

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

Date: February 24, 2000

Subject: Acute toxicity data review for Chlorpropham product, Trade name: Sprout Nip 7A

EPA Reg.No.: 34704-614
DP Barcode: D262716
Case No.: 0271

Handwritten notes: W/Me March 2, 00 MDP

From: Hari Mukhoty, DVM, PhD
Product Reregistration Branch (PRB)
Special Review and Reregistration Division (SRRD), Mail Code: 7508C

To: Cynthia Williams, CRM
PRB, SRRD, Mail Code: 7508C
Special Review and Reregistration Division (7508C)

Applicant: Platte Chemical Co
P. O. Box 667
Greely, CO 80632

FORMULATION FROM EPA Reg.No. 34704-614 LABEL:

Table with 2 columns: Ingredient(s) and % by wt.
Active Ingredient(s): Chlorpropham... 78.500%
Inert Ingredient(s): ... 21.500%
Total 100.00%

BACKGROUND: The Platte Chemical Company has cited the acute toxicity data from product EPA Reg. No. 2749-517 (MRIDs 44330401- 6 for 81-1 to 81-6 respectively) to support the reregistration of their product EPA Reg. No. 34704-614. The trade name of the product is "Sprout Nip 7A". The studies were conducted by Product Safety Labs., and completed in the month of June, 1997. Both aforesaid formulations are chemically similar as determined by comparing the Basic Formulation CSFs of the subject product with the cited product (dated 5-24-91 Vs. 11-1-94).

Product EPA Reg. No.34704-614 has been placed in ' BATCH 4' of Table 1 of the Chlorpropham RED and EPA Reg. No. 2749-517 has not been addressed in that RED.

RECOMMENDATIONS:

The acute toxicity data requirements for the undermentioned product are satisfied.

The acute toxicity profile for EPA Reg.No. 34704-614 is currently:

Acute Oral Toxicity	III	Acceptable
Acute Dermal Toxicity	III	Acceptable
Acute Inhalation Toxicity	IV	Acceptable
Primary Eye Irritation	III	Acceptable
Primary Dermal Irritation	IV	Acceptable
Dermal Sensitization	non-sensitizer	Acceptable

LABELING:

ID #: 34704-614 SPROUT NIP 7A

INGREDIENT LABELING:

Contains Methanol

SIGNAL WORD: DANGER PELIGRO
POISON SKULL and CROSSBONES symbol

FIRST AID:

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

IF ON SKIN: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call Poison Control Center or Physician for treatment advice.

2

IF SWALLOWED: Call a Poison Control Center or Doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to by a Poison Control Center or Doctor.

PRECAUTIONARY STATEMENTS (HAZARDS TO HUMANS AND DOMESTIC ANIMALS) : Harmful if swallowed or absorbed through the skin. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Methanol may cause blindness. Wear long-sleeved shirt and long pants, socks and shoes and chemical resistant gloves (such as Barrier Laminate, Butyl/Nitrile/Neoprene rubber/PVC/Viton \geq 14 mils).

User Safety Recommendations:

Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove contaminated clothing and wash clothing before reuse.

NOTE TO PHYSICIAN: The following note to physician statement is required for the subject product:

NOTE TO PM/CRM/Registrant: The proposed label should contain a Note to Physician which addresses the presence methanol.

The following statements are suggested types of information that may be included:

- technical information on symptomatology,
- use of supportive treatments to main life functions,
- medicine that will counter act the specific physiological effects of the pesticide,
- company telephone number to specific medical personnel who can provide specialized medical advice

DATA REVIEW FOR ACUTE ORAL TOXICITY (§81-1,870.1100)

Product Manager: Jim Tompkins, 25
MRID No.: 443304-01

Reviewer: Hari Mukhoty
Study Completion Date: 06-12-1997
Report No.: PSL5171

Testing Facility: Product Safety Labs., NJ
Author: Gary Wnorowski

Quality Assurance (40 CFR §160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1: 20 v/v water)

Species: Sprague-Dawley derived albino rats
Age: Young adult, not specific
Weight: males = 184-230 grams; females = 162-191 grams at initiation
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LD₅₀ (mg/kg):**

Males :	mg/kg
Females :	mg/kg
Combined:	3,670 mg/kg

2. **Tox. Category:** **III** **Classification:** Acceptable

Procedure (Deviations from §81-1): None

Procedure: After acclimation to the laboratory, 30 healthy rats were selected for test and equally distributed into three dose groups of five males and five females each. Dose levels of 2000, 3500, and 5000 milligrams of the test substance per kilogram of bodyweight was administered to healthy rats by oral gavage. The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days or until mortality. Body weights were recorded prior to administration and again on days 7 and 14 (termination) or after death. Necropsies were performed on all animals.

Results: Following test substance administration most animals from all dose levels exhibited one or more of the clinical signs of abnormal posture, hypoactivity, piloerection, and or irregular respiration. Prior to death, one decedent animal from the 5,000 mg/kg dose level also developed tremors. All survivors recovered from the above symptoms by Day 3 and gained bodyweight over the 14-day observation period.

4

INCIDENCE OF MORTALITY AT EACH DOSE LEVEL

Dose level (mg/kg)	Males	Females	Total
2,000	0/5	0/5	0/10
2,500	2/5	1/5	3/10
5,000	5/5	5/5	10/10

Gross Necropsy: Gross necropsy of the decedents revealed discoloration of the lungs, liver and intestines at 5,000 mg/kg dose level. At lower dose levels gross necropsy findings at terminal sacrifice were generally unremarkable. Apart from red lung discoloration consistent with euthanasia by carbon dioxide inhalation, all other tissues and organs appeared normal.

5

DATA REVIEW FOR ACUTE DERMAL TOXICITY (§81-2,870.1100)

Product Manager: Jim Tompkins, 25
MRID No.: 443304-02

Reviewer: Hari Mukhoty
Study Completion Date: 06-13-97
Report No.: PSL 5172

Testing Laboratory: Product Safety Labs, NJ
Author: Gary Wnorowski

Quality Assurance (40 CFR § 160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1: 20 v/v water)

Species: Sprague-Dawley derived albino rats

Weight: males = 238-254 grams; females = 215-240 grams at initiation.

Age: none stated

Source: Ace Animals, Inc, Boyertown, PA

Summary:

1. **LD₅₀ (mg/kg):** Males
Females
Combined >2,000 mg/kg

2. **Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations From §81-2): None

Methods: 2000 mg/kg of bodyweight the test material was applied as received to the skin of ten healthy rats for 24 hours. The test substance was applied evenly over a dose area of approximately 2" x 3" (approximately 10% of the body surface) and covered with a 2" x 3", 6-ply gauze pad. The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days. Bodyweights were recorded prior to application and again on Days 7 and 14 (termination). Necropsies were performed on all animals at terminal sacrifice.

Results: All animals survived, gained weight and appeared active and healthy. Apart from dermal irritation (erythema and edema) observed at the dose site of all animals between Days 1 and 2, there were no other signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

Results:**Reported Mortality**

DOSAGE (mg/kg)	(number deaths/number tested)		
	Males	Females	Combined
2,000	0/5	0/5	0/10

Gross Necropsy Findings: Gross necropsy findings at terminal sacrifice were generally unremarkable (lungs slightly red customarily seen with carbon dioxide inhalation, euthanasia procedure).

DATA REVIEW FOR ACUTE INHALATION-TOXICITY TESTING (§81-3,870.1300)

Product Manager: Jim Tompkins, 25
MRID No.: 443304-03

Reviewer: Hari Mukhoty
Study Completion Date: 06-17-1997
Report No.: PSL 5176

Testing Laboratory: Product Safety Labs., NJ
Author: Gary Wnorowski

Quality Assurance (40 CFR §160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1:20 v/v water)

Exposure Type : Whole body chamber exposure

Species: Sprague-Dawley derived albino rats
Weight: males = 214-231 grams; females = 185-222 grams at initiation
Age: Young adult, not specific days
Source: Ace Animals, Inc., Boyertown, PA

Summary:

1. **LC₅₀ (mg/L):**
Males = mg/L
Females = mg/L
Combined = 2.03 mg/L
2. **MMAD:** 2.4 micrometers
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Deviation From §81-3): None

Methods : After establishing the desired generation procedures during pre-test trials, ten young adult healthy rats were selected for test and exposed to test atmosphere for 4 hours. each. Exposure level of and 2.0 mg/L were selected for testing. Each group of animals was exposed to the test atmosphere for four hours. Chamber concentration and particle size distribution of the test substance were determined periodically during the exposure period. The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days. Bodyweights were recorded prior to exposure and again on Days 7 and 14 (termination) or after death. Necropsies were performed on all animals at terminal sacrifice.

Results: Following exposure, animals exhibited clinical signs including ocular and nasal discharge, facial staining, abnormal respiration, hunched posture and hypoactivity. Upon removal from the exposure chamber animals showed test substance on the fur.

8

All animals survived exposure to the test atmosphere.

SUMMARY OF PRE-TEST EXPOSURE TRIALS

Trial No.	Chamber concentration (mg/L)	Mass Median Aerodynamic Diameter (micrometer)
2	2.08	2.9
4	2.13	2.9

SUMMARY OF PARTICLE SIZE DISTRIBUTION

Sample No.	Sample time	Collection time	MMAD	GSD
1	1.5 hours	2 minutes	2.4 micrometers	1.73
2	3 hours	2 minutes	2.5 micrometers	1.84

SUMMARY OF MORTALITY DATA

Exposure Level	Mortality			
	mg/L	Males	Females	Total
2.03		0/5	0/5	0/10

Gross Necropsy Findings:

Lungs were slightly to moderately red. This is customarily seen with Carbon dioxide inhalation, euthanasia procedure. Gross necropsy findings at terminal sacrifice were generally unremarkable.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4,870.2400)

Product Manager: Jim Tompkins, 25
MRID No.: 443304-04

Reviewer: Hari Mukhoty
Study Completion Date: 06-13-97
Report No.: PSL 5173

Testing Laboratory: Product safety Labs. NJ
Author: Gary Wnorowski

Quality Assurance (40 CFR §160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1:20 v/v water)

Dosage: 0.1 mL of the test substance (Liquid) instilled into conjunctival sac of right eye, as received, with upper & lower lids gently held together for 1 sec.

Species: New Zealand albino rabbit

Sex: 3 males and 3 females

Weight: Not provided

Age: Young adult, not specific in days

Source: Davidson's Mill Farm, South Brunswick, NJ

Summary:

1. **Toxicity Category:** III
2. **Classification:** Acceptable

Procedure (Deviations From §81-4): None

Methods: Three males and Three females young adult New Zealand albino rabbits were used to assess eye irritation of the aforesaid product. Prior to instillation, both eyes were examined using fluorescein dye procedure. One drop 2% dye was instilled in both eyes. The eyes were rinsed with physiological saline 30 seconds post instillation. The eyes were examined with compact 4 watt UV lamp. 0.10 mL of the test substance was instilled into the conjunctival of the right eye of each rabbit. The lids were gently held together for about 1 second. The other eye of each rabbit remain untreated. Ocular irritation was evaluated using a high-intensity white light at 1, 24, 48, and 72 hours post instillation.

Results: All animals appeared active and healthy during the study. Apart from eye irritation noted below, there were no other signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

No corneal opacity or iritis was noted during the study. One and 24 hours after the test substance instillation, all treated eyes exhibited conjunctivitis. The overall incidence and severity of irritation decrease with time. By 72 hours, all animals were free from ocular

irritation.

INCIDENCE OF EYE IRRITATION

Time Post Instillation	UNRINSED			RINSED++		
	Corneal Opacity	Iritis	Conjunctivitis	Corneal Opacity	Iritis	Conjunctivitis
1 hour	0/6	0/6	6/6			
24 hours	0/6	0/6	6/6			
48 hours	0/6	0/6	5/6			
72 hours+	0/6	0/6	0/6			
Day 4						
Day 7						
Day 10						

+ Study terminated at 72 hours

++ Not applicable

11

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5,870.2500)

Product Manager: Jim Tompson, 25
MRID No.: 443304-05

Reviewer: Hari Mukhoty
Study Completion Date: 06-13-1997
Report No.: PSL 5174

Testing Laboratory: Product Safety Labs., NJ
Author: Gary Wnorowski

Quality Assurance (40 CFR §160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1:20 v/v water)

Dosage: 0.5 mL of the test substance as received (liquid) applied topically to 6 cm square of body surface.

Species: New Zealand albino rabbits

Age: Young adult, not specified in days

Sex: 3 males and 3 females **Weight:** Not specified

Source: Davidson's Mill Farm, S. Brunswick, NJ

Summary:

1. **Toxicity Category:** IV
2. **Classification:** Acceptable

Procedure (Deviations From §81-5): None

Methods : Five-tenth of a milliliter of the test substance as received (liquid) was applied to the skin of six young adult healthy New Zealand albino rabbits for 4 hours. The test substance was applied to one 6 cm square intact dose site on each animal and covered with a 1" x 1", 4-ply gauze pad. The pad and the entire trunk of each animal were then wrapped with semi-occlusive 3" Micropore tape to avoid dislocation of the pad. After 4 hours the pads were removed and individual dose sites were scored at approximately 1, 24, 48, 72 hours (Termination) after patch removal.

Results: All animals appeared active and healthy. Apart from the dermal irritation noted below, there were no other signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

At one and 24 hours of patch removal, very slight erythema was noted at 5 of 6 treated sites. Very slight edema was also evident in one rabbits. The incidence and severity of irritation decreased thereafter. All animals were free from dermal irritation within 48 hours.

The test material is classified as slightly irritating to the skin when applied as received.

12

Results:

OBSERVATIONS	(number "positive"/number tested)					
	minutes	hours			days	
	30-60	24	48	72	7*	14
erythema	6/6	6/6	0/6	0/6		
edema	1/6	1/6	0/6	0/6		

* The study terminated at 72 hours.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6,870.2600)

Product Manager: Jim Tompson, 25

MRID No.: 443304-06

Reviewer: Hari Mukhoty

Study Completion Date: 06-18-97

Report No.: PSL 5175

Testing Laboratory: Product Safety Lab., New Jersey

Author: Gary Wnorowski

Quality Assurance (40 CFR §160.12): Provided

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1:20 v/v water)

Positive Control Material: Dinitrobenzene (0.4 mL of 0.08 % DNCB in 80% aqueous ethanol for induction phase)

Species: Hartley albino Guinea pigs

Weight: Males 298-384 grams, at initiation

Age: Young adult, no specific in days

Source: Davidson's Mill Farms, New Jersey

Method: Buehler Method

Summary:

1. This Product is not a Dermal Sensitizer.

2. Classification: Acceptable

Procedure (Deviation From §81-6): None

Methods and Results :

Range Finding Test: Four animals were used to determine the highest non-irritating concentration (HNIC) of the test substance prior to the challenge dose. The fur was removed from the dorsal area and flanks of each guinea pig. The area was divided into 4 test sites on each animal. The test substance was applied neat (100%), and was also diluted with distilled water to yield concentrations of 75%, 50%, and 25% w/w. Each concentration was applied to a test site using an occlusive 25 mm Hilltop Chamber. After 6 hours of exposure, the chambers were removed. 24 hours post application each site was evaluated for local reactions.

Based on the findings, the HNIC selected for the challenge phase was a 100%.

The above methods were also used to determine the HNIC of DNCB dissolved in 0.04 % w/w solution in acetone for challenge phase.

Induction phase: Once each week for three weeks, four-tenths of a milliliter of the test substance was applied as received to the left side of each test animal. After 6-hour exposure period the chambers were removed. The same procedures were followed by applying 0.4 mL of 0.08 % DNCB in 80% aqueous ethanol to the positive control animals. 24 and 48 hours after each induction application, readings were made of local reactions.

Test Animals (applied as received, 100%): Transient, very faint erythema was noted at two test sites during the induction phase.

Positive Control Animals (0.08% DNCB in 80% aqueous ethanol): Very faint to severe erythema was noted at all positive control sites during the induction phase. Overall, the incidence and severity of irritation increased with each successive application, with eschar evident at several sites following the third dose.

Challenge phase: Thirteen days after the last induction dose, 0.4 mL of the HNIC of the test substance (100%) was applied to a naive site on the right side of each animal as a challenge dose, using methods stated above. The same procedures were followed by applying 0.4 mL of 0.04 % DNCB in acetone to the positive control animals for the challenge phase. These sites were evaluated for a sensitization response at 24 and 48 hours after the challenge application.

In addition to the test and positive control animals, 10 guinea pigs from the same shipment were maintained under identical environmental conditions and were treated with the HNIC of the test or positive control substance (five animals each) at challenge only. These animals constituted the two "naive" groups.

Test Animals (applied as received, 100%) : No irritation was noted at any test site following challenge.

Naive Control Animals (applied as received, 100%) : No irritation at any naive control sites following challenge.

Positive Control Animals (0.04% DNCB in acetone) : All positive control animals exhibited signs of sensitization response at 24 and/or 48 hours after challenge.

Positive Naive Control Animals (0.04% DNCB in acetone): Very faint erythema was noted at 1 positive naive control sites 24 hours after challenge. Irritation cleared from the affected sites by 24 after challenge.

Conclusion: Based on these findings and on the evaluation system used, the test substance is not considered to be a contact sensitizer. The positive responses to 0.04 % DNCB in acetone validates the test system used in this study.

ACUTE TOX ONE-LINER

1. PC CODE: 018301
2. CURRENT DATE: February 25, 2000
3. TEST MATERIAL: CIPC 7A, EPA Reg. No. 2749-517, Batch # 04C126386, Amber liquid, pH 5.85 (1:20 v/v water)

Study/Species/Lab/ Study # / Date	MRID #	Results	Tox. Cat.	Core Grade
acute oral toxicity/rats/ Product Safety Labs/ PSL5171 /06-12-1997	44330401	LD ₅₀ = 3,670 mg/kg	III	A
acute dermal toxicity/ rats/ Product Safety Labs/ PSL 5172 /06-13-1997	44330402	LD ₅₀ > 2000 mg/kg	III	A
acute inhalation toxicity/rats/ Product Safety Labs./ PSL5176 / 06-17-1997	44330403	LC ₅₀ > 2.03 mg/L	IV	A
primary eye irritation/ rabbits/ Product Safety Labs / PSL5173 / 06-13-1997	44330404	All ocular irritation cleared within 72 hours	III	A
primary dermal irritation/ rabbits/ Product Safety Labs/ PSL5174/ 06-13-1997	44330405	No visible irritation at 48 hours	IV	A
skin sensitization/ Guinea pigs/ Product Safety Labs/ PSL 5175/06-18-1997	44330406	Non-sensitizer	--	A

Core Grade Keys: A = Acceptable, S = Supplementary (upgradeable), U = Unacceptable
V = self-Validated

16