

Scientific Associates

1474 S. VANDEVENTER AVE. - ST. LOUIS 10, MO.

September 13, 1954

CERTIFICATE OF ANALYSIS

SUBJECT -

The Toxicological Investigation of Fluid OS-57

HydrouL 150

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

Monsanto Project No.: SA-77

EXPERIMENTAL PROCEDURE -

(A) Acute Oral Toxicity

Measured single doses of undiluted Fluid OS-57 were introduced into the stomachs of Sprague Dawley strain albino rats by means of a rubber catheter attached to a hypodermic syringe. The material was found to be non-lethal at the highest dose fed which was 28.5 grams per kilogram. The animals were held for seven days observation following treatment, but no autopsies were performed in view of the results. The data are given in Table I.

(B) Toxicity By Skin Absorption

Fluid OS-57 was applied in varying amounts to the closely clipped intact skin of albino rabbits in an effort to find the Minimum Lethal Dose. The treated areas were covered with plastic shields to retard evaporation. The data are shown in Table II.

(C) Skin Irritation In Rabbits

The degree of skin irritation was determined according to the method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 4, Dec. 1944). Observations made over a period of several days on the intact skin of three rabbits treated with Fluid OS-57 are scored in Table III.

(D) Ocular Irritation

0.1 ml. of Fluid OS-57 was placed in the conjunctival sac of the right eye of each of three albino rabbits and the amount of inflammation resulting was scored according to the method of Draize, Woodard and Calvery. The results are shown in Table IV.

(E) Vapor Inhalation In Rats

Four mature male rats were placed in a small metal chamber and exposed for six hours to a saturated atmosphere of atomized Fluid OS-57 produced by passing a stream of compressed air at a rate of three liters per minute

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through a container of the liquid placed inside the chamber. The animals, all of which survived, were held for seven days observation following exposure. The data are found in Table V.

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TABLE I
THE ACUTE ORAL TOXICITY OF
FLUID OS-57 FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	220	0.3	+ 4.5	Survived
2- Male	210	0.8	+ 6.0	Survived
3- Female	195	1.1	+ 8.0	Survived
4- Female	175	2.0	+ 4.0	Survived
5- Female	230	3.3	+ 7.0	Survived
6- Male	245	5.2	+ 3.0	Survived
7- Male	215	7.0	+ 4.0	Survived
8- Female	200	8.9	0.0	Survived
9- Female	185	11.3	0.0	Survived
10- Male	235	16.0	- 2.0	Survived
11- Male	250	21.7	- 6.0	Survived
12- Male	240	24.0	- 5.5	Survived
13- Female	180	28.5	- 10.0	Survived
14- Male	190	29.5	- 6.5	Survived

DISCUSSION -

All animals survived even when the dose reached 28.5 grams per kilogram which was the largest amount fed. There was severe diarrhea at levels above 7.0 grams per kilogram and in all probability much of the Fluid OS-57 was excreted unchanged. Appetite of the animals was affected for the duration of the diarrhea which was 2 to 3 days. Otherwise, there were no outward signs of toxicity.

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TABLE II
 THE TOXICITY OF FLUID OS-57
 BY SKIN ABSORPTION IN RABBITS

Animal No.- Sex	Weight Kilograms	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	1.8	1.8	+ 4.0	Survived
2- Male	2.1	3.3	+ 2.0	Survived
3- Male	1.9	5.2	+ 3.0	Survived
4- Male	1.8	7.0	0.0	Survived
5- Male	2.2	8.8	0.0	Survived
6- Male	1.7	9.5	0.0	Survived

DISCUSSION -

The maximum dose of 9.5 grams per kilogram was non-lethal by skin absorption. The activity of the animals was not markedly affected by the treatment. There appeared to be some discomfort and partial loss of appetite for 2 to 3 days, but evidently the Fluid OS-57 had little or no systemic effect.

TABLE III
 SKIN IRRITATION OF
 FLUID OS-57 IN RABBITS

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF			
	2 Hours	24 Hours	48 Hours	72 Hours
1- Male	1	1	1	0
2- Male	1	2	1	0
3- Male	1	1	1	1
Average	1.0	1.3	1.0	0.3

DISCUSSION -

Slight erythema with no edema was present on the skin in two hours. The condition remained about the same for two days and had cleared completely in two of the rabbits by the third day. There was no evidence of subcutaneous damage. Fluid OS-57 was considered to be a very mild to mild skin irritant.

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T A B L E I V

OCULAR IRRITATION OF
 FLUID OS-57 IN RABBITS

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF			
	1 Hour	24 Hours	48 Hours	72 Hours
1- Male	8	6	2	0
2- Male	6	4	0	0
3- Male	10	5	2	0
Average	8.0	5.0	1.3	0.0

DISCUSSION -

Eye irritation consisted of mild conjunctival redness, slight swelling of the eyelids and slight, temporary corneal dullness. This added up to an average score of 8.0 out of a possible maximum of 110 after one hour. The score dropped to 5.0 in 24 hours and the inflammation had disappeared in one rabbit after 48 hours and had all but disappeared in the other two animals. There was no damage of a permanent nature.

T A B L E V

VAPOR INHALATION TOXICITY OF
 FLUID OS-57 FOR RATS

Animal No.	Fate	Concentration Of Fumes Inside Chamber	Average Temperature Inside Chamber °F.	Average Relative Humidity Inside Chamber %
1	Survived	Saturated	81.8	73.5
2	Survived	Atmosphere		
3	Survived			
4	Survived			

DISCUSSION -

The animals survived the six hours exposure as well as the following seven days observation period. A moderately dense cloud of atomized Fluid OS-57 resulted from the operation. Eye and nasal irritation were mild to moderate and ocular irritation had practically disappeared after twenty-four hours. There was a trace of bronchial rales in two of the animals for 3 to 4 days. The rats were moderately lethargic during the exposure, but regained normal activity rapidly when removed from the chamber.

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SUMMARY -

Fluid OS-57 was non-lethal when given orally to rats in doses as high as 28.5 grams per kilogram. Much of the material was apparently excreted unchanged.

A maximum dose of 9.5 grams per kilogram placed on intact rabbit skin was not fatal.

Skin irritation amounted to slight erythema with no edema for a maximum average score of 1.3 out of a possible 8.0.

Eye irritation consisted of mild erythema with slight swelling of the eyelids for an average maximum score of 8.0 out of a possible 110.

Exposure to a saturated atmosphere for six hours of atomized Fluid OS-57 was not fatal to four mature rats.

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