YOUNGER LABORATORIES
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Certificate of Analysis

July 3rd, 1962

C+25AM

SUBJECT -

Toxicological Investigation Of: Aroclor 4465
Monsanto Sample Number 46
Monsanto Project Number Y-62-44

STUDY CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats)

The diluted compound was fed by stomach tube to Sprague-Dawley strain albino 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)

The diluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white 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, together with the dilution at which the compound was applied, are shown in Table II.

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EXPERIMENTAL PROCEDURES - (Continued)

C) Skin Irritation (Rabbits)

The finely ground powder and a 50.0% solution in corn oil were applied to the clipped, intact skin of albino rabbits and removed after twenty-four hours with soap and warm water. 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)

Twenty (20.0) milligrams of finely ground sample were placed in the conjunctival sac of the right eye of each of three albino 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 -

Aroclor 4465

A) Oral L_{50} (Rats)

The Oral L_{50} for male and female rats was placed at 16,000 milligrams per kilogram with lower and upper limits of 13,760 to 18,560 milligrams per kilogram.

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

B) Skin Absorption MLD (Rabbits)

The Minimum Lethal Dose by skin absorption in 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 female rabbits.

C) Skin Irritation (Rabbits)

The compound was classed as a moderate skin irritant.
The average maximum score was 3.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits)

The compound was classed as a mild eye irritant.
The average maximum score was 19.6 out of a possible 110 in four hours.

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Fred M. Younger

BY: FRED M. YOUNGER

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TABLE I

THE ORAL LD_{50} OF Aroclor 4465* FOR RATS

Sample Fed As A 50.0% Solution In Corn Oil

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	200	10,000	Survived
2- Female	190	10,000	Survived
3- Female	215	10,000	Survived
4- Male	230	10,000	Survived
5- Male	225	10,000	Survived
6- Male	240	12,600	Survived
7- Female	210	12,600	Survived
8- Female	225	12,600	Survived
9- Female	215	12,600	Survived
10- Male	240	12,600	Died
11- Male	250	15,800	Survived
12- Male	235	15,800	Died
13- Female	220	15,800	Survived
14- Female	215	15,800	Died
15- Female	210	15,800	Survived
16- Male	235	20,000	Died
17- Male	250	20,000	Survived
18- Male	230	20,000	Died
19- Female	215	20,000	Died
20- Male	240	20,000	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 16,000 milligrams per kilogram with lower and upper limits of 13,760 to 18,560 milligrams per kilogram.

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

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

Toxic symptoms included severe diarrhea, loss of appetite, and increasing weakness.

At autopsy there was inflammation of the gastric mucosa, liver discoloration, and renal hyperemia macroscopically.

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TABLE II

THE MINIMUM LETHAL DOSE OF 'Aroclor 4465'
BY SKIN ABSORPTION IN RABBITS

Sample Applied As 50.0% Solution In Corn Oil

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.3	794	+ 0.2	Survived
2 - Female	2.6	1260	+ 0.1	Survived
3 - Female	2.5	2000	- 0.2	Survived
4 - Female	2.7	2000	- 0.1	Survived
5 - Female	2.5	3160	- 0.3	Died - 21 Days
6 - Female	2.6	5010	- 0.3	Died - 9 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in 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 female rabbits.

Survival time was nine to twenty-one days.

Toxic symptoms included lethargy and reduced appetite after several days. Those succumbing developed tremors and an anemia-like appearance several days before death.

At autopsy there was liver discoloration and pulmonary hyperemia macroscopically.

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T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'Aroclor 4465'

Sample Applied as Finely Ground Powder
Sample Applied as 50.0% Solution In Corn Oil

Animal Number	Numerical Evaluation at The End Of 1 Hour	4 Hours	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
FINELY GROUND POWDER							
1	0	2	4	4	3	2	1
2	0	1	3	3	3	1	0
3	0	2	4	4	3	2	0
average	0.0	1.6	3.6	3.6	3.0	1.6	0.3

DISCUSSION -

The compound was classed as a moderate skin irritant.

FINELY GROUND POWDER:
No skin change was noted after one hour. Slight to well defined erythema with no edema developed within four hours for an average score of 1.6 out of a possible 8. Overnight there was slight edema, increasing the average score to 3.6. Although the application was removed, no substantial change was noted until the fifth day when the average score dropped to 1.6. Edema had disappeared but slight redness was still present.

50% SOLUTION IN CORN OIL:
A 50.0% solution in corn oil produced almost identical data to that shown above, placing it in the 'moderate skin irritant' category.

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T A B L E IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'Aroclor 4465'

Sample (20.0 Milligrams) Applied As Finely Ground Powder

Animal Number	Numerical Evaluation at The End Of						
	1 Hour	4 Hours	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1	15	18	13	9	4	2	0
2	12	18	18	12	8	4	0
3	15	21	18	14	8	4	0
Average	14.0	19.6	16.3	11.6	6.6	2.6	0.0

DISCUSSION -

The compound was classed as a mild eye irritant.

Discomfort was mild immediately following application.

After one hour there was moderate discharge, mild redness of the conjunctivae, mild edema, and slight iris congestion for an average score of 14.0 out of a possible 110. Dullness increased slightly in four hours and little change was noted overnight. After irrigation the inflammation gradually reduced so that by the fifth day iris and cornea were normal. Slight redness of the palpebral conjunctivae remained for an average score of 2.6.

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