

US EPA ARCHIVE DOCUMENT

DATA EVALUATION REPORT

PEBULATE

STUDY TYPE: ACUTE INHALATION - RAT (81-3)

Prepared for

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

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Task Order No. 98-18F

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Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S.
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DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
 OPPTS 870.1300 [§81-3]

DP BARCODE: D247841

SUBMISSION CODE: S546073

P.C. CODE: 041403

TOX. CHEM. NO.: 710

TEST MATERIAL (PURITY): Pebulate Technical (96.1%)

SYNONYMS: Tillam®, S-Propyl butylethylthiocarbamate

CITATION: Miller, J. (1978) Acute inhalation toxicity of Tillam Technical in albino rats. Richmond Toxicity Laboratory Inhalation Facility, Stauffer Chemical Company, de Guigne Technical Center, Richmond, CA 94804. Study no. T-6456, December 20, 1978. MRID 00143575. Unpublished.

SPONSOR: ICI Americas Inc., Agricultural Products, Wilmington, DE

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 00143575), groups of young adult Sprague-Dawley rats (10/sex) were exposed (whole body) to Pebulate Technical (96.1%) aerosol for 4 hours at concentrations of 2.2, 3.0, 3.2, 3.6, 3.9, or 4.8 mg/L (MMAD= 3.3-4.0 μ m). Animals were then observed for 14 days.

All deaths occurred within 3 days of exposure. Clinical signs included depression, prostration, dyspnea, reddish brown stains around anogenital region, and highly nervous behavior. The clinical signs appeared more severe in the higher-dosed groups. Necropsy showed reddened lungs in two males of the 3.9 mg/L group and two males and one female of the 3.0 mg/L group, small white and pink patches on the lung surface of one male and one female exposed to 3.6 mg/L, and dark red lungs in seven males and five females exposed to 2.2 mg/kg.

LC₅₀ Males = 3.7 mg/L (95% C.L. 3.4-4.0 mg/L)

LC₅₀ Females = 3.5 mg/L (95% C.L. 3.2-3.8 mg/L)

The Combined LC₅₀ = 3.6 mg/L (95% C.L. 3.38-3.86 mg/L)

Pebulate Technical is in TOXICITY CATEGORY IV for Acute Inhalation Toxicity.

This acute inhalation study is classified as **Acceptable (Guideline)**. It does satisfy the guideline requirement for an acute inhalation study (81-3) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and flagging statements were not provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Pebulate Technical
Description: amber liquid
Lot/Batch #: CGB-0201
Purity: 96.1% a.i.
2. Vehicle and/or positive control
None
3. Test animals
Species: rat
Strain: Sprague-Dawley
Age and weight at dosing: ~7 weeks; males: 172-249 g, females: 156-208 g
Source: Charles River, Portage, MI
Acclimation period: ten days
Diet: Purina Rat Chow[®], Ralston Purina, St. Louis, MO, *ad libitum*
Water: tap water, *ad libitum*
Housing: 5/sex/plastic cages with stainless steel wire mesh bottoms
Environmental conditions:
Temperature: 21±2°C
Humidity: not reported
Air changes: not reported
Photoperiod: 10 hour light/14 hour dark

B. STUDY DESIGN AND METHODS

1. In life dates
Not reported
2. Exposure conditions
Temperature (19-20°C) and humidity (65-80%) were recorded at 30-minute intervals throughout the 4-hour exposure period.
3. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Rats were exposed to Pebulate Technical by whole-body exposure for four hours. They were observed throughout the 4-hour exposure and twice daily thereafter. The animals were weighed on days 0, 7, and 14 during the study. Survivors were killed and a necropsy was performed.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated						
Nominal conc. (mg/L)	Analytical conc. (mg/L)	MMAD μ m	GSD	Males	Females	Combined
6.73	2.2	3.6	1.8	0/10	0/10	0/20
8.69	3.0	3.5	1.7	2/10	3/10	5/20
6.91	3.2	3.3	1.6	0/10	1/10	1/20
8.02	3.6	3.4	1.6	7/10	3/10	10/20
9.20	3.9	3.3	1.7	4/10	9/10	13/20
12.5	4.8	4.0	2.0	10/10	10/10	20/20

Data taken from Tables 2-14, pp.48-60, MRID 143575.

4. Generation of the test atmosphere and description of the chamber

The animals were placed in individual partitioned stainless steel wire cages inside a 447 L whole-body exposure chamber. Exposure atmospheres were generated using an aerosol discharger. Conditioned room air was drawn through an absolute filter into the inhalation chamber under negative pressure. The total air flow through the chamber was adjusted to 110 liter/minute. Exposure samples were collected at 60 minute intervals from the breathing zone of the rats during each exposure. Time to chamber equilibrium was approximately 18 min.

Analytical chemistry - The filter was extracted with organic solvent and the amount of the test material was determined by gas-liquid chromatography using a nitrogen selective detector.

Test atmosphere concentration - The total particulate concentration within the animal's breathing zone was measured analytically. The average results are in Table 1 above.

Particle size determination - Two air samples at a sampling rate of 0.75 L/min were taken using a low-volume cascade impactor. The amount of test material collected was determined by GLC and the particle size distribution was determined using a graphical method.

5. Statistics

The LC₅₀ was calculated using the Litchfield and Wilcoxon method.

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. All deaths occurred within 3 days of exposure. Two of ten males and 3/10 females exposed to 3.0 mg/L, 1/10 females exposed to 3.2 mg/L, 7/10 males and 3/10 females exposed to 3.6 mg/L, 4/10 males and 9/10 females exposed to 3.9 mg/L, and all 4.8 mg/L dosed rats died following treatment.

LC₅₀ Males = 3.7 mg/L (95% C.L. 3.4-4.0 mg/L)

LC₅₀ Females = 3.5 mg/L (95% C.L. 3.2-3.8 mg/L)

The Combined LC₅₀ = 3.61 mg/L (95% C.L. 3.38-3.86 mg/L)^a

^aCalculated by reviewer using Litchfield & Wilcoxon method

B. CLINICAL OBSERVATIONS

Depression, prostration, dyspnea, reddish brown stains around anogenital region, and highly nervous behavior were seen among all rats with the exception of the 2.2 mg/L group. The 2.2 mg/L group developed depression and blood-like flecks about the face. The clinical signs appeared more severe in the higher-dosed groups. All surviving rats recovered by day 6.

C. BODY WEIGHT

The non-surviving rats lost weight prior to death. The surviving rats had gained weight by day 7 and at the end of the study.

D. NECROPSY

Reddened lungs in two males in the 3.9 mg/L group and in two males and one females in the 3.0 mg/L group, small white and pink patches on the lung surface of one male and one female exposed at 3.6 mg/L, dark red lungs in seven males and five females dosed at 2.2 mg/kg appeared to be treatment related.

E. DEFICIENCIES

No study deficiencies were identified.

SignOff Date:	4/13/99
DP Barcode:	D254687
HED DOC Number:	013311
Toxicology Branch:	TOX1