PROJECT NO: Y-69-41
REPORT

YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

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Certificate of Analysis

May 5th, 1969

SUBJECT -

Toxicological Investigation Of: MCS 900

Monsanto Sample Number 51

Monsanto Project Number Y-69-41

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

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

The diluted 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 test animals were examined macroscopically.

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

B) Skin Absorption MLD (Rabbits, 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 symptoms 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)

The undiluted compound was applied to the clipped, intact skin of albino male and female rabbits and removed after twenty-four hours. The application was covered with plastic strips to retard evaporation and avoid contamination.

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

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

D) Eye Irritation (Rabbits, Mixed Sex)

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

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

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

E) Vapor Inhalation (Male Rats)

Six mature male rats were placed in a metal chamber of 70 liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 204 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 and since there were no deaths, all were held for ten days observation, then sacrificed for macroscopic examination.

The data are shown in Table V.

SUMMARY -

MCS 900

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

The Oral LD_{50} for male and female rats was placed at 1280 milligrams per kilogram with lower and upper limits of 1180 to 1380 milligrams per kilogram.

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

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SUMMARY - (Continued)

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The highest application of 7940 milligrams per kilogram was found to be non-lethal by skin absorption in male and female rabbits.

The compound was classed as practically non-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 2.0 out of a possible 8 in twenty-four 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 10.6 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: MELVIN D. BIRCH

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TABLE I

THE ORAL LD_{50} OF 'MCS 900' FOR RATS

Sample Fed As A 10.0% Solution In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	225	794	Survived
2- Male	245	794	Survived
3- Female	210	794	Survived
4- Male	250	794	Survived
5- Female	220	794	Survived
6- Male	260	1000	Died
7- Female	250	1000	Survived
8- Male	255	1000	Survived
9- Female	235	1000	Survived
10- Male	245	1000	Survived
11- Female	220	1260	Died
12- Male	250	1260	Died
13- Female	250	1260	Survived
14- Male	245	1260	Survived
15- Female	220	1260	Died
16- Male	250	1580	Died
17- Female	225	1580	Died
18- Male	240	1580	Survived
19- Female	225	1580	Died
20- Male	260	1580	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 1280 milligrams per kilogram with lower and upper limits of 1180 to 1380 milligrams per kilogram.

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

Survival time was one to three days with most deaths occurring during the second day.

Toxic symptoms included reduced appetite for two to three days, increasing weakness, and collapse.

At autopsy there was jaundice areas of the liver, lung hyperemia, and distended coronaries.

Surviving animals were sacrificed nine days after dosing. Macroscopic examination showed discolored areas of the liver and lung hyperemia at the higher dosage levels; slight discoloration of the liver was noted at the lower dosage levels.

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TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS 900'
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	2.4	2000	+ 0.1	Survived
2 - Male	2.4	3160	0.0	Survived
3 - Female	2.5	5010	- 0.1	Survived
4 - Male	2.2	7940	- 0.2	Survived
5 - Female	2.4	7940	- 0.1	Survived

DISCUSSION -

The highest application of 7940 milligrams per kilogram was found to be non-lethal by skin absorption in male and female rabbits.

The compound was classed as practically non-toxic by skin absorption in male and female rabbits.

Toxic symptoms included reduced appetite and slight weakness in animals #3 through #5; weight loss in fourteen days was 0.5 kilogram to 0.7 kilogram.

Surviving animals were sacrificed fourteen days after dosing. Macroscopic examination showed mottled and discolored liver, and gaseous intestines in animals #4 and #5. Areas of slight discoloration of the liver were noted in animals #2 and #3. The viscera of animal #1 appeared normal.

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TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF

'MCS 900'

Sample 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	1	2	1	0	0	0
2 - Female	1	2	1	0	0	0
3 - Male	1	2	1	0	0	0
Average	1.0	2.0	1.0	0.0	0.0	0.0

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

Within minutes after application there was twitching of the skin and barely perceptible redness was noted.

At the one hour reading there was barely perceptible redness with no edema.

Within twenty-four hours there was barely perceptible redness and very slight edema.

Within forty-eight hours edema had disappeared.

All animals received a score of zero within three days.

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TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'MCS 900'

Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of					
	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	10	4	2	0	0	0
2 - Female	10	4	0	0	0	0
3 - Female	12	4	2	0	0	0
Average	10.6	4.0	1.3	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 10.6 out of a possible 110 in one hour.

There was mild to moderate discomfort with blinking and closed lids immediately following application.
Within ten minutes there was slight erythema and edema, and discharge.
At the one hour reading erythema was slight, edema mild, and there was moderate discharge with traces of whitish exudate. There was no corneal cloudiness.
Within twenty-four hours discharge had ceased and erythema and edema were slight.
Within forty-eight hours there was barely perceptible erythema; edema had disappeared.
All animals received a score of zero within three days.

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TABLE V

INHALATION OF

'MCS 900' VAPORS BY RATS

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

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

Amount of Sample -- To start ..... 204.0 Grams
Recovered ..... 202.9 Grams
Vaporized or left in equipment ..... 1.1 Grams (0.54%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No immediate effect ...
2 - Male	Survived	No apparent discomfort or lethargy ...
3 - Male	Survived	
4 - Male	Survived	No weakness or nasal discharge ...
5 - Male	Survived	Normal respiration.
6 - Male	Survived	

DISCUSSION -

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

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

There were no visible signs of weakness or distress of any consequence observed during the exposure period. Ocular and nasal mucosae remained free of inflammation.

The ten day observation period was uneventful. Weight gain was normal.

Test animals were sacrificed ten days after exposure. Macroscopic examination revealed slight areas of lung congestion in all animals; otherwise the viscera appeared normal.