

1. ~~Mr. M. E. Eisenhower~~ Texas City Plant
2. ~~Mr. R. N. Wheeler~~ South Charleston Plant
3. Dr. W. R. Manning-Building 2000 Tech. Center-South Chas.

You may find of interest. Not warning
on peroral dose rate. May wish to file with the
Food Production project.

ABSteele

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SEP 27 1971

M. E. EISENHOUR

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R. N. WHEELER

Chemical Hygiene Fellowship
MELLON INSTITUTE
Carnegie-Mellon University

Miscellaneous Toxicity Studies

Editor: C. S. Weil
For: UNION CARBIDE CORPORATION, Chemicals and Plastics Operations Division

SEVIN and/or Phenothiazine

Samples 33-162 and 33-56

Peroral, Single Dose to Female Rats

SEVIN LD50 = 0.224 (0.117 to 0.432) gm/kg; 1 ml = 0.05 gm in corn oil

Phenothiazine LD50 = 2.99 (2.02 to 4.42) gm/kg; 1 ml = 0.25 gm in corn oil

SEVIN plus Phenothiazine LD50 = 0.933 (0.631 to 1.38) gm/kg; 1 ml = 0.30
in corn oil

Predicted/observed = $0.978/0.933 = 1.05$; additive joint action.

TEMIK Oxime

2-Methyl-2-(methylthio)propionaldehyde oxime

Sample 34-113

Peroral, Single Dose to Rats

LD50 = 0.707 (0.281 to 1.78) ml/kg, undiluted.

UC 30948

2-Methyl-2-[2-methyl-2-(methylthiopropylideneaminoxy)]propionaldehyde

O-(methylcarbamoyl)oxime

Sample 34-107

Peroral, Single Dose to Rats

LD50 = 0.0238 (0.00952 to 0.0594) gm/kg; 1 ml = 0.05 gm in PEG-400

A D.O.T. Class B poison perorally.

UC 44123

2',6'-Diisopropyl-3',5'-dinitro-2,2,2-trichloroacetanilide

Sample 34-112

Peroral, Single Dose to Rats

LD50 > 5.0 gm/kg; 1 ml = 0.20 gm in PEG-400

Skin Irritation, Rabbit, Uncovered

No irritation on 5 rabbits from 20% in PEG-400

Eye Irritation, Rabbit

No, or trace, irritation from powder or 20% in PEG-400.

UC 46207

2-[O-(methylcarbamoyl)oximino]-1,4-dithiane

Sample 34-128

Peroral, Single Dose to Rats

LD50 = 0.0154 (0.0114 to 0.0208) gm/kg; 1 ml = 0.10 gm in corn oil

A D.O.T. Class B poison perorally.

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A. B. STEELE

Vinylidene Chloride

Sample 32-222

Peroral, Single Dose to Rats

LD50 = 0.406 (0.295 to 0.559) ml/kg undiluted.

Inhalation - 4 Hour LC50 = 38,060 (24,940 to 58,070) ppm.

Repeated Peroral Dosing Aimed at Finding any Circulatory Disturbances in Toes or Tail

Groups of 10 male and 10 female, Harlan Wistar, 90 to 120 gram, weanling rats were given undiluted vinylidene chloride by daily stomach intubation to a maximum of 29 doses. The dosage schedule was as follows:

<u>Gm/Kg</u>	<u>Days</u>	<u>Gm/Kg</u>	<u>Days</u>
0.203	7	0.511	3
0.256	3	0.644	2
0.323	5	0.811	3
0.406	2	1.02	2
		1.28	2

Animals received various dosages before death or sacrifice ensued. Cumulative dosage ranged from 3.8 ml/kg to 14.5 ml/kg.

Tissues were taken from the rats that died or that were killed for histopathological examination. The pathologist reported lesions related to gastritis, enteritis and esophagitis with some being sufficiently severe to become perforating ulcers. Particular attention was paid to the toes and tails based on the hypothesis that if this compound was implicated in acro-osteolysis that circulatory failure and lesions of the most distal portions of the body would be affected as is the case in man. No single lesion occurred with sufficient frequency to implicate the compound in this regard. Detailed reports on pathology are available.

Protocol sheets and Standard Test Procedures are available for each entry upon request.



Carol S. Weil, M.A.
Senior Fellow

Approved:



Charles P. Carpenter, Ph.D.
Administrative Fellow

Typed: September 13, 1971 - md

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Vinylidene Chloride

M. I. Sample No. 32-222 Initiator A. B. Steele
Date Started 10-20-69 Sample Identification _____

Peroral, Single Dose to Rats

LD50 - 0.406 (0.295 to 0.559) ml/kg, undiluted.

Conditions - standard.

Dosage; ml/kg	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
1.0	5/5	0,0,0,0,0	-	Abdomen's distended - death in 3 hours.
0.5	4/5	2,2,3,3,	+49	At autopsy intestinal irritation. One rat had blood on genitalia and one had a dark red spot on the tail.
0.25	0/5	-	81 to 104	

Conclusions - highly toxic following acute peroral administration.

Inhalation, Single, by Rats

Conditions - Procedure D.

Proce- dure	Time	Concen- tration	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
D	1.5 hrs	64,000 ppm.	6/6	All in exposure.	-	All prostrate at 8 min.
D	4 hrs	32,000 ppm.	2/6	1 in ex- posure, 1 at 1 day.	+31 to +53	Poor coordination at 8 min. Prostrate at 45 min.

Gross Pathology - Victims - scattered hemorrhage of lungs, capillary injection in oviducts.

Survivors - large, dark spleen; light brown areas on lungs.

Conclusions - 4-hour LC50 = 38,060 (24,940 to 58,070) ppm.

FOR DESCRIPTION OF TESTS REFER TO STANDARD TEST PROCEDURES

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Standard Test Procedures

In all tests, the nonfasted animals are maintained on appropriate Rockland diets and water ad lib except during period of manipulation or confinement. Dosage levels differ by a factor of 2 in a geometric series. LD50s or LC50s are calculated by the moving average method based on a 14-day observation period.

Peroral. Compounds administered by stomach intubation to Wistar derived male rats, 90-120 grams in weight and 3 to 4 weeks of age, reared in our own colony.

Skin Penetration. Male albino rabbits, 3 to 5 months of age, are immobilized during the 24-hour contact period with the compound retained under impervious sheeting on the clipped intact skin of the trunk. Thereafter, excess fluid is removed to prevent ingestion. Maximum dosage that can be retained is 20 ml./kg.

Inhalation. Procedure A. Concentrated vapor is generated in a gas washing bottle by passing dried air at 2.5 liters/min. through a fritted glass disc immersed to a depth of at least 1-1/2 inches in the chemical which is delivered to rats in a 9-liter glass exposure chamber. Mean vapor concentration is calculated from the loss in weight of the liquid or estimated from the vapor pressure at the actual temperature of the chemical during aeration.

Procedure B. Substantially saturated vapor is prepared by spreading 50 grams of chemical over 200 cm.² area on shallow tray placed near the top of a 120-liter glass chamber which is then sealed for at least 16 hours while an intermittently operated fan agitates the internal chamber atmosphere. Rats are then introduced in a gasketed drawer-type cage designed and operated to minimize vapor loss.

Procedure C. Mist, vapor and any oxidation or decomposition products of the chemical held at 170°C. are generated and delivered as in A.

Procedure D. Vapor at metered concentration, not checked analytically, is generated by feeding the liquid at a constant rate down the inside of a spirally corrugated surface of a minimally heated one inch Pyrex tube, through which metered air is passed. Resultant vapor is delivered as in A.

Procedure E. Spray - Solutions or suspensions are atomized in a glass VAPONEFRIN nebulizer using dried compressed air at 9 liters/min. (corrected) and 22 p.s.i. The resultant aerosol of droplets averaging 2 microns in diameter is conducted directly into a 60-liter cubic glass chamber containing rats. Mean aerosol concentration is calculated from the amount of material atomized.

Procedure F. Dust - Dust clouds are generated by a baffled Wright Dust Feed through which air is passed at 20 liters/min. (uncorrected) at 15 p.s.i. The dust is delivered directly to a 120-liter plexiglas chamber containing rats. Airborne dust concentrations are measured gravimetrically every half hour.

Skin Irritation. Chemical is applied in 0.01 ml. amounts to clipped, uncovered intact skin of 5 rabbit bellies either undiluted or in progressive dilutions of 10, 1, 0.1, and 0.01% in solvent. Ten grades are recognized based on appearance of moderate or marked capillary injection, erythema, edema or necrosis within 24 hours. No injury from undiluted = Grade 1.

Eye Irritation. Eyes not staining with 5% fluorescein in 20 seconds contact are accepted. Single instillation of 0.005, 0.02, 0.10 or 0.5 ml. undiluted or of 0.5 ml. of 40, 15, 5 and 1% dilutions are made into conjunctival sac of 5 rabbits. Read immediately unstained and after fluorescein at 24 hours, with ten grades recognized. Trace or no injury from 0.5 ml. undiluted = Grade 1.

MAILING LIST

Summary of the Miscellaneous Toxicity Studies Report is being mailed to the following List B and Agricultural Chemicals List.

List B

Medical Directors

4 - C. U. Dernehl
1 - E. Q. Hull
1 - R. E. Joyner
1 - T. N. Spencer
1 - R. J. Sexton

Other Distributions

1 - M. B. VerNooy
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Libraries

2 - Chemicals Division (1 set each
Library) Building 701 and 770
Libraries, South Charleston, W. Va.

Agricultural Chemicals

1 - R. C. Back
1 - W. J. Bartley
1 - R. A. Bleidt
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1 - R. L. Masker
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Library

1 - Union Carbide Corporation
Library - Building 740
P. O. Box 8361
South Charleston, W. Va.

The summary of this report will be included in the COLLECTED SUMMARIES for the month of Sept. and mailed to the following List A.

List A

1 { G. H. Daniels
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1 - W. B. Ackart
1 - E. A. Barr
1 - F. W. Tauber

Pertinent protocol sheets and Standard Test Procedures, along with the Summary pages, are being mailed to the following project initiators:

Project Initiators

1 - J. K. Chan
1 - J. F. Lacount
1 - A. B. Steele

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