REPORT FILE

YOUNGER LABORATORIES
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# *Certificate of Analysis*

September 14th, 1970

SUBJECT -

Toxicological Investigation Of: MC S 1007 - Pydraul F-9A (Amendment 1)
Monsanto Sample Number 93
Monsanto Project Number Y-70-87

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

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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 six levels designed to blanket the toxicity range thereby supplying data for calculation of the $LD_{50}$ which was done according to the method of E. J. de Beer.

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

Observations were made for toxic signs and the viscera of the test animals were examined macroscopically.

The data are shown in Table II.

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EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits, Mixed Sex)

0.5 Milliliter of undiluted sample was applied to the clipped, intact skin of three albino male and female rabbits under a one inch by one inch square patch, two single layers thick. The patches were held in place with adhesive tape. The trunk of each animal was wrapped with plastic strips, to avoid contamination and retard evaporation, for the twenty-four hour exposure period.

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

The data, scored according to the method of Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Rabbits, Mixed Sex)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino male and female rabbits and observations made over a period of seven days for inflammation.

The eyes were rinsed with warm isotonic saline solution after twenty-four hours.

The data, scored according to the method of Draize, et al, are shown in Table IV.

E) Vapor Inhalation (Male Rats) - Ambient Temperature

Six mature male rats were placed in a metal chamber of 35-liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 113.3 grams 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 four liters per minute as measured by a calibrated rotameter. This was sufficient to violently agitate the liquid. No supplementary air was introduced inasmuch as the above supply was ample for the animals oxygen requirements.

The animals were observed for behavior during exposure and for ten days following exposure. The viscera of the test animals were examined macroscopically.

SUMMARY -

MCS 1007 - Pydraul F-9A (Amendment 1)

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

The Oral $LD_{50}$ for male and female rats was placed at 8,100 milligrams per kilogram with lower and upper limits of 7,370 to 8,910 milligrams per kilogram.

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



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SUMMARY - (Continued)

B) Skin Absorption MLD (Rabbits, Mixed Sex)

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

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

C) Skin Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 3.0 out of a possible 8 in seventy-two hours.

D) Eye Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 10.0 out of a possible 110 in one hour.

E) Vapor Inhalation (Male Rats) - Ambient Temperature

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, INC.

BY: MELVIN D. BIRCH

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# TABLE I

## THE ORAL $LD_{50}$ OF

## 'MCS 1007 - Pydraul F-9A (Amendment 1)'

## FOR RATS

Sample Fed Undiluted

| Animal No. - Sex | Weight Gm. | Dose Mg./Kg. | Fate |
|---|---|---|---|
| 1- Female | 190 | 3,980 | Survived |
| 2- Male | 210 | 3,980 | Survived |
| 3- Female | 200 | 3,980 | Survived |
| 4- Male | 190 | 3,980 | Survived |
| 5- Female | 200 | 3,980 | Survived |
| 6- Male | 230 | 5,010 | Survived |
| 7- Female | 220 | 5,010 | Survived |
| 8- Male | 250 | 5,010 | Survived |
| 9- Female | 205 | 5,010 | Died |
| 10- Male | 200 | 5,010 | Survived |
| 11- Female | 210 | 6,310 | Survived |
| 12- Male | 200 | 6,310 | Survived |
| 13- Female | 195 | 6,310 | Survived |
| 14- Male | 195 | 6,310 | Survived |
| 15- Female | 195 | 6,310 | Died |
| 16- Male | 210 | 7,940 | Survived |
| 17- Female | 220 | 7,940 | Died |
| 18- Male | 210 | 7,940 | Died |
| 19- Female | 195 | 7,940 | Survived |
| 20- Male | 200 | 7,940 | Survived |
| 21- Female | 200 | 10,000 | Died |
| 22- Male | 195 | 10,000 | Died |
| 23- Female | 200 | 10,000 | Survived |
| 24- Male | 200 | 10,000 | Survived |
| 25- Female | 195 | 10,000 | Died |
| 26- Male | 195 | 12,600 | Died |
| 27- Female | 250 | 12,600 | Died |
| 28- Male | 210 | 12,600 | Died |
| 29- Female | 195 | 12,600 | Died |
| 30- Male | 255 | 12,600 | Died |

DISCUSSION -

The Oral $LD_{50}$ for male and female rats was placed at 8,100 milligrams per kilogram with lower and upper limits of 7,370 to 8,910 milligrams per kilogram.

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



Continued

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TABLE I -- DISCUSSION (Continued)

Survival time was one to four days with most deaths occurring during second and third day.

Toxic signs included reduced appetite and activity (for one to four days in survivors), lethargy, increasing weakness, collapse, and death.

At autopsy there was hemorrhagic lungs, liver discoloration, and gastrointestinal inflammation.

Surviving animals were sacrificed seven days after dosing. Macroscopic examination revealed slight areas of lung congestion in upper dosage levels; viscera of animals in lower dosage levels appeared normal.

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## TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS 1007 - Pydraul F-9A (Amendment 1)'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

| Animal No. - Sex | Weight Kg. | Dose Mg./Kg. | Weight Change 5 Days Later Kg. | Fate |
|---|---|---|---|---|
| 1 - Male | 1.8 | 1260 | 0.0 | Survived |
| 2 - Female | 1.8 | 2000 | - 0.1 | Survived |
| 3 - Male | 1.8 | 2000 | 0.0 | Survived |
| 4 - Female | 2.0 | 2000 | - 0.1 | Survived |
| 5 - Male | 1.8 | 3160 | - 0.1 | Died -- 9 Days |
| 6 - Female | 2.5 | 5010 | - 0.3 | Died -- 6 Days |

DISCUSSION -

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

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

Survival time was six to nine days.

Toxic signs included reduced appetite and activity (for five to ten days in survivors), slight diarrhea noted on fourth to fifth day, increasing weakness, collapse, and death.

At autopsy there was congestion of the lungs, enlarged gall bladder, mottled and discolored liver, slight discoloration of kidneys, and slight gastrointestinal inflammation.

Surviving animals were sacrificed fourteen days after dosing. Macroscopic examination revealed slight congestion of the lungs and slight liver discoloration.



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## T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF
'M C S 1007 - Pydraul F-9A (Amendment 1)'

Sample (0.5 Milliliter) Applied Undiluted

| Animal No. - Sex | Numerical Evaluation At The End Of | | | | | |
|---|---|---|---|---|---|---|
| | 1 Hour | 24 Hours | 48 Hours | 72 Hours | 120 Hours | 168 Hours |
| 1 - Male | 0 | 1 | 2 | 3 | 2 | 2 |
| 2 - Female | 0 | 2 | 3 | 3 | 2 | 2 |
| 3 - Male | 0 | 1 | 3 | 3 | 2 | 2 |
| Average | 0.0 | 1.3 | 2.6 | 3.0 | 2.0 | 2.0 |

DISCUSSION -

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

The average maximum score was 3.0 out of a possible 8 in seventy-two hours.

Observations following application --

| | |
|---|---|
| 1-Hour: | No skin changes; zero readings |
| 24-Hours: | Barely perceptible to slight erythema; no edema |
| 48-Hours: | Barely perceptible to slight erythema, barely perceptible edema |
| 72-Hours: | Barely perceptible erythema, slight edema |
| 120- 168-Hours: | No erythema; slight edema (slight thickening of the skin, still remained after fourteen days) |

Note: Sample had a slight drying effect on the skin causing the skin to scale off in seven to ten days.



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T A B L E  I V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF

'MCS 1007 -- Pydraul F-9A (Amendment 1)'

Sample (0.1 Milliliter) Applied Undiluted

| | Numerical Evaluation At The End Of | | | | | |
|---|---|---|---|---|---|---|
| Animal No. - Sex | 1 Hour | 24 Hours | 48 Hours | 72 Hours | 120 Hours | 168 Hours |
| 1 - Male | 10 | 0 | 0 | 0 | 0 | 0 |
| 2 - Female | 10 | 2 | 0 | 0 | 0 | 0 |
| 3 - Male | 10 | 2 | 0 | 0 | 0 | 0 |
| Average | 10.0 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 |

DISCUSSION -

The compound was classed as a slight eye irritant in male and female rabbits. The average maximum score was 10.0 out of a possible 110 in one hour.

Observations following application --

| | |
|---|---|
| Immediate: | Discomfort was slight |
| 10-Minutes: | Slight erythema, barely perceptible edema, moderate discharge |
| 1-Hour: | Moderate erythema and discharge, barely perceptible edema |
| 24-Hours: | Slight erythema in two instances; no edema or discharge |
| 48-Hours: | Eyes normal; zero readings |
| 72- 168-Hours: | Eyes normal; zero readings |

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# T A B L E V

## INHALATION OF

## 'M C S 1007 - Pydraul F-9A (Amendment 1)' VAPORS BY RATS

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

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

Average Concentration Of Sample Entering Chamber ..... 0.21 cc/$M^3$

Amount of Sample -- To start ..... 113.3 Grams
Recovered ..... 113.0 Grams
Vaporized or left
in equipment ..... 0.3 Gram (0.2 %)

| Animal No. - Sex | Fate | Observations During Exposure |
|---|---|---|
| 1 - Male | Survived | No nasal or ocular discharge ... |
| 2 - Male | Survived | No weakness or drowsiness of consequence ... |
| 3 - Male | Survived | |
| 4 - Male | Survived | Normal respiration. |
| 5 - Male | Survived | |
| 6 - Male | Survived | |

DISCUSSION -

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

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

Observations following exposure --

All animals appeared normal when removed from the chamber.
There was reduced appetite and activity for one to two days. In three to four days all animals recovered initial weight and in ten days all showed normal weight gain.

Surviving animals were sacrificed ten days following exposure. The viscera appeared normal by macroscopic examination.



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