7-28-93

FINAL

DATA EVALUATION REPORT

Fortress

Study Type: Acute Inhalation Toxicity

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Prepared by:

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Date: 8/9/93

DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation Toxicity (Rat); Guideline 81-3

EPA IDENTIFICATION NUMBERS

CAS No.: 54593-83-8

MRID No.: 417368-32

PC Number: 129006

Tox. Chem. No.: 663P

TEST MATERIAL: Fortress® 5G

SYNONYMS: IN 43898-54; DPX-43898-54; Phosphorothioic acid, 0,0-diethyl 0-(1,2,2,2-tetrachloroethyl) ester

SPONSOR: Agricultural Products Department, E.I. du Pont de Nemours and Company, Wilmington, DE

STUDY NUMBER: HLR 135-90

TESTING FACILITY: E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE

TITLE OF REPORT: Acute Inhalation Toxicity Study with IN 43898-54 in Rats

AUTHOR: J.C. Stadler

STUDY COMPLETED: April 2, 1990

CONCLUSIONS: Tested in Crl:CD®BR rats

Estimated acute inhalation LC_{50} in males: 0.205 mg/L
(with 95% C.I. of 0.175-0.595 mg/L)

Estimated acute inhalation LC_{50} in females: 0.064 mg/L
(with 95% C.I. of 0.042-0.106 mg/L)

TOXICITY CATEGORY: II--Males; ~~I~~--Females Tox II per WPS Guidelines. TPChin 6/9/95

CORE CLASSIFICATION: Core Minimum Data. This study meets the minimum requirements set forth under EPA Guideline Series 81-3 for an acute inhalation toxicity study.

A. MATERIALS

Test Compound

Test material:	IN 43898-54 (5G Formulation)
Identification number:	18,103
Purity:	5.2%
Physical description:	Brown powder
Storage condition:	Not reported
Stability:	Not reported

Actual Exposure Levels: Males--0.148, 0.149, 0.165, 0.170, or 0.238 mg/L
Females--0.028, 0.040, 0.041, 0.054, 0.056, 0.124, or 0.148 mg/L

In a preliminary test, 5 males and 5 females were exposed to 0.148 mg/L of test material. All females died while none of the males died. Therefore, males and females were subsequently given different concentrations.

Controls: None were used

Test Animals

Species:	Rat
Strain:	Crl:CD®BR
Source:	Charles River Breeding Laboratories, Raleigh, NC
Sex:	Male and Female
Age:	52 to 76 days at exposure
Weight:	Males--237-316 g; Females--181-253 g on Day 1
No. animals/dose:	10/sex (except for the 0.148 mg/L dose group where there were 5/sex)

B. TEST PERFORMANCE

Environmental Conditions:

Temperature	23° ± 3°C
Humidity	50% ± 10%

A 12/12 hour light/dark cycle was maintained

Inhalation Chamber: A cylindrical glass exposure chamber having an internal volume of 38 L was used. Animals were held in perforated stainless steel cylinders with conical nose pieces which were subsequently inserted into the face plate of the exposure chamber. Samples (20 L) from the breathing zone were drawn through a glass fiber filter and two impingers containing 10 mL acetone.

Chamber Monitoring: Recorded at 30 minute intervals

Temperature	19°-22°C
Humidity	49%-64%
Air flow	36 L/min
Oxygen content	20.9%

Dose Preparation/Generation of Test Atmospheres: The test atmospheres were prepared by milling AGsorb LVM-MS 25/50 clay until particles of a respirable size were produced. A propylene glycol/milled clay mixture was then mixed with the active ingredient to produce the test mixture. The test atmosphere (monitored at 30-minute intervals) was produced by suspending the test mixture in a stream of conditioned, filtered air. The test material was monitored with a K-Tron Model T20 twin-screw volumetric feeder and K-Tron series 6300 digital speed controller into a Fluid Energy Processing and Equipment Model 00 Jet-O-Mizer. The Jet-O-Mizer sent the test material through a series of glass elutriators which retained the larger particles and allowed the smaller particles to pass into the exposure chamber. Chamber concentrations were controlled by varying the rates that test material was fed into the Jet-O-Mizer.

Analytical Determinations: The difference in pre- and post-sampling filter weights were determined to estimate atmospheric concentrations of particulate Fortress. Gravimetric analysis was used to determine total particulate from randomly selected (i.e., not all) filters. Gas chromatography was used (on samples from the acetone on the impingers) to determine concentrations of active ingredient released as a vapor. Results from these analyses showed that animals were exposed to active ingredient combined with particulate and released as a vapor. Mean exposure levels of 8 samples for each exposure (shown in the mortality table in Results) demonstrated great variations as indicated by the large standard deviations. Of the total weight, 1%-3% constituted vaporized active ingredient and <1% active ingredient remained in the test substance on the filters, although there were great variations between exposures. Apparently, some material evaporated prior to weighing. The author stated that "It could not be accurately determined how much material may have evaporated from the dust between the time of sampling and the time of analysis."

Because of the known toxicity of the active ingredient, it was felt that handling of the test material should be minimized. Therefore, with the exception of one time when the test material was used, partical size distribution and characterization of the test system were conducted using samples of the milled clay containing no active ingredient. In addition, nominal concentrations for each exposure were not determined. Particle size distribution was determined using a Sierra® Series 210 cyclone preseparator/cascade impactor and Sierra® Series 110 constant Flow Air Sampler. Analytical results are summarized below:

Sample No.	Total Particulate (mg/L)	MMAD (μm)	% Particles <1 μm	<3 μm	<10 μm
Inert Clay Dust					
1	0.115	0.74	58	85	>99
2	0.084	1.00	50	82	>99
3	0.104	0.67	60	87	>99
IN 43898-54					
1	0.051	0.64	66	>99	>99

Particle Size Determination: The percent of particles <1 μm ranged from 50 to 66.

Duration of Exposure: 4 hrs; nose-only exposure

Observation Period: 14 days

Observation Frequency: Immediately following exposure; daily thereafter

Body Weight Interval: Daily, except on weekends

Gross Pathology: YES

Histopathology: NO

C. RESULTS

Mortality: Mortality was observed at almost all exposure levels. Results are summarized below.

Males		Females	
Dose (mg/L) ± S.D.	Mortality[a]	Dose (mg/L) ± S.D.	Mortality[a]
0.148 ± 0.145	0/ 5	0.028 ± 0.010	0/10
0.149 ± 0.063	3/10	0.040 ± 0.010	0/10
0.165 ± 0.035	3/ 9[b]	0.041 ± 0.038	1/10
0.170 ± 0.099	1/10	0.054 ± 0.010	6/10
0.238 ± 0.076	7/10	0.056 ± 0.024	0/10
		0.124 ± 0.052	8/10
		0.148 ± 0.145	5/ 5

[a]Mortality is expressed as No. deaths/No. exposed.
[b]One rat died as a result of a tight fitting restrainer and was not included in the analysis

Death occurred either during exposure or during the first 4 days after exposure.

Clinical Observations: Among both males and females, common clinical signs included discharge from the nose and eyes, tremors, salivation, hunched posture, lethargy, and irregular respiration. These signs were in general only seen during the first two days following exposure.

Body Weight: Surviving rats lost weight during the first 2-4 days. All animals then gained weight throughout the rest of the observation period. Mean body weights (g) are summarized below:

Sex	Dose mg/L	Day 1	Day 7	Day 14
Males	0.148	270	300	350
	0.149	272	268	332
	0.165	291	286	348
	0.170	252	285[a]	337[b]
	0.238	261	292[a]	363[b]
Females	0.028	234	241[a]	250
	0.040	203	231	246
	0.041	218	237	256
	0.054	206	213	242
	0.056	231	241	252
	0.124	219	208	249
	0.148	210	--	--

[a]Represents Day 8 Body Weights
[b]Represents Day 15 Body Weights

Gross Necropsy: No specific target organs were identified. Common findings, seen only in animals that died, included discoloration of the lungs and nose, stained skin, oral and nasal cavity discharge, chromodacryorrhea, and small intestines distended with gas. No findings were noted in animals that survived to term.

LC_{50} Determination: The estimated acute inhalation LC_{50}, calculated by probit analysis, was 0.205 mg/L in males (95% C.I. 0.175-0.595 mg/L) and 0.064 mg/L in females (95% C.I. 0.042-0.106 mg/L). An earlier study had shown an LC_{50} of the active ingredient to be 0.58 ppm.

D. REVIEWER'S COMMENTS

This study was well designed, conducted, and reported. The reviewers appreciate the difficulties involved in handling a highly toxic compound such as Fortress and the need to minimize potential exposure for the employees. Thus, the approach to estimate the MMAD from the milled clay material without test substance and sampling the clay with test substance only once, was accepted. There was an unresolved problem, as acknowledged by the author, with test material vaporizing from the filters. The reviewers suggest further investigation of this issue, but recommend, nevertheless, that the study be classified as Minimum.

E. QUALITY ASSURANCE MEASURES

Was the test performed under GLPs? YES

A Quality Assurance Statement, signed and dated March 30, 1990 was submitted and included dates when findings were reported. (The findings were not specified.)