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
1921 Jefferson Davis Highway
Arlington, VA 22202

4/13/1999

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 98-18F

Primary Reviewer:
Susan Chang, M.S.

Signature: _____
Date: _____

Secondary Reviewers:
H.Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.

Signature: _____
Date: _____

Robert H. Ross, M.S., Group Leader

Signature: _____
Date: _____

Quality Assurance:
LeeAnn Wilson, M.A.

Signature: _____
Date: _____

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. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Yung G. Yang, Ph.D. _____, Date _____
Toxicology Branch 1 (7509C)
EPA Work Assignment Manager: S. Diwan, Ph.D. _____, Date _____
Toxicology Branch 1(7509C)

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 Unpublished.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 μm). 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.

LC_{50} Males = 3.7 mg/L (95% C.L. 3.4-4.0 mg/L)
LC_{50} Females = 3.5 mg/L (95% C.L. 3.2-3.8 mg/L)
The Combined LC_{50} = 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 LC_{50} 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.

LC_{50} Males = 3.7 mg/L (95% C.L. 3.4-4.0 mg/L)
LC_{50} Females = 3.5 mg/L (95% C.L. 3.2-3.8 mg/L)
The Combined LC_{50} = 3.61 mg/L (95% C.L. 3.38-3.86 mg/L)[a]
[a]Calculated 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