US EPA ARCHIVE DOCUMENT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

August 9, 2000

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 70871-RG / AM3651PI
DP Barcode: D266606
Case No: 068900

To: Velma Noble, PM 31
Regulatory Management Branch
Antimicrobials Division (7510C)

From: Ian Blackwell, Biologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Through: Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant: Bioshield Technologies, Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Didecyl dimethyl ammonium chloride	2.88
3-Trimethyoxysilyl)propyldimethyloctadecyl ammonium chloride	36.05
Alkyl dimethyl benzyl ammonium chloride	6.40
Octyl decyl dimethyl ammonium chloride	4.80
Dioctyl dimethyl ammonium chloride	1.92
Other Ingredient(s):	47.95
Total:	100.00%

BACKGROUND: Bioshield Technologies, Inc., has submitted a set, or "six-pack", of acute toxicity studies to support the registration of their product "AM3651PI". These studies were conducted by Stillmeadow, Inc. The MRID Numbers are 451213-03 through -08. These studies were reviewed for PSB/AD by the EPA contractor Oak Ridge Laboratories.

RECOMMENDATIONS: PSB findings are:

Each of the six submitted studies is acceptable to support the registration of this new product.

The acute toxicity profile for EPA File Symbol 70871-RG is currently:

acute oral toxicity	III	acceptable
acute dermal toxicity	IV	acceptable
acute inhalation toxicity	III	acceptable
primary eye irritation	I/CORROSIVE	acceptable
primary skin irritation	III	acceptable
dermal sensitization	Nonsensitizer	acceptable

LABELING:

INGREDIENT LABELING:

Contains Methanol.

SIGNAL WORD: DANGER

POISON SKULL and CROSSBONES symbol

PRECAUTIONARY STATEMENTS:

Corrosive. Causes irreversible eye damage. Harmful if swallowed or inhaled. Do not get in eyes or on clothing. Avoid contact with skin. Avoid breathing spray mist. Methanol may cause blindness. Wear goggles or face shield. Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting

unless told to by a poison control center or doctor. Do not give anything by mouth to an unconscious person.

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

IF INHALED: Move person to fresh air. If person is not breathing, call 911 or ambulance, then give artificial respiration, preferably mouth-to-mouth, if possible. Call a poison control center or doctor for further treatment advice.

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN:

Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician." The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

The following "Note to Physician" statement is required for the subject product:

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT [870.1100 (81-1)]
MRID 45121303

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: [signature]
Date: JUL 0 5 2000

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

Signature: [signature]
Date: JUL 0 5 2000

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

Signature: [signature]
Date: JUL 0 5 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: [signature]
Date: JUL 0 5 2000

Disclaimer

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

Oak Ridge National Laboratory Managed and Operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Ian Blackwell, M.S. Date 8/9/00
EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date _____
Antimicrobials Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat [OPPTS 870.1100 (§81-1)]

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: Kuhn, J.O. (1999) Acute oral toxicity study in rats. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4850-98, April 21, 1999. MRID 45121303. Unpublished.

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

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 45121303) groups of five male and five female fasted young adult Sprague-Dawley rats were given a single oral 500 (females only), 1000, 2000, 3000 (females only), or 5050 mg/kg dose of AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3) and observed for 14 days.

None of the 1000 mg/kg males or 500 mg/kg females died during the study. One 1000 mg/kg female, one male and one female in the 2000 mg/kg group, and five males and four females in the 5000 mg/kg group were found dead on days 1 or 2. Two 2000 mg/kg males, three 3000 mg/kg females, and one 5000 mg/kg female were found dead between days 4 and 6. All 500 mg/kg female rats appeared normal during the study. Respiratory chirp/gurgle, diarrhea, red crust on muzzle, piloerection, polyuria, decreased defecation/soft feces, swollen face, dark stain around eyes, sensitivity to touch, decreased activity, walking on tiptoe, salivation, muzzle brown/red crust, and/or ptosis were noted from the rats in the higher dose groups. The survivors recovered by day 13. Alopecia on the anogenital area was noted from four rats. Two 1000 mg/kg and one 2000 mg/kg males had withdrawn testes on days 4 and/or 5. The decedents had ataxia, nasal and ocular discharge, distended abdomens, and/or gasping prior to death. One 1000 mg/kg female, one male and one female in the 2000 mg/kg group, and one 3000 mg/kg female did not gain weight or lost weight during the first week, but all gained weight during the second week of the study. All other surviving rats gained weight during the study. The decedents had brown, white paste, green, or red slurry in the stomach; a red, orange gel,

green, or yellow liquid in intestines; mottled red/dark red lungs, distended gastrointestinal tracts; undersized livers; dark spleens; thickened stomach mucosa; and/or distended stomach with yellow/white semisolid matter and yellow fluid. No observable abnormalities were noted from the surviving rats at necropsy.

The oral LD_{50}s for males, females, and combined were 1920 mg/kg (95% C.L. 1581-2333 mg/kg), 2090 mg/kg (95% C.L. 82-53139 mg/kg), and 1892 mg/kg (95% C.L. 1153-3104 mg/kg), respectively.

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

This acute oral study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for an acute oral study [870.1100 (§81-1)] 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:SD
   Age and/or weight at dosing: age not reported; males: 222-310 g, females: 155-227 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 bottom
   Environmental conditions:
   Temperature: 22±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
500	-	-	2/24/99	3/10/99
1000	1/27/99	2/10/99	2/10/99	2/24/99
2000	1/20/99	2/3/99	1/20/99	2/3/99
3000	-	-	1/27/99	2/10/99
5050	1/13/99	1/15/99	1/13/99	1/19/99

2. Animal assignment and treatment

Following an overnight fast, groups of five rats/sex were given a single 500 (females only), 1000, 2000, 3000 (females only), or 5050 mg/kg dose of the test material by gavage (Table 1). The animals were observed for mortality and clinical signs of toxicity at least three times post dosing and at least once daily thereafter for 14 days. They were weighed prior to dosing and on study days 7 and 14. All rats were necropsied.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
500	-	0/5	-
1000	0/5	2/5	2/10
2000	3/5	1/5	4/10
3000	-	3/5	-
5050	5/5	5/5	10/10

Data taken from p. 8, MRID 45121303.

3. Statistics

Calculation of the oral LD_{50} was by the Litchfield and Wilcoxon method.

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. None of the 1000 mg/kg males or 500 mg/kg females died as a result of AM 3651P toxicity. One 1000 mg/kg female, one 2000 mg/kg male, and three males and two females in the 5000 mg/kg group were found dead on day 1. One 2000 mg/kg female and two males and two females in the 5000 mg/kg group were found dead on day 2. Two 2000 mg/kg males, three 3000 mg/kg females, and one 5000 mg/kg female were found dead between days 4 and 6.

The oral LD_{50}s for males, females, and combined were 1920 mg/kg (95% C.L. 1581-2333 mg/kg), 2090 mg/kg (95% C.L. 82-53139 mg/kg), and 1892 mg/kg (95% C.L. 1153-3104 mg/kg), respectively. This places AM 3651P in TOXICITY CATEGORY III.

B. CLINICAL OBSERVATIONS

All 500 mg/kg female rats appeared normal during the study. Respiratory chirp/gurgle, diarrhea, red crust on muzzle, piloerection, polyuria, decreased defecation/soft feces, swollen face, dark stain around eyes, sensitivity to touch, decreased activity, walking on tiptoe, salivation, muzzle brown/red crust, and/or ptosis were noted from the rats in the higher dose groups. The survivors recovered by day 13. Alopecia on the anogenital area was noted from four rats on days 4, 7, or 11 through 14. Two 1000 mg/kg and one 2000 mg/kg males had withdrawn testes on days 4 and/or 5. The decedents also had ataxia, nasal and ocular discharge, distended abdomens, and/or gasping prior to death.

C. BODY WEIGHT

One 1000 mg/kg female and one 3000 mg/kg female did not gain weight and one male and one female in the 2000 mg/kg group lost weight during the first week, but all gained weight during the second week of the study. All other surviving rats gained weight during the study.

D. NECROPSY

The decedents had brown, white paste, green, or red slurry in the stomach; red, orange gel, green, or yellow liquid in intestines; mottled red or dark red lungs; distended gastrointestinal tracts; under sized livers; dark spleens; thickened stomach mucosa, and/or distended stomach with a yellow or white semisolid matter and yellow fluid. No observable abnormalities were noted from the surviving rats.

E. DEFICIENCIES

In the study report, it was listed that the rats were born on November 6, December 2 and 11, 1999 and were received on December 31, 1998 and January 21 and February 4, 1999. Corrections need to be made. These would not affect the study results.

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: ACUTE DERMAL TOXICITY - RABBIT [870.1200 (81-2)]
MRID 45121304

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: S. Chang
Date: JUL 05 2000

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

Signature: H.T. Borges
Date: JUL 05 2000

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

Signature: Robert H. Ross
Date: JUL 05 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: JUL 05 2000

Disclaimer

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

Oak Ridge National Laboratory Managed and Operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Ian Blackwell, M.S.
EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date 8/3/00
Antimicrobials Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit [OPPTS 870.1200 (§81-2)]

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: Kuhn, J.O. (1999) Acute dermal toxicity study in rabbits. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4851-98, April 21, 1999. MRID 45121304. Unpublished.

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

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 45121304) approximately 10% of the body surface area of groups of five male and five female young adult New Zealand White rabbits was dermally exposed to 500 (females only), 3500 (females only), 5050, or 5500 (females only) mg/kg AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3) for 24 hours. The animals were observed for 14 days.

None of the male rabbits and the females in 500 and 5500 mg/kg group died during the study. Two 3500 mg/kg females and two 5050 mg/kg females were found dead on days 1, 2, or 3. All 500 mg/kg female rabbits appeared normal during the study. Diarrhea, soft feces, decreased and no defecation, and/or not eating were noted from a few of the rabbits. The surviving rabbits recovered by day 12 or earlier. Very slight to severe erythema, very slight to moderate edema, atonia, coriaceousness, desquamation, eschar, and/or necrosis were noted on all animals. Three males and one female in the 5050 mg/kg group and four 5500 mg/kg females lost weight during the first week, but all gained weight during the second week. However, one male and one female only regained their original weight and one 5500 mg/kg female never regained her original weight. All other survivors gained weight during the study. Fluid in the stomach, gaseous bowl loops/small intestines, brown lungs with atelectasis, friable stomach wall and liver, food in the abdominal cavity, and/or green abdominal walls were noted from three decedents. No observable abnormalities were noted from the survivors and one decedent 5050 mg/kg female at necropsy.

The dermal LD_{50} for males, females, and combined was > 5050 mg/kg.

AM 3651P is in TOXICITY CATEGORY IV based on the LD_{50}.

This acute dermal study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for an acute dermal study [870.1200 (81-2)] in the rabbit.

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: rabbit
   Strain: New Zealand White
   Age and/or weight at dosing: approximately 11 weeks; males: 2.3-2.9 kg, females: 2.075-3.35 kg
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: 5 days
   Diet: PMI Feeds Inc.,™ Lab Rabbit Diet No. 5321, in measured amounts
   Water: municipal water, *ad libitum*
   Housing: individually in suspended stainless steel cages with wire bottom
   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
500	-	-	2/18/99	3/4/99
3500	-	-	1/28/99	2/11/99
5050	1/7/99	1/21/99	1/7/99	1/21/99
5500	-	-	1/28/99	2/11/99

2. Animal assignment and treatment

The study was first conducted as a limit test using five male and five female rabbits given a single 5050 mg/kg dose of AM 3651P applied to a clipped area on the dorsal trunk (approximately 10% of the body surface). In addition, groups of five female rabbits were treated with 500, 3500, or 5500 mg/kg test material in the same manner as the limit test (Table 1). The application site was covered with a gauze patch, secured with non-irritating adhesive tape, and wrapped with an orthopedic stockinette and secured with tape. The covering was removed 24 hours later and the site washed with tap water and a cloth to remove residual test material. The animals were observed for mortality and clinical signs of toxicity at least three times on the day of dosing and at least daily thereafter for 14 days. They were weighed prior to test material application, and on study days 7 and 14. All rabbits were necropsied.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
500	-	0/5	-
3500	-	2/5	-
5050	0/5	2/5	2/10
5500	-	0/5	-

Data taken from p. 9, MRID 45121304.

3. Statistics

Calculation of the dermal LD_{50} was not required.

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. None of the male rabbits or the females in 500 and 5500 mg/kg group died during the study. One 3500 mg/kg female and one 5050 mg/kg female were found dead on day 1. One 5050 mg/kg female was found dead on day 2. One 3500 mg/kg female was found dead on day 3.

The dermal LD_{50} for males, females, and combined was > 5050 mg/kg. This places AM 3651P in TOXICITY CATEGORY IV.

B. CLINICAL OBSERVATIONS

All 500 mg/kg female rabbits appeared normal during the study. Diarrhea, soft feces, decreased and no defecation, and/or not eating were noted from a few of the rabbits. The surviving rabbits recovered by day 12 or earlier. Very slight to severe erythema, very slight to moderate edema, atonia, coriaceousness, desquamation, eschar, and/or necrosis were noted on all animals.

C. BODY WEIGHT

Three males and one female in the 5050 mg/kg group and four 5500 mg/kg females lost weight during the first week, but all gained weight during the second week. However, one male and one female only regained their original weight and one 5500 mg/kg female never regained her original weight. All other survivors gained weight during the study.

D. NECROPSY

Fluid in stomach, gaseous bowl loops/small intestines, brown lungs with atelectasis, friable stomach wall/liver, food in the abdominal cavity, and/or green abdominal wall were noted from three decedents. No observable abnormalities were noted from the survivors and one decedent 5050 mg/kg female.

E. DEFICIENCIES

None

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
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: Ross Chang
Date: JUL 0 5 2000

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

Signature: H T Borges
Date: JUL 0 5 2000

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

Signature: Robert H. Ross
Date: JUL 0 5 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: JUL 0 5 2000

Disclaimer

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Oak Ridge National Laboratory Managed and Operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Ian Blackwell, M.S. Date 8/9/00
EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date _____
Antimicrobials Division (9510C)

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)*	GSD (µm)*	Particles ≤4.3 µm (%)*	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.
* 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 lōst 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

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT [870.2400 (81-4)]
MRID 45121306

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: Ross Chang
Date: JUL 0 5 2000

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

Signature: H T Borges
Date: JUL 0 5 2000

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

Signature: Robert H. Ross
Date: JUL 0 5 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: JUL 0 5 2000

Disclaimer

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

Oak Ridge National Laboratory Managed and Operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

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EPA Reviewer: Ian Blackwell, M.S. Date 8/9/00
EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date _____
Antimicrobials Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit [OPPTS 870.2400 (§81-4)]

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: Kuhn, J.O. (1999) Primary eye irritation study in rabbits. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4853-98, March 31, 1999. MRID 45121306. Unpublished.

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

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 45121306) 0.1 mL of AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3) was instilled into the right conjunctival sac of nine adult male/female New Zealand white rabbits. The eyes of three rabbits were rinsed with deionized water for one minute beginning 30 seconds after test material instillation. All treated eyes were washed with deionized water for one minute immediately after the 24 hour scoring. The contralateral eye of all rabbits served as control. The unwashed and washed eyes were scored for ocular irritation according to the Draize method 1, 24, 48, and 72 hours and 4, 7, 10, 14, 17, and 21 days after instillation and the irritation classified according to the method of Kay and Calandra.

Due to test material film opacity or the severity of chemosis and/or discharge, the corneal condition at several observation points and on several rabbits with washed or nonwashed eyes was not scored. Nonwashed eyes: Of the rabbits that could be scored, corneal opacity was noted on 2/2 rabbits at the day 4 observation and on 1/1 rabbit at the 21 day observation. Iritis was noted on 2/2 at the day 4 observation and on 1/1 rabbit at the day 14, 17, and 21 observations. Washed eyes: Corneal opacity was noted on one rabbit 48 hours after test material instillation through the end of the study, on one rabbit 24 hours after test material instillation, and on one rabbit 24 and 48 hours after test material instillation. Iritis was noted on one rabbit 48 hours through day 4 and on another rabbit at 24 and 48 hours, and at day 4 observations. All rabbits with nonwashed eyes showed corneal necrosis one to 24 hours after test material instillation and could not be checked afterwards due to the severity of chemosis and discharge. Thickened schlera was noted

on 3/3 rabbits with washed eyes one hour after test material instillation. The test material induced positive conjunctival irritation on all rabbits one hour after test material instillation through the end of the study. The maximum mean total scores for unwashed eyes and washed eyes were 31.7 at 4 days after treatment and 51.0 at 24 hours after treatment, respectively. The scores would have been higher if all observations could be scored.

In this study, AM 3651P was corrosive and is in TOXICITY CATEGORY I for primary eye irritation.

This study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for a primary eye irritation study [870.2400 (§81-4)] in the rabbit.

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

   None

3. Test animals

   Species: rabbit
   Strain: New Zealand White
   Age and weight at dosing: approximately 13 weeks; males: 2.275-2.975 kg and females: 2.275-2.725 kg
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: 5 days
   Diet: PMI Feeds, Inc.™ Lab Rabbit Diet No. 5321, in measured amounts
   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

Start: January 11, 1999; end: February 1, 1999

2. Animal assignment and treatment

The test material (0.1 mL) was instilled into the right conjunctival sac of three male and six female rabbits and the eye lids held together for approximately 1 second. The eyes of three female rabbits were rinsed with deionized water for one minute beginning 30 seconds after test material instillation. The eyes of six rabbits were not washed. The contralateral eye of all rabbits served as control. All treated eyes were washed with deionized water for one minute immediately after the 24 hour scoring. The animals were scored for ocular irritation 1, 24, 48, and 72 hours and 4, 7, 10, 14, 17, and 21 days after instillation according to the Draize method and the degree of irritation classified according to the method of Kay and Calandra.

II. RESULTS AND DISCUSSION

A. Nonwashed eyes: Due to the test material film opacity, the corneal condition one hour after test material instillation was not determined. Corneal opacity was noted on 2/2 rabbits that could be scored at the day 4 observation and on 1/1 rabbit at the 21 day observation. Iritis was noted on 2/2 at the day 4 observation and on 1/1 rabbit at the day 14, 17, and 21 observations. During the rest of the study period and for the rest of the rabbits, the severity of chemosis and discharge made the scoring of corneal opacity and iritis impossible. The test material induced positive conjunctival irritation one hour after test material instillation through the end of the study. All rabbits showed necrosis of the cornea one to 24 hours after test material instillation and could not be checked afterwards due to the severity of chemosis and discharge. Washed eyes: Corneal opacity was noted on one rabbit 48 hours after test material instillation through the end of the study, on one rabbit 24 hours after test material instillation, and on one rabbit 24 and 48 hours after test material instillation. Iritis was noted on one rabbit 48 hours through day 4 and on another rabbit at 24, 48, and day 4 observations. Due to the severity of chemosis and/or discharge or test material film made the scoring on the rabbits during other observation periods impossible. The test material induced positive conjunctival irritation one hour after test material instillation through the end of the study. Thickened schlera was noted on 3/3 rabbits one hour after test material instillation. The maximum mean total scores for unwashed eyes and washed eyes were 31.7 at 4 days after treatment and 51.0 at 24 hours after treatment, respectively. The scores would have been higher if all observations could be scored.

This classifies the test material as corrosive. AM 3651P is in TOXICITY CATEGORY I.

B. DEFICIENCIES

None

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT [870.2500 (81-5)]
MRID 45121307

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: Ross Chang
Date: JUL 05 2000

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

Signature: H T Borges
Date: JUL 05 2000

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

Signature: Robert H. Ross
Date: JUL 05 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: JUL 05 2000

Disclaimer

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EPA Reviewer: Ian Blackwell, M.S. Date 8/31/00

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date _____

Antimicrobials Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit [OPPTS 870.2500 (§81-5)]

DP BARCODE: D266606 SUBMISSION CODE: S580646

P.C. CODE: 069149 CASE NO.: 068900

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

SYNONYMS: not reported

CITATION: Kuhn, J.O. (1999) Primary dermal irritation study in rabbits. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4854-98, March 31, 1999. MRID 45121307. Unpublished.

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

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 45121307) three male and three female adult New Zealand White rabbits were dermally exposed to 0.5 mL AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3) for 4 hours on the dorsal trunk. The animals were observed for 14 days. Irritation was scored by the method of Draize.

Very slight erythema was noted on 1/6, 1/6, and 2/6 rabbits 1 hour, 10 days, and 14 days after patch removal, respectively, and severe erythema was noted on 2/6 rabbits at the end of the study. Well defined erythema was noted on all rabbits at other observation periods. Very slight to moderate edema was noted on all rabbits one hour after patch removal. Very slight to slight edema was noted on all rabbits 24 hours after patch removal. By 48 and 72 hours, very slight edema was noted on 5/6 rabbits that resolved on 2/6 rabbits by day 7 and on 2/6 rabbits by day 14. Very slight edema persisted on one rabbit through the end of the study. The primary dermal irritation index was 3.2.

In this study, AM 3651P was moderately irritating and is in TOXICITY CATEGORY III for primary dermal irritation.

This study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for a primary dermal irritation study [870.2500 (81-5)] in the rabbit.

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

   None

3. Test animals

   Species: rabbit
   Strain: New Zealand White
   Age and weight at dosing: approximately 12 weeks; males: 2.55-3.00 kg and females: 2.55-3.10 kg
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: 5 days
   Diet: PMI Feeds, Inc.™ Lab Rabbit Diet No. 5321, in measured amounts
   Water: municipal water, *ad libitum*
   Housing: individually in suspended stainless steel cages with wire bottom
   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

   Start: January 12, 1999; end: January 26, 1999

2. Animal assignment and treatment

   Three male and three female animals were given a single 0.5 mL dose of AM 3651P applied to a 8 x 8 cm clipped intact site on the dorsal trunk. The application sites were covered with 2.5 x 2.5 cm gauze, secured with non-irritating adhesive tape, and wrapped with a semi-permeable dressing. The dressings were left in place for 4 hours, after which they were removed and the application sites washed with water and a cloth to remove residual test material. The sites were scored for erythema and edema according to the Draize method 1, 24, 48, and 72 hours and 7, 10, and 14 after patch removal.

II. RESULTS AND DISCUSSION

A. With the exception of very slight erythema that was on 1/6, 1/6, and 2/6 rabbits 1 hour, 10 days, and 14 days after patch removal, respectively, and severe erythema that was noted on 2/6 rabbits at the end of the study, well defined erythema was noted on all rabbits one hour after patch removal throughout the study. Very slight to moderate edema was noted on all rabbits one hour after patch removal. Very slight to slight edema was noted on all rabbits 24 hours after patch removal. By 48 and 72 hours, very slight edema was noted on 5/6 rabbits that resolved on 2/6 rabbits by day 7 and on 2/6 rabbits by day 14. Very slight edema persisted on one rabbit through the end of the study. The primary dermal irritation index was 3.2.

AM 3651P was moderately irritating and is in TOXICITY CATEGORY III.

B. DEFICIENCIES

None

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(AM 3651P)

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG [870.2600 (81-6)]
MRID 45121308

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K0215

Primary Reviewer:
Susan Chang, M.S.

Signature: Susan Chang
Date: JUL 05 2000

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

Signature: H T Borges
Date: JUL 05 2000

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

Signature: Robert H. Ross
Date: JUL 05 2000

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: JUL 05 2000

Disclaimer

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Oak Ridge National Laboratory Managed and Operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

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EPA Reviewer: Ian Blackwell, M.S. Date 8/4/00
EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Date _____
Antimicrobials Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea Pig [OPPTS 870.2600 (§81-6)]

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: Kuhn, J.O. (1999) Dermal sensitization study in guinea pigs. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. Laboratory study number 4855-98, May 7, 1999. MRID 45121308. Unpublished.

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

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 45121308) with AM 3651P (55.2% total quaternary ammonium chloride, Batch No. B129828B-2 and B129828B-3), 20 young adult male/female Hartley guinea pigs were tested using the Buehler method.

Very faint usually nonconfluent erythema was noted on 1/10 animals, 24 hours after the first induction with resolution by 48 hours. Very faint usually nonconfluent erythema was noted on 9/10 animals after the second induction. Very faint usually nonconfluent to strong erythema was noted on 10/10 animals after the third induction. After three weekly inductions, dermal irritation suggestive of sensitization was not observed on the test animals after challenge. The study report include a DNCB positive control study which was carried out within six months of the current study. The results were appropriate.

In this study, AM 3651P was not a dermal sensitizer.

This study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirements for a dermal sensitization study [870.2600 (§81-6)] in the guinea pig.

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 positive control

Vehicle: deionized water; positive control: 1-Chloro-2,4-dinitrobenzene (DNCB) (historical data)

3. Test animals

Species: guinea pig
Strain: Hartley
Age and weight at start of treatment: age not reported; males: 509-557 g and females: 444-552 g
Source: Charles River Laboratories, Wilmington, MA
Acclimation period: 5 days
Diet: PMI Feeds, Inc.™ Guinea Pig Diet No. 5025, *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

Start: January 13, 1999; end: February 12, 1999

2. Animal assignment and treatment

The animals were induced and challenged according to the method of Buehler. The back of the trunk of 10 male and 10 female guinea pigs were clipped prior to each treatment. For the induction phase, 0.4 mL of 75% v/v test material in deionized water was applied to the animal beneath a 3.8 x 5 cm Coverlet adhesive dressing and was covered with polyethylene film and taped. Each animal was then placed in a restrainer for approximately six hours. The procedure was repeated once each week for three weeks. Guinea pigs were left untreated for two weeks before challenge. The animals were challenged

with 0.4 mL of 50% v/v test material in deionized water under occlusion to naive sites. A naive control group was treated with 0.4 mL of 50% v/v test material in deionized water at challenge only. Reactions were scored 24 hours after induction and challenge and, in addition, 48 hours after the first induction and challenge.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

Very faint usually nonconfluent erythema (score = 0.5) was noted on 1/10 animals, 24 hours after the first induction with resolution by 48 hours. Very faint usually nonconfluent erythema was noted on 9/10 animals after the second induction. Very faint usually nonconfluent to strong erythema was noted on 10/10 animals after the third induction.

B. CHALLENGE REACTIONS AND DURATION

Very faint usually nonconfluent erythema was noted on 4/10 test animals and 1/10 naive control animals, respectively, 24 hours following challenge with resolution by 48 hours.

AM 3651P was not a dermal sensitizer.

C. POSITIVE CONTROL

The study report include a DNCB positive control study which was carried out within six months of the current study. The results were appropriate.

D. ADDITIONAL TESTING

It is the reviewer's opinion that the study was conducted in a manner suitable to detect the sensitization potential of the test material. No additional testing is needed.

E. DEFICIENCIES

None