YOUNGER LABORATORIES
Biochemists . . . Pharmacologists . . . Analysts

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Certificate of Analysis

January 22nd, 1969

SUBJECT -

Toxicological Investigation Of: FLUORINATED AROCLOR 1254

Monsanto Sample Number 170

Monsanto Project Number I-68-133

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

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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 animals that succumbed 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 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 Calvary (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.

SUMMARY -

FLUORINATED AROCLOR 1254

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

The Oral LD_{50} for male and female rats was placed at 1430 milligrams per kilogram with lower and upper limits of 1240 to 1645 milligrams per kilogram.

The compound was classed as mildly 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 158 milligrams per kilogram and less than 251 milligrams per kilogram.

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

C) Skin Irritation (Rabbits, Mixed Sex)

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

The average maximum score was 3.3 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.

YOUNGER LABORATORIES

BY: MELVIN D. BIRCH

TABLE I

THE ORAL LD_{50} OF 'FLUORINATED AROCLOR 1254' FOR RATS

Sample Fed As A 20.0% Solution In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	210	1260	Survived
2- Male	255	1260	Survived
3- Female	225	1260	Died
4- Male	240	1260	Survived
5- Female	195	1260	Survived
6- Male	215	1580	Died
7- Female	215	1580	Died
8- Male	230	1580	Survived
9- Female	205	1580	Survived
10- Male	250	1580	Died
11- Female	220	2000	Died
12- Male	240	2000	Died
13- Female	235	2000	Died
14- Male	235	2000	Survived
15- Female	210	2000	Died
16- Male	220	2510	Died
17- Female	215	2510	Died
18- Male	240	2510	Died
19- Female	190	2510	Died
20- Male	230	2510	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 1430 milligrams per kilogram with lower and upper limits of 1240 to 1645 milligrams per kilogram.

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

Survival time was two to five days with most deaths occurring in three to four days.

Toxic symptoms included weakness, loss of appetite, collapse, and death. Diarrhea was present in a few animals.

At autopsy there was extensive renal, liver, and pulmonary hyperemia.

TABLE II

The Minimum Lethal Dose Of 'FLUORINATED AROCLOR 1254'
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	2.2	63.1	0.0	Survived
2 - Male	2.4	100	+ 0.2	Survived
3 - Female	2.2	158	+ 0.1	Survived
4 - Male	2.3	251	+ 0.1	Died -- 6 Days
5 - Female	2.0	398	0.0	Died -- 7 Days
6 - Male	2.5	631	0.0	Died -- 7 Days
7 - Female	2.2	1000	- 0.1	Died -- 7 Days
8 - Male	2.4	1580	-----	Died -- 5 Days
9 - Female	1.9	2510	-----	Died -- 5 Days
10 - Male	2.1	3980	- 0.1	Died -- 6 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 158 milligrams per kilogram and less than 251 milligrams per kilogram.

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

Survival time was five to seven days.

Slight weakness and loss of appetite was evident after the third day. Appetite and activity appeared normal after the fifth day in those animals that survived.

At autopsy there was renal, liver, and pulmonary hyperemia by macroscopic examination.

T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'FLUORINATED AROCLOR 1254'

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	0	3	3	1	0	0
2 - Female	0	3	3	1	0	0
3 - Male	0	4	4	1	0	0
Average	0.0	3.3	3.3	1.0	0.0	0.0

DISCUSSION -

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

The average maximum score was 3.3 out of a possible 8 in twenty-four hours.

No skin changes were noted in one hour.
Marked redness and moderate edema were present in twenty-four hours.
Following removal of the compound edema disappeared in seventy-two hours and only slight redness remained.
All animals received a score of zero in five days.

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T A B L E IV

E Y E IRRITATION IN RABBITS AFTER APPLICATION OF 'FLUORINATED AROCLOR 1254'

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 - Female	10	2	0	0	0	0
2 - Male	12	4	2	0	0	0
3 - Female	10	2	0	0	0	0
Average	10.6	2.6	0.6	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 no apparent discomfort immediately following application.

Slight edema, mild to moderate erythema and discharge developed the first hour. Within twenty-four hours only a slight redness of the palpebral conjunctivae remained.

Redness disappeared from two animals within forty-eight hours and all were free of color within three days.