Project Report 41-70
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CHEMICAL HYGIENE FELLOWSHIP
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UCAR Resin LPCA-5011 (80% in CELLOSOLVE Acetate)

Range Finding Toxicity Studies

Sponsor: *Union Carbide Corporation*

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Summary

Stomach Intubation, rat - LD50 = 14.9 ml/kg; dosed as received.
Skin Penetration, rabbit - LD50 > 16.0 ml/kg; dosed as received.
Inhalation, rat -
Substantially saturated vapor, static conditions at 24°C.
8 hours killed 0 of 6.
Uncovered Skin Irritation, rabbit - None, Grade 1.
Covered Skin Irritation, rabbit FHSA test - Primary irritation score = 0.0; not an "irritant".
Eye Injury, rabbit - Moderate, Grade 5.
Eye Injury, rabbit FHSA test - 6 of 6 eyes "positive"; an "irritant".

Interpretation

UCAR Resin LPCA-5011 (80% in CELLOSOLVE acetate) was slightly toxic following single stomach intubation and had an extremely low order of toxicity following single covered dermal application. Administration of the undiluted material resulted in no irritation to uncovered rabbit skin and in moderate corneal injury, with iritis, in rabbit eyes. When tested by Federal Hazardous Substances Act (FHSA) conditions (Draize scoring), it was not an "irritant" to covered rabbit skin but was an "irritant" to the eyes. No hazard is anticipated from the infrequent inhalation of substantially saturated vapor evolved at room temperature under normal handling conditions. With the exception of eye irritation, the LPCA-5011 in CELLOSOLVE acetate was no more toxic or irritating than CELLOSOLVE acetate alone (tested previously). The present study indicates somewhat more severe eye injury than noted for CELLOSOLVE acetate alone.

Samples

Quantity: 0.5 pt; 1 pt
Date Received: 12-19-77; 2-1-78
CHF Sample No.: 40-485; 41-33

Submitted By: H. G. France
Division: Chemicals and Plastics, South Charleston, WV

Identification: 511-01-6642; 511-01-0414 (viscous yellow liquid)
Charge No.: 03986

Peroral, Single Dose to Rats

LD50 - 14.9 (10.1 to 22.1) ml/kg; dosed as received.

Conditions - Standard. See attached page of standard test procedures.

Dosage; ml/kg	Dead / Dosed	Days to Death	Weight Change	Signs
64.0	5/5	1,1,1,1,1	-	Heavy breathing, sluggish 2 min.
32.0	5/5	1,1,1,1,1	-	-
16.0	3/5	2,2,2	115 to 119 gm	Coughing 1 min.
8.0	0/5	-	86 to 138 gm	-
4.0	0/3	-	111 to 129 gm	-

Gross Pathology - In victims, petechiae of the lungs; livers mottled, visceral surfaces pale; stomachs transparent, distended, gas or fluid-filled; kidneys mottled, sections congested; adrenals congested; intestines transparent, yellow or white, fluid-filled. In survivors, nothing remarkable.

Conclusions - Slightly toxic following acute peroral intubation.

Skin Penetration, Single Dose to Rabbits

LD50 > 16.0 ml/kg; dosed as received.

Conditions - Standard. Dosed under polyethylene sheeting.

Dosage; ml/kg	Dead / Dosed	Days to Death	Weight Change	Skin Irritation	Signs
16.0	1/7	12	135 to 340 gm	-	-

Gross Pathology - In victim, lungs with dark red areas; liver dark purple; intestines hemorrhaged; mucous discharge from anus. In survivors, kidneys pale.

Conclusions - Extremely low order of toxicity following acute covered dermal application.

Inhalation, Single, by Rats

Conditions - Static exposure at 24°C. Procedure B of standard test procedures.

Procedure	Time	Concentration	Dead / Dosed	Death	Weight Change	Signs
B	8 hr	Substantially saturated vapor	0/6	-	53 to 82 gm	-

Gross Pathology - Nothing remarkable.

Conclusions - No hazard is anticipated from the infrequent inhalation of substantially saturated vapor evolved at room temperature under normal handling conditions.

Skin Irritation, Rabbit, Uncovered

Conditions - Standard. Applied undiluted.

Conclusions - No irritation on 5 rabbits. Grade 1.

Skin Irritation, Rabbit, Covered

Conditions - FHSA procedure; 24-hour contact.

Conclusions - Primary irritation score = 0.0. Not an "irritant" by FHSA definition.

Eye Irritation, Rabbit

Conditions - Standard. Instilled undiluted.

Conclusions - Moderate corneal injury, with iritis, from 0.02 ml per eye; trace corneal injury on one of 5 eyes from 0.005 ml per eye. Grade 5.

Eye Irritation, Rabbit

Conditions - FHSA procedure.

Conclusions - See separate sheet. Six of 6 eyes "positive" for corneal, iridal and conjunctival injury. An "irritant" by FHSA definition.

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Acknowledgments:

Single Peroral Tests	Robin A. Turney, B.S. Technologist
Skin Penetration, Irritation Tests	Naomi I. Condra, B.S. Scientist
Inhalation Studies	Donald J. Nachreiner, B.S. Assistant Scientist

Date: April 24, 1978

Typed: *sac*

Standard Test Procedures

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

Toxicity Terminology for Peroral and 24-Hr Dermal LD50s (A)/Inhalation 4-Hr LC50 (B)

	A, gm/kg	B, ppm		A, gm/kg	B, ppm
Extremely low order	> 15	> 100M	Highly	0.05-0.5	100-1M
Slightly	5-15	10M-100M	Seriously	0.001-0.05	10-100
Moderately	0.5-5	1M-10M	Dangerously	< 0.001	< 10

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

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 16 to 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 to 100 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 psi. 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 14 liters/min (uncorrected) at 5 psi. 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.

EYE IRRITATION - DRAIZE (FHSA) SCORING

Material UCAR Resin LPCA-5011 (80% in CELLOSOLVE Acetate) Sample Number 40-485

Rabbit Number	77-72199			77-72098			77-72130			77-72109			77-71043			77-71055		
Time After Dose (Hours)	24	48	72	24	48	72	24	48	72	24	48	72	24	48	72	24	48	72
Observation	SCORE																	
(1) Cornea																		
Opacity	2	2	2	1	1	0	2	2	1	2	2	2	1	1	1	2	2	2
Area Involved	2	2	1	2	1	0	4	4	3	4	3	3	4	3	2	4	3	1
Subtotal	20	20	10	10	5	0	40	40	15	40	30	30	20	15	10	40	30	10
(2) Iris																		
Subtotal	5	0	0	5	0	0	5	0	0	5	5	5	5	5	5	5	5	5
(3) Conjunctivae																		
Redness	3	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	2
Chemosis	2	1	1	2	1	0	3	1	0	3	2	2	2	2	1	2	1	1
Discharge	3	2	2	2	1	0	3	1	0	3	2	2	2	3	2	2	2	2
Subtotal	16	10	10	12	6	2	16	8	2	16	12	12	12	14	10	12	10	10
T tal Score	41	30	20	27	11	2	61	48	17	61	47	47	37	34	25	57	45	25

Median Score

	Cornea	Iris	Conjunctivae	Total
24 Hours	30	5	14	49.0
48 Hours	25	2.5	10	37.5
72 Hours	10	2.5	10	22.5

Comments: 6 of 6 eyes "positive" for corneal, iridal and conjunctival injury; an "irritant".

Signed: William J. Conroy Date Applied 1-10-78