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Certificate of Analysis

THE TOXICITY OF THE THERMAL DECOMPOSITION PRODUCTS OF 'PYRAUL 625'

Study Conducted For
MONSANTO CHEMICAL COMPANY, ST. LOUIS, MISSOURI

INTRODUCTION

The experiment was designed to determine the effect upon laboratory rats when exposed to a fog of thermal decomposition products produced by dropping PYRAL 625, Lot A-1505, a product of Monsanto Chemical Company, on a surface heated to a temperature of 2000° Fahrenheit. Various intensities of fog were generated for different groups of animals.

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EXPERIMENTAL PROCEDURE

Half of a fifteen inch McDanel high temperature combustion tube (inside diameter seven-eighth's inch, non-porous vitreous material) was wound with special sixteen gauge nickel-chromium wire. The wire was attached to a variable transformer for controlling temperature. After being wrapped in asbestos paper, the tube was insulated with four inches of mineral wool and then surrounded with a container made of asbestos board.

The tube was clamped at an angle of approximately 70 degrees with several inches of the unwound end protruding from the container. A thermocouple was inserted to the center of the tube and the temperature measured by an indicating pyrometer. At the upper end of the container two openings were made; one large enough for a small funnel to be inserted. The liquid to be volatilized was dropped from a burette

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at a measured rate, through the funnel to the inner surface of the heated combustion tube. The tube was slanted to prevent the drops from falling through and at the same time allow them to spatter against the sides, making for rapid volatilization.

Curved, three-fourths inch copper tubing was attached to the other opening. The tubing rose to a height of two and one-half feet above the combustion chamber and then returned about the same distance to a one liter flask from which an opening led into a five gallon glass bottle connected to a metal inhalation chamber of seventy liters capacity.

Animals were placed in the chamber, the chamber sealed, and connected to a vacuum pump with rubber tubing. The fluid was dropped at a measured rate onto the inner surface of the combustion tube heated to 2000° F. Sufficient suction was supplied by the pump to pull the combustion products through the copper tubing into the liter flask and five gallon bottle and then into the exposure chamber. From here the fog was drawn into an air trap and a calcium chloride trap attached directly before the vacuum pump. No cooling bath was used for the fog; temperature reduction was achieved by passing the combustion products through the copper tube and the five gallon bottle before entering the chamber. It was desired to expose the animals as nearly as possible to the fog as generated. The liter flask removed some solid particles of combustion.

Supplemental air for the animals' oxygen requirements was supplied by an air compressor and introduced into the five gallon bottle for mixing with the combustion products before entry into the exposure chamber.

The flow of filtered and dried air was controlled by means of a calibrated rotameter.

GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

Eight mature male rats were exposed for one hour three days per week for two weeks to a moderate concentration of PYDRAUL 625 volatilized at 2000° F. The concentration

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was clearly evident in the chamber but not sufficient to obscure the animals.

The fate of the animals is shown in Table I.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

Eight mature male rats were exposed for fifteen minutes to a heavy concentration of PYDRAUL 625 mist produced by volatilization at 2000° F. The concentration was practically as heavy as obtainable. The animals in the front of the chamber were nearly obscured.

The data on the animals is shown in Table II.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

Eight mature male rats were exposed for one hour to a heavy concentration of PYDRAUL 625 mist produced by volatilization at 2000° F. The concentration was practically as heavy as obtainable. The animals in the front of the chamber were nearly obscured.

The results are shown in Table III.

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Figure 1 — Inhalation Chamber And Equipment For Generating Mist

Figure 2 — Close-Up Of Inhalation Chamber During Generation Of Moderate Concentration Of Mist

Figure 3 — Close-Up Of Inhalation Chamber During Generation Of Heavy Concentration Of Mist

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TABLE I

EXPOSURE TO 'PYDRAUL 625' MIST (MODERATE CONCENTRATION)
ONE HOUR DAILY, THREE DAYS PER WEEK FOR TWO WEEKS (SIX HOURS TOTAL)

Average Temperature Inside Chamber ..... 86.0° F.
Average Relative Humidity Inside Chamber ..... 73.5 %
Volatilization Rate ..... 6.1 ML./Hour (Equivalent to 8.2 Gm./Hour
Supplemental Air Supply ..... 6.0 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change 2 Weeks After Last Exposure Gm.	Weight Change 4 Weeks After Last Exposure Gm.	Fate
1	235	- 10	0	Survived
2	250	0	+ 15	Survived
3	240	- 25	----	Died - 21 Days
4	260	+ 5	+ 20	Survived
5	245	- 15	----	Died - 18 Days
6	230	0	+ 10	Survived
7	245	- 10	+ 5	Survived
8	255	- 15	0	Survived

DISCUSSION -

No deaths resulted during the exposure time although two of the rats died eighteen and twenty-one days after the final exposure.

The fog produced a moderate degree of irritation each time, most of which, outwardly at least, appeared to have cleared up by the time for the next exposure two days later.

There was salivation, nasal discharge, some instances of irregular breathing, and moderate lethargy. The animals were reasonably steady when moving about the chamber and none appeared in danger of collapse when removed.

Temperature and humidity were higher than normal in the chamber due to the steady influx of the mist. This contributed somewhat to the discomfort of the animals. Activity between exposures remained about normal. The fur of the rats was damp from condensate after each exposure. Several of the animals developed sniffles as

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the experiment progressed but respiratory inflammation did not reach the stage of bronchial rales.

The majority of the rats lost weight for approximately two weeks after inhalation was concluded. Four weeks after the final exposure, all rats with the exception of the two that died at eighteen and twenty-one days, had gained weight and appeared to be in healthy condition.

The animals that succumbed became emaciated, developed colds, and gradually lost weight. A streptococcus organism was isolated from the pulmonary tract of one rat. It is impossible to state whether exposure to mist was a direct cause of death in both instances. It is likely that this, in combination with high humidity, were contributing factors.

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TABLE II

EXPOSURE TO 'PYDRAUL 625' MIST (HEAVY CONCENTRATION)
FOR FIFTEEN MINUTES

Average Temperature Inside Chamber ..... 81.5° F.
Average Relative Humidity Inside Chamber ..... 65.0 %
Volatilization Rate ..... 10.9 Ml./Hour (Equivalent to 14.7 Gm./Hour
Supplemental Air Supply ..... 3.5 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	215	+ 15	Considerable discomfort after a few minutes —
2	235	+ 10	
3	220	+ 20	Copious nasal discharge with some lacrimation —
4	240	+ 5	Reduced Activity —
5	210	+ 25	Animals obscured except in front part of cage.
6	230	+ 10	
7	235	+ 15	
8	245	0	

DISCUSSION -

No deaths resulted from fifteen minutes exposure to a saturated atmosphere of PYDRAUL 625 thermal decomposition products.

Reduced activity and irregular breathing were noted when the animals were removed from the chamber. They were not in danger of collapse.

Examination thirty minutes after exposure showed a cessation of nasal discharge but moderate edema of the nasal mucosa and redness around the eyes.

The animals had gained in weight when weighed two weeks later.

They appeared normal by outward observation.

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TABLE III

EXPOSURE TO 'PYDRAUL 625' MIST (HEAVY CONCENTRATION)
FOR ONE HOUR

Average Temperature Inside Chamber ..... 84.0° F.
Average Relative Humidity Inside Chamber ..... 69.0 %
Volatilization Rate ..... 10.9 Ml./Hour (Equivalent to 14.7 Gm./Hour
Supplemental Air Supply ..... 4.5 Liters/Minute

Animal Number	Starting Weight Gm.	Weight Change After 2 Weeks Gm.	Observations During Exposure
1	205	+ 15	Salivation and nasal discharge in a few minutes —
2	220	+ 5	
3	195	- 5	Breathing gradually becoming short and irregular —
4	220	+ 10	
5	235	0	Considerable activity for 10 to 15 minutes —
6	215	+ 5	Definite weakness within 30 minutes —
7	240	0	
8	225	+ 10	All animals at the point of collapse when removed from chamber.

DISCUSSION -

The heavy concentration of acrid fog was nearly fatal to the animals exposed for one hour.

They were in a semi-comatose state when taken from the chamber. The majority were on their feet within thirty minutes but showed marked weakness. Breathing was difficult and irregular. Considerable improvement was noted overnight. However, lethargy and poor appetite were evident for several days. After two weeks all animals were still alive and acting normally with one exception. This animal appeared unthrifty but the condition did not appear to be confined solely to the respiratory tract.

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St. Louis, Missouri
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SUMMARY

HYDRAUL 625 was volatilized by dropping the liquid onto a non-porous, vitreous surface heated to a temperature of 2000° F. The thermal decomposition products were drawn into an inhalation chamber and groups of rats exposed to various concentrations of the mist.

The results were as follows:

GROUP A: EXPOSURE TO MODERATE MIST (SIX HOURS TOTAL)

Considerable discomfort, irritation, and lethargy resulted from the exposures, but there were no deaths until eighteen and twenty-one days after the final exposure when two of the eight animals succumbed.

GROUP B: EXPOSURE TO HEAVY CONCENTRATION OF MIST (FIFTEEN MINUTES TOTAL)

Fifteen minutes exposure to a heavy concentration of mist produced copious nasal discharge and lacrimation, indicative of irritation. The animals showed some weakness when removed from the chamber but all survived.

GROUP C: EXPOSURE TO HEAVY CONCENTRATION OF MIST (ONE HOUR TOTAL)

One hour exposure to a heavy concentration of mist resulted in weakness to the point of collapse in all animals. Breathing difficulties gradually disappeared as the animals gained strength. After two weeks they appeared normal with the exception of one animal.

The pH of the condensate from the volatilized HYDRAUL 625 was in the range of 3.5 to 4.5.

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Fred M. Younger

BY: FRED M. YOUNGER

September 29th, 1958

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