

PROJECT NO: Y-66-165
PORT FILE

YOUNGER LABORATORIES

Biochemists ... Pharmacologists ... Analysts

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Certificate of Analysis

November 9th, 1966

SUBJECT - SANTOSAFA 330

Toxicological Investigation Of: MCS 528

Monsanto Sample Number 190

Monsanto Project Number Y-66-165

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)

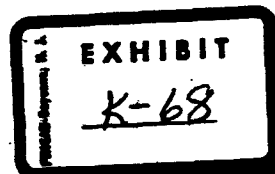
The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits.

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 528

A) Oral LD₅₀ (Rats, Mixed Sex)

The Oral LD₅₀ for male and female rats was placed at 8400 milligrams per kilogram with lower and upper limits of 6885 to 10,250 milligrams per kilogram.

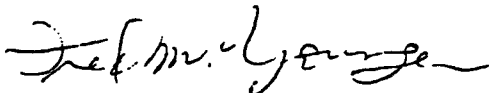
The compound was classed as practically non-toxic by oral ingestion in male and female rats.

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

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

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BY: FRED M. YOUNGER

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TABLE I

THE ORAL LD₅₀ OF 'MCS 528' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	210	6,310	Survived
2- Male	240	6,310	Survived
3- Female	225	6,310	Survived
4- Male	250	6,310	Survived
5- Female	215	6,310	Died
6- Male	235	7,940	Survived
7- Female	220	7,940	Survived
8- Male	260	7,940	Died
9- Female	215	7,940	Died
10- Male	245	7,940	Survived
11- Female	230	10,000	Died
12- Male	265	10,000	Died
13- Female	210	10,000	Died
14- Male	240	10,000	Survived
15- Female	225	10,000	Died
16- Male	235	12,600	Died
17- Female	215	12,600	Died
18- Male	245	12,600	Survived
19- Female	220	12,600	Died
20- Male	250	12,600	Died

DISCUSSION -

The Oral LD₅₀ for male and female rats was placed at 8,400 milligrams per kilogram with lower and upper limits of 6,885 to 10,250 milligrams per kilogram.

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

Survival time was one to five days.

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

At autopsy the lungs were hemorrhagic and there was liver congestion.

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T A B L E II

THE MINIMUM LETHAL DOSE OF 'MCS 528'
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	2.5	794	- 0.1	Survived
3 - Male	3.0	1260	- 0.2	Died -- 7 Days
4 - Female	2.5	2000	- 0.3	Died -- 5 Days
5 - Male	2.7	3160	- 0.2	Died -- 5 Days
6 - Female	2.4	5010	-----	Died -- 4 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 794 milligrams per kilogram and less than 1260 milligrams per kilogram.

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

Survival time was four to seven days.

Toxic symptoms included weakness in two to three days, loss of appetite, reduced activity, and paralysis.

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

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