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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 20, 1998

MEMORANDUM:

Subject: Acute Toxicity Reviews for EPA Reg. No.: 432-667
Scourge Insecticide with SBP-1382/PBO 18+54% MF Formula II
DP Barcode: 202910
Case No: 038172

From: Jane Smith, Chemist
Technical Review Branch
Registration Division (7505C)

JCS 5/20/98

To: Susan Lewis
Insecticide Branch
Registration Division (7505C)

Applicant: AGREVO Environmental Health

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Resmethrin	18.00%
Piperonyl Butoxide	54.00%
Inert Ingredient(s):	28.00%
Total:	100%

BACKGROUND: AGREVO Environmental Health has submitted three acute toxicity studies (guidelines 81-3, -4 and -6) in support of EPA Reg. No. 432-667. The MRID #s are 431994-01through -03. The studies were conducted by Stillmeadow, Inc, Sugar Land, Texas.

RECOMMENDATIONS:

The acute toxicity profile* for **this submission** for reg. no. 432-667 is currently:

Study	Toxicity Category	Evaluation
acute inhalation toxicity	IV	acceptable
primary eye irritation	III	acceptable
dermal sensitization	IV	acceptable

*See below for entire acute toxicity profile.

LABELING:

Date: 05/20/98 LABEL REVIEW SYSTEM

ID #: 000432-00667 SCOURGE INSECTICIDE WITH SBP-1382/PBO 18+54% MF FORM.II

RESTRICTED USE CLASSIFICATION RECOMMENDED:

Due to dermal irritation toxicity category.

The PM Team should decide if restricted use classification is necessary or if alternative labeling will allay the requirement for restricted use classification.

SIGNAL WORD: WARNING

PRECAUTIONARY STATEMENTS:

Causes skin irritation. Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Do not get on skin or on clothing. Avoid contact with eyes. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Drink promptly a large quantity of milk, egg whites, gelatin solution, or if these are not available, drink large quantities of water. Avoid alcohol.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention. For Category III, add "if symptoms persist."

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

Probable mucosal damage may contraindicate the use of gastric lavage.

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ACUTE TOX ONE-LINER

1. PC CODE: 097801 Resmethrin, 067501 Piperonyl Butoxide

2. CURRENT DATE: May 19, 1998

3. TEST MATERIAL: Scourge insecticide with SBP-1382 (resmethrin)/PBO 18 + 54% MF Formula II

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat	Core Grade
acute oral toxicity / rats / M.B. Research Laboratories / 83-6700A / **1983**	250875	LD_{50} 2600mg/kg	III	A
acute dermal toxicity / rabbits / M.B. Research Laboratories / 83-6700B / **1983**	250875	LD_{50} >2000 mg/kg	III	A
acute inhalation toxicity / rat / Stillmeadow, Inc. / 7381-90 / **1-22-91**	431994-01	LC_{50} >2.61 (mg/L)	IV	A
primary eye irritation / rabbits / Stillmeadow, Inc. / 9382-90 / **1-17-91**	431994-02	No irritation in the 72 hour study. Mild conjunctival effects and corneal stippling subsiding by 48 hours.	III	A
primary eye irritation / rabbits / M. B. Research Laboratories / 83-6999D / **1983**	252817	No corneal opacity, mild to medium conjunctival redness, chemosis and discharge clearing by day 3.	III	A
primary eye irritation / rabbits / M. B. Research Laboratories / 83-6700D / **1983**	unknown	corneal opacity and 4/6 rabbits eyes not clear at 21 days.	I**	A
primary dermal irritation / rabbits / M. B. Research Laboratories / 83-6999C / **1983**	250875	The irritation increased to level of 4 for erythema and eschar through day 7 .	II	A
dermal sensitization / guinea pig / Stillmeadow, Inc. / 7383-90 / **1-14-91**	431994-03	not a sensitizer	—	A

** Registrant reported mix-up of samples had occurred. Resubmitted an eye study (Accession #252817)

A = Acceptable
U = Unacceptable
S = Supplementary
V = self-Validated

DATA EVALUATION RECORD

SBP-1382/PBO 18-54%

Study Type: Acute Pack (§81-3, -4, and -6)

Work Assignment No. 3-54 (D202910)

Prepared for

Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall II
Arlington, VA 22202

Prepared by

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Dynamac Corporation
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Primary Reviewer:
Christie E. Padova, B.S.

Signature: Christie E. Padova
Date: 5-6-98

Project Manager:
Mary L. Menetrez, Ph.D.

Signature: Mary L Menetrez
Date: 5-6-98

Disclaimer

This Data Evaluation Record may have been altered by the Registration Division subsequent to signing by Dynamac Corporation personnel. .

EPA Reviewer: Jane Smith
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
OPPTS Number: 870.1300 OPP Guideline Number: §81-3
MRID # 431994-01
Study Completion Date: 1/22/91
Laboratory Study Number: 7381-90

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified

CITATION: Holbert, M. (1991) Acute inhalation toxicity study in rats with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7381-90. January 22, 1991. MRID 43199401. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 43199401), five young adult Sprague Dawley rats/sex were exposed by whole-body inhalation to Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide) at 2.64 mg/L (>limit concentration) for 4 hours. Animals were observed for clinical signs and mortality for up to 14 days following exposure.

Inhalation LC_{50} Males = >2.64 mg/L (observed)
Females = >2.64 mg/L (observed)

Scourge Insecticide w/SBP-1382/PBO 18%-54% is classified as **TOXICITY CATEGORY IV** based on the observed LC_{50} values in both sexes.

All animals survived the 14-day observation period. Clinical effects were observed between 0.5 hours into exposure through day 3 and included piloerection, activity decreases, ptosis, nasal discharge, salivation, and ataxia. No significant treatment-related effect on the body weights of males was observed; however, 3/5 females lost weight between 0 and 7 days. All females then gained weight between 7 and 14 days and exhibited overall increases ranging from 0.38 to 7.6% (mean of 5.6%). Necropsy of animals sacrificed after 14 days revealed no observable abnormalities.

This study is classified **acceptable (§81-3)** and satisfies the guideline requirement for an acute inhalation study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide
   CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: HSD:(SD)
   Age: Young adult
   Weight: 284-333 g males; 209-261 g females
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥1 Week
   Diet: Purina Formulab Chow (#5008), ad libitum, except during exposure
   Water: Purified (reverse osmosis) tap water, ad libitum, except during exposure
   Housing: 1-3 Animals/cage, separated by sex
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: November 12 - 26, 1990

2. Exposure conditions: A stainless steel dynamic-flow exposure chamber (200 L) of New York University design was used; the animals were housed in individual stainless steel cages inside the chamber during exposure.

   Test atmosphere was generated using a Spraying System's 1/4 JSS air atomizer equipped with a nebulizer ball. The resultant aerosol was directed through a baffling chamber (volume not specified) and diluted with dried filtered air prior to entering the exposure chamber. The air flow, recorded every 30 minutes, averaged 69.1 L/min during exposure (range of 62.3 to 77.6 L/min); the study author reported that this was sufficient to ensure an oxygen content of at least 19%. The 99% equilibration time was 14.8 minutes, and the exposure period was extended to allow for equilibration.

   The nominal test atmosphere concentration was determined at the end of the exposure period by dividing the total amount of test material delivered to the chamber by the total air volume that passed through the chamber during the exposure time. The actual test atmosphere concentration was determined analytically once per hour during exposure. At each interval, samples (12.5 L) were drawn from the breathing zone of the animals through two chloroform impingers. Aliquots of the extracts were analyzed for resmethrin using gas chromatography in conjunction with flame-ionization detection (GC/FID). The nominal and average analytically-determined time-weighted test concentrations were 7.35 and 2.637 mg/L, respectively.

   Particle size was determined twice, at 2.25 and 4.00 hours, using an Andersen cascade impactor. Samples (21.23 L) were collected from the breathing zone of the animals. The calculated average mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were 2.92 and 2.28 µm, respectively. The average percentage of particles ≤4.7 µm was 74.14%.

   The temperature and relative humidity, recorded at 30-minute intervals during exposure, ranged from 72-74 °F and 54-69%, respectively.

3. Animal assignment and treatment: Five young adult Sprague Dawley rats/sex were exposed via whole-body inhalation to Scourge Insecticide w/SBP-1382/PBO 18%-54% at 2.64 mg/L (>limit

concentration) for 4 hours. The animals were observed for signs of toxicity and/or mortality at 0.5, 1.0, and 2.5 hours into exposure (only one animal/sex was visible), 30 minutes and 2 hours following exposure, and once daily thereafter for up to 14 days. Body weights were recorded at 0 (prior to exposure), 7, and 14 days. After 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

4. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: All animals survived the 4-hour exposure and 14-day observation periods.

Inhalation LC_{50} Males = >2.64 mg/L (observed)
Females = >2.64 mg/L (observed)

B. Clinical observations: Both visible animals exhibited piloerection, activity decreases, ptosis, and nasal discharge during exposure. Thirty minutes following exposure, piloerection, activity decreases, nasal discharge, salivation, and ataxia were observed in 10/10 animals. Effects completely subsided from all animals by day 4.

C. Body Weight: No significant treatment-related effect on the body weights of males was observed; all males gained weight, with an overall (0-14 days) average increase of 15%. In females, a treatment-related effect on body weight was apparent between 0 and 7 days, with 3/5 animals exhibiting decreases. All females then gained weight between 7 and 14 days and exhibited overall increases ranging from 0.38 to 7.6% (mean of 5.6%).

D. Necropsy: Necropsy of animals sacrificed after 14 days revealed no observable abnormalities.

E. Deficiencies: The aerodynamic particle size should have been determined hourly during the exposure. This deficiency is considered minor since the individual particle size values were comparable and within the ideal respirable range of 1-4 µm.

EPA Reviewer: Jane Smith
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS Number: 870.2400 OPP Guideline Number: §81-4

MRID # 431994-02
Study Completion date: 1/17/1998
Laboratory Study Number: 7382-90

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified

CITATION: Kuhn, J. (1991) Primary eye irritation study in rabbits with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7382-90. January 17, 1991. MRID 43199402. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 43199402), 0.1 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide) was instilled into the conjunctival sac of the left eye of nine young adult New Zealand White rabbits (three male and six female). Thirty seconds following instillation, 3/9 treated eyes (all female) were flushed 1 minute with deionized water. The animals were observed for up to 72 hours following treatment, and eye irritation was scored by the Draize method.

No positive ocular irritation was observed in the treated eyes (unwashed and washed) during the 72-hour study. Effects between unwashed and washed eyes were similar and included mild conjunctival effects and corneal stippling. These effects subsided from all eyes by 48 hours.

In this study, **Scourge Insecticide w/SBP 1382/PBO 18%-54%** is classified as **TOXICITY CATEGORY IV** for primary eye irritation.

This study is classified **acceptable (§81-4)** and satisfies the guideline requirements for a primary eye irritation study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide

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CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult (3-6 months)
   Weight: Not specified
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: 6 Days
   Diet: Purina Rabbit Chow, unspecified measured amount/animal/day
   Water: Tap water, ad libitum
   Housing: Individual
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: September 10 - 13, 1990

2. Animal assignment and treatment: A 0.1-mL aliquot of Scourge Insecticide w/SBP-1382/PBO 18%-54% was instilled into the conjunctival sac of the left eye of nine young adult New Zealand White rabbits (three male and six female). The upper and lower lids were held together for 1 second before releasing to prevent loss of the material. Thirty seconds after instillation, 3/9 treated eyes (all female) were flushed for 1 minute with room temperature deionized water. The right eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24, 48, and 72 hours following instillation. At the 24-hour and subsequent (if necessary) observations, fluorescein dye was used to confirm the presence or absence of corneal ulceration. Eye irritation was scored by the Draize method.

II. RESULTS AND DISCUSSION:

A. Clinical observations: No positive ocular irritation was observed in the treated unwashed eyes during the 72-hour study. One hour following instillation, slight conjunctival redness (score of 1) was observed in 6/6 eyes, very slight conjunctival chemosis (score of 1) was observed in 1/6 eyes, and slight to moderate conjunctival discharge (scores of 1-2) was observed in 3/6 eyes. Conjunctival irritation subsided from all eyes by 48 hours. Corneal stippling was also observed in up to 3/6 eyes between 1 and 24 hours. No other ocular effects were observed. In this study, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a significant ocular irritant.

Similarly, no positive ocular irritation was observed in the treated washed eyes. At 1 hour, slight conjunctival redness (score of 1) was observed in 3/3 eyes, and moderate conjunctival discharge (score of 2) was observed in 2/3 eyes. Conjunctival irritation subsided from all eyes by 48 hours. Corneal stippling was also observed in 1/3 eyes at 1 hour. No other ocular effects were observed.

B. Deficiencies: Aside from ocular irritation, individual observations for the entire day of dosing and individual daily observations were not provided. These deficiencies, however, have no effect on the results of the study and are considered minor.

EPA Reviewer: Jane Smith
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS Number: 870.2600 OPP Guideline Number: §81-6

MRID # 431994-03
Study Competion date: 1/14/98
Laboratory Study number: 7383-90

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified

CITATION: Kuhn, J. (1991) Dermal sensitization study in guinea pigs with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7383-90. January 14, 1991. MRID 43199403. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 43199403) conducted with Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide), ten male Hartley albino guinea pigs were tested using methods based on those derived by Buehler. A concurrent positive control study was conducted in the same manner using 1-chloro-2,4-dinitrobenzene.

Very slight erythema was observed at 1/10 and 2/10 sites 24 and 48 hours, respectively, following challenge with 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to virgin sites of previously-induced animals. Although a naive control group of animals was not included for comparison, these incidences are less that those observed following the initial induction application using 100% test material. Acceptable positive control data were provided to validate the test methodology. As a result, **Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer**.

This study is classified **acceptable (§81-6)** and satisfies guideline requirements for a dermal sensitization study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide
   CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle and positive control: No test substance vehicle was used.

   Concurrent positive control data were generated using 0.06% (w:v) 1-chloro-2,4-dinitrobenzene (DNCB; purity not specified) in ethanol for both phases.

3. Test animals: Species: Guinea pig
   Strain: Hartley-Albino
   Age: Not specified (young adult based on weight)
   Weight: 295-345 g (both test groups)
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥1 Week
   Diet: Purina Guinea Pig Diet (#5025), ad libitum
   Water: Tap water, ad libitum
   Housing: Five animals/cage
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: September 12 - October 19, 1990 (both definitive and positive control studies)

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Buehler [Buehler, E., Arch. Dermatol. 91:171-177(1965)]. Based on the results of preliminary testing using two male animals and 0.5 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54% either as received (100%), or as 1, 10, and 50% dilutions in an unspecified vehicle, the test substance was administered at 100% for both phases of the definitive study.

   For the induction phase, fur from the dorsal trunk area (at least 8 x 10 cm) of 10 young adult Hartley albino guinea pigs was clipped 1 day prior to dermal administration with 0.5 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54%. The test substance was applied as received using a Coverlet adhesive dressing (1.6- x 2.8-cm gauze patch attached to a 3.8- x 5-cm piece of adhesive). One patch was attached to the left front quadrant of each animal, each patch was covered with a strip of clear polyethylene film secured with tape, and the animals were placed in restrainers. After a 6-hour exposure period, the animals were removed from the restrainers, the coverings were removed, and the animals were returned to their cages. Application of the undiluted test substance was repeated three times weekly at 2- to 3-day intervals to the same site for 2 consecutive weeks for a total of 10 applications.

   Two weeks following the final induction treatment, a single challenge exposure was conducted in the same manner as described with 0.5 mL of 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to both the previously-treated left front quadrant and to the naive right rear quadrant. A naive control group was not included in this study.

   The guinea pigs were observed for dermal irritation 24 hours following each induction and challenge exposure; in addition, observations were recorded 48 hours following induction applications 1 and 10, and after the challenge treatment. Erythema and edema were scored separately using the Draize scale. Body weights of each animal were recorded 1 day prior to the first induction treatment and 1 day prior to the challenge treatment.

   The positive control study was conducted in an identical manner as described.

II. **RESULTS AND DISCUSSION**:

A. Induction reactions and duration: The incidence and/or degree of dermal irritation gradually increased during the induction phase. After 24 hours, very slight erythema (score of 1) was observed at 7/10 sites following the first treatment and at 10/10 sites following the third and fourth treatments. Twenty-four hours following the fifth treatment, very slight to well-defined erythema (scores of 1-2) was observed at 10/10 sites and very slight edema (score of 1) developed at 8/10 sites. Twenty-four and 48 hours following the tenth treatment, very slight to well-defined erythema (scores of 1-2) and very slight edema (score of 1) were observed at 10/10 sites.

B. Challenge reactions and duration: Irritation following challenge with 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to the previously-induced test sites was generally consistent with that observed during induction phase: very slight erythema (score of 1) was observed at 7/10 sites after 24 and 48 hours. Application to the virgin site of previously-induced animals resulted in very slight erythema at 1/10 and 2/10 sites after 24 and 48 hours, respectively. No edema was observed following the applications. A naive control group of animals was not included for comparison. Based on the data provided, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer.

C. Positive control: The incidence and severity of dermal irritation increased with each successive application of DNCB. No dermal irritation was observed following the first application; 24 hours following the fourth treatment, very slight erythema (score of 1) was observed at 10/10 sites; and 24 hours following the ninth and tenth applications, moderate/severe to severe erythema (scores of 3-4), slight to moderate edema (scores of 2-3), and eschar formation were observed at 10/10 sites.

   Irritation following challenge with 0.06% DNCB to the previously-induced test sites was generally consistent with that observed during induction phase: well-defined to severe erythema (scores of 2-4; mean 2.3) and slight to moderate edema (scores of 2-3) were observed at 10/10 sites after 24 and 48 hours. Eschar formation was also observed at up to 4/10 sites after 24 or 48 hours. Application to the virgin site of previously-induced animals resulted in very slight to well-defined erythema and very slight to slight edema (scores of 1-2) at 10/10 sites after 48 hours (higher scores observed at 48 hours); therefore, 100% of the animals exhibited dermal sensitization. Although a naive control group of animals was not included for comparison, these data demonstrate the adequacy of the test species and methods employed.

D. Deficiencies: To further support the obtained data, the study should have included groups of naive controls (treated only at challenge) for both the test material and positive control substance. However, the data clearly demonstrate that although a very slight dermal irritant, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer, and therefore this deficiency is considered minor.

EPA Reviewer:
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
OPPTS Number: 870.1300 OPP Guideline Number: §81-3

DP BARCODE: D202910 SUBMISSION CODE:
P.C. CODE: TOX. CHEM. NO.:
EPA REG. NO.: MRID# 43199401 lab # 7381-90 computed 1/22/91

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified Still Meadow INC

CITATION: Holbert, M. (1991) Acute inhalation toxicity study in rats with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7381-90. January 22, 1991. MRID 43199401. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 43199401), five young adult Sprague Dawley rats/sex were exposed by whole-body inhalation to Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide) at 2.64 mg/L (>limit concentration) for 4 hours. Animals were observed for clinical signs and mortality for up to 14 days following exposure.

Inhalation LC_{50} Males = >2.64 mg/L (observed)
Females = >2.64 mg/L (observed)

Scourge Insecticide w/SBP-1382/PBO 18%-54% is classified as **TOXICITY CATEGORY IV** based on the observed LC_{50} values in both sexes.

All animals survived the 14-day observation period. Clinical effects were observed between 0.5 hours into exposure through day 3 and included piloerection, activity decreases, ptosis, nasal discharge, salivation, and ataxia. No significant treatment-related effect on the body weights of males was observed; however, 3/5 females lost weight between 0 and 7 days. All females then gained weight between 7 and 14 days and exhibited overall increases ranging from 0.38 to 7.6% (mean of 5.6%). Necropsy of animals sacrificed after 14 days revealed no

observable abnormalities.

This study is classified **acceptable (§81-3)** and satisfies the guideline requirement for an acute inhalation study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide
   CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: HSD:(SD)
   Age: Young adult
   Weight: 284-333 g males; 209-261 g females
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥1 Week
   Diet: Purina Formulab Chow (#5008), ad libitum, except during exposure
   Water: Purified (reverse osmosis) tap water, ad libitum, except during exposure
   Housing: 1-3 Animals/cage, separated by sex
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: November 12 - 26, 1990

2. Exposure conditions: A stainless steel dynamic-flow exposure chamber (200 L) of New York University design was used; the animals were housed in individual stainless steel cages inside the chamber during exposure.

   Test atmosphere was generated using a Spraying System's 1/4 JSS air atomizer equipped with a nebulizer ball. The resultant aerosol was directed through a baffling chamber (volume not specified) and diluted with dried filtered air prior to entering the exposure chamber. The air flow, recorded every 30 minutes, averaged 69.1

L/min during exposure (range of 62.3 to 77.6 L/min); the study author reported that this was sufficient to ensure an oxygen content of at least 19%. The 99% equilibration time was 14.8 minutes, and the exposure period was extended to allow for equilibration.

The nominal test atmosphere concentration was determined at the end of the exposure period by dividing the total amount of test material delivered to the chamber by the total air volume that passed through the chamber during the exposure time. The actual test atmosphere concentration was determined analytically once per hour during exposure. At each interval, samples (12.5 L) were drawn from the breathing zone of the animals through two chloroform impingers. Aliquots of the extracts were analyzed for resmethrin using gas chromatography in conjunction with flame-ionization detection (GC/FID). The nominal and average analytically-determined time-weighted test concentrations were 7.35 and 2.637 mg/L, respectively.

Particle size was determined twice, at 2.25 and 4.00 hours, using an Andersen cascade impactor. Samples (21.23 L) were collected from the breathing zone of the animals. The calculated average mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were 2.92 and 2.28 μm, respectively. The average percentage of particles $\leq$4.7 μm was 74.14%.

The temperature and relative humidity, recorded at 30-minute intervals during exposure, ranged from 72-74 °F and 54-69%, respectively.

3. Animal assignment and treatment: Five young adult Sprague Dawley rats/sex were exposed via whole-body inhalation to Scourge Insecticide w/SBP-1382/PBO 18%-54% at 2.64 mg/L (>limit concentration) for 4 hours. The animals were observed for signs of toxicity and/or mortality at 0.5, 1.0, and 2.5 hours into exposure (only one animal/sex was visible), 30 minutes and 2 hours following exposure, and once daily thereafter for up to 14 days. Body weights were recorded at 0 (prior to exposure), 7, and 14 days. After 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

4. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: All animals survived the 4-hour exposure and 14-day observation periods.

Inhalation LC_{50} Males = >2.64 mg/L (observed)
Females = >2.64 mg/L (observed)

B. Clinical observations: Both visible animals exhibited piloerection, activity decreases, ptosis, and nasal discharge during exposure. Thirty minutes following exposure, piloerection, activity decreases, nasal discharge, salivation, and ataxia were observed in 10/10 animals. Effects completely subsided from all animals by day 4.

C. Body Weight: No significant treatment-related effect on the body weights of males was observed; all males gained weight, with an overall (0-14 days) average increase of 15%. In females, a treatment-related effect on body weight was apparent between 0 and 7 days, with 3/5 animals exhibiting decreases. All females then gained weight between 7 and 14 days and exhibited overall increases ranging from 0.38 to 7.6% (mean of 5.6%).

D. Necropsy: Necropsy of animals sacrificed after 14 days revealed no observable abnormalities.

E. Deficiencies: The aerodynamic particle size should have been determined hourly during the exposure. This deficiency is considered minor since the individual particle size values were comparable and within the ideal respirable range of 1-4 μm.

EPA Reviewer: _____
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden _____
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS Number: 870.2400 OPP Guideline Number: §81-4

DP BARCODE: D202910 SUBMISSION CODE:
P.C. CODE: TOX. CHEM. NO.:
EPA REG. NO.: Wind# 43199402 Lab# 7382-90 date unspecified 1/7/91

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified

CITATION: Kuhn, J. (1991) Primary eye irritation study in rabbits with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7382-90. January 17, 1991. MRID 43199402. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 43199402), 0.1 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide) was instilled into the conjunctival sac of the left eye of nine young adult New Zealand White rabbits (three male and six female). Thirty seconds following instillation, 3/9 treated eyes (all female) were flushed 1 minute with deionized water. The animals were observed for up to 72 hours following treatment, and eye irritation was scored by the Draize method.

No positive ocular irritation was observed in the treated eyes (unwashed and washed) during the 72-hour study. Effects between unwashed and washed eyes were similar and included mild conjunctival effects and corneal stippling. These effects subsided from all eyes by 48 hours.

In this study, **Scourge Insecticide w/SBP 1382/PBO 18%-54% is not a significant ocular irritant**, and is classified as **TOXICITY CATEGORY IV** for primary eye irritation.

This study is classified **acceptable (§81-4)** and satisfies the guideline requirements for a primary eye irritation study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide
   CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult (3-6 months)
   Weight: Not specified
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: 6 Days
   Diet: Purina Rabbit Chow, unspecified measured amount/animal/day
   Water: Tap water, ad libitum
   Housing: Individual
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: September 10 - 13, 1990

2. Animal assignment and treatment: A 0.1-mL aliquot of Scourge Insecticide w/SBP-1382/PBO 18%-54% was instilled into the conjunctival sac of the left eye of nine young adult New Zealand White rabbits (three male and six female). The upper and lower lids were held together for 1 second before releasing to prevent loss of the material. Thirty seconds after instillation, 3/9 treated eyes (all female) were flushed for 1 minute with room temperature deionized water. The right eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24, 48, and 72 hours following instillation. At the 24-hour and subsequent (if necessary) observations,

fluorescein dye was used to confirm the presence or absence of corneal ulceration. Eye irritation was scored by the Draize method.

II. RESULTS AND DISCUSSION:

A. Clinical observations: No positive ocular irritation was observed in the treated unwashed eyes during the 72-hour study. One hour following instillation, slight conjunctival redness (score of 1) was observed in 6/6 eyes, very slight conjunctival chemosis (score of 1) was observed in 1/6 eyes, and slight to moderate conjunctival discharge (scores of 1-2) was observed in 3/6 eyes. Conjunctival irritation subsided from all eyes by 48 hours. Corneal stippling was also observed in up to 3/6 eyes between 1 and 24 hours. No other ocular effects were observed. In this study, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a significant ocular irritant.

Similarly, no positive ocular irritation was observed in the treated washed eyes. At 1 hour, slight conjunctival redness (score of 1) was observed in 3/3 eyes, and moderate conjunctival discharge (score of 2) was observed in 2/3 eyes. Conjunctival irritation subsided from all eyes by 48 hours. Corneal stippling was also observed in 1/3 eyes at 1 hour. No other ocular effects were observed.

B. Deficiencies: Aside from ocular irritation, individual observations for the entire day of dosing and individual daily observations were not provided. These deficiencies, however, have no effect on the results of the study and are considered minor.

EPA Reviewer: _____
Registration Division, Technical Review Branch (7505C)

EPA Work Assignment Manager: John C. Redden _____
Registration Division, Technical Review Branch (7505C)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS Number: 870.2600 OPP Guideline Number: §81-6

DP BARCODE: D202910 SUBMISSION CODE:
P.C. CODE: MRID 43199403 TOX. CHEM. NO.:
EPA REG. NO.: Lab # 7383-90 complete 1/14/91

TEST MATERIAL (PURITY): Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide)

SYNONYMS: None specified

CITATION: Kuhn, J. (1991) Dermal sensitization study in guinea pigs with Scourge Insecticide w/SBP-1382/PBO 18%-54% Ref. #12411 Lot No. 2150 ALM 02. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 7383-90. January 14, 1991. MRID 43199403. Unpublished.

SPONSOR: Roussel Bio Corporation, 170 Beaver Brook Road, Lincoln Park, NJ.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 43199403) conducted with Scourge Insecticide w/SBP-1382/PBO 18%-54% (18% resmethrin and 54% piperonyl butoxide), ten male Hartley albino guinea pigs were tested using methods based on those derived by Buehler. A concurrent positive control study was conducted in the same manner using 1-chloro-2,4-dinitrobenzene.

Very slight erythema was observed at 1/10 and 2/10 sites 24 and 48 hours, respectively, following challenge with 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to virgin sites of previously-induced animals. Although a naive control group of animals was not included for comparison, these incidences are less that those observed following the initial induction application using 100% test material. Acceptable positive control data were provided to validate the test methodology. As a result, **Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer.**

This study is classified **acceptable (§81-6)** and satisfies guideline requirements for a dermal sensitization study 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: Scourge Insecticide w/SBP-1382/PBO 18%-54%
   Description: Clear, brown liquid
   Lot/Batch #: 2150 ALM 02
   Composition: 18% Resmethrin and 54% piperonyl butoxide
   CAS #: 10453-86-8 and 51-03-6, respectively

2. Vehicle and positive control: No test substance vehicle was used.

   Concurrent positive control data were generated using 0.06% (w:v) 1-chloro-2,4-dinitrobenzene (DNCB; purity not specified) in ethanol for both phases.

3. Test animals: Species: Guinea pig
   Strain: Hartley-Albino
   Age: Not specified (young adult based on weight)
   Weight: 295-345 g (both test groups)
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥1 Week
   Diet: Purina Guinea Pig Diet (#5025), ad libitum
   Water: Tap water, ad libitum
   Housing: Five animals/cage
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: September 12 - October 19, 1990 (both definitive and positive control studies)

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Buehler [Buehler, E., Arch. Dermatol. 91:171-177(1965)]. Based on the results of preliminary testing using two male animals and 0.5 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54% either as received (100%), or as 1, 10, and 50% dilutions in an unspecified vehicle, the test substance was administered at 100% for both phases of the definitive study.

   For the induction phase, fur from the dorsal trunk area (at least 8 x 10 cm) of 10 young adult Hartley albino guinea pigs was clipped 1 day prior to dermal administration with 0.5 mL of Scourge Insecticide w/SBP-1382/PBO 18%-54%. The test substance was applied

as received using a Coverlet adhesive dressing (1.6- x 2.8-cm gauze patch attached to a 3.8- x 5-cm piece of adhesive). One patch was attached to the left front quadrant of each animal, each patch was covered with a strip of clear polyethylene film secured with tape, and the animals were placed in restrainers. After a 6-hour exposure period, the animals were removed from the restrainers, the coverings were removed, and the animals were returned to their cages. Application of the test substance was repeated three times weekly at 2- to 3-day intervals to the same site for 2 consecutive weeks for a total of 10 applications.

Two weeks following the final induction treatment, a single challenge exposure was conducted in the same manner as described with 0.5 mL of 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to both the previously-treated left front quadrant and to the naive right rear quadrant. A naive control group was not included in this study.

The guinea pigs were observed for dermal irritation 24 hours following each induction and challenge exposure; in addition, observations were recorded 48 hours following induction applications 1 and 10, and after the challenge treatment. Erythema and edema were scored separately using the Draize scale. Body weights of each animal were recorded 1 day prior to the first induction treatment and 1 day prior to the challenge treatment.

The positive control study was conducted in an identical manner as described.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: The incidence and/or degree of dermal irritation gradually increased during the induction phase. After 24 hours, very slight erythema (score of 1) was observed at 7/10 sites following the first treatment and at 10/10 sites following the third and fourth treatments. Twenty-four hours following the fifth treatment, very slight to well-defined erythema (scores of 1-2) was observed at 10/10 sites and very slight edema (score of 1) developed at 8/10 sites. Twenty-four and 48 hours following the tenth treatment, very slight to well-defined erythema (scores of 1-2) and very slight edema (score of 1) were observed at 10/10 sites.

B. Challenge reactions and duration: Irritation following challenge with 100% Scourge Insecticide w/SBP-1382/PBO 18%-54% to the previously-induced test sites was generally consistent with that observed during induction phase: very slight erythema (score of 1) was observed at 7/10 sites after 24 and 48 hours. Application to the virgin site of previously-induced animals resulted in very slight erythema at 1/10 and 2/10 sites after 24 and 48 hours, respectively. No edema was observed following the applications. A naive control group of animals was not included for comparison. Based on the data provided, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer.

C. Positive control: The incidence and severity of dermal irritation increased with each successive application of DNCB. No dermal irritation was observed following the first application; 24 hours following the fourth treatment, very slight erythema (score of 1) was observed at 10/10 sites; and 24 hours following the ninth and tenth applications, moderate/severe to severe erythema (scores of 3-4), slight to moderate edema (scores of 2-3), and eschar formation were observed at 10/10 sites.

Irritation following challenge with 0.06% DNCB to the previously-induced test sites was generally consistent with that observed during induction phase: well-defined to severe erythema (scores of 2-4; mean 2.3) and slight to moderate edema (scores of 2-3) were observed at 10/10 sites after 24 and 48 hours. Eschar formation was also observed at up to 4/10 sites after 24 or 48 hours. Application to the virgin site of previously-induced animals resulted in very slight to well-defined erythema and very slight to slight edema (scores of 1-2) at 10/10 sites after 48 hours (higher scores observed at 48 hours); therefore, 100% of the animals exhibited dermal sensitization. Although a naive control group of animals was not included for comparison, these data demonstrate the adequacy of the test species and methods employed.

D. Deficiencies: To further support the obtained data, the study should have included groups of naive controls (treated only at challenge) for both the test material and positive control substance. However, the data clearly demonstrate that although a very slight dermal irritant, Scourge Insecticide w/SBP-1382/PBO 18%-54% is not a dermal sensitizer, and therefore this deficiency is considered minor.