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MELLON INSTITUTE OF INDUSTRIAL RESEARCH
SPECIAL REPORT

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Range Finding Tests on Trimethoxysilane

Union Carbide Chemicals Co., U.C.C.

Industrial Fellowship 274-25

Summary

Stomach Intubation, rat - LD₅₀ = 9.33 ml./kg.

Skin Penetration, rabbit - LD₅₀ = 6.30 ml./kg.

Inhalation, rat -

Concentrated vapor generated at 24°C.

15 minutes killed 6 of 6
(approximately 71,000 PPM.)

Metered Concentrations - 4 hours

62.5 PPM. killed 5 of 6

31.25 PPM. killed 1 of 6

Uncovered Skin Irritation, rabbit - ~~moderate~~, Grade 3.

Eye Injury, rabbit - moderate, Grade 5.

Trimethoxysilane has slight acute toxicity by the peroral and skin penetration routes but presents a definite hazard by inhalation under ordinary handling conditions. Rats failed to survive after a 15-minute inhalation period in a concentrated vapor atmosphere. The calculated concentration, based on weight loss of sample in relation to dilution air, was 71,000 PPM. Obviously, high concentrations of trimethoxysilane are readily built-up in the air, therefore, precautions must be taken to protect those handling this chemical. The uncovered rabbit skin responded to contact with the undiluted material with capillary injection only but rabbit eyes had moderately severe corneal necrosis from instillation of 0.02 ml. amounts. Vapor from trimethoxysilane caused only trace injuries to rabbit eyes after a three-minute exposure period. Forty-eight hours later, all eyes were normal.

Methanol has been studied previously by this laboratory as has its esters. The following table affords comparison of these three materials with trimethoxysilane.

<u>Material</u>	<u>Peroral LD₅₀ ml./kg.</u>	<u>Skin Penetration LD₅₀ ml./kg.</u>	<u>Inhalation of Concentrated Vapor</u>	<u>Uncovered Skin Irritation</u>	<u>Eye Injury</u>	<u>Report Number</u>
Methanol	15.4	20	8 hrs. killed 5/6 4 hrs. killed 0/6	None	Minor	14-68 19-132
Trimethoxy- silane	9.33	6.30	15 min. killed 6/6 (62.5 PPM. for 4 hrs. killed 5/6, 31.25 PPM. for 4 hrs. killed 1/6)	Minor	Moderate	This Report 25-22

Sample

On December 7, 1961, one-pint of trimethoxysilane bearing Lot Number 1008-61-28; D72 was received from Sistersville, West Virginia, for toxicity assay as requested by R. C. Maier, Silicones Division.

Single Peroral Doses

Trimethoxysilane has an acute LD₅₀ of 9.33 (6.69 to 13.0) ml./kg. when administered undiluted by stomach intubation to male albino rats.

Carworth Farms-Elias nonfasted rats, five to six weeks of age and 90-120 grams in weight were dosed at levels differing by a factor of 2.0 in a geometric series. The rats were reared in our own colony and maintained from time of weaning on Rockland rat diet (complete). The method of moving average for calculating the median-effective dose (LD₅₀) was applied to the 14-day mortality data.

The animals became sluggish soon after dosing. Deaths on the highest dosage level (20 ml./kg.) occurred within the ensuing four-hour period while most of those on the lower level were delayed for two days. At autopsy, gross examination revealed slightly congested lungs (on delayed deaths only), congested kidneys and adrenals, and some gastrointestinal hemorrhage. The livers were mottled and congested with burned areas evident on surfaces that lay in apposition to stomachs which still contained part of the dose.

Skin Penetration

By rabbit skin penetration, the LD₅₀ is 6.30 (4.66 to 8.52) ml./kg. undiluted. Marked erythema of the skin resulted from these covered applications.

Male albino New Zealand strain rabbits, three to five months of age and averaging 2.5 kg. in weight were immobilized and kept in a hood to prevent the inhalation of vapor from trimethoxysilane during the 24-hour skin contact period. Thereafter, the polyethylene sheeting used to retain the dose in contact with the clipped skin of the trunk was removed and the animals were caged for the remainder of the 14-day observation period. The rabbits were procured locally and maintained on Rockland rabbit ration. The moving average method of calculating the LD₅₀ was used.

Deaths occurred on the first, second, third and fourth day after application of the chemical. Gross findings at autopsy included congested lungs, mottled livers, and bright mottled kidneys with prominent surface markings. All survivors gained weight during the subsequent 14-day observation period.

Inhalation

Concentrated Vapor

Concentrated vapor, generated at approximately 24°C. by passing dried air at the rate of 2.5 liters/minute through a fritted glass disc immersed to a depth of at least one inch in 50 ml. of trimethoxysilane, killed six of six CFE, female albino rats within 1-1/2 hours after a 15-minute inhalation period in a 9-liter chamber. Death was attributed to lung hemorrhage. The calculated concentration, based on weight loss of sample in relation to dilution air, was 71,000 PPM.

Metered Concentrations

A metered concentration of 62.5 PPM. killed five of six female rats after a four-hour inhalation period but 31.25 PPM., inhaled for a similar interval, killed only one of six rats.

All deaths were delayed for 10 to 13 days after the inhalation period. Gross examination at autopsy disclosed considerable lung hemorrhage. The survivors lost an average of 35 grams of body weight during the subsequent two-week observation period, and at sacrifice on the 14th day, had from 10 to 80% consolidation of the lungs.

24-Hour Irritation Tests

Uncovered application of 0.01 ml. amounts of trimethoxysilane to the clipped skin of the rabbit belly caused minimal capillary injection on three animals and marked injection on two others. Grade 3 in our ten-grade rating system.

Rabbit eyes suffered moderately severe corneal necrosis from the instillation of 0.02 ml. amounts of the undiluted chemical while only minor corneal injury resulted from 0.005 ml. amounts. Grade 5 in our ten-grade rating system.

Vapor from trimethoxysilane, evolved at the rate of 1 liter/minute, caused trace corneal injury in rabbit eyes after a three-minute exposure period. The lids were injected and some pus was present. After 48 hours, all eyes were normal although some precipitate remained at the site of contact.

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Acknowledgments

Skin Penetration, Irritation Tests

Inhalation Studies

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Table 25-61

Trimethoxysilane (24-323)

Single Doses to Male Albino Rats Fed Undiluted by Stomach Tube

<u>Rat Number</u>	<u>1961 Date Dosed</u>	<u>Grams Weight</u>	<u>Weight Change in 14 Days</u>	<u>Dosage; ML. Per Kilo</u>	<u>Dose in ML.</u>	<u>Days to Death</u>
46746	12-19	94	-	20.0	1.9	0
46808	12-19	98	-	20.0	2.0	0
46362	12-19	102	-	20.0	2.0	0
46983	12-19	118	-	20.0	2.4	0
46961	12-19	120	-	20.0	2.4	0
46803	12-12	106	-	10.0	1.1	0
46780	12-12	112	-	10.0	1.1	2
46805	12-12	102	-	10.0	1.0	2
46778	12-12	113	+12	10.0	1.1	-
46907	12-12	113	+34	10.0	1.1	-
46804	12-12	111	+54	5.0	0.56	-
46786	12-12	116	+69	5.0	0.58	-
46080	12-12	99	+67	5.0	0.50	-
46109	12-12	119	+58	5.0	0.60	-
46038	12-12	119	+59	5.0	0.60	-
46100	12-12	111	+58	2.5	0.28	-
46207	12-12	97	+50	2.5	0.24	-
46101	12-12	103	+44	2.5	0.25	-
46106	12-12	110	+74	2.5	0.28	-
46969	12-12	94	+73	2.5	0.24	-

LD₅₀ = 9.33 (6.69 to 13.0) ml./kg.

Table 25-62

Trimethoxysilane (24-323)

Single Doses to Male Albino Rabbits by Skin Penetration
Administered Undiluted Under Polyethylene Dam for 24 Hours

<u>Rabbit Number</u>	<u>Date Clipped</u>	<u>Date Applied</u>	<u>Grams Weight</u>	<u>Weight Change in 14 Days</u>	<u>Dosage; Ml. Per Kilo</u>	<u>Dose in Ml.</u>	<u>Days to Death</u>
42424	12-11-61	12-13-61	2648	-	10.0	26.5	4
42425	12-11-61	12-13-61	2326	-	10.0	23.3	1
46465	1-2-62	1-3-62	2964	-	10.0	29.6	2
46467	1-2-62	1-3-62	3048	-	10.0	30.5	1
46479	12-19-61	12-21-61	2534	-	5.0	12.7	3
46480	12-19-61	12-21-61	2614	+ 26	5.0	13.1	-
46481	12-19-61	12-21-61	3044	+292	5.0	15.2	-
46482	12-19-61	12-21-61	2624	+186	5.0	13.1	-

LD₅₀ = 6.30 (4.66 to 8.52) ml./kg.

Table 25-63

Trimethoxysilane (24-323)

Single Inhalation by A Group of Female Albino Rats of
Concentrated Vapor Generated at Approximately 24°C.

<u>Rat Number</u>	<u>Date and Duration of Inhalation</u>	<u>Conc. Mg./L.</u>	<u>Initial Weight Grams</u>	<u>Days to Death</u>
46825			136	0
46876	12-21-61		136	0
46879	15 minutes in	353.86	132	0
46889	9-Liter		120	0
46901	Chamber		122	0
46913			116	0

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Table 25-64

Trimethoxysilane (24-323)

Single Inhalation by Groups of Female Albino Rats of Metered Concentrations

<u>Rat Number</u>	<u>Date and Duration of Inhalation</u>	<u>Conc. P.P.M.</u>	<u>Initial Weight Grams</u>	<u>Weight Change in 14 Days</u>	<u>Days to Death</u>
50056			128	-	10
50062	2-21-62		154	-	10
50090	4 Hours in	62.5	140	-	10
50085	9-Liter		148	-	12
50060	Chamber		146	-	13
50061			144	-32	-
50042			206	-	11
50043	3-7-62		204	-36	-
50044	4 Hours in	31.25	184	-30	-
50046	9-Liter		208	-54	-
50378	Chamber		164	+ 8	-
50409			200	-66	-