UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

07/20/00

MEMORANDUM

Subject: D260933
Z-1, EPA File Symbol 3573-AO

From: Wallace Powell, Biologist
Product Science Branch
Antimicrobials Division (7510C)

Thru: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

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

To: Velma Noble, Product Manager, Team 31
Jacquie Campbell, Team Reviewer, Team 31
Regulatory Management Branch I
Antimicrobials Division (7510C)

BACKGROUND

The applicant, The Procter & Gamble Company, has submitted studies of acute oral toxicity, acute dermal toxicity, primary eye irritation, acute inhalation toxicity, primary dermal irritation, and dermal sensitization – MRID's 449560-07 through 449560-12, respectively. The studies were submitted to support registration of Z-1, EPA File Symbol 3573-AO, a spray product intended for deodorizing fabrics. The studies were reviewed for Product Science Branch (PSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum.

The product is labeled with the following active ingredients:

Active Ingredient	% by weight	EPA code
Didecyl dimethyl ammonium chloride	0.13	069149

RECOMMENDATION

The product has one Basic and seven Alternate formulations. Their compositions are specified in the Confidential Statements of Formula (CSF) dated 06/13/00 (EPA Received date 06/19/00). The eight formulations appear substantially similar to each other. Acute toxicity data supporting any one of them can support the others.

Submitted Studies:

PSB concurs with the acute Toxicity Categories assigned in the attached reviews of the submitted studies. These Categories are listed below:

Acute oral toxicity	Category IV
Acute dermal toxicity	IV
Acute inhalation tox.	IV
Eye irritation	Unacceptable
Skin irritation	IV
Skin sensitization	Non-sensitizer

Eye Irritation Data:

The applicant submitted a Low Volume Eye Test (LVET), MRID 449560-09. A review of this study is attached. Irritation signs observed in the study were as follows:

Corneal opacity: None.
Iridal involvement: None.
Conjunctival irritation: No 'positive' conjunctival redness or swelling.
No additional signs of ocular damage were observed.

If this were a Draize study, it would indicate Toxicity Category IV.

The applicant also submitted a toxicology summary, in a letter dated 10/25/99. It appears that the summary is intended to show correlation between the submitted LVET results and consumer incident data. The summary indicates that, during the period of May 1996 through September 1999, 195 cases of accidental eye exposure were reported to the applicant's 1-800 consumer health and safety hotline for the applicant's Febreze Fabric Refresher, as representing 4.2×10^{-6} eye comments per liter of product shipped. Times to clear were obtained for 46% of the 195 cases (although the reported times to clear were probably representative of the large majority of the cases) and averaged 14.6 hours, though the median was 2 hours. All cases involving symptoms were characterized as mild and transient. 23% of all cases reported symptoms as "none." In 87% of all cases, any symptoms (whether they be actual or "none") cleared within 24 hours; in about 96%, within 48 hours.

The test material in the submitted LVET study was identified as SS0637.01. Its formulation appears substantially similar to the subject product, so that any eye irritation data supporting SS0637.01 could support the subject product also.

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The consumer incident data summarized in the applicant's toxicology summary represents the applicant's Febreze product (Febreze Fabric Refresher). The applicant has specified two Febreze formulations – one that was used from May 1996 to Dec. 1998, and one that has been used from December 1998 through the time of the applicant's letter. Neither one of the Febreze formulations appears quite similar enough to the subject product to allow for it to be accepted for eye irritation assessment in lieu of the subject product formulation.

PSB does not consider an LVET study to be an acceptable fulfillment of the eye irritation data requirement. PSB shares the following concerns with various other reviewers in the Office of Pesticide Programs (OPP) in this agency:

> The Procter & Gamble study which developed support for the LVET used a limited range of product types, most of which would tend to produce rather low levels of eye irritation.
>
> The use of consumer incident data as the standard for comparing LVET & Draize test results is questionable. The value of incident reports is limited by any limitations in consumer participation. The value of incident reports is also limited by the uncertainty as to whether or not participants' eyes were rinsed, and the exact amounts of product that participants were exposed to.
>
> The LVET is thought to be less adequate for characterizing potential irritation than typical irritation. In this sense it is not an adequate substitute for the Draize test.
>
> Limiting placement of test material to the cornea may result in disparately milder irritation scores in the LVET than in the Draize test.
>
> The Interagency Regulatory Advisory Group (IRAG) recommended limiting the regulatory use of the LVET to use as a screening tool to characterize a test material either as an irritant or as potentially a non-irritant.

Conclusion:

The acute Toxicity Categories assigned to the product are listed above under the "Submitted Studies" heading. The eye irritation data requirement has not been met because a specific acute Toxicity Category for eye irritation is not apparent based on the submitted study, the submitted study is non-Guideline, and the submitted incident data offer too little support to the submitted study. Once the eye irritation data requirement is met, the precautionary (human hazard) and first-aid statements for the product label can be determined.

12-13-99

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DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT [870.1100(81-1)]
MRID 44956007

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. K0143

Primary Reviewer:
Susan Chang, M.S.

Signature: [signature]
Date: DEC 13 1999

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

Signature: H.T Borges
Date: DEC 13 1999

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

Signature: Robert H. Ross
Date: DEC 13 1999

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: DEC 13 1999

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.

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EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Douds, D.A. (1999) An acute oral toxicity study in rats with SS0637.01. Springborn Laboratories, Inc., Ohio Research Center, 640 North Elizabeth Street, Spencerville, OH 45887. Study No. 3029.2202, August 5, 1999. MRID 44956007. Unpublished.

SPONSOR: The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44956007) five male and five female fasted young adult Sprague-Dawley rats were given a single oral 5000 mg/kg dose of SS0637.01 (Lot No. 01) and observed for 14 days.

No rats died during the study. Transient incidences of fecal stain, soft/mucoid stools, and/or dark material around the nose were noted from two males and two females with recovery by day 4. All rats had normal body weight gains. No significant gross internal findings were observed at necropsy.

The oral LD_{50} for males, females, and combined was > 5000 mg/kg (Limit Test).

SS0637.01 is in TOXICITY CATEGORY IV based on the LD_{50}.

This acute oral study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirement for an acute oral study [870.110 (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: SS0637.01

Description: clear colorless liquid
Lot/Batch #: 01
Density: 1.01 g/mL
Composition: not reported

2. Vehicle and/or positive control

None

3. Test animals

Species: rat
Strain: Hsd: Sprague-Dawley® SD®
Age and/or weight at dosing: approximately 8-12 weeks; males: 206-239 g, females: 166-172 g
Source: Harlan Sprague Dawley, Inc., Indianapolis, IN
Acclimation period: ≥5 days
Diet: PMI Certified Rodent Chow No. 5002 (Purina Mills, Inc.), *ad libitum*
Water: treated municipal tap water, *ad libitum*
Housing: individually in suspended stainless steel cages
Environmental conditions:
Temperature: 72-74°F
Humidity: 32-63%
Air changes: 10-15 per hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: April 9, 1999; end: April 23, 1999

2. Animal assignment and treatment

Following an overnight fast, five rats/sex were given a single 5000 mg/kg dose of the test material by gavage. The animals were observed for clinical signs of toxicity twice on study day 0 and daily thereafter for 14 days. A general health/mortality check was performed twice daily throughout the study. They were weighed prior to fasting and on study days 0, 7, and 14. All rats were sacrificed and necropsied.

3. Statistics

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

II. RESULTS AND DISCUSSION

A. MORTALITY

None of the rats died as a result of SS0637.01 toxicity.

The oral LD_{50} for males, females, and combined was > 5000 mg/kg. **This places SS0637.01 in TOXICITY CATEGORY IV.**

B. CLINICAL OBSERVATIONS

Three males and three females had no clinical signs during the study. Transient incidences of fecal stain, soft/mucoid stools, and/or dark material around the nose were noted from the other rats with recovery by day 4.

C. BODY WEIGHT

All rats had normal body weight gains.

D. NECROPSY

No significant gross internal findings were observed at necropsy.

E. DEFICIENCIES

None

12-13-99
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DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: ACUTE DERMAL - RABBIT [870.1200 (81-2)]
MRID 44956008

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. 0143

Primary Reviewer:
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Signature: [signature]
Date: DEC 13 1999

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Date: DEC 13 1999

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

Signature: [signature]
Date: DEC 13 1999

Quality Assurance:
LeeAnn Wilson, M.A.

Signature: [signature]
Date: DEC 13 1999

Disclaimer

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

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EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Douds, D.A. (1999) An acute dermal toxicity study in rabbits with SS0637.01. Springborn Laboratories, Inc., Ohio Research Center, 640 North Elizabeth Street, Spencerville, OH 45887. Study No. 3029.2203, August 11, 1999. MRID 44956008. Unpublished.

SPONSOR: The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44956008) approximately 10% of the body surface area of five male and five female adult New Zealand White rabbits was dermally exposed to 5000 mg/kg (Limit Test) SS0637.01 (Lot No. 01) for 24 hours. The animals were observed for 14 days.

None of the animals died during the study. Feces small in size, dark material around mouth/nose, soft/mucoid stools, and/or few feces were noted from three males and five females. The animals recovered by day 11. Erythema, edema, blanching, and/or superficial lightening were present at the site of test material application. No significant gross internal findings were observed at necropsy.

The dermal LD_{50} for males, females, and combined was > 5000 mg/kg (Limit Test).

SS0637.01 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 requirement 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: SS0637.01

Description: clear colorless liquid
Lot/Batch #: 01
Density: 1.01 g/mL
Composition: not reported

2. Vehicle and/or positive control

None

3. Test animals

Species: rabbit
Strain: New Zealand White
Age and/or weight at dosing: 12 weeks; males: 2375-2737 g, females: 2200-2409 g
Source: Myrtle's Rabbitry, Thompson Station, TN
Acclimation period: ≥5 days
Diet: PMI Certified Rabbit Chow No. 5322 (Purina Mills, Inc.), *ad libitum*
Water: treated municipal tap water, *ad libitum*
Housing: individually in suspended stainless steel cages
Environmental conditions:
Temperature: 66-74°F
Humidity: 41-63%
Air changes: 10-15 per hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: April 6, 1999; end: April 20, 1999

2. Animal assignment and treatment

The study was conducted as a limit test using five male and five female rabbits. Animals were given a single 5000 mg/kg dose of SS0637.01 applied to a clipped area (approximately 10% of the body surface). The application site was covered with a gauze dressing, plastic wrap, and then wrapped with elastic wrap. The covering was removed 24 hours later and the excess test material was removed using gauze moistened with deionized water. The animals were observed for clinical signs of toxicity twice on study day 0 (post dosing) and daily thereafter for 14 days. Dermal irritation was examined daily following patch removal. A mortality check was performed twice daily throughout the study. They were weighed prior to test material application, and on study days 7 and 14. All rabbits were sacrificed and necropsied.

3. Statistics

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

II. RESULTS AND DISCUSSION

A. MORTALITY

None of the rabbits died during the study.

The dermal LD_{50} for males, females, and combined was > 5000 mg/kg. This places SS0637.01 in TOXICITY CATEGORY IV.

B. CLINICAL OBSERVATIONS

Feces small in size, dark material around mouth/nose, soft/mucoid stools, and/or few feces were noted from three males and five females. The animals recovered by day 11. Erythema, edema, blanching, and/or superficial lightening were present at the site of test material application.

C. BODY WEIGHT

All animals had normal body weight gains.

D. NECROPSY

No significant gross internal findings were observed at necropsy. One incidence of cysts on the oviducts were observed, however, this was not considered treatment-related.

E. DEFICIENCIES

None

12-13-99
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DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT [870.2400 (81-4)]
MRID 44956009

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
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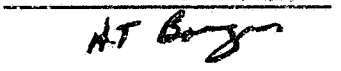
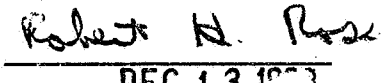
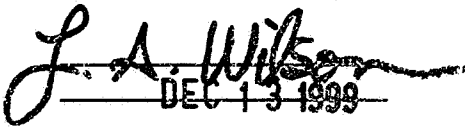
Oak Ridge, TN 37831
Action No. K0143

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	 DEC 13 1999
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	 DEC 13 1999
Robert H. Ross, M.S., Group Leader	Signature: Date:	 DEC 13 1999
Quality Assurance: Lee Ann Wilson, M.A.	Signature: Date:	 DEC 13 1999

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EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Douds, D.A. (1999) A low volume eye irritation study in rabbits with SS0637.01. Springborn Laboratories, Inc., Ohio Research Center, 640 North Elizabeth Street, Spencerville, OH 45887. Study No. 3029.2204, July 23, 1999. MRID 44956009. Unpublished.

SPONSOR: The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44956009) 0.01 mL of SS0637.01 (Lot No. 01) was placed directly on the cornea between the center of the cornea and the superior limbus of the right eye of six adult male/female New Zealand white rabbits. The eyes were scored for ocular irritation according to the Draize method 1, 24, 48, 72 hours after instillation.

No corneal opacity or iritis were found on any rabbit. The test material induced no conjunctival irritation.

In this study, SS0637.01 was not an eye irritant.

This study is classified as **Unacceptable/Guideline** and does not satisfy the subdivision F guideline requirement for a primary eye irritation study [870.2400 (81-4)] in the rabbit. Only 0.01 mL of test material was instilled into each eye, but the guideline requires 0.1 mL.

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

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: SS0637.01

   Description: clear colorless liquid
   Lot/Batch #: 01
   Composition: not reported

2. Vehicle

None

3. Test animals

Species: rabbit
Strain: New Zealand white
Age and weight at dosing: adult; male: 2.630 kg, females: 2.335-2.845 kg
Source: Myrtle's Rabbitry, Thompson Station, TN
Acclimation period: ≥5 days
Diet: PMI Certified Rabbit Chow No. 5322, *ad libitum*
Water: treated municipal tap water, *ad libitum*
Housing: individually in suspended stainless steel cages
Environmental conditions:
Temperature: 68-71°F
Humidity: 43-63%
Air changes: 10-15 per hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: April 8, 1999; end: April 11, 1999

2. Animal assignment and treatment

The test material (10 μL) was placed directly on the cornea between the center of the cornea and the superior limbus of the right eye of one male and five female adult New Zealand white rabbits. Following instillation, the eyelids were released without forced blinking or manipulation. The contralateral eye of all rabbits served as control. The eyes were rinsed with physiological saline to remove any residual test material. The animals were scored for ocular irritation 1, 24, 48, and 72 hours after instillation. Ocular irritation was scored according to the Draize method.

II. RESULTS AND DISCUSSION

A. No corneal opacity or iritis were found on any rabbit. The test material induced no positive conjunctival irritation.

This classifies the test material as non-irritating.

B. DEFICIENCIES

No explanation was given for why only 0.01 mL of test material was used in the study. The guideline requires 0.1 mL.

12-13-99
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DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: ACUTE INHALATION - RAT [870.1300 (81-3)]
MRID 44956010

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. K0143

Primary Reviewer:
Susan Chang, M.S.

Signature: Ross Chang
Date: DEC 13 1999

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

Signature: H.T Borges
Date: DEC 13 1999

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

Signature: Robert H. Ross
Date: DEC 13 1999

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: DEC 13 1999

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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: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Ulrich, C.E. (1999) An inhalation toxicity study of SS0637.01 in albino rats. WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281. Laboratory study number WIL-28037, September 30, 1999. MRID 44956010. Unpublished.

SPONSOR:The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 44956010), five male and five female young adult Sprague-Dawley rats were exposed nose-only to SS0637.01 (Lot No. 01) for 4 hours at a concentration of 2.1 mg/L. Approximately 75% of particles had an aerodynamic diameter < 3.2 μm. The mass median aerodynamic diameter and geometric standard deviation were estimated to be 1.7 and 2.44 μm, respectively. The animals were observed for 14 days.

No rats died during the study. Red material around the nose/eye and wet red facial areas were noted from four males and five females immediately following exposure. The rats recovered by day 1. All male rats had normal body weight gains. One female did not gain weight from days 0-3 and another female did not gain weight from days 3-7. By the end of the study, all females had gained weight. No significant changes were observed at necropsy.

The LC_{50} for males, females, and combined was > 2.1 mg/L (Limit Test).

SS0637.01 is in TOXICITY CATEGORY IV based on the LC_{50}.

This acute inhalation study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirement 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: SS0637.01

Description: clear colorless liquid
Lot/Batch #: 01
Purity: 100%
Composition: 1.25% nonvolatiles

2. Vehicle and/or positive control

None

3. Test animals

Species: rat
Strain: Crl:CD®(SD)IGS BR
Age and weight at dosing: approximately 52 days; males: 287-295 g, females: 220-229 g
Source: Charles River Laboratories, Kingston, NY 12484
Acclimation period: ≥7 days
Diet: PMI Nutrition International, Inc., Certified Rodent Chow No. 5002, *ad libitum*
Water: treated municipal water, *ad libitum*
Housing: individually suspected wire-mesh cages
Environmental conditions:
Temperature: 67-74°F
Humidity: 49-58%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 6, 1999; end: July 20, 1999

2. Exposure conditions

Temperature and humidity were recorded approximately every 30 minutes throughout the four hour exposure.

3. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Rats were exposed to SS0637.01 by nose-only exposure for four hours. They were observed once daily throughout the 14-day study. They were weighed prior to test material exposure and on days 3, 7, and 14. All rats were sacrificed and necropsied.

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

Nominal Conc. (mg/L)	Grav. Conc. (mg/L)	MMAD (μm)	GSD (μm)	Particles <3.2 μm (%)	Temp. (°C)	Humidity (%)	Male	Female	Combined
3.6	2.1	1.7	2.44	75	21	32	0/5	0/5	0/10

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

The test material was metered and pumped to a Spraying System atomizer (Type J body, No. 1650 fluid nozzle and No. 64 air cap). Dry compressed air was supplied to the air port of the atomizer. The aerosol was sprayed into a six-liter glass atomization chamber to remove the large droplets produced during the atomization process. The resulting aerosol was piped to the nose-only exposure system. The average total airflow was 22-25 liters/min and the nose-only exposure chamber volume was 10 L.

Time to equilibrium was not specified in the study report.

Analytical chemistry - None

Test atmosphere concentration - Gravimetric samples were collected using glass fiber filters held in an in-line filter holder position in the center spacer ring between the two animal exposure sections of the exposure system. Eight samples were collected. The filters were dried and weighed. The average results are in Table 1 above.

Particle size determination - Particle size of each exposure concentration was determined using a seven-stage cascade impactor. The test material concentration collected by each stage was determined gravimetrically. Results are in Table 1 above.

5. Statistics

Calculation of the inhalation LC_{50} was not required.

II. RESULTS AND DISCUSSION

A. MORTALITY

No rats died during the study.

The LC_{50} for males, females, and combined was > 2.1 mg/L.

This places SS0637.01 in TOXICITY CATEGORY IV.

B. CLINICAL OBSERVATIONS

Red material around the nose/eye and wet red facial areas were noted from four males and five females immediately following exposure. The rats recovered by day 1.

C. BODY WEIGHT

All male rats had normal body weight gains. One female did not gain weight from days 0-3 and another female did not gain weight from days 3-7. By the end of the study, all females had gained weight.

D. NECROPSY

Diffuse red discoloration of all lung lobes in two males and dark red areas of the lobes in one male and one female were observed. The study author suggested that air was trapped within the alveoli. One male had multiple, pinpoint, dark red areas on the thymus. The study author stated that this is a common finding in laboratory rats and was not considered treatment-related.

E. DEFICIENCIES

The air change frequency and photoperiod of the animal room were not reported. These would not affect the study results.

12-13-99
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DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT (81-5)
MRID 44956011

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. K0143

Primary Reviewer:
Susan Chang, M.S.

Signature: Susan Chang
Date: DEC 13 1999

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

Signature: H.T. Borges
Date: DEC 13 1999

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

Signature: Robert H. Ross
Date: DEC 13 1999

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: DEC 13 1999

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.

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EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Douds, D.A. (1999) A primary skin irritation study in rabbits with SS0637.01. Springborn Laboratories, Inc., Ohio Research Center, 640 North Elizabeth Street, Spencerville, OH 45887. Study No. 3029.2205, August 11, 1999. MRID 44956011. Unpublished.

SPONSOR: The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44956011) three male and three female adult New Zealand white rabbits were dermally exposed to 0.5 mL SS0637.01 (Lot No. 01) for 4 hours on the clipped dorsal trunk. The animals were observed for 72 hours. Irritation was scored by the method of Draize.

Very slight erythema was noted on all rabbits one hour following patch removal with recovery by 24 hours. The calculated primary irritation index for the test material was 0.25.

In this study, SS0637.01 is essentially non-irritating and is in TOXICITY CATEGORY IV for primary dermal irritation.

This study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirement 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: SS0637.01

   Description: clear colorless liquid
   Lot/Batch #: 01
   Composition: not reported

2. Vehicle

None

3. Test animals

Species: rabbit
Strain: New Zealand white
Age and weight at dosing: adult; males: 2.358-2.455 kg; females: 2.485-2.650 kg
Source: Myrtle's Rabbitry, Thompson Station, TN
Acclimation period: ≥5days
Diet: PMI Certified Rabbit Chow No. 5322 (Purina Mills, Inc.), *ad libitum*
Water: treated municipal tap water, *ad libitum*
Housing: individually in suspended stainless steel cages
Environmental conditions:
Temperature: 65-71°F
Humidity: 45-59%
Air changes: 10-15 per hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: April 5, 1999; end: April 8, 1999

2. Animal assignment and treatment

Three male and three female animals were given a single 0.5 mL dose of SS0637.01 applied under a 1 inch x 1 inch gauze patch on the clipped site on the dorsal trunk. The gauze patch was held in contact with the skin at the cut edges with a nonirritating tape. Removal and ingestion of the test material was prevented by placing an elastic wrap over the trunk and test area (semi-occlusive binding). A collar was placed on each animal after dosing throughout the study. The dressing was left in place for 4 hours, after which it was removed and the residual test material was removed with distilled water and dry gauze. The site was scored for erythema and edema according to the Draize method 1, 24, 48, and 72 hours after patch removal.

II. RESULTS AND DISCUSSION

A. Very slight erythema was noted on all rabbits one hour following patch removal with recovery by 24 hours. The calculated primary irritation index for the test material was 0.25.

SS0637.01 is essentially non-irritating and is in TOXICITY CATEGORY IV.

B. DEFICIENCIES

None

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12-13-99
C

DATA EVALUATION REPORT

DIDECYL DIMETHYL AMMONIUM CHLORIDE
(SS0637.01)

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG (81-6)
MRID 44956012

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
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. K0143

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Date: DEC 13 1999

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Date: DEC 13 1999

Robert H. Ross, M.S., Group Leader
Signature: Robert H Ross
Date: DEC 13 1999

Quality Assurance:
Lee Ann Wilson, M.A.
Signature: L. A. Wilson
Date: DEC 13 1999

Disclaimer

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

DIDECYL DIMETHYL AMMONIUM CHLORIDE Dermal Sensitization Study [870.2600 (81-6)]

EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____

EPA Work Assignment Manager: Nader Elkassabany, Ph.D._____ Date: _____

DATA EVALUATION RECORD

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

DP BARCODE: D260933
P.C. CODE: 069149

SUBMISSION CODE: S570933
CASE NO.: 065046

TEST MATERIAL: SS0637.01

SYNONYMS: not reported

CITATION: Douds, D. (1999) A dermal sensitization study in guinea pigs with SS0637.01 - Modified Buehler design. Springborn Laboratories, Inc., Ohio Research Center, 640 North Elizabeth Street, Spencerville, OH 45887. Study No. 3029.2206, July 27, 1999. MRID 44956012. Unpublished.

SPONSOR: The Procter & Gamble Company, 11530 Reed Hartman Highway, Cincinnati, OH 45241

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44956012) with SS0637.01 (Lot No. 01), 30 young adult male and female Hartley guinea pigs were tested using the Buehler method.

Slight patchy erythema was noted 24-48 hours after induction. No positive reaction was noted on any test or naive control animal following challenge. The study report included a HCA positive control study which was carried out just beyond six months of the current study. The results were appropriate.

In this study, SS0637.01 was not a dermal sensitizer.

This study is classified as **Acceptable/Guideline** and satisfies the subdivision F guideline requirement 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.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: SS0637.01

Description: clear colorless liquid
Lot/Batch #: 01
Composition: not reported

2. Vehicle and positive control

Vehicle: distilled water (challenge); positive control: α-hexylcinnamaldehyde (HCA)

3. Test animals

Species: guinea pig
Strain: Hartley
Age and weight at start of treatment: young adult; males: 351-439 g, females: 383-444 g
Source: Hilltop Lab Animals, Inc., Scottdale, PA
Acclimation period: ≥5 days
Diet: PMI Certified Guinea Pig Chow No. 5026 (Purina Mills, Inc.), *ad libitum*
Water: treated municipal tap water, *ad libitum*
Housing: individually in suspended stainless steel cages
Environmental conditions:
Temperature: 59-74°F
Humidity: 35-65%
Air changes: 10-15 per hour
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: April 6, 1999; end: May 7, 1999

2. Animal assignment and treatment

The animals were induced and challenged according to the method of Buehler. The side of 15 male and 15 female guinea pigs were clipped. For each induction, 0.3 mL of undiluted test material was applied with a Hilltop chamber for approximately six hours once each week for three weeks to the left side. Guinea pigs were left untreated for two weeks before challenge. The animals were challenged with 0.3 mL of 50% test material in distilled water under occlusion to naive sites for 6 hours. A naive control group was

treated with 0.3 mL of 50% test material in distilled water at challenge only. Reactions were scored 24 and 48 hours post exposure.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

Slight patchy erythema was noted on 2/20 animals 24 hours after the first induction with recovery by 48 hours. Slight patchy erythema was noted on 6/20 and 1/20 animals 24 and 48 hours, respectively, after the second induction. Slight patchy erythema was noted on 3/20 animals 24 hours after the third induction with recovery by 48 hours.

B. CHALLENGE REACTIONS AND DURATION

Slight patchy erythema was noted on 7/20 and 3/20 test animals 24 and 48 hours, respectively, after challenge. Slight patchy erythema was noted on 3/10 and 1/10 naive control animals 24 and 48 hours, respectively, after challenge. No responses indicative of sensitization were observed after challenge.

SS0637.01 was not a dermal sensitizer.

C. POSITIVE CONTROL

The study report included a HCA positive control study which was carried out just beyond six months of the current study and the results were appropriate.

E. 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.

F. DEFICIENCIES

The positive control study was done on October 1, 1998 through October 30, 1998. The current study was done on April 6, 1999 through May 7, 1999.