

YOUNGER LABORATORIES

Biochemists... Pharmacologists... Analysts

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Certificate of Analysis

November 9th, 1966

SUBJECT -

Toxicological Investigation Of: MCS 404
Monsanto Sample Number 189
Monsanto Project Number Y-66-164

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD₅₀ (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 LD₅₀ 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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SUMMARY -

MCS 404

A) Oral LD₅₀ (Rats, Mixed Sex)

The Oral LD₅₀ for male and female rats was placed at 15,000 milligrams per kilogram with lower and upper limits of 10,875 to 20,700 milligrams per kilogram.

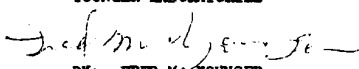
The compound was classed as practically non-toxic by oral ingestion in male and female rats.

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 1260 milligrams per kilogram and less than 2000 milligrams per kilogram.

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

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BY: FRED M. YOUNGER

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— Monsanto Company

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TABLE I

THE ORAL LD₅₀ OF 'MCS 404' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight	Dose	Fate
	Gm.	Mg./Kg.	
1- Female	230	10,000	Survived
2- Male	245	10,000	Survived
3- Female	215	10,000	Survived
4- Male	240	10,000	Survived
5- Female	220	10,000	Died
6- Male	250	12,600	Died
7- Female	215	12,600	Survived
8- Male	260	12,600	Survived
9- Female	225	12,600	Died
10- Male	240	12,600	Survived
11- Female	210	15,800	Died
12- Male	235	15,800	Survived
13- Female	225	15,800	Survived
14- Male	270	15,800	Died
15- Female	230	15,800	Survived
16- Male	250	20,000	Died
17- Female	220	20,000	Died
18- Male	260	20,000	Survived
19- Female	215	20,000	Died
20- Male	255	20,000	Died

DISCUSSION -

The Oral LD₅₀ for male and female rats was placed at 15,000 milligrams per kilogram with lower and upper limits of 10,875 to 20,700 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 six days.

Toxic symptoms included severe diarrhea, lacrimation, tremors, dyspnea, and collapse.

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

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T A B L E II
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	2.4	501	+ 0.1	Survived
2 - Male	2.9	794	- 0.1	Survived
3 - Female	2.4	1260	- 0.3	Survived
4 - Male	2.7	2000	- 0.2	Died -- 8 Days
5 - Female	2.3	3160	- 0.3	Died -- 5 Days
6 - Male	2.7	5010	----	Died -- 4 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 1260 milligrams per kilogram and less than 2000 milligrams per kilogram.

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

Survival time was four to eight days.

Toxic symptoms included increasing weakness, tremors, dyspnea, and paralysis.

At autopsy there was liver and pulmonary congestion.

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