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July 13, 1955

CERTIFICATE OF ANALYSIS

SUBJECT -

Toxicological Investigation of Pydraul 600.

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

Monsanto Project No.: SA-55-43

Monsanto Sample No.: 56, Lot 107

EXPERIMENTAL PROCEDURE -

(A) Oral LD_{50} In Rats

The acute oral toxicity was found by the introduction of measured single doses of undiluted Pydraul 600 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 blanket the toxicity range thereby supplying data for calculation of the LD_{50}.

Selected animals from those succumbing were autopsied and macroscopic examination made of the viscera. The data are shown in Table I.

(B) Toxicity By Skin Absorption In Rabbits

The Minimum Lethal Dose was found by the application of increasing single doses of undiluted Pydraul 600 to the closely clipped intact skin of New Zealand white rabbits. The treated areas were covered with plastic shields and the animals were placed in special cages to prevent them from licking off the sample. Observations were made for outward signs of toxicity and the vital organs of selected animals from those succumbing were examined macroscopically. The data are given 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. 4, December 1944) was used in evaluating Pydraul 600 as a skin irritant. Observations made over a period of several days following application of the undiluted liquid to intact rabbit skin are scored in Table III.

(D) Eye Irritation In Rabbits

0.1 ml. of undiluted Pydraul 600 was placed in the conjunctival sac of the right eye of each of three albino rabbits and the resulting irritation scored according to Draize, et al. The results, based on several days observation, are shown in Table IV.

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(E) Vapor Inhalation In Rats

Four mature male rats were placed in a metal chamber of approximately 30 liters capacity and exposed for six hours to a concentrated atmosphere of atomized Pydraul 600 obtained by passing a stream of compressed air through a container of fluid inside the chamber. Air pressure was 22 pounds per square inch.

The animals were observed through the clear plastic top and, inasmuch as there were no deaths, all animals were held for seven days observation. The data are shown in Table V.

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TABLE I

THE ORAL LD_{50} OF PIDRAUL 600 FOR RATS

Animal No.- Sex	Weight Grams	Dose G./Kg.	Fate
1- Male	275	22.7	Survived
2- Female	215		Survived
3- Female	230		Survived
4- Female	195		Survived
5- Male	240		Survived
6- Male	220	26.0	Survived
7- Female	210		Survived
8- Female	235		Died
9- Male	250		Survived
10- Male	245		Survived
11- Male	220	29.2	Died
12- Male	260		Survived
13- Female	225		Survived
14- Female	240		Survived
15- Female	215		Died
16- Male	240		Survived
17- Male	250	32.5	Died
18- Male	245		Died
19- Female	210		Died
20- Female	200		Died
21- Female	190		Died

DISCUSSION -

The oral LD_{50} was placed at 30.5 grams per kilogram. Survival time was 2 to 6 days. Severe diarrhea developed in all animals dosed at the above levels as might be expected. There was loss of appetite and considerable lethargy present.

At autopsy no specific abnormalities were observed by macroscopic examination with the exception of moderately severe gastrointestinal inflammation and a gaseous condition in the stomach.

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TABLE II

THE MINIMUM LETHAL DOSE OF PYDRAUL 600
BY SKIN ABSORPTION IN RABBITS

Animal No.- Sex	Weight Kilograms	Dose G./Kg.	Weight Change 5 Days After Dosing %	Fate
1- Male	1.8	0.7	+ 6.0	Survived
2- Male	2.1	1.3	+ 5.0	Survived
3- Male	1.8	2.6	0.0	Survived
4- Male	1.6	3.9	- 4.0	Survived
5- Male	2.3	5.2	- 8.0	Died--8 Days
6- Male	2.0	6.5	-15.0	Died--5 Days
7- Male	1.8	7.8	-11.0	Died--7 Days

DISCUSSION -

The Minimum Lethal Dose was found to be 3.9 to 5.2 grams per kilogram. Survival time was 5 to 8 days. The animals gradually became less active and lost appetite. This resulted in a weight loss for all rabbits dosed at levels above 2.6 grams per kilogram. Moderate weakness of the hind quarters with some unsteadiness developed.

At autopsy no definite changes were noted in the viscera by macroscopic examination.

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TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF PYDRAUL 600

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 2 Hours	24 Hours	48 Hours	72 Hours	120 Hours
1- Male	2	2	1	1	0
2- Female	2	3	2	2	0
3- Female	2	2	2	2	0
Average	2.0	2.3	1.6	1.6	0.0

DISCUSSION -

The average score after 2 hours was 2.0 out of a possible 8.0. There was slight to moderate redness with no observable edema. The average score stayed within the range of 2.3 to 1.6 for three days with slight differences in the degree of erythema being the only changes noted. Within five days the inflammation had disappeared.

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF PYDRAUL 600

Animal No.- Sex	NUMERICAL EVALUATION AT THE END OF 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours
1- Female	18	16	6	2	0
2- Female	20	12	8	3	0
3- Female	14	10	4	0	0
Average	17.3	10.6	6.0	1.6	0.0

DISCUSSION -

There was little immediate reaction on the part of the animals. The average score after 1 hour was 17.3 out of a possible 110. Moderate erythema and lacrimation with slight edema developed. The iris and cornea were not actually affected excepting for the temporary film of Pydraul 600 that gave the corneal area the appearance of dullness. This film cleared within a few hours. Overnite the average score reduced to 10.6 and continued to decrease until no irritation was observed on the fifth day.

TABLE V

VAPOR INHALATION OF PYDRAUL 600 BY RATS

Animal No.- Sex	Fate	Concentration Of Atomized Pydraul 600 Inside Chamber	Average Temperature Inside Chamber °F.	Average Relative Humidity Inside Chamber %
1- Male	Survived	Concentrated Atmosphere	81.0	69.5
2- Male	Survived			
3- Male	Survived			
4- Male	Survived			

DISCUSSION -

No deaths resulted from the six hour exposure nor during the following seven day observation period. A fairly dense fog developed although the atmosphere was probably less than saturated. The nature of the fluid made it difficult to atomize even at 22 pounds pressure.

Ocular and nasal irritation were mild to moderate. Activity and breathing gradually slowed as exposure time increased. The animals were quite lethargic when removed from the chamber, but appeared normal the following day.

SUMMARY -

The oral LD_{50} of Pydraul 600 for rats was 30.5 grams per kilogram.

The Minimum Lethal Dose by skin absorption in rabbits was found to be 3.9 to 5.2 grams per kilogram.

Skin irritation in rabbits amounted to slight to moderate erythema for a maximum average score of 2.3 out of a possible 8.0 in 24 hours.

Eye irritation consisted of moderate erythema and lacrimation with slight edema for an average maximum score of 17.3 out of a possible 110 in 1 hour.

No deaths resulted in rats from a six hour exposure to a concentrated atmosphere of atomized Pydraul 600.

SCIENTIFIC ASSOCIATES

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