Scientific Associates

1474 S. Vandeventer Ave. · St. Louis 10, Mo.

February 3, 1955

CERTIFICATE OF ANALYSIS

SUBJECT -

Toxicological Investigation of Fluid CB-43

TESTS CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.
Monsanto Project No. 54-91

EXPERIMENTAL PROCEDURE -

A) Acute Oral Toxicity
The Oral LD_{50} was found by the introduction of measured single doses of undiluted compound into the stomachs of Sprague-Dawley-strain albino rats by means of a rubber catheter attached to a hypodermic syringe.
After the approximate Minimum Lethal Dose was determined, groups of rats were fed at levels designed to bracket the toxicity range thereby supplying data for calculation of the LD_{50}.
Selected animals from these ensembling tests were autopsied and macroscopic examination made of the viscera.
The data are shown in Table I.

B) Toxicity By Skin Absorption
Undiluted Fluid CB-43 was applied in varying amounts to the closely clipped intact skin of albino rabbits in order to find the Minimum Lethal Dose. The treated areas were covered with plastic shields to retard evaporation and the animals were placed in opaque cages to prevent them from licking off the sample.
The results are found in Table II.

C) Skin Irritation in Rabbits
The scoring method of Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944) was used in evaluating Fluid CB-43 as a skin irritant.
Observations made over a period of several days, after the compound was placed on intact rabbit skin, are scored in Table III.

D) Eye Irritation in Rabbits
Undiluted compound in the amount of 0.1 ml. was placed in the conjunctival sac of the right eye of each of three albino rabbits and the degree of irritation scored according to Draize, Woodard and Calvery (J. of Pharm. and Exp. Therapeutics, Vol. 82, No. 2, Dec. 1944).
The results are given in Table IV.

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EXPERIMENTAL PROCEDURE - (Continued)

E) Vapor Inhalation

Four mature male rats were placed in a small metal drum and exposed for six hours to a saturated atmosphere of Fluid GB-43 by passing a stream of compressed air at a pressure of 15 pounds per square inch through a container of Fluid placed inside the chamber. The animals were checked for symptoms of toxicity and all were held for seven days observation following exposure.

The data are shown in Table V.

SUMMARY -

The Oral LD_{50} of Fluid GB-43 for rats was found to be 17.0 grams per kilogram.

The Minimum Lethal Dose by skin absorption in rabbits was 2.4 to 3.0 grams per kilogram.

Skin irritation amounted to mild erythema with practically no edema for an average maximum score of 2.0 out of a possible 8.0.

The average maximum score for eye irritation was 13.0 out of a possible 110. There was slight to moderate redness of the eyelids with mild edema.

A six hour exposure to a saturated atmosphere of Fluid GB-43 was non-lethal for rats.

SCIENTIFIC ASSOCIATES

Fred M. Younge

Dr. FRED M. YOUNGE

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The material in this report is to be used in development [illegible] and may be given to [illegible] [illegible] in [illegible] [illegible] in formal [illegible] may be [illegible] [illegible] ment in [illegible] toxicity are to be referred as before to the Medical Department in St. Louis for reply.

— Monsanto Chemical Company

To: Monsanto Chemical Company,
St. Louis, Missouri.
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TABLE I

TO [illegible] LD_{50} OF FLUID [illegible] FOR [illegible]

Animal No. - Sex	Weight Gm.	Dose Gm. / Kg.	Rate
1- Female	135	15.0	Survived
2- Female	220	15.0	Survived
3- Male	240	15.0	Survived
4- Male	230	15.0	Died
5- Female	215	15.0	Survived
6- Male	250	18.0	Died
7- Male	210	18.0	Died
8- Female	195	18.0	Survived
9- Female	225	18.0	Died
10- Female	190	18.0	Survived
11- Male	210	21.0	Died
12- Male	235	21.0	Died
13- Female	220	21.0	Died
14- Female	195	21.0	Survived
15- Female	24[illegible]	21.0	Died
16- Male	260	24.0	Died
17- Male	245	24.0	Died
18- Male	230	24.0	Survived
19- Male	250	24.0	Died
20- Female	215	24.0	Died

DISCUSSION -

The Oral LD_{50} was found to be about 17.0 grams per kilogram. Survival time was two to seven days. Severe diarrhea developed causing weight losses up to 25 % in some rats. It is likely that part of the dose was excreted before complete digestion took place. Loss of appetite and muscular incoordination developed in 24 to 48 hours.

At autopsy there was evidence of liver dysfunction in addition to severe gastro-intestinal irritation.

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TABLE II

THE MINIMUM LETHAL DOSE OF FLUID CR-63

BY SKIN ABSORPTION

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	1.8	1.2	- 5.0%	Survived
2 - Female	2.0	2.4	- 7.0%	Survived
3 - Male	2.1	3.0	- 10.0%	Died — 6 Days
4 - Male	1.7	3.6	- [illegible]	Died — 8 Days
5 - Female	1.8	4.8	- [illegible]	Died —14 Days
6 - Female	1.7	6.1	—	Died — 3 Days

DISCUSSION -

The Minimum Lethal Dose by skin absorption was 2.4 to 3.0 grams per kilogram. All animals dosed lost weight and those succumbing lost as much as 30%. There was a gradual wasting away with partial paralysis of the hind quarters and a convulsive-like movement of the head as outward symptoms of toxicity. Survival time was three to fourteen days.

At autopsy there were no gross[illegible] abnormalities observed by macroscopic examination. The compound apparently affects the nerve tissue.

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TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION
OF FLUID CB - 63

Animal No. - Sex	Numerical Evaluation At The End Of 30 Min.	24 Hrs.	48 Hrs.	72 Hrs.
1 - Female	2	2	1	1
2 - Female	2	3	2	0
3 - Female	2	2	2	1
Average	2.0	2.3	1.6	0.6

Discussion -
Skin irritation consisted of mild erythema with practically no edema for an average score of 2.0 after one hour. There was no appreciable change until the third day when the average score dropped to 0.6. At this time one animal was free of inflammation and only a trace of redness remained on the other two rabbits.

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TABLE V

INHALATION OF FLUID 35-63 VAPORS BY RATS

Animal No. - Sex	Fate	Concentration Of Fluid 35 - 63 Vapors Inside Chamber	Average Temperature Inside Chamber	Average Relativ Humidity Inside Chamber
1 - Male	Survived	Saturated Atmosphere	79.0°F.	72.0 %
2 - Male	Survived			
3 - Male	Survived			
4 - Male	Survived			

DISCUSSION -

The Fluid 35-63 fumes were non-lethal over a six hour exposure. Ocular and nasal irritation was moderate. The animals gradually became lethargic and developed irregular breathing but none collapsed during exposure. The fog produced settled quite rapidly on the chamber walls.

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