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Certificate of Analysis

August 3rd, 1956

SUBJECT -

Toxicological Investigation Of Pydrawl AC (OE-67).

Monsanto Sample No. 134 - Y-776
Monsanto Project No. Y-56-40

TEST CONDUCTED FOR -

Monsanto Chemical Company, St. Louis, Missouri.

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} In Rats
Undiluted Pydrawl AC was introduced 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 found, groups of rats were fed at levels designed to bracket the toxicity range thereby supplying data for calculation of the LD_{50}.

Observations were made for outward symptoms of toxicity and the viscera of selected animals from those succumbing was examined macroscopically.

The data are given in Table I.

B) The Minimum Lethal Oral Dose For Rabbits
Undiluted Pydrawl AC was fed by stomach tube in varying amounts to New Zealand white rabbits in order to find the lethal range.

Observations were made for outward symptoms of toxicity and the viscera of those animals that succumbed was examined macroscopically.

The data are shown in Table II.

C) Toxicity By Skin Absorption In Rabbits
Undiluted Pydrawl AC was applied in varying amounts to the closely clipped, intact skin of New Zealand white rabbits and the treated areas covered with plastic shields. A leather collar was placed around the neck of each rabbit to prevent them from turning their head sufficiently to get at the application.

Observations were made for outward evidence of toxicity and the viscera of all animals that succumbed was examined macroscopically.

The data are found in Table III.

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EXPERIMENTAL PROCEDURE - (Continued)

E) Skin Irritation In Rabbits
Undiluted Pydrasl AC was applied to the closely clipped, intact skin of three albino rabbits and observations made over a period of several days for irritation.

The results, based on the scoring technique of Draize, Woodard and Calvery (J. of Pharm. & Exp. Therapeutics, Vol. 82, No. 4 (Dec.) 1944), are given in Table IV.

F) Eye Irritation In Rabbits
0.1 Milliliter of undiluted Pydrasl AC was placed in the conjunctival sac of the right eye of each of three albino rabbits and the resulting irritation scored according to Draize, Woodard and Calvery (J. of Pharm. & Exp. Therapeutics, Vol. 82, No. 4 (Dec.) 1944).

Data from several days observation are shown in Table V.

F) Vapor Inhalation In Rats
Four mature male rats were placed in a metal chamber of 25 liters capacity and exposed for six hours to an atmosphere of Pydrasl AC vapors produced by aspirating the liquid at room temperature. The sample was poured into a three hole, round bottom flask and compressed air passed over an orifice, the lower end of which was immersed in the liquid. A glass tube led from the flask into the chamber. A glass baffle was placed in the line to break up droplets and allow, as nearly as practicable, only vapors to pass. Air pressure averaged about 4.4 pounds per square inch.

The animals were observed for toxic symptoms, and, since there were no deaths, all were held for ten days observation.

The data are shown in Table VI.

YOUNGER LABORATORIES

Fred M. Younger

BY: FRED M. YOUNGER

[redacted]

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TABLE I

THE ORAL LD_{50} OF 'FYDRAUL AC (OS 67)'
FOR RATS

Animal No. - Sex	Weight Gm.	Dose Gm./Kg.	Fate
1- Male	260	40.0	Survived
2- Male	245	40.0	Survived
3- Male	275	40.0	Died
4- Female	220	40.0	Survived
5- Female	210	40.0	Survived
6- Male	240	45.0	Died
7- Male	235	45.0	Survived
8- Female	225	45.0	Survived
9- Male	250	45.0	Survived
10- Female	195	45.0	Died
11- Female	210	50.0	Died
12- Female	225	50.0	Survived
13- Female	200	50.0	Survived
14- Male	260	50.0	Survived
15- Male	280	50.0	Died
16- Female	215	55.0	Died
17- Female	205	55.0	Died
18- Female	235	55.0	Survived
19- Female	245	55.0	Died
20- Male	230	55.0	Died
21- Male	240	55.0	Survived

[redacted] -

The Oral LD_{50} was placed at 52.0 grams per kilogram. Survival time was overnite to four days. There was severe diarrhea in all animals as might be expected from the high feeding levels necessary to obtain kills. Weakness and lethargy of several days duration developed. There was three instances of moderate muscular incoordination in the survivors. The condition cleared in seven to ten days.

At [redacted] pulmonary congestion was the only important visceral change noted [redacted]ically.

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TABLE II

THE MINIMUM LETHAL ORAL DOSE OF 'PYDRAUL AC (OS-67)'
FOR RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	2.8	2.0	- 4.0 %	Survived
2 - Female	2.5	3.5	-10.0 %	Survived
3 - Female	3.0	4.5	- 6.0 %	Died - 11 Days
4 - Male	3.2	5.5	-14.0 %	Died - 6 Days
5 - Male	2.9	7.5	-12.0 %	Died - 11 Days
6 - Male	2.8	10.0	-10.0 %	Died - 8 Days

DISCUSSION -

The Minimum Lethal Oral Dose range was found to be 3.5 to 4.5 grams per kilogram. Survival time was six to eleven days. All animals lost weight for several days after being fed. Those succumbing continued to lose weight and became very weak before dying. There appeared to be slight paralysis.

At autopsy there was liver discoloration and moderate pulmonary hyperemia.

TABLE III

TOXICITY OF 'PYDRAUL AC (OS-67)' BY SKIN ABSORPTION
IN RABBITS

Animal No. - Sex	Weight Kg.	Dose Gm./Kg.	Weight Change 5 Days After Dosing	Fate
1 - Male	2.7	2.0	+ 4.0 %	Survived
2 - Male	2.4	3.0	0.0	Survived
3 - Male	2.5	4.0	- 3.0 %	Survived
4 - Male	2.2	5.0	- 4.0 %	Died - 21 Days
5 - Male	2.7	6.0	- 8.0 %	Died - 10 Days
6 - Male	2.8	7.5	- 5.0 %	Died - 8 Days
7 - Male	2.2	9.0	-10.0 %	Died - 12 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption was 4.0 to 5.0 grams per kilogram. Survival time was eight to twenty-one days and weight losses ran from fifteen to twenty-eight per cent. The animals gradually lost appetite and weight. This was followed by unsteadiness and some muscular incoordination, the latter becoming evident a few days before death.

At autopsy no specific abnormalities were observed macroscopically.

TABLE IV

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF 'PYRENAL AC (05-67)'

Animal No. - Sex	Numerical Evaluation At The End Of 2 Hours	24 Hours	48 Hours	72 Hours	120 Hours
1 - Female	0	1	1	0	0
2 - Male	1	2	1	1	0
3 - Female	0	1	1	1	0
Average	0.3	1.3	1.0	0.6	0.0

DISCUSSION -

One animal out of three showed an average score of 0.3 out of a possible 8.0. Desquamation, erythema ranging from slight to fairly well defined appeared on all the animals for an average maximum score of 1.3. At this time the skin was wiped free of Pyrenal AC. A slight amount of redness with no edema was still present on top of the animals after seventy-two hours. However, all received a score of zero on the fifth day. Pyrenal AC was classed as a mild skin irritant.

TABLE V

EYE IRRITATION IN RABBITS AFTER APPLICATION OF 'PYRENAL AC (05-67)'

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours
1 - Male	6	2	0	0
2 - Male	8	4	2	0
3 - Female	8	4	0	0
Average	7.3	3.3	0.6	0.0

DISCUSSION -

No immediate discomfort of consequence was observed upon application. The average score after one hour was 7.3 out of a possible 110. There was moderate redness of the palpebral conjunctivae, considerable lacrimation, and slight edema. The iris and cornea were little affected. Lacrimation and edema practically disappeared thereafter. The average score at this time was 3.3. Two of the animals were free of inflammation in forty-eight hours. Pyrenal AC was classed as a mild eye irritant.

TABLE VI

SIX HOUR INHALATION OF 'PYDRAUL AC (OB-67)' VAPORS BY RATS

Average Relative Humidity Inside Chamber ..... 64.0 %

Average Temperature Inside Chamber ..... 76.5° F.

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	Rather Mild Discomfort,
2 - Male	Survived	no pawing at the nose.
3 - Male	Survived	Breathing about normal.
4 - Male	Survived	

DISCUSSION -

All animals survived the six hours exposure as well as the ten day observation period. The animals were not seriously affected by the vapors. Breathing remained regular and irritation was sufficient to produce only a slight degree of lacrimation and salivation. The nasal mucosa was slightly redder than normal when the animals were removed from the chamber but no edema was observed. Appetite seemed to be unaffected the day following exposure.

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SUMMARY -

The Oral LD_{50} of Pydraul AC (08-67) for rats was found to be 52.0 grams per kilogram. Such a high figure indicates that the compound is practically innocuous when fed orally to rats.

The Minimum Lethal Oral Dose for rabbits was 3.5 to 4.5 grams per kilogram.

The Minimum Lethal Dose by Skin Absorption in rabbits was 4.0 to 5.0 grams per kilogram.

Skin Irritation in rabbits consisted of slight to well defined erythema with no edema for an average maximum score of 1.3 out of a possible 8.0. The compound was classed as a mild skin irritant.

The average maximum score for Eye Irritation was 7.3 out of a possible 110. It was also classed as a mild eye irritant.

Rats survived a six hour exposure to Pydraul AC vapors which were found to be only slightly irritating.

The [illegible] in formal publications [illegible] may be made without [illegible] ment in St. Louis. Customer [illegible] toxicity are to be referred [illegible] ment in St. Louis for reply.

— Monsanto Chemical Company