DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: ACUTE INHALATION TOXICITY - RAT [870.1300 (81-3)]
MRID 45121305

Prepared for
Antimicrobials Division
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U.S. Environmental Protection Agency
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DATA EVALUATION RECORD

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

DP BARCODE: D266606
P.C. CODE: 069149

SUBMISSION CODE: S580646
CASE NO.: 068900

TEST MATERIAL: AM 3651P (55.2% total quaternary ammonium chloride)

SYNONYMS: not reported

CITATION: Bennick, J.E. (1999) Acute inhalation toxicity study in rats. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4852-98, April 26, 1999. MRID 45121305. Unpublished.

SPONSOR: BioShield Technologies, Inc., 4405 International Blvd., Suite B-109, Norcross, GA 30093

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 45121305), groups of five male and five female young adult Sprague-Dawley rats were exposed nose-only to AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3) for 4 hours at concentrations of 0.72 (males only), 0.95, 1.42, or 3.19 mg/L. The mass median aerodynamic diameter was estimated to be 1.1-4.1 μm and the geometric standard deviation was 1.9-10.4 μm. Approximately 28-100% of particles had an aerodynamic diameter ≤4.3 μm. The animals were observed for 14 days.

Three males and two females in the 3.19 mg/L group died during or within two hours of exposure. One male and one female in the 0.95 mg/L group, one male and two females in the 1.42 mg/L group, and one 3.19 mg/L female were found dead on day 1. One 0.72 mg/L male, one 0.95 mg/L male, and three 1.42 mg/L males were found dead between days 3 and 10. Piloerection, decreased activity, respiratory gurgles, ptosis, red crust on nose/eyes, aggressiveness, gasping, sensitivity to touch, and/or decreased defecation were noted from the rats with recovery in the survivors by day 8. Decreased activity and respiratory gurgles of two 0.95 mg/L females persisted through the end of the study. One 0.72 mg/L male decedent had discolored eyes, polyuria, and withdrawn testes. Two 0.72 mg/L males, three males and three females in the 0.95 mg/L group, one male and two females in the 1.42 mg/L group, and one 3.19 mg/L male lost weight during the first week. Most of the rats gained weight during the second week, but one 0.95 mg/L male and one 1.42 mg/L female did not regain their original weight and one 0.95 mg/L female and one 1.42 mg/L female lost weight during the second week. All other survivors

gained weight during the study. Discolored/swollen lungs, discolored stomachs and contents, and/or gas in the gastrointestinal tract were noted from the decedents. Discolored lungs were noted from three surviving rats (one 0.95 mg/L female, one 1.42 mg/L female, and one 3.19 mg/L male). No observable abnormalities were noted from the other survivors at necropsy.

The LC_{50}s for males, females, and combined were 1.32 mg/L (95% C.L. 0.53-3.35 mg/L), 2.24 mg/L (95% C.L. 0.97-5.20 mg/L), and 1.75 mg/L (95% C.L. 0.92-3.36 mg/L), respectively.

AM 3651P is in TOXICITY CATEGORY III based on the LC_{50}.

This acute inhalation study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for an acute inhalation study [870.1300 (§81-3)] in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: AM 3651P

   Description: pale yellow liquid
   Lot/Batch #: B129828B-2 and B129828B-3
   Composition: 55.2% total quaternary ammonium chloride

2. Vehicle and/or positive control

   None

3. Test animals

   Species: rat
   Strain: HSD:Sprague-Dawley
   Age and weight at dosing: approximately 8-9 weeks; males: 237-354 g, females: 181-228 g
   Source: Harlan Sprague Dawley, Inc., Indianapolis, IN
   Acclimation period: 5 days
   Diet: PMI Feeds Inc.,™ Formula No. 5008, *ad libitum*
   Water: municipal water, *ad libitum*
   Housing: individually in suspended stainless steel cages with wire bottoms
   Environmental conditions:
   Temperature: 20±3°C

Humidity: 30-70%
Air changes: 10-12/hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Dose	Male		Female	
mg/kg	Start Date	End Date	Start Date	End Date
0.72	1/26/99	2/9/99	-	-
0.95	1/19/99	2/2/99	1/19/99	2/2/99
1.42	1/18/99	2/1/99	1/18/99	2/1/99
3.19	1/14/99	1/28/99	1/14/99	1/28/99

2. Exposure conditions

Temperature and humidity were recorded every 30 minutes for the 4 hour exposure.

3. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Rats were exposed to AM 3651P by nose-only exposure for four hours. Rats were observed frequently on the day of exposure and at least once daily thereafter for 14 days. They were weighed prior to test material exposure and on days 7 and 14. All rats were necropsied.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated

Nominal Conc. (mg/L)	Grav. Conc. (mg/L)	MMAD (µm)[a]	GSD (µm)[a]	Particles ≤4.3 µm (%)[a]	Temp. (°C)	Humidity (%)	Male	Female	Combined
0.90	0.72	1.9, 1.1	5.3, 1.9	67, 100	72	55	1/5	-	-
2.46	0.95	3.1, 4.1	5.3, 3.2	35, 28	72	57	2/5	1/5	3/10
2.51	1.42	1.7, 2.9	10.4, 4.2	57, 53	72	56	4/5	2/5	6/10
4.50	3.19	2.8, 2.6	4.3, 2.0	50, 47	72	56	3/5	3/5	6/10

Data were taken from pp. 23 and 25-34, MRID 45121305.
[a] Determined at two time period during exposure

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

The exposure atmosphere was generated by a pressure operated Spraying System air atomizer (1/4 JSS) which aspirated the test material and elutriated the aerosol through a baffling chamber. The aerosol was diluted with filtered air and drawn into the nose-only exposure chamber. The average total airflow was 207 (0.72 mg/L dose) and 153 (0.95, 1.42, and 3.19 mg/L doses) liters/min and the exposure chamber volume was 500 L.

Time to equilibrium was not reported.

Analytical chemistry - None

Test atmosphere concentration - Gravimetric samples were collected using filters twice per hour from the breathing zone of the animals. The gravimetric concentration was determined by passing a known volume of exposure air through a pre-weighted filter and dividing the amount of test material deposited on the filter by the volume of air which passed through the filter. The nominal concentration was determined by dividing the loss in weight of the test material after the exposure by the total volume of air that passed through the chamber. The average results are in Table 1 above.

Particle size determination - Particle size was determined twice during each exposure using an eight-stage cascade impactor. The aerodynamic mass median diameter and geometric standard deviation were calculated by a computer program utilizing probit analysis. Results are in Table 1 above.

5. Statistics

The inhalation LC_{50} was calculated by probit analysis.

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. Two 3.19 mg/L males died during exposure. One male and two females in the 3.19 mg/L group died within two hours of post exposure. One male and one female in the 0.95 mg/L group, one male and two females in the 1.42 mg/L group, and one 3.19 mg/L female were found dead on day 1. One 0.72 mg/L male, one 0.95 mg/L male, and three 1.42 mg/L males were found dead between days 3 and 10.

The LC_{50}s for males, females, and combined were 1.32 mg/L (95% C.L. 0.53-3.35 mg/L), 2.24 mg/L (95% C.L. 0.97-5.20 mg/L), and 1.75 mg/L (95% C.L. 0.92-3.36 mg/L), respectively. This places AM 3651P in TOXICITY CATEGORY III.

B. CLINICAL OBSERVATIONS

Piloerection, decreased activity, respiratory gurgles, ptosis, red crust on nose/eyes, aggressiveness, gasping, sensitivity to touch, and/or decreased defecation were noted from the rats with recovery for the survivors by day 8. Decreased activity and respiratory gurgles of two 0.95 mg/L females persisted through the end of the study. One 0.72 mg/L male decedent had discolored eyes, polyuria, and withdrawn testes.

C. BODY WEIGHT

Two 0.72 mg/L males, three males and three females in the 0.95 mg/L group, one male and two females in the 1.42 mg/L group, and one 3.19 mg/L male lost weight during the first week. Most of the rats gained weight during the second week, but one 0.95 mg/L male and one 1.42 mg/L female did not regain their original weight and one 0.95 mg/L female and one 1.42 mg/L female lost weight during the second week. All other survivors gained weight during the study.

D. NECROPSY

Discolored/swollen lungs, discolored stomachs and contents, and/or gas in the gastrointestinal tract were noted from the decedents. Discolored lungs were noted from three surviving rats (one 0.95 mg/L female, one 1.42 mg/L female, and one 3.19 mg/L male). No observable abnormalities were noted from the other survivors.

E. DEFICIENCIES

None