per kilogram.

Survival time was overnight to three days.

There was diarrhea, salivation, tremors, and coma.

At autopsy the gastrointestinal tract was gaseous and inflamed. There was liver discoloration due in part to congestion.

TOWOLDMON0001951

T A B L E II

THE MINIMUM LETHAL DOSE OF '08-95' BY SKIN ABSORPTION IN RABBITS

Animal No. - Sex	Weight Kg.	Dose Mg. / Kg.	Weight Change 5 Days After Dosing Kg.	Fate
1 - Female	2.3	450	- 0.2	Survived
2 - Female	2.1	625	- 0.2	Survived
3 - Male	2.6	1,250	- 0.3	Died - 11 Days
4 - Male	2.6	2,500	- 0.2	Died - 5 Days
5 - Male	2.4	5,000	- 0.2	Died - 5 Days
6 - Female	2.1	7,500	- 0.4	Died - 4 Days
7 - Male	2.5	10,000	- 0.4	Died - 3 Days

DISCUSSION -

The Minimum Lethal Dose range was found to be 625 to 1,250 milligrams per kilogram. Survival time was three to eleven days.

Appetite was soon affected resulting in weight losses. This was about the only toxic symptom for two days. Weakness and lethargy were noted thereafter. Violent convulsions developed in two of the animals several hours before death.

At autopsy there were extensive hemorrhagic areas in the lungs and moderate kidney congestion.

TOWOLDMON0001952

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'OS-95'

Animal Number	Numerical Evaluation At The End Of 2 Hours	24 Hours	48 Hours	72 Hours	120 Hours
1	2	3	2	1	1
2	2	3	2	2	1
3	1	3	2	1	1
Average	1.6	3.0	2.0	1.3	1.0

DISCUSSION -

After two hours there was slight to well defined erythema with no edema for an average score of 1.6 out of a possible 8.0. Overnight the average score increased to 3.0 on the basis of more redness and slight edema.

The application was removed in twenty-four hours but the irritation decreased rather slowly. Slight erythema was still present on all animals on the fifth day.

OS-95 was classed as a moderate skin irritant.

TOWOLDMON0001953

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'CS-95'

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1	12	8	4	2	0
2	10	6	4	0	0
3	12	8	4	2	0
Average	11.3	7.3	4.0	1.3	0.0

DISCUSSION -

There was mild immediate discomfort shown upon application. The average score after one hour was 11.3 out of a possible 110.0. Irritation consisted of moderate erythema of the conjunctivae with mild edema and lacrimation. The details of the iris were slightly obscured due to some congestion. The latter condition improved overnight resulting in an average score of 7.3. One animal was free of inflammation in seventy-two hours and all were given a score of zero in five days.

CS-95 was classed as a mild eye irritant.

TOWOLDMON0001954

TABLE V

INHALATION OF 'OS-95' VAPORS BY RATS

Average Temperature Inside Chamber . . . . . 76.0° F.
Average Relative Humidity Inside Chamber . . . . . 59.5 %
Amount Of 'OS-95' Vaporized. . . . . 6.4 Grams

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Little immediate reaction -
2 - Male	Survived	Activity about normal -
3 - Male	Survived	Animals continue to explore chamber -
4 - Male	Survived	Discomfort slight after four hours.

DISCUSSION -

The rats survived the six hour exposure with no aftermath of bronchial rales or other evidence of respiratory injury. Activity was not affected to any noticeable extent. The animals remained steady and were observed eating and drinking at intervals. Nasal and ocular irritation was not sufficient to stimulate a discharge.

6.4 Grams, equivalent to 2.5 per cent of the sample, was vaporized. Considerable agitation was maintained at a pressure of three pounds per square inch. However, the chamber atmosphere remained quite clear with only a very slight haze detectable by reflected light.

It was concluded that a concentrated atmosphere of OS-95 vapors was only slightly irritating to rats exposed for six hours.

GBRN002864

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Biochemists . . . Pharmacologists . . . Analysts

ROUTE 9 — BOX 281
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Certificate of Analysis

THE TOXICITY OF THE THERMAL DECOMPOSITION PRODUCTS OF 'PYDRAUL 625'

Study Conducted For
MONSANTO CHEMICAL COMPANY, ST. LOUIS, MISSOURI

COPY

INTRODUCTION

The experiment was designed to determine the effect upon laboratory rats when exposed to a fog of thermal decomposition products produced by dropping PYDRAL 625, Lot A-1505, a product of Monsanto Chemical Company, on a surface heated to a temperature of 2000° Fahrenheit. Various intensities of fog were generated for different groups of animals.

EXPERIMENTAL PROCEDURE

Half of a fifteen inch McDaniel high temperature combustion tube (inside diameter seven-eighth's inch, non-porous vitreous material) was wound with special sixteen gauge nickel-chromium wire. The wire was attached to a variable transformer for controlling temperature. After being wrapped in asbestos paper, the tube was insulated with four inches of mineral wool and then surrounded with a container made of asbestos board.

The tube was clamped at an angle of approximately 70 degrees with several inches of the unwound end protruding from the container. A thermocouple was inserted to the center of the tube and the temperature measured by an indicating pyrometer. At the upper end of the container two openings were made; one large enough for a small funnel to be inserted. The liquid to be volatilized was dropped from a buret

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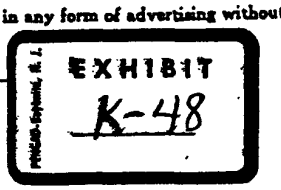

at a measured rate, through the funnel to the inner surface of the heated combustion tube. The tube was slanted to prevent the drops from falling through and at the same time allow them to spatter against the sides, making for rapid volatilization.

Curved, three-fourths inch copper tubing was attached to the other opening. The tubing rose to a height of two and one-half feet above the combustion chamber and then returned about the same distance to a one liter flask from which an opening led into a five gallon glass bottle connected to a metal inhalation chamber of seventy liters capacity.

Animals were placed in the chamber, the chamber sealed, and connected to a vacuum pump with rubber tubing. The fluid was dropped at a measured rate onto the inner surface of the combustion tube heated to 2000° F. Sufficient suction was supplied by the pump to pull the combustion products through the copper tubing into the liter flask and five gallon bottle and then into the exposure chamber. From here the fog was drawn into an air trap and a calcium chloride trap attached directly before the vacuum pump. No cooling bath was used for the fog; temperature reduction was achieved by passing the combustion products through the copper tube and the five gallon bottle before entering the chamber. It was desired to expose the animals as nearly as possible to the fog as generated. The liter flask removed some solid particles of combustion.

Supplemental air for the animals' oxygen requirements was supplied by an air compressor and introduced into the five gallon bottle for mixing with the combustion products before entry into the exposure chamber.

The flow of filtered and dried air was controlled by means of a calibrated rotameter.

GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

Eight mature male rats were exposed for one hour three days per week for two weeks to a moderate concentration of PYDRAUL 625 volatilized at 2000° F. The concentration

TOWOLDMON0001957

was clearly evident in the chamber but not sufficient to obscure the animals.

The fate of the animals is shown in Table I.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

Eight mature male rats were exposed for fifteen minutes to a heavy concentration of PYDRAUL 625 mist produced by volatilization at 2000° F. The concentration was practically as heavy as obtainable. The animals in the front of the chamber were nearly obscured.

The data on the animals is shown in Table II.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

Eight mature male rats were exposed for one hour to a heavy concentration of PYDRAUL 625 mist produced by volatilization at 2000° F. The concentration was practically as heavy as obtainable. The animals in the front of the chamber were nearly obscured.

The results are shown in Table III.

- - - - - - - - - - -

Figure 1 — Inhalation Chamber And Equipment For Generating Mist

Figure 2 — Close-Up Of Inhalation Chamber During Generation Of Moderate Concentration Of Mist

Figure 3 — Close-Up Of Inhalation Chamber During Generation Of Heavy Concentration Of Mist

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— Monsanto Chemical Company

TOWOLDMON0001958

TABLE I

EXPOSURE TO 'PYDRAUL 625' MIST (MODERATE CONCENTRATION)
ONE HOUR DAILY, THREE DAYS PER WEEK FOR TWO WEEKS (SIX HOURS TOTAL)

Average Temperature Inside Chamber ..... 86.0° F.
Average Relative Humidity Inside Chamber ..... 78.5 %
Volatilization Rate ..... 6.1 Ml./Hour (Equivalent to 8.2 Gm./Hour
Supplemental Air Supply ..... 6.0 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change 2 Weeks After Last Exposure Gm.	Weight Change 4 Weeks After Last Exposure Gm.	Fate
1	235	- 10	0	Survived
2	250	0	+ 15	Survived
3	240	- 25	——	Died - 21 Days
4	260	+ 5	+ 20	Survived
5	245	- 15	——	Died - 18 Days
6	230	0	+ 10	Survived
7	245	- 10	+ 5	Survived
8	255	- 15	0	Survived

DISCUSSION -

No deaths resulted during the exposure time although two of the rats died eighteen and twenty-one days after the final exposure.

The fog produced a moderate degree of irritation each time, most of which, outwardly at least, appeared to have cleared up by the time for the next exposure two days later.

There was salivation, nasal discharge, some instances of irregular breathing, and moderate lethargy. The animals were reasonably steady when moving about the chamber and none appeared in danger of collapse when removed.

Temperature and humidity were higher than normal in the chamber due to the steady influx of the mist. This contributed somewhat to the discomfort of the animals. Activity between exposures remained about normal. The fur of the rats was damp from condensate after each exposure. Several of the animals developed sniffles as

TOWOLDMON0001959

the experiment progressed but respiratory inflammation did not reach the stage of bronchial rales.

The majority of the rats lost weight for approximately two weeks after inhalation was concluded. Four weeks after the final exposure, all rats with the exception of the two that died at eighteen and twenty-one days, had gained weight and appeared to be in healthy condition.

The animals that succumbed became emaciated, developed colds, and gradually lost weight. A streptococcus organism was isolated from the pulmonary tract of one rat. It is impossible to state whether exposure to mist was a direct cause of death in both instances. It is likely that this, in combination with high humidity, were contributing factors.

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TABLE II

EXPOSURE TO 'PYDRAUL 625' MIST (HEAVY CONCENTRATION)
FOR FIFTEEN MINUTES

Average Temperature Inside Chamber ..... 81.5° F.
Average Relative Humidity Inside Chamber ..... 65.0 %
Volatilization Rate ..... 10.9 Ml./Hour (Equivalent to 14.7 Gm./Hour
Supplemental Air Supply ..... 3.5 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	215	+ 15	Considerable discomfort after a few minutes —
2	235	+ 10	
3	220	+ 20	Copious nasal discharge with some lacrimation —
4	240	+ 5	Reduced Activity —
5	210	+ 25	Animals obscured except in front part of cage.
6	230	+ 10	
7	235	+ 15	
8	245	0	

DISCUSSION -

No deaths resulted from fifteen minutes exposure to a saturated atmosphere of PYDRAUL 625 thermal decomposition products.

Reduced activity and irregular breathing were noted when the animals were removed from the chamber. They were not in danger of collapse.

Examination thirty minutes after exposure showed a cessation of nasal discharge but moderate edema of the nasal mucosa and redness around the eyes.

The animals had gained in weight when weighed two weeks later.

They appeared normal by outward observation.

TABLE III

EXPOSURE TO 'PYDRAUL 625' MIST (HEAVY CONCENTRATION) FOR ONE HOUR

Average Temperature Inside Chamber ..... 84.0° F.
Average Relative Humidity Inside Chamber ..... 69.0 %
Volatilization Rate ..... 10.9 ML./Hour (Equivalent to 14.7 Gm./Hour
Supplemental Air Supply ..... 4.5 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	205	+ 15	Salivation and nasal discharge in a few minutes —
2	220	+ 5	
3	195	- 5	Breathing gradually becoming short and irregular —
4	220	+ 10	
5	235	0	Considerable activity for 10 to 15 minutes —
6	215	+ 5	Definite weakness within 30 minutes —
7	240	0	
8	225	+ 10	All animals at the point of collapse when removed from chamber.

DISCUSSION -

The heavy concentration of acrid fog was nearly fatal to the animals exposed for one hour.

They were in a semi-comatose state when taken from the chamber. The majority were on their feet within thirty minutes but showed marked weakness. Breathing was difficult and irregular. Considerable improvement was noted overnight. However, lethargy and poor appetite were evident for several days. After two weeks all animals were still alive and acting normally with one exception. This animal appeared unthrifty but the condition did not appear to be confined solely to the respiratory tract.

TOWOLDMON0001962

To: Monsanto Chemical Co. ..ny,
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 8

SUMMARY

PYDRAUL 625 was volatilized by dropping the liquid onto a non-porous, vitreous surface heated to a temperature of 2000° F. The thermal decomposition products were drawn into an inhalation chamber and groups of rats exposed to various concentrations of the mist.

The results were as follows:

GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

Considerable discomfort, irritation, and lethargy resulted from the exposures, but there were no deaths until eighteen and twenty-one days after the final exposure when two of the eight animals succumbed.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

Fifteen minutes exposure to a heavy concentration of mist produced copious nasal discharge and lacrimation, indicative of irritation. The animals showed some weakness when removed from the chamber but all survived.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

One hour exposure to a heavy concentration of mist resulted in weakness to the point of collapse in all animals. Breathing difficulties gradually disappeared as the animals gained strength. After two weeks they appeared normal with the exception of one animal.

The pH of the condensate from the volatilized PYDRAUL 625 was in the range of 3.5 to 4.5.

YOUNGER LABORATORIES

Fred M. Younger

BY: FRED M. YOUNGER

September 29th, 1958

GBRN002872

TOWOLDMON0001963

YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

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Certificate of Analysis

October 20th, 1958

SUBJECT -

Toxicological Investigation Of CS-95.

Monsanto Sample Number 102 - Lot 7501-3677;
Monsanto Sample Number 17 - Lot S-59

Monsanto Project Number Y-58-29

TESTS CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Skin Absorption MLD (Rabbits)

The undiluted compound was applied in varying amounts to the closely clipped, intact skin of albino rabbits and the animals placed in wooden stocks for eight hours after which the trunk was wrapped in plastic strips and the animals returned to individual cages.

Observations were made for toxic symptoms and the viscera of selected animals from those succumbing was examined macroscopically.

The data are shown in Table I.

B) Skin Irritation (Rabbits)

0.1 Milliliter of undiluted CS-95 was applied to the clipped, intact skin of albino rabbits and observations made over a period of several days for irritation.

The results, scored according to Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, 377 (1944)), are shown in Table II.

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BY: FRED M. YOUNGER

GBRN002873

EXHIBIT
K-49

TABLE I

TOXICITY OF 'OS-95' BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
SAMPLE 102, Lot 7501-3677				
1 - Male	2.1	1000	0.0	Survived
2 - Female	1.8	1500	- 0.2	Survived
3 - Female	2.0	2000	- 0.3	Died - 7 Days
4 - Male	2.4	2000	- 0.1	Survived
5 - Male	2.3	2500	- 0.2	Died - 6 Days
6 - Male	2.4	2500	- 0.1	Died - 14 Days
7 - Female	2.0	3500	- 0.3	Died - 5 Days
SAMPLE 17, Lot S-59				
1 - Female	2.3	1000	- 0.1	Survived
2 - Male	2.6	1250	0.0	Survived
3 - Male	2.5	1250	- 0.2	Died - 17 Days
4 - Male	2.3	1500	- 0.3	Died - 9 Days
5 - Female	2.2	1500	- 0.2	Died - 7 Days
6 - Female	2.1	2000	- 0.2	Died - 7 Days
7 - Male	2.6	2500	- 0.3	Died - 6 Days

DISCUSSION -

There was one death and one survival at 2000 milligrams per kilogram on Sample 102, Lot 7501-3677.
Survival time ranged from five to fourteen days. Gradual loss of appetite with increasing lethargy and weakness developed.

On Sample 17, Lot S-59 there was one death and one survival at 1250 milligrams per kilogram.
Survival time was six to seventeen days. Toxic symptoms were very similar to those already described.

At autopsy there appeared to be degenerative changes in the liver by macroscopic examination. Pulmonary hyperemia was also observed.

GBRN002874

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TABLE II

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'OS-95'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	4 Hours	24 Hours	48 Hours	72 Hours	120 Hours
SAMPLE 102, Lot 7501-3677						
1	0	0	2	1	1	0
2	0	1	3	2	1	0
3	0	1	2	2	1	0
Average	0.0	0.6	2.3	1.6	1.0	0.0
SAMPLE 17, LOT S-59						
1	0	1	3	2	2	1
2	0	1	2	2	1	0
3	0	1	3	2	1	0
Average	0.0	1.0	2.6	2.0	1.3	0.3

DISCUSSION -

No irritation was observed on either sample one hour after exposure. Two out of three animals on sample 102 showed barely perceptible erythema after four hours for an average score of 0.6 out of a possible 8.0. Overnight there was well defined erythema with one instance of slight edema increasing the average score to 2.3. Removal of the application reduced the irritation to barely perceptible redness on the third day.

There was practically no difference between the two samples as the data in the table indicate. The average twenty-four hour score for number 17 was 2.6 as compared to 2.3 for number 102.

The two samples of OS - 95 were classed as mild to moderate skin irritants.

The material in this report is to be used in development of ... but it is not to be used for ... GBRN002875

SUMMARY --

The Minimum Lethal Dose range by skin absorption in rabbits was determined on two samples of CS - 95.

Number 102, Lot 7501-3677 gave a range of 2000 to 2500 milligrams per kilogram.

Number 17, Lot S-59 gave a range of 1250 to 1500 milligrams per kilogram.

Both samples were classed as mild to moderate skin irritants. The average maximum score for number 102 was 2.3 out of a possible 8.0 in twenty-four hours. Number 17 scored an average of 2.6 after the same time interval.

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Certificate of Analysis

THE TOXICITY OF THE THERMAL DECOMPOSITION PRODUCTS OF
'OS-95'

Study Conducted For
MONSANTO CHEMICAL COMPANY, ST. LOUIS, MISSOURI

COPY

INTRODUCTION

The experiment was designed to determine the effect upon laboratory rats when exposed to a fog of thermal decomposition products produced by dropping OS-95, Lot 7501-3679, a product of Monsanto Chemical Company, on a surface heated to a temperature of 1000° Fahrenheit. Various intensities of fog were generated for different groups of animals.

EXPERIMENTAL PROCEDURE

Half of a fifteen inch McDaniel high temperature combustion tube (inside diameter seven-eighth's inch, non-porous vitreous material) was wound with special sixteen gauge nickel-chromium wire. The wire was attached to a variable transformer for controlling temperature. After being wrapped in asbestos paper, the tube was insulated with four inches of mineral wool and then surrounded with a container made of asbestos board.

The tube was clamped at an angle of approximately 70 degrees with several inches of the unwound end protruding from the container. A thermocouple was inserted to the center of the tube and the temperature measured by an indicating pyrometer.

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EXHIBIT
K-50

TOWOLDMON0001968

At the upper end of the container two openings were made; one large enough for a small funnel to be inserted. The liquid to be volatilized was dropped from a burette at a measured rate, through the funnel to the inner surface of the heated combustion tube. The tube was slanted to prevent the drops from falling through and at the same time allow them to spatter against the sides, making for rapid volatilization.

Curved, three-fourths inch copper tubing was attached to the other opening. The tubing rose to a height of two and one-half feet above the combustion chamber and then returned about the same distance to a one liter flask from which an opening led into a five gallon glass bottle connected to a metal inhalation chamber of seventy liters capacity.

Animals were placed in the chamber, the chamber sealed, and connected to a vacuum pump with rubber tubing. The fluid was dropped at a measured rate onto the inner surface of the combustion tube heated to 1000° F. Sufficient suction was supplied by the pump to pull the combustion products through the copper tubing into the liter flask and five gallon bottle and then into the exposure chamber. From here the fog was drawn into an air trap and a calcium chloride trap attached directly before the vacuum pump. No cooling bath was used for the fog; temperature reduction was achieved by passing the combustion products through the copper tube and the five gallon bottle before entering the chamber. It was desired to expose the animals as nearly as possible to the fog as generated. The liter flask removed some solid particles of combustion.

Supplemental air for the animals' oxygen requirements was supplied by an air compressor and introduced into the five gallon bottle for mixing with the combustion products before entry into the exposure chamber.

The flow of filtered and dried air was controlled by means of a calibrated rotameter.

GBRN002878

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GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

Eight mature male rats were exposed for one hour three days per week for two weeks to a moderate to moderately heavy concentration of OS-95 volatilised at 1000° F. The concentration of fog was sufficient to partially obscure the animals at a depth of six inches within the chamber. Those at the rear of the chamber (a depth of eighteen to twenty-four inches) were all but obscured.

The fate of the animals is shown in Table I.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

Eight mature male rats were exposed for fifteen minutes to a heavy concentration of OS-95 mist produced by volatilization at 1000° F. The concentration was as heavy as obtainable. The animals in the front of the chamber were nearly obscured. Those at a depth of six inches were completely obscured.

The data on the animals is shown in Table II.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

Eight mature male rats were exposed for one hour to a heavy concentration of OS-95 mist produced by volatilisation at 1000° F. The concentration was as heavy as obtainable. The animals in the front of the chamber were nearly obscured. Those at a depth of six inches were completely obscured.

The results are shown in Table III.

GBRN002879

TOWOLDMON0001970

TABLE I

EXPOSURE TO 'CS-95' MIST (MODERATELY HEAVY CONCENTRATION)
ONE HOUR DAILY, THREE DAYS PER WEEK FOR TWO WEEKS (SIX HOURS TOTAL)

Average Temperature Inside Chamber ..... 75.5° F.
Average Relative Humidity Inside Chamber ..... 56.0 %
Volatilization Rate ..... 6.0 ML./ Hour (Equivalent To 8.4 Gm./Hour)
Supplemental Air Supply ..... 6.0 Liters / Minute

Animal Number	Starting Weight Gm.	Weight Change 1 Week After Last Exposure Gm.	Weight Change 2 Weeks After Last Exposure Gm.	Fate
1	215	- 5	0	Survived
2	230	- 15	- 10	Survived
3	220	- 10	- 5	Survived
4	235	+ 5	+ 10	Survived
5	225	0	0	Survived
6	210	- 10	0	Survived
7	240	0	+ 5	Survived
8	225	0	+ 10	Survived

DISCUSSION -

Two weeks after the last one hour exposure in the series of six, all animals were alive and practically normal in outward appearance and behavior. Breathing was quiet and regular with no nasal discharge. Six of the eight animals were either maintaining their starting weight or had gained slightly. Appetite of the remaining two animals had improved over that shown the first week following the last exposure.

Fog from CS-95 decomposed at 1000° F. caused considerable discomfort within a few minutes. Nasal discharge, salivation, moderate lacrimation, and rapid breathing followed by shallow breathing was observed. The animals were usually quite active for ten to fifteen minutes after which they became lethargic and changed position in the chamber less often.

GBRN002880

TOWOLDMON0001971

To: Monsanto Chemical Company,
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 5

Some weakness was noted in the animals at the end of each one hour exposure but they were not in danger of collapse. However, they were less resistant to the fog during the second week and five of the eight developed sniffles. The inflammatory condition did not reach the stage of bronchial rales.

TOWOLDMON0001972

To: Monsanto Chemical Company,
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 6

T A B L E II

EXPOSURE TO 'OS-95' MIST (HEAVY CONCENTRATION) FOR FIFTEEN MINUTES

Average Temperature Inside Chamber ..... 76.5° F.
Average Relative Humidity Inside Chamber ..... 53.5 %
Volatilization Rate ..... 10.4 Ml. / Hour (Equivalent To 14.5 Gm. / Hour)
Supplemental Air Supply ..... 3.5 Liters / Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	225	+ 15	Spasmodic breathing pattern --
2	210	+ 5	Copious salivation and nasal
3	240	+ 10	discharge --
4	235	+ 15	Moderate lacrimation --
5	250	+ 10	Animals fairly steady, can be
6	220	+ 25	seen in front part of cage only.
7	225	+ 20	
8	235	+ 15	

DISCUSSION -

All animals survived the fifteen minutes exposure to a heavy concentration of OS-95 decomposition products. They were lethargic and weak when removed from the chamber but were not in immediate danger of collapse. Oral and nasal discharge had about ceased within an hour. Moderate inflammation of the nasal mucosa was evident for twenty-four to thirty-six hours.

The fog was as dense as could be generated and was sufficient to obscure the animals excepting when they were in the immediate front section of the chamber.

Weight gains ran from five to twenty-five grams two weeks after exposure.

TOWOLDMON0001973

To: Monsanto Chemical Company,
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 7

T A B L E III

EXPOSURE TO 'OS-95' MIST (HEAVY CONCENTRATION) FOR ONE HOUR

Average Temperature Inside Chamber ..... 78.0° F.

Average Relative Humidity Inside Chamber ..... 52.0 %

Volatilization Rate ..... 10.4 Ml./Hour (Equivalent To 14.5 Gm./Hour)

Supplemental Air Supply ..... 4.5 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	235	+ 10	Increasing lethargy —
2	210	+ 20	Almost no activity after
3	240	+ 20	twenty minutes —
4	215	+ 5	Breathing reduced, shallow and
5	225	+ 15	irregular —
6	205	+ 10	Several instances of gasping near
7	230	+ 5	end of exposure —
8	220	+ 15	Nasal and oral discharge — Lacrimation.

DISCUSSION -

The one hour exposure to a heavy concentration of fog resulted in collapse for three of the animals and near collapse for the remainder. There were no deaths however. Fairly rapid recovery was noted after removal from the chamber. The animals were moving about in fifteen to forty-five minutes although weak. Several days were required before activity and appetite returned to normal. Pulmonary congestion, insofar as could be determined by outward observation of breathing rate, had subsided materially in seven to ten days.

All animals showed weight gains two weeks after treatment and it appeared that they would continue to thrive.

TOWOLDMON0001974

THE TOXICITY OF THE THERMAL DECOMPOSITION PRODUCTS OF 'OS-95'

To: Monsanto Chemical Company,
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 8

SUMMARY

GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

All animals survived the schedule of six, one hour exposures spread over a period of two weeks. Copious nasal discharge, salivation, lethargy, and moderate weakness developed. The fog caused considerable inflammation and discomfort but the cumulative effect was not lethal.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

No deaths resulted from fifteen minutes exposure to a heavy concentration of fog. There was irritation but the animals were not in danger of collapse.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

Collapse and near collapse developed in the latter stages of the one hour exposure. No deaths resulted. The animals were moving about in fifteen to forty-five minutes after exposure. Weakness was evident for several days.

YOUNGER LABORATORIES

Fred M. Younger

BY: FRED M. YOUNGER

December 8th, 1958
Monsanto Project Y-58-46

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— Monsanto Chemical Company

GBRN002884

TOWOLDMON0001975

YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

123 CLIFF CAVE ROAD
ST. LOUIS 29, MISSOURI
PHONE: TILDEN 6-2540

Certificate of Analysis

March 4th, 1963
C+2 AM

SUBJECT -

Toxicological Investigation Of: Pyranol 1470
Monsanto Sample Number 21
Monsanto Project Number I-63-11

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

COPY

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.

GBRN002885

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EXHIBIT
K-51

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 32.6 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

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 -

Pyranol 1470

A) Oral LD_{50} (Rats)

The Oral LD_{50} for male and female rats was placed at 2250 milligrams per kilogram with lower and upper limits of 1990 to 2555 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 2000 milligrams per kilogram and less than 3160 milligrams per kilogram. Animal #3, dosed at 2000 milligrams per kilogram, very nearly succumbed.

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

TOWOLDMON0001978

TABLE I

THE ORAL LD_{50} OF 'Pyranol 1470' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	225	1580	Survived
2- Female	210	1580	Survived
3- Male	235	1580	Survived
4- Male	250	1580	Survived
5- Female	215	1580	Survived
6- Female	220	2000	Survived
7- Male	240	2000	Survived
8- Male	245	2000	Survived
9- Female	230	2000	Died
10- Female	215	2000	Survived
11- Male	235	2510	Died
12- Male	240	2510	Survived
13- Female	220	2510	Died
14- Female	210	2510	Died
15- Male	235	2510	Died
16- Male	225	3160	Died
17- Female	220	3160	Died
18- Female	215	3160	Died
19- Male	235	3160	Died
20- Male	245	3160	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 2250 milligrams per kilogram with lower and upper limits of 1990 to 2555 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 three days with most deaths occurring in two to three days.

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

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

TOWOLDMON0001979

TABLE II

THE MINIMUM LETHAL DOSE OF 'Pyranol 1470'
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	2.5	794	- 0.1	Survived
2 - Female	2.2	1260	- 0.1	Survived
3 - Female	2.3	2000	- 0.2	Survived
4 - Female	2.6	3160	- 0.3	Died - 10 Days
5 - Female	2.5	5010	- 0.2	Died - 7 Days
6 - Female	2.5	7940	- 0.4	Died - 7 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.

Animal #3, dosed at 2000 milligrams per kilogram, very nearly succumbed.

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

Survival time was seven to ten days.

Toxic symptoms included loss of appetite, lethargy, and increasing weakness. Weight losses ran to forty per cent of starting weight.

At autopsy there was liver discoloration and renal hyperemia macroscopically.

TOWOLDMON0001980

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'Pyranol 1470'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	3	5	4	3	2	1
2	2	4	3	2	1	0
3	3	5	4	2	2	1
Average	2.6	4.6	3.6	2.3	1.6	0.6

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.

Well-defined redness with very slight edema developed within an hour for an average score of 2.6 out of a possible 8. Overnight there was well-defined to moderate erythema and slight edema increasing the average score to 4.6. No blistering was observed. Inflammation gradually receded following removal of the application. After seven days one animal was given a score of zero but very slight redness was still present on the remaining animals.

TOWOLDMON0001981

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'Pyranol 1470'

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	26	17	12	6	0
2	28	21	13	8	4	0
3	35	30	20	12	6	0
Average	32.6	25.6	16.6	10.6	5.3	0.0

DISCUSSION -

The compound was classed as a moderate eye irritant.

The average maximum score was 32.6 out of a possible 110 in one hour.

There was intermittent pawing at the eyes for several minutes following application.

After one hour the average score was 32.6 out of a possible 110. Slight edema, slight to moderate redness of the conjunctivae, copious discharge, and slight iris congestion developed. The corneal area cleared somewhat in twenty-four hours and within five days iris and cornea were normal. Conjunctivitis and edema cleared completely within seven days.

TOWOLDMON0001982

TABLE V

INHALATION OF 'Pyranol 1470' VAPORS BY RATS

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

Average Relative Humidity Inside Chamber ..... 42 %

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Occasional pawing at the eyes in ten to fifteen minutes ...
2 - Male	Survived	Slight nasal discharge ...
3 - Male	Survived	Some discomfort ...
4 - Male	Survived	No real weakness ...
		Occasional irregular breathing.

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.

The vapors produced mild nasal and eye inflammation as well as some discomfort. No weakness of consequence was noted at the end of exposure and no bronchial rales developed.

Activity and appetite returned to normal within twenty-four hours. Nasal inflammation disappeared within seventy-two hours. No respiratory complications developed during the ten day observation period.

TOWOLDMON0001983

PROJECT NO. Y-63-88
REPORT FILE

ORIGINAL

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

128 CLIFF CAVE ROAD
ST. LOUIS 29, MISSOURI

PHONE: TILDEN 6-2540

Certificate of Analysis

December 19th, 1963

SUBJECT -

Toxicological Investigation Of: MCS - 300
Monsanto Sample Number 112
Monsanto Project Number Y-63-88

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

COPY

EXPERIMENTAL PROCEDURE -

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

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino male and female rats.

After the approximate Minimum Lethal Dose was determined, groups of male and female rats were fed in increasing doses at increments of 0.1 fractional log intervals at four levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to a modification of the method of E. J. de Beer.

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

The data are shown in Table I.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits.

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

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

The data are shown in Table II.

GBRN002893

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EXHIBIT
K-52

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.

A) 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 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 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 -

MCS-300

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

The Oral LD_{50} for male and female rats was placed at 8,920 milligrams per kilogram with lower and upper limits of 7,045 to 11,325 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 3980 milligrams per kilogram and less than 6310 milligrams per kilogram.

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

TOWOLDMON0001985

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 mild eye irritant.

The average maximum score was 19.6 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

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— Monsanto Chemical Company

GBRN002895

TABLE I

THE ORAL LD_{50} OF 'MCS-300' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	220	6,310	Survived
2- Female	235	6,310	Survived
3- Male	230	6,310	Survived
4- Male	240	6,310	Died
5- Female	240	6,310	Survived
6- Female	225	7,940	Survived
7- Male	245	7,940	Died
8- Male	250	7,940	Died
9- Female	215	7,940	Survived
10- Female	220	7,940	Survived
11- Male	250	10,000	Died
12- Male	235	10,000	Died
13- Female	205	10,000	Survived
14- Female	215	10,000	Survived
15- Male	235	10,000	Died
16- Male	240	12,600	Died
17- Female	220	12,600	Survived
18- Female	225	12,600	Died
19- Male	235	12,600	Died
20- Male	240	12,600	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 8,920 milligrams per kilogram with lower and upper limits of 7,045 to 11,325 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 two to three days.

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

At autopsy there was inflammation of the gastrointestinal mucosa with liver and renal hyperemia.

GBRN002896

TOWOLDMON0001987

TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS-300' 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	2.2	1,000	0.0	Survived
2 - Male	2.5	1,580	- 0.2	Survived
3 - Female	2.2	2,510	- 0.2	Survived
4 - Male	2.4	3,980	- 0.4	Survived
5 - Female	2.3	6,310	- 0.3	Died — 5 Days
6 - Male	2.6	10,000	———	Died — 3 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 3980 milligrams per kilogram and less than 6310 milligrams per kilogram.

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

Survival time was three to five days.

Toxic symptoms included weakness, tremors, and muscular impairment after forty-eight to seventy-two hours.

At autopsy no visceral changes of consequence were noted, excepting for pulmonary hyperemia.

GBRN002897

TOWOLDMON0001988

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-300'

Sample Applied Undiluted

Animal Number	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	0	4	4	3	2	1
2	0	5	4	3	3	2
3	0	4	3	3	2	2
Average	0.0	4.3	3.6	3.0	2.6	1.6

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.

No skin changes were noted after one hour. Overnight there was well-defined erythema with slight to moderate edema for an average score of 4.3. No blistering developed but the edges of the treated areas were outlined by definite raising. Reduction of inflammation was gradual following removal of the application. After seven days slight redness and swelling were still present.

TOWOLDMON0001989

T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-300'

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	18	16	11	7	2	0
2	18	13	9	4	0	0
3	23	18	13	9	4	0
Average	19.6	15.6	11.0	6.6	2.0	0.0

DISCUSSION -

The compound was classed as a mild eye irritant.

The average maximum score was 19.6 out of a possible 110 in one hour.

Discomfort was moderate immediately following application.

Mild redness of the conjunctivae, slight edema, little or no discharge, and slight corneal dullness developed within one hour for an average score of 19.6. Congestion decreased slightly in twenty-four hours. In five days, iris and cornea were clear and only a trace of erythema remained for an average score of 2.0.

TOWOLDMON0001990

T A B L E V

INHALATION OF 'MCS-300' VAPORS BY RATS

Average Temperature Inside Chamber ..... 77° F.

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

Amount Of Sample -- To Start ..... 150 cc
Recovered ..... 148 cc
Vaporized or left in the apparatus ..... 2 cc (1.3%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Mild lethargy after thirty to sixty minutes ...
2 - Male	Survived	No discomfort ...
3 - Male	Survived	Normal breathing rate ...
4 - Male	Survived	No inflammation.

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. No signs of irritation or discomfort were noted during the test. Nasal and ocular mucosae were free of inflammation upon examination at the end of the six hours. The ten days observation period was uneventful.

TOWOLDMON0001991

PROJECT NO: Y-65-214
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

Certificate of Analysis

January 12th, 1966

SUBJECT -

Toxicological Investigation Of: MCS - 404

Monsanto Sample Number 245

Monsanto Project Number Y-65-214

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.

GBRN002901

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EXHIBIT
K-53

TOWOLDMON0001992

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 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 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.

TOWOLDMON0001993

SUMMARY -

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

The Oral LD_{50} for male and female rats was placed at 19,800 milligrams per kilogram with lower and upper limits of 17,030 to 23,165 milligrams per kilogram.

The compound was classed as practically non-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 1000 milligrams per kilogram and less than 1580 milligrams per kilogram.

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

D) Skin Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 0.6 out of a possible 8 in twenty-four hours.

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 11.6 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 relatively non-toxic under conditions of the test.

YOUNGER LABORATORIES

BY: FRED M. YOUNGER

GBRN002903

TOWOLDMON0001994

T A B L E I

THE ORAL LD_{50} OF 'M C S - 404' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Rate
1- Female	230	12,600	Survived
2- Male	245	12,600	Survived
3- Female	220	12,600	Survived
4- Male	240	12,600	Survived
5- Female	225	12,600	Survived
6- Male	250	15,800	Survived
7- Female	235	15,800	Survived
8- Male	260	15,800	Survived
9- Female	240	15,800	Died
10- Male	265	15,800	Survived
11- Female	235	20,000	Died
12- Male	255	20,000	Survived
13- Female	225	20,000	Died
14- Male	250	20,000	Died
15- Female	230	20,000	Survived
16- Male	270	25,100	Died
17- Female	235	25,100	Died
18- Male	255	25,100	Survived
19- Female	240	25,100	Died
20- Male	260	25,100	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 19,800 milligrams per kilogram with lower and upper limits of 17,030 to 23,165 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 three to four days.

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

At autopsy the gastreintestinal tract was gaseous and there was liver congestion.

GBRN002904

TOWOLDMON0001995

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 5 (1/12/66) - Y-65-214

T A B L E II

THE MINIMUM LETHAL ORAL DOSE OF 'MCS - 404' FOR RABBITS

Sample Fed Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.3	1000	+ 0.2	Survived
2 - Male	2.4	1580	+ 0.1	Survived
3 - Female	2.6	2510	- 0.2	Died -- 5 Days
4 - Male	3.1	2510	- 0.3	Died -- 7 Days
5 - Female	2.7	3980	- 0.2	Died -- 8 Days
6 - Male	2.7	6310	- 0.3	Died -- 8 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 five to eight days.
Toxic symptoms included gradual loss of appetite with increasing weakness, lethargy, and collapse.

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

The material in this report is to be used in development of the product and may be given to [illegible] sales contacts, but it is not to be used [illegible] [illegible] [illegible] of toxicity are to be [illegible] to the Medical Department in St. Louis for reply.

— Monsanto Chemical Company

GBRN002905

TOWOLDMON0001996

TABLE III

THE MINIMUM LETHAL DOSE OF 'MCS-404' 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	2.7	631	+ 0.1	Survived
2 - Male	3.3	1000	- 0.1	Survived
3 - Female	2.5	1580	- 0.2	Died — 6 Days
4 - Male	2.6	2510	- 0.4	Died -- 9 Days
5 - Female	2.3	3980	- 0.2	Died - 14 Days
6 - Male	2.8	6310	- 0.3	Died — 5 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1000 milligrams per kilogram and less than 1580 milligrams per kilogram.

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

Survival time was five to fourteen days.
Toxic symptoms included weakness after three to six days, reduced appetite, dyspnea, collapse, and paralysis.

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

GBRN002906

TOWOLDMON0001997

T A B L E IV

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-404'

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	0	0	0	0
3 - Male	0	1	0	0	0
Average	0.0	0.6	0.3	0.0	0.0

DISCUSSION -

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

The average maximum score was 0.6 out of a possible 8 in twenty-four hours.

No skin changes were noted at the end of one hour. Overnight there were two instances of very slight redness with no edema for an average score of 0.6. Within seventy-two hours all animals were free of inflammation.

TOWOLDMON0001998

T A B L E V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS-404'

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	11	9	4	2	0
2 - Male	11	6	2	0	0
3 - Female	13	8	4	4	0
Average	11.6	7.6	3.3	2.0	0.0

DISCUSSION -

The compound was classed as a slight eye irritant.
The average maximum score was 11.6 out of a possible 110 in one hour.

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

Mild discharge, slight redness, very slight edema, and slight corneal dullness was recorded after one hour. Edema and discharge disappeared overnight. Within three days only a trace to slight erythema remained on two animals.

TOWOLDMON0001999

T A B L E VI

INHALATION OF 'MCS-404' VAPORS BY RATS

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

Average Relative Humidity Inside Chamber ..... 44 %

Amount of Sample -- To start ..... 100.0 cc
Recovered ..... 99.5 cc
Vaporized or left in equipment ..... 0.5 cc (0.5%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No immediate effect ...
2 - Male	Survived	Lethargy after one hour ...
3 - Male	Survived	No discomfort ...
4 - Male	Survived	Normal respiration ...
		No weakness.

DISCUSSION -

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

It was concluded that the vapors were relatively non-toxic under conditions of the test.

With the exception of moderate lethargy, the animals showed no reaction to the vapors. Weakness was absent and no nasal or ocular inflammation was noted. Activity and appearance were normal the day following exposure and no respiratory complications developed during the ten day observation period.

TOWOLDMON0002000

Y-64-7

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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PHONE: TILDEN 6-2840

Certificate of Analysis

February 13th, 1964

SUBJECT -

Toxicological Investigation Of: FE - 145

Monsanto Sample Number 7

Monsanto Project Number Y-64-7

STUDY CONDUCTED FOR -

Monsanto Chemical 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 female and male 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.

GBRN002910

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EXHIBIT K-54

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Absorption MLD (Rabbits, Mixed Sex)

The undiluted compound was applied in increasing doses at increments of [illegible] 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)

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 IV.

E) 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 V.

F) Vapor Inhalation (Male Rats)

Four 150-gram male rats were placed in a glass desiccator, [illegible] mm in diameter, and exposed for 6 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 5 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.

GBRN002911

TOWOLDMON0002002

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

SUMMARY -

FE-145

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

The Oral LD_{50} for male and female rats was placed at 6680 milligrams per kilogram with lower and upper limits of 5375 to 8285 milligrams per kilogram.

The compound was classed as practically non-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 1000 milligrams per kilogram and less than 1580 milligrams per kilogram.

The compound was classed as mildly 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)

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

The average maximum score was 4.0 out of a possible 8 in twenty-four hours.

E) Eye Irritation (Rabbits)

The compound was classed as a mild to moderate eye irritant.

The average maximum score was 23.6 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 slightly toxic under conditions of the test.

YOUNGER LABORATORIES

BY: FRED N. YOUNGER

GBRN002912

TOWOLDMON0002003

TABLE I

THE ORAL LD_{50} OF 'FW-145' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gms.	Dose Mg./Kg.	Rats
1- Female	215	5,010	Survived
2- Female	250	5,010	Died
3- Male	245	5,010	Survived
4- Male	240	5,010	Survived
5- Female	225	5,010	Survived
6- Female	230	6,310	Survived
7- Male	250	6,310	Died
8- Male	260	6,310	Survived
9- Female	235	6,310	Died
10- Female	235	6,310	Survived
11- Male	240	7,940	Survived
12- Male	260	7,940	Died
13- Female	225	7,940	Died
14- Female	235	7,940	Survived
15- Male	240	7,940	Survived
16- Male	250	10,000	Died
17- Female	220	10,000	Died
18- Female	225	10,000	Died
19- Male	240	10,000	Died
20- Male	245	10,000	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 6680 milligrams per kilogram with lower and upper limits of 5375 to 8285 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.

Toxic symptoms included gradually increasing weakness, diarrhea, tremors, and coma of up to twenty-four hours duration.

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

TOWOLDMON0002004

TABLE II

THE MINIMUM LETHAL ORAL DOSE OF 'Fi-145' FOR RABBITS

Sample Fed Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Male	3.0	651	+ 0.2	Survived
2 - Female	2.0	1000	0.0	Survived
3 - Male	3.1	1580	-----	Died -- 3 Days
4 - Female	2.8	2510	-----	Died -- 2 Days
5 - Male	3.2	3980	-----	Died -- 2 Days
6 - Female	2.7	6310	-----	Died -- 1 Day

DISCUSSION -

The Minimum Lethal Oral Dose for male and female rabbits was found to be greater than 1000 milligrams per kilogram and less than 1580 milligrams per kilogram.

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

Survival time was one to three days.

Toxic symptoms included tremors after several hours, salivation, increasing weakness, and collapse.

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

GBRN002914

TOWOLDMON0002005

TABLE III

THE MINIMUM LETHAL DOSE OF 'FM-145'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Date
1 - Female	2.8	631	+ 0.1	Survived
2 - Male	3.1	1000	0.0	Survived
3 - Female	2.6	1580	- 0.2	Survived
4 - Male	3.0	2510	- 0.4	Survived
5 - Female	2.6	3980	-----	Died -- 2 Days
6 - Male	3.1	6310	-----	Died -- 2 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 two days for animals #5 and #6.

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

At autopsy there was liver discoloration and renal congestion by macroscopic examination.

GBRN002915

TOWOLDMON0002006

T A B L E IV

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'FR-145'

Sample Applied Undiluted

	Numerical Evaluation At The End Of					
Animal Number	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	2	4	5	2	1	0
2	1	4	5	2	0	0
3	2	4	4	2	1	0
Average	1.6	4.0	4.3	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 4.0 out of a possible 8 in twenty-four hours.

After one hour there was slight to well-defined redness for an average score of 1.6. Inflammation increased in twenty-four hours to slight edema and well-defined to moderate erythema.

After removal of the application, irritation diminished to a trace of redness in five days.

GBRN002916

TOWOLDMON0002007

T A B L E V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'FH-145'

Sample (0.1 Milliliter, Applied Undiluted

Animal Number	Numerical Evaluation At The End Of					
	1 Hour	4 Hours	15 Hours	72 Hours	120 Hours	168 Hours
1	22	15	8	4	[illegible]	0
2	27	21	14	9	4	0
3	22	18	10	7	2	0
Average	23.6	18.0	10.6	6.6	2.0	0.0

DISCUSSION -

The compound was classed as a mild to moderate eye irritant.

The average maximum score was 23.6 out of a possible 110 in one hour.

Considerable discomfort was shown immediately upon application.

After one hour there was moderate lacrimation, slight edema, mild to moderate redness of the palpebral conjunctivae, mild iris congestion, and slight corneal dullness for an average score of 23.6. Discharge ceased in twenty-four hours and congestion reduced, lowering the average score to 18.0. Iris and cornea were normal in five days. A slight degree of redness was still present in two instances.

GBRN002917

TOWOLDMON0002008

T A B L E VI

INHALATION OF 'FH-145' VAPORS BY RATS

Average Temperature Inside Chamber ..... 73° F.

Average Relative Humidity Inside Chamber ..... 54 %

Amount Of Sample - To Start ..... 150.0 cc
Recovered ..... 148.5 cc
Vaporized or Left In Apparatus ..... 1.5 cc (1.0%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Some discomfort in ten to fifteen minutes ...
2 - Male	Survived	Mild nasal discharge ...
3 - Male	Survived	Lethargy ...
4 - Male	Survived	Occasional shallow breathing ...
		No weakness of consequence.

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.

Inhalation of the vapors caused some discomfort but the animals were not weakened to any extent. No bronchial rales or other evidence of respiratory inflammation was noted either immediately following exposure or during the ten day observation period.

TOWOLDMON0002009