PROJECT NO. Y-66-151
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

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

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Certificate of Analysis

October 17th, 1966

SUBJECT -

Toxicological Investigation Of: MCS 990

Monsanto Sample Number 176

Monsanto Project Number Y-66-151

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

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

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

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

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

The data are shown in Table I.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

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

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

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

The data are shown in Table II.

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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, et al, are shown in Table IV.

E) Vapor Inhalation (Male Rats)

Four mature male rats were placed in a metal chamber of 35 liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 100 milliliters of the compound contained in a 250-milliliter Erlenmeyer flask.

Vapors from the flask passed into a one liter bottle to remove droplets and then into the chamber.

Air flow through the sample was four liters per minute as measured by a calibrated rotameter. This was sufficient to violently agitate the liquid. No supplementary air was introduced inasmuch as the above supply was ample for the animals oxygen requirements.

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

The data are shown in Table V.

SUMMARY -

MCS 90

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

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

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

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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 slight irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 1.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

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

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

E) Vapor Inhalation (Male Rats)

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

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

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BY: FRED M. YOUNGER

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TABLE I

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

Sample Fed Undiluted

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

DISCUSSION -

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

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

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

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

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

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TABLE II

THE MINIMUM LETHAL DOSE OF 'MCS 90'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Male	2.8	501	+ 0.1	Survived
2 - Female	2.3	794	+ 0.2	Survived
3 - Male	2.9	1260	0.0	Survived
4 - Female	2.5	2000	- 0.2	Survived
5 - Male	2.8	3160	- 0.4	Died -- 6 Days
6 - Female	2.6	5010	-----	Died -- 2 Days

DISCUSSION -

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

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

Survival time was two to six days.

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

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

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T A B L E III

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

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1 - Male	0	1	1	0	0
2 - Female	0	2	1	1	0
3 - Male	0	2	2	1	0
Average	0.0	1.6	1.3	0.6	0.0

DISCUSSION -

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

The average maximum score was 1.6 out of a possible 8 in twenty-four hours.

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

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TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'MCS 90'

Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of					
	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	29	20	13	9	4	0
2 - Female	24	17	9	4	0	0
3 - Male	31	24	15	9	4	0
Average	28.0	20.3	12.3	7.3	2.6	0.0

DISCUSSION -

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

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

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

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TABLE V

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

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

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

DISCUSSION -

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

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

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

No respiratory complications developed during the ten day observation period.

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