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

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AUG - 1 1997

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Reviews of 6 Acute Studies with Milo-Pro 4L Herbicide (43.9% Propazine)

DP Barcode: D219175 PC Code: 080808
Submission: S493489 Tox Chem No: 184

TO: Jim Tompkins, PM 25
Herbicide Branch
Registration Division (7505C)

FROM: Kit Farwell
Reregistration Branch 1
Health Effects Division (7509C)

Kit Farwell 7-31-97

THRU: Whang Phang, Senior Scientist
Reregistration Branch 1
Health Effects Division (7509C)

Whang Phang 7/31/97

REGISTRANT: Griffin Corporation, Valdosta, GA

CONCLUSIONS: The six acute studies with Milo-Pro 4L Herbicide (43.9% Propazine) are all Acceptable/Guideline and satisfy the respective 81-1 through 81-6 guideline requirements. Following is a table summarizing the acute studies. The complete DERs are attached.

ACTION REQUESTED: Review and evaluate the following studies:

Acute Studies with Milo-Pro 4L Herbicide (43.9% Propazine):

Kuhn, J. (1994) Acute oral toxicity study in rats. Stillmeadow, Inc. Study Number 1324-94. October 27, 1994. MRID 43474107.

Kuhn, J. (1994) Acute dermal toxicity study in rabbits. Stillmeadow, Inc. Study Number 1325-94. August 31, 1994. MRID 43474108.

Holbert, M. (1994) Acute inhalation toxicity study in rats. Stillmeadow, Inc. Study Number 1326-94. November 9, 1994. MRID 43474109.

Kuhn, J. (1994) Primary eye irritation study in rabbits. Stillmeadow, Inc. Study Number 1327-94. August 31, 1994. MRID 43474110.

Kuhn, J. (1994) Primary dermal irritation study in rabbits. Stillmeadow, Inc. Study Number 1328-94. August 31, 1994. MRID 43474111.

Kuhn, J. (1994) Dermal sensitization study in guinea pigs. Stillmeadow, Inc. Study Number 1329-94. October 26, 1994. MRID 43474112.

Acute Toxicity of Milo-Pro 4L Herbicide (43.9% Propazine)

Study Type (MRID #)	Results	Tox Category	TB Evaluation
81-1 Acute Oral (43474107)	Male LD_{50} > 5050 mg/kg/day Female LD_{50} = 3922 mg/kg	III	Acceptable
81-2 Acute Dermal (43474108)	LD_{50} >5050 mg/kg	IV	Acceptable
81-3 Acute Inhalation (43474109)	LC_{50} > 2.13 mg/L	IV	Acceptable
81-4 Primary Eye Irritation (43474110)	Negative	IV	Acceptable
81-5 Primary Skin Irritation (43474111)	Negative	IV	Acceptable
81-6 Dermal Sensitization (43474112)	Negative	N/A	Acceptable

cc Catherine Eiden, RCAB

ATTACHMENTS: DERs

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DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Acute Oral Toxicity (81-1)

Work Assignment No. 2-21A (MRID 43474107)

Prepared for

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

Prepared by

Pesticide Health Effects Group
Sciences Division
Dynamac Corporation
2275 Research Boulevard
Rockville, MD 20850-3268

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

Signature: Christie E. Padova
Date: 8-22-96

Quality Assurance:
Mike Norvell, Ph.D.

Signature: Mike Norvell
Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J. Spangler
Date: 9/10/96

Disclaimer

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EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Kuhn, J. (1994) Acute oral toxicity study in rats. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1324-94. October 27, 1994. MRID 43474107. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 43474107), groups of five young adult Sprague-Dawley albino rats/sex were given single oral doses of undiluted Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25) at 5,050 mg/kg (limit concentration) for males and 2,500, 3,500, 4,500, or 5,050 mg/kg for females. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Oral LD_{50} Males = >5,050 mg/kg (observed)
Females = 3,922 (3,373-4,561) mg/kg (95% C.I.)

Milo-Pro 4L Herbicide is classified as **TOXICITY CATEGORY III** based on the calculated LD_{50} values for female animals.

Mortality occurred in 10/15 female animals tested at ≥3,500 mg/kg between 1 and 3 days following administration. Effects were observed primarily in animals that died during the study and included piloerection, activity decreases, hypersensitivity, nasal discharges, polyuria, ptosis, salivation, and withdrawn testes. Ataxia, chromodacryorrhea, decreased defecation, and rapid shallow breathing were observed only in decedent animals. Effects subsided from all surviving animals by day 8. Gross necropsies of decedent animals revealed slightly swollen and/or discolored red lungs (10/10), discolored livers (7/10), abnormal contents of the gastrointestinal tracts (9/10), and black mesenteric lymph nodes (2/10). Necropsy of animals sacrificed

after 14 days revealed discolored red lungs (3/15), discolored liver surface (1/15), and gas-distended large intestine (1/15).

This study is classified **acceptable**, and satisfies the guideline requirements for an acute oral study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: HSD:SD, albino
   Age: Young adult
   Weight: 207-250 g males; 188-236 g females
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥5 days
   Diet: Purina Formulab Chow (#5008), ad libitum
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: June 29-August 10, 1994

2. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1. Following a fasting period (length not specified), rats were given a single oral dose of undiluted Milo-Pro 4L Herbicide by gavage; dosing volumes ranged from 2.31 to 4.66 mL/kg. The rats were observed for signs of toxicity and/or mortality at 1, 2, and 4 hours following administration, and at least once daily thereafter for the remainder of the 14-day study. Body weights were recorded at study days 0 (prior to dosing), 7, and 14. At 14 days, the surviving animals were sacrificed, and all animals were necropsied and examined for gross pathological changes.

   TABLE 1. Doses, mortality/animals treated

Dose, mg/kg	Males	Females	Combined
2,500	--	0/5	--
3,500	--	1/5	--
4,500	--	5/5	--
5,050	0/5	4/5	4/10

3. Statistics: The acute oral LD_{50} value (with 95% C.I.) for female animals was calculated by a computer program utilizing probit analysis.

II. RESULTS AND DISCUSSION:

A. Mortality: Mortality data are presented in Table 1. Mortality occurred in 10/15 female animals tested at ≥3,500 mg/kg between 1 and 3 days following administration.

Oral LD_{50} Males = >5,050 mg/kg (observed)
Females = 3,922 (3,373-4,561) mg/kg (95% C.I.)
Combined = Not determined

B. Clinical observations: Piloerection and activity decrease were observed in animals from all dose groups; effects observed primarily in animals that died during the study included hypersensitivity, nasal discharge, polyuria, ptosis, salivation, and withdrawn testes. In addition, ataxia, chromodacryorrhea, decreased defecation, and rapid shallow breathing were observed only in decedent females. Effects subsided from surviving female animals by day 5, and from male animals by day 8. Individual observations were not provided.

C. Body Weight: No treatment-related effects on body weight were observed in surviving animals, with overall (0-14 days) average body weight increases of 27% for males and 15-21% for females.

D. Necropsy: Gross necropsies of decedent female animals revealed slightly swollen and/or discolored red lungs (10/10), discolored (primarily edges) livers (7/10), abnormal contents of the gastrointestinal tract (including stomach, large intestines, and small intestines; 9/10), black mesenteric lymph nodes (2/10), and yellow fatty tissue (1/10). In addition, a perforated stomach and clear tan liquid in abdominal cavity were observed in a single decedent female from the 4,500-mg/kg dose group.

Gross necropsy of animals sacrificed after 14 days revealed discolored red lungs (3/15), discolored liver surface (1/15), and gas-distended large intestine (1/15).

E. Deficiencies: Clinical observations should have been provided on an individual animal basis. As a result, effects observed in decedent versus surviving animals and/or the number of affected animals could not accurately be determined. However, this deficiency did not alter the results of this study and is considered minor.

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DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Acute Dermal Toxicity (81-2)

Work Assignment No. 2-21B (MRID 43474108)

Prepared for

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

Prepared by

Pesticide Health Effects Group
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Dynamac Corporation
2275 Research Boulevard
Rockville, MD 20850-3268

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

Signature: Christie E. Padova
Date: 8-22-96

Quality Assurance:
Mike Norvell, Ph.D.

Signature: mike norvell
Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J Spangler
Date: 9/10/96

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EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Kuhn, J. (1994) Acute dermal toxicity study in rabbits. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1325-94. August 31, 1994. MRID 43474108. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 43474108), five young adult New Zealand White rabbits/sex were dermally exposed to Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25) at 5,050 mg/kg (>2X limit concentration) for 24 hours. The test substance was applied to approximately 10% of the total body surface area. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

Milo-Pro 4L Herbicide is classified as **TOXICITY CATEGORY IV** based on the observed LD_{50} values in both sexes.

A single female died 3 days following administration. Clinical signs of toxicity were observed between 1 and 6 days and included decreased defecation, diarrhea, nasal discharge, and aggression. Very slight to moderate/severe erythema, very slight edema, and/or desquamation were observed at 7/9 treatment sites between 1 and 10 days. The body weight of a single surviving female decreased 12% during the study, and the body weight of a single male animal remained unchanged. Gross necropsy of the single decedent female revealed green, black, and purple abdominal muscles and swollen lungs containing a white liquid. Necropsies of animals sacrificed after 14 days revealed brick red lungs with white discolorations.

This study is classified **acceptable**, and satisfies the guideline requirements for an acute dermal study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

2. Vehicle: None employed.

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult (3-6 months)
   Weight: 2.55-2.90 kg males; 2.75-2.95 kg females
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: ≥5 days
   Diet: Purina Rabbit Chow, unspecified measured amount/animal/day
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: June 23-July 7, 1994

2. Animal assignment and treatment: Fur from the dorsal trunk areas of five young adult animals/sex was clipped 1 day prior to dermal administration of Milo-Pro 4L Herbicide at 5,050 mg/kg (>2X limit concentration). The test substance was evenly applied as received to an 8- x 4-inch region of the clipped skin (equivalent to 206.4 cm^2 or approximately 10% of the total body surface area). Each application site was covered with a 8- x 4-inch surgical gauze patch secured with non-irritating adhesive tape, and the entire trunk of each animal was wrapped with plastic film secured with non-irritating adhesive tape. After 24 hours, the coverings were removed, and the sites were gently washed with tap water and a clean wet cloth. The rabbits were observed for signs of toxicity and/or mortality at 1, 2, and 4 hours following treatment,

and at least once daily thereafter for the remainder of the 14-day study. Erythema and edema were scored separately according to the Draize scale at 1, 3, 7, 10, and 14 days of study. In addition, body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, the surviving animals were sacrificed, and all animals were necropsied and examined for gross pathological changes.

3. Statistics: Not applicable for this study.

II. RESULTS AND DISCUSSION:

A. Mortality: A single female animal died 3 days following administration.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

B. Clinical observations: Clinical signs of toxicity observed during the study included decreased defecation, diarrhea, nasal discharges (males only), and aggression (females only). Effects were observed between 1 and 6 days following administration. Individual observations were not provided.

Very slight to moderate/severe erythema (scores of 1-3) and very slight edema (score of 1) were observed in males between days 1 and 7. In addition, desquamation was observed at 3/4 sites of females between days 3 and 10. All dermal irritation had subsided by day 14.

C. Body Weight: The body weights of two females decreased between 1 and 7 days, and the body weight of one of those rabbits continued to decrease between 7 and 14 days. Overall (0-14 days), the body weight of this animal decreased 12%; the body weights of the remaining three surviving females increased 6.4-9.1%. The body weight of a single male remained unchanged during the study; otherwise, all males gained weight (12-16%).

D. Necropsy: Gross necropsy of the single decedent female revealed green, black, and purple abdominal muscles and swollen lungs containing a white liquid. Necropsies of animals sacrificed after 14 days revealed brick red lungs with white discolorations and a white caudal lobe of the liver in a single male animal, and a small stomach filled with a mass of fibrous material (probably hair) in a single female animal.

E. Deficiencies: Clinical observations should have been provided on an individual animal basis; however, this deficiency did not alter the results of this study and is considered minor.

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DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Acute Inhalation Toxicity (81-3)

Work Assignment No. 2-21C (MRID 43474109)

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
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Prepared by

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Primary Reviewer:
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Signature: Christie E. Padova
Date: 8-22-96

Quality Assurance:
Mike Norvell, Ph.D.

Signature: mike norvell
Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J Spangler
Date: 9/10/96

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EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/19/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Holbert, M. (1994) Acute inhalation toxicity study in rats. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1326-94. November 9, 1994. MRID 43474109. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 43474109), a group of five young adult Sprague-Dawley albino rats/sex was exposed by whole-body inhalation to Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25) at 2.13 mg/L (limit concentration) for 4 hours. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postexposure.

Inhalation LC_{50} Males = >2.13 mg/L (observed)
Females = >2.13 mg/L (observed)

Milo-Pro 4L Herbicide is classified as **TOXICITY CATEGORY IV** based on the observed LC_{50} values for both sexes.

All animals survived the 4-hour exposure and 14-day observation periods. Piloerection, activity decreases, fur coated with test material, and red crusts on noses were observed in up to 10/10 animals between chamber removal and 3 days following exposure. Effects initially subsided from all animals by day 4; however, piloerection, ptosis, red crusts on noses, and alopecia were observed primarily in females between 8 and 14 days. Gross necropsies after 14 days revealed slightly swollen and red mottled lungs in three males.

This study is classified **acceptable**, and satisfies the guideline requirements for an acute inhalation study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

2. Vehicle and/or positive control: Water (not further characterized)

3. Test animals: Species: Rat
   Strain: HSD:SD, albino
   Age: Young adult
   Weight: 213-228 g males; 207-218 g females
   Source: Harlan Sprague Dawley, Inc., Houston, TX
   Acclimation period: ≥5 days
   Diet: Purina Formulab Chow (#5008), ad libitum, except during exposure
   Water: Tap water, ad libitum, except during exposure

B. STUDY DESIGN and METHODS:

1. In-life dates: August 19-September 2, 1994

2. Exposure conditions: A whole-body, dynamic-flow exposure chamber (200 L) constructed of stainless steel and containing individual stainless steel wire mesh cages (New York University design) was utilized in the study.

   Based on the results of preliminary trials, the test material was diluted to 80% with water prior to use in order to obtain the maximum test concentration. Test atmosphere was generated into the top of the exposure chamber using a pressure-operated Spraying System's air atomizer (1/4 JSS). The total airflow through the exposure chamber was maintained at 76.4 L/min (equivalent to 22.9 chamber turnovers/hour). The time required for 99% equilibration was 12 minutes.

   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 once per hour during the exposure period. Samples (15.66 L) obtained from the breathing zone of the animals were drawn through chloroform traps. Samples of the chloroform were analyzed for propazine using a Tracor 560 gas chromatograph in conjunction with flame ionization detection. The nominal and average analytically-determined test concentrations were 259.1 and 2.13 mg/L, respectively.

Particle size was determined twice per exposure period using an Anderson cascade impactor. Samples (56.6 L) were collected from the breathing zone of the animals at 0.75 and 3.00 hours into exposure. The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) averaged 6.17 and 2.56 µm, respectively. The percentage of particles <9, <4.7, and <1.1 µm averaged 73.18, 38.38, and 3.40%, respectively.

During the exposure period, the mean temperature was 69 °F, the mean relative humidity was 95%, and the oxygen level was reportedly maintained above 19%.

3. Animal assignment and treatment: Five young adult rats/sex were exposed to Milo-Pro 4L Herbicide at 2.13 mg/L via whole-body inhalation for 4 hours. The animals were observed for signs of toxicity and/or mortality at 0.5, 1.0, 2.5, 4.5, and 6.0 hours following the initiation of exposure, and at least once daily thereafter for the remainder of the 14-day study. Body weights were recorded at 0 (prior to exposure), 7, and 14 days. After 14 days, surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

4. Statistics: Not applicable for this study.

II. RESULTS AND DISCUSSION:

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

Inhalation LC_{50} Males = >2.13 mg/L (observed)
Females = >2.13 mg/L (observed)

B. Clinical observations: Piloerection, activity decreases, fur coated with test material, and red crusts on noses were observed in up to 10/10 animals between chamber removal (4.5 hours) and 3 days following exposure. Effects initially subsided from all animals by day 4; however, piloerection was observed in one rat/sex between 8 and 10 days, ptosis was observed in a single female between 8 and 10 days, red crusts on noses were observed in a single female between 8 and 9 days, and alopecia of the jaw was observed in a single female between 8 and 14 days.

C. Body Weight: The body weight of a single female decreased between 0 and 7 days, then increased between 7 and 14 days; otherwise, no significant treatment-related effects on body weight were observed. Overall (0-14 days), all animals gained weight, with average increases of 19% for males and 11% for females.

D. Necropsy: Gross necropsies after 14 days revealed slightly swollen and red mottled lungs in three male animals.

E. Deficiencies: The average MMAD was 6.17 μm, exceeding the ideal respirable range of 1-4 μm. However, data from preliminary trials indicate that the highest concentration attained with a MMAD within the ideal respirable range was 1.19 mg/L. As a result, this study is deemed as a "best effort".

The aerodynamic particle size should have been determined hourly during each exposure period; however, since the size was determined twice/exposure, and since the calculated MMAD values were comparable, this deficiency is considered minor.

The relative humidity was a constant 95% during the exposure period. Although this greatly exceeds the 40-60% range specified in Subdivision F guidelines, water was used as a test substance vehicle, and this percentage is considered normal and should have had no adverse effects on the results of this study.

DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Primary Eye Irritation (81-4)

Work Assignment No. 2-21D (MRID 43474110)

Prepared for

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

Prepared by

Pesticide Health Effects Group
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Primary Reviewer:
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Signature: Christie E. Padova
Date: 8-22-96

Quality Assurance:
Mike Norvell, Ph.D.

Signature: mike norvell
Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J Spangler
Date: 9/10/96

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EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/19/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Kuhn, J. (1994) Primary eye irritation study in rabbits. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1327-94. August 31, 1994. MRID 43474110. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 43474110), 0.1 mL of Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25) was instilled into the conjunctival sac of the right 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. All treated eyes were washed after 24 hours. The animals were observed for up to 72 hours following treatment.

Slight conjunctival redness was observed in 6/6 treated unwashed eyes 1 hour following instillation. No corneal opacity, iridial changes, or other conjunctival effects were observed during the 72-hour observation period, and all conjunctival redness subsided by 24 hours.

Based on the results of this study, **Milo-Pro 4L Herbicide is not an ocular irritant**, and is classified as **TOXICITY CATEGORY IV.**

This study is classified **acceptable**, and satisfies the guideline requirements for a primary eye irritation study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   pH: 7.64
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

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 provided
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: ≥5 days
   Diet: Purina Rabbit Chow, unspecified measured amount/animal/day
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: June 27-30, 1994

2. Animal assignment and treatment: A 0.1-mL aliquot of Milo-Pro 4L Herbicide was instilled into the conjunctival sac of the right 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. Twenty-four hours after instillation, all treated eyes were flushed in the same manner. The left eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24 (prior to washing), 48, and 72 hours following instillation. At the 24-hour observation, fluorescein dye was used to confirm the presence or absence of corneal ulceration. Eye irritation was scored using the Draize method.

II. **RESULTS AND DISCUSSION:**

A. Clinical observations: Slight conjunctival redness (score of 1) was observed in 6/6 treated unwashed eyes 1 hour following instillation. No corneal opacity, iridial changes, or other conjunctival effects were observed during the study, and all conjunctival redness subsided by 24 hours. Based on the results of this study, Milo-Pro 4L Herbicide is not an ocular irritant.

Effects observed in the treated washed eyes were slightly more severe. Slight to moderate conjunctival redness (scores of 1-2) was observed in 3/3 eyes, and very slight conjunctival chemosis (score of 1) was observed in 2/3 eyes. No corneal opacity or iridial changes were observed during the study, and all conjunctival effects subsided by 24 hours.

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

DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Primary Dermal Irritation (81-5)

Work Assignment No. 2-21E (MRID 43474111)

Prepared for

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

Prepared by

Pesticide Health Effects Group
Sciences Division
Dynamac Corporation
2275 Research Boulevard
Rockville, MD 20850-3268

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

Signature: Christie E. Padova
Date: 8-22-96

Quality Assurance:
Mike Norvell, Ph.D.

Signature: Mike Norvell
Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J. Spangler
Date: 9/10/96

Disclaimer

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

EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/19/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Kuhn, J. (1994) Primary dermal irritation study in rabbits. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1328-94. August 31, 1994. MRID 43474111. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 43474111), three young adult New Zealand White rabbits/sex were dermally exposed to 0.5 mL of Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25) for 4 hours; the test substance was applied as to a single intact <25-cm^2 site/animal. Animals were observed for dermal irritation for up to 72 hours following application, and irritation was scored by the Draize method.

No dermal irritation was observed during the 72-hour observation period. Based on the results of this study, **Milo-Pro 4L Herbicide is not a dermal irritant**, and is classified as **TOXICITY CATEGORY IV** for primary dermal irritation.

This study is classified as **acceptable**, and satisfies the guideline requirements for a primary dermal irritation study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   pH: 7.64
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

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 provided
   Source: Ray Nichols Rabbitry, Lumberton, TX
   Acclimation period: ≥5 days
   Diet: Purina Rabbit Chow, unspecified measured amount/animal/day
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: June 21-24, 1994

2. Animal assignment and treatment: Fur from the dorsal trunk area (approximately 8 x 8 cm/animal) of three young adult animals/sex was clipped 1 day prior to dermal administration with 0.5 mL of Milo-Pro 4L Herbicide. The test substance was applied as received to a single intact application site/animal, covered with a two-ply 25-cm^2 surgical gauze patch secured with non-irritating tape, and the trunk of each animal was then loosely wrapped with an orthopedic stockinette secured with adhesive tape. Following a 4-hour exposure period, the coverings were removed, and the test sites were gently washed with tap water and a clean cloth. The rabbits were observed for dermal irritation at 0.5, 24, 48, and 72 hours following patch removal. Erythema and edema were scored separately using the Draize method.

II. **RESULTS AND DISCUSSION:**

A. Clinical observations: No dermal irritation was observed during the 72-hour observation period. Based on the results of this study, Milo-Pro 4L Herbicide is not a dermal irritant.

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

DATA EVALUATION RECORD

Milo-Pro 4L Herbicide
(Propazine)

Study Type: Dermal Sensitization (81-6)

Work Assignment No. 2-21F (MRID 43474112)

Prepared for

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

Prepared by

Pesticide Health Effects Group
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Date: 8-22-96

Quality Assurance:
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Date: 8/23/96

Project Manager:
William Spangler, Ph.D.

Signature: William J Spangler
Date: 9/10/96

Disclaimer

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EPA Reviewer: W. Greear, MPH, DABT W. Greear, Date 9/18/96
Review Section IV, Toxicology Branch I (7509C)
EPA Secondary Reviewer: M. Copley, DVM, DABT M Copley, Date 9/19/96
Review Section IV, Toxicology Branch I (7509C)

DATA EVALUATION RECORD

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

DP BARCODE: D219175 SUBMISSION CODE: S493489
P.C. CODE: 080808 TOX. CHEM. NO.:
EPA REG. NO.:

TEST MATERIAL (PURITY): Milo-Pro 4L Herbicide (an end-use-product containing 43.9% propazine)

SYNONYMS: None specified

CITATION: Kuhn, J. (1994) Dermal sensitization study in guinea pigs. Stillmeadow, Inc., Sugar Land, TX. Laboratory Study Number 1329-94. October 26, 1994. MRID 43474112. Unpublished.

SPONSOR: Griffin Corporation, Rocky Ford Road, Valdosta, GA.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 43474112) conducted with Milo-Pro 4L Herbicide (43.9% propazine, Lot# 4067-25), five guinea pigs/sex were tested using methods based on those derived by Buehler.

No dermal irritation was observed 24 or 48 hours following a single challenge application to either previously-induced or naive control animals. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, **Milo-Pro 4L Herbicide is not a dermal sensitizer.**

This study is classified as **acceptable**, and satisfies the guideline requirements for a dermal sensitization study (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: Milo-Pro 4L Herbicide
   Description: White liquid
   Lot/Batch #: 4067-25
   Purity: 43.9% Propazine
   Density: 1.0827 g/mL (temperature not specified)
   CAS #: 139-40-2

2. Vehicle and positive control: None employed

   Summarized positive control data were provided (Stillmeadow Study Number 1372-94; July 8-September 16, 1994) using 1.0 and 0.15% (w:v) 1-chloro-2,4-dinitrobenzene (DNCB; approximately 95% purity) in ethanol for the induction and challenge phase treatments, respectively.

3. Test animals: Species: Guinea pig
   Strain: Hartley-Albino
   Age: Not specified
   Weight: 357-410 g males; 328-396 g females
   Source: SASCO Inc., Madison, WI
   Acclimation period: ≥5 days
   Diet: Purina Guinea Pig Chow, ad libitum
   Water: Tap water, ad libitum
   Housing: 1-4/cage, separated by sex

B. STUDY DESIGN and METHODS:

1. In-life dates: July 6-August 5, 1994

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Buehler [Ritz, H., and E. Buehler, Current Concepts in Cutaneous Toxicity, p. 28 (1980)]. Based on the results of preliminary testing using two animals/sex and 0.4 mL of Milo-Pro 4L Herbicide (100%) or 0.4 mL of 5, 20, or 50% dilutions (v:v) in deionized water, the test substance was administered at 100% in both phases of the definitive study.

   For the induction phase, fur from the dorsal trunk area (at least 8 x 10 cm) of five animals/sex was clipped 1 day prior to dermal administration of 0.4 mL of Milo-Pro 4L Herbicide. The test substance was applied 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, the entire trunk was

wrapped in polyethylene film, and the animals were placed in restrainers for a 6-hour exposure period. Removal of the test substance from the skin was not described. Application of the test substance was repeated once weekly to the same site for 2 consecutive weeks (three total applications).

For the challenge phase, a single Milo-Pro 4L Herbicide treatment was administered in the same manner as described, to the previously untreated right rear quadrant 2 weeks following the final induction treatment. To serve as naive controls, an additional five animals/sex were included for the challenge treatment. The guinea pigs were observed for dermal irritation 24 hours following each induction and challenge exposure; in addition, observations were recorded 48 hours following the first induction and challenge treatments. Erythema was scored according to the following scale:

0 - No reaction
0.5 - Very faint, usually nonconfluent
1 - Faint, usually confluent
2 - Moderate
3 - Strong, with or without edema

Body weights of each animal were recorded on days 0 (1 day prior to the first induction treatment) and 28 (1 day prior to the challenge treatment).

Although many details concerning the induction and challenge phases of the positive control study were not provided, the test animals were obtained from the same supplier as in the definitive study, and the study was conducted according to the Buehler method. In addition, vehicle control tests were conducted.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: No dermal irritation was observed during the induction phase.

B. Challenge reactions and duration: No dermal irritation was observed 24 or 48 hours following a single challenge application to either previously-induced or naive control animals. Based on the results of this study, Milo-Pro 4L Herbicide is not a dermal sensitizer.

No significant treatment-related effects on body weight were observed between animals from the treated and naive control groups, with average increases of 57% for males and 42-46% for females.

C. Positive control: Twenty-four hours following the first induction application, very faint erythema (score of 0.5) was observed at 1/10 sites; after 48 hours, very faint to moderate erythema (scores of 0.5-2) was observed at 5/10 sites. Twenty-four hours following the second and third induction applications, severe erythema (score of 3) was observed at 10/10 sites.

Twenty-four hours following a single challenge treatment to previously-induced animals, very faint to severe erythema (scores of 0.5-3) was observed at 10/10 sites and persisted or worsened at all sites after 48 hours. In contrast, no dermal irritation was observed 24 or 48 hours following application to naive control sites. These data confirm the adequacy of the test species and method employed.

Deficiencies: Although the age of the test animals was not specified, based on the body weights provided, they were probably young adult animals at study initiation, and this deficiency is considered minor.

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Chemical:	**Propazine (ANSI)**
PC Code:	**080808**
HED File Code	**13000 Tox Reviews**
Memo Date:	**08/01/1997**
File ID:	**TX014091**
Accession Number:	**412-01-0120**

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