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December 14th, 1970

Certificate of Analysis C+25AM

SUBJECT -

Toxicological Investigation Of: MCS 1004 -- AROCLOR 4273
Lot Number: OR 151723-3

Monsanto Sample Number 122

Monsanto Project Number Y-70-116

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

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EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (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 six levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to the method of E. J. Le Beer.

Observations were made for toxic signs and the viscera of the test animals 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 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 signs 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)

0.5 Milliliter of undiluted compound was applied to the clipped, intact skin of New Zealand white male and female rabbits under a one inch by one inch square patch, two single layers thick. The patches were held in place with adhesive tape. The trunk of each animal was wrapped with plastic strips, to retard evaporation and avoid contamination, for the twenty-four hour exposure period.

Observations were made over a period of seven 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 seven 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) - Sample warmed to 45°C. to Liquefy

Six mature male rats were placed in a metal chamber of 35-liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 178.7 grams of the compound contained in a 500-milliliter erlenmeyer flask. The sample was warmed to 45°C. to liquefy.

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 liquid. No supplementary air was introduced inasmuch as the above supply was ample for the animals oxygen requirements.

The animals were observed for behavior during exposure and for ten days following exposure. The viscera of the test animals were examined macroscopically.

The data are shown in Table V.

SUMMARY -

MCS 1004 -- ARCOLOR 4273 -- Lot OR 151723-3

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

The Oral LD_{50} for male and female rats was placed at 8920 milligrams per kilogram with lower and upper limits of 8030 to 9930 milligrams per kilogram.

The compound was classed as practically non-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 2000 milligrams per kilogram and less than 3160 milligrams per kilogram.

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

C) Skin Irritation (Rabbits, Mixed Sex)

The compound was classed as non-irritating when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 0.0 out of a possible 8 during the seven day observation period.

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 12.0 out of a possible 110 in one hour.

E) Vapor Inhalation (Male Rats) - Sample warmed to 45°C. to liquefy

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

It was concluded that the vapors were practically non-toxic under conditions of the test.

YOUNGER LABORATORIES, INC.

BY: MELVIN D. BIRCH

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TABLE I

THE ORAL LD_{50} OF

'MCS 1004 — AROCLOR 4273 -- Lot OR 151723-3'

FOR RATS

Sample Fed Undiluted (Sample warmed to 45°C. to Liquefy)

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	210	5,010	Survived
2- Male	195	5,010	Survived
3- Female	210	5,010	Survived
4- Male	225	5,010	Survived
5- Female	220	5,010	Survived
6- Male	215	6,310	Survived
7- Female	210	6,310	Survived
8- Male	205	6,310	Survived
9- Female	205	6,310	Died
10- Male	225	6,310	Survived
11- Female	200	7,940	Survived
12- Male	200	7,940	Survived
13- Female	200	7,940	Survived
14- Male	250	7,940	Died
15- Female	205	7,940	Died
16- Male	245	10,000	Died
17- Female	200	10,000	Survived
18- Male	245	10,000	Survived
19- Female	200	10,000	Died
20- Male	235	10,000	Died
21- Female	205	12,600	Died
22- Male	245	12,600	Survived
23- Female	200	12,600	Died
24- Male	200	12,600	Died
25- Female	200	12,600	Died
26- Male	235	15,800	Died
27- Female	205	15,800	Died
28- Male	215	15,800	Died
29- Female	200	15,800	Died
30- Male	210	15,800	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 8920 milligrams per kilogram with lower and upper limits of 8030 to 9930 milligrams per kilogram.

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

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TOXSTUDIES0968

DISCUSSION -- TABLE I -- (Continued)

Survival time was one to five days with most deaths occurring within two days. Toxic signs included reduced appetite and activity, lethargy, slight tremors, increasing weakness, collapse, and death.

At autopsy there was hemorrhagic lungs, slight liver discoloration, and gastrointestinal inflammation (acute in some cases).

Surviving animals were sacrificed seven days after dosing. Macroscopic examination revealed slight lung congestion in upper dosage levels; viscera of animals on lower dosage levels appeared normal.

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TABLE II

THE MINIMUM LETHAL DOSE OF

'MCS 1004 -- AROCLOR 4273 -- Lot OR 151723-3'

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	1.9	1260	- 0.2	Survived
2 - Female	2.6	2000	- 0.5	Survived
3 - Male	2.1	2000	- 0.2	Survived
4 - Female	2.0	2000	- 0.3	Survived
5 - Male	2.0	3160	- 0.3	Died -- 9 Days
6 - Female	2.7	5010	- 0.5	Died -- 7 Days
7 - Male	2.1	7940	- 0.3	Died --11 Days
8 - Female	2.5	7940	- 0.6	Died --13 Days
9 - Male	1.8	7940	- 0.4	Died -- 8 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and 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 male and female rabbits.

Survival time was seven to thirteen days.

Toxic signs included reduced appetite and activity (four to eight days in survivors), lethargy, diarrhea, increasing weakness, collapse, and death.

At autopsy there was mottled and discolored liver, enlarged gall bladder, and gastrointestinal inflammation (acute in some cases).

Surviving animals were sacrificed fourteen days after dosing. Macroscopic examination revealed slight liver discoloration and slight gastrointestinal inflammation.

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T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF
'MCS 1004 -- AROCLOR 4273 -- Lot OR 151723-3'

Sample (0.5 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	0	0	0	0	0	0
2 - Male	0	0	0	0	0	0
3 - Female	0	0	0	0	0	0
Average	0.0	0.0	0.0	0.0	0.0	0.0

DISCUSSION -

The compound was classed as non-irritating when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 0.0 out of a possible 8 during the seven day observation period.

Observations following application -

1- Hour: No skin changes; zero readings
24- 168- Hours: No skin changes; zero readings

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TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'MCS 1004 -- AROCLOR 4273 -- Lot OR 151723-3'

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 - Male	12	8	2	0	0	0
2 - Female	12	8	2	0	0	0
3 - Male	12	8	0	0	0	0
Average	12.0	8.0	1.3	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 12.0 out of a possible 110 in one hour.

Observations following application -

Immediate:	Discomfort was slight
10-Minutes:	Moderate erythema, barely perceptible to slight edema, copious discharge
1-Hour:	Moderate erythema, barely perceptible edema, copious discharge
24-Hours:	Moderate erythema, barely perceptible edema, slight discharge
48-Hours:	Slight erythema in two instances; no edema or discharge
72-Hours:	Eyes normal; zero readings
120- 168-Hours:	Eyes normal; zero readings

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TABLE V

INHALATION OF 'MCS 1004 -- ARCLOR 4273 -- Lot OR 151723-3'
VAPORS BY RATS *

Average Temperature Inside Chamber ..... 74° F.
Average Relative Humidity Inside Chamber ..... 65 %

Amount of Sample -- To start ..... 178.7 Grams
Recovered ..... 178.7 Grams
Vaporized or left in equipment ..... 0.0 Gram (0.0 %)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	No nasal or ocular discharge ...
2 - Male	Survived	No weakness or drowsiness of
3 - Male	Survived	consequence ...
4 - Male	Survived	Normal respiration.
5 - Male	Survived	
6 - Male	Survived	

DISCUSSION -

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

It was concluded that the vapors were practically non-toxic under conditions of the test.

Observations following exposure --

The animals appeared normal when removed from the chamber. There were no bronchial rales or other evidence of respiratory complications. The ten day observation period was uneventful.

Weight gain was normal.

Surviving animals were sacrificed ten days following exposure. The viscera appeared normal by macroscopic examination.

* Sample warmed to 45°C. to Liquefy

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