PROJECT NO. Y-69-53
REPORT FILE

YOUNGER LABORATORIES
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Certificate of Analysis

July 7th, 1969

SUBJECT -

Toxicological Investigation Of: Fluorinated Aroclor 1254 (OR 16827)
Monsanto Sample Number 63
Monsanto Project Number Y-69-53

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, et al, are shown in Table IV.

E) Vapor Inhalation (Male Rats) - Ambient Temperature

Four 150-gram male rats were placed in a glass desiccator, 250 mm in diameter, and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 64.5 grams 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 agitate the viscous 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 held for ten days following exposure. The viscera of the test animals were examined macroscopically.

The data are shown in Table V.

SUMMARY -

Fluorinated Aroclor 1254 (OR 16827)

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

The Oral LD_{50} for male and female rats was placed at 1120 milligrams per kilogram with lower and upper limits of 1020 to 1220 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 Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 200 milligrams per kilogram and less than 316 milligrams per kilogram.

The compound was classed as moderately 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 4.0 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 8.0 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 slightly toxic under conditions of the test.

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BY: MELVIN D. BIRCH

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T A B L E I

THE ORAL LD_{50} OF

'Fluorinated Aroclor 1254 (OR 16827)'

FOR RATS

Sample Fed As A 20.0% Solution In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	220	794	Survived
2- Male	225	794	Survived
3- Female	240	794	Died
4- Male	260	794	Survived
5- Female	225	794	Survived
6- Male	225	1000	Died
7- Female	220	1000	Survived
8- Male	245	1000	Survived
9- Female	220	1000	Survived
10- Male	255	1000	Survived
11- Female	220	1260	Died
12- Male	230	1260	Died
13- Female	260	1260	Died
14- Male	220	1260	Survived
15- Female	225	1260	Survived
16- Male	240	1580	Died
17- Female	225	1580	Died
18- Male	230	1580	Died
19- Female	225	1580	Died
20- Male	225	1580	Died

DISCUSSION -

The ORAL LD_{50} for male and female rats was placed at 1120 milligrams per kilogram with lower and upper limits of 1020 to 1220 milligrams per kilogram.

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

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

Toxic symptoms included diarrhea for one to two days, greatly reduced appetite, lethargy, increasing weakness, and collapse.
Most survivors showed a weight loss ten days after dosing.

At autopsy there was liver discoloration and gastrointestinal inflammation with some cases of hemorrhagic areas of the lungs.

Surviving animals were sacrificed ten days after dosing. Macroscopic examination showed hemorrhagic areas in the lungs, mottled and discolored areas of the liver, discoloration of the kidneys, and gastrointestinal inflammation.

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TABLE II

THE MINIMUM LETHAL DOSE OF
'Fluorinated Aroclor 1254 (OR 16827)'
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	2.1	200	+ 0.2	Survived
2 - Female	2.0	316	+ 0.1	Died -- 9 Days
3 - Male	1.9	501	- 0.1	Died -- 6 Days
4 - Female	2.5	794	- 0.2	Died -- 5 Days
5 - Male	2.0	1260	- 0.2	Died -- 6 Days
6 - Female	2.4	2000	- 0.3	Died -- 5 Days
7 - Male	2.3	3160	- 0.2	Died -- 5 Days
8 - Female	2.1	5010	- 0.2	Died -- 5 Days
9 - Male	2.4	7940	- 0.3	Died -- 6 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 200 milligrams per kilogram and less than 316 milligrams per kilogram.

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

Survival time was five to nine days.

Toxic symptoms included reduced appetite and activity, increasing weakness, and collapse.

Note: Surviving animal (#1) began losing weight after the fifth day following dosing. Fifteen days after dosing animal weighed 2.1 kilograms (same as starting weight).

At autopsy there was jaundiced liver, slight discoloration of kidneys, hemorrhagic lungs, and distended coronaries.

Surviving animal (#1) sacrificed fifteen days after dosing. Macroscopic examination showed mottled and discolored liver and enlarged gall bladder.

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T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF
'Fluorinated Aroclor 1254 (OR 16827)'

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 - Female	1	4	4	3	1	0
2 - Male	1	4	3	2	0	0
3 - Male	1	4	3	1	0	0
Average	1.0	4.0	3.3	2.0	0.3	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 4.0 out of a possible 8 in twenty-four hours.

Observations following application:

Immediate:	Moderate discomfort
1-Hour:	Barely perceptible erythema, no edema
24-Hours:	Well defined erythema, slight edema
48-Hours:	Well defined erythema, barely perceptible to slight edema
72-Hours:	Very slight erythema; no edema on one animal, Barely perceptible to slight edema on remaining two animals
120-Hours:	Very slight erythema, no edema on one animal; zero reading on remaining two animals
168-Hours:	Skin normal; zero reading

Note: Sample had a defatting effect on the skin. The epidermis flaked off in seven to ten days. There was no injury in depth.

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T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF

'Fluorinated Aroclor 1254 (OR 16827)'

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	8	2	0	0	0	0
2 - Male	8	0	0	0	0	0
3 - Male	8	2	0	0	0	0
Average	8.0	1.3	0.0	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 8.0 out of a possible 110 in one hour.

Observations following application:

Immediate:	Mild discomfort
10-Minutes:	Moderate erythema, slight edema and discharge; Slight dilatation of the pupil
1-Hour:	Moderate erythema, slight edema and discharge; Pupil normal
24-Hours:	Very slight redness in two of three animals, no edema or discharge
48-Hours:	Eye normal; zero reading
72- 168 Hours:	Eye normal; zero reading

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TABLE V

INHALATION OF 'Fluorinated Aroclor 1254 (OR 16827)'
VAPORS BY RATS

Average Temperature Inside Chamber ..... 75° F.

Average Relative Humidity Inside Chamber ..... 56 %

Amount of Sample -- To start ..... 64.5 Grams
Recovered ..... 64.0 Grams
Vaporized or left
in equipment ..... 0.5 Gram (0.8%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Mild ocular irritation (slight redness and eyes closed) ...
2 - Male	Survived	
3 - Male	Survived	Mild lethargy ...
4 - Male	Survived	Slow reflexes.

DISCUSSION -

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

It was concluded that the vapors were slightly toxic under conditions of the test.

Observations during and following exposure:

Immediate:	No effect
10-Minutes:	Mild ocular irritation (slight redness, tearing, and eyes closed)
30-Minutes:	Mild lethargy, mild ocular irritation, slow reflexes
1-Hour:	Mild lethargy, moderate ocular irritation, slow reflexes
3-Hours:	No change
6-Hours:	No change

Within twenty-four hours after removal from the chamber eyes were normal and appetite and activity appeared normal.

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

The test animals were sacrificed ten days after exposure. The viscera appeared normal by macroscopic examination.

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