UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

March 21, 2000

MEMORANDUM:

Subject: EPA Reg. No.: 2749-517
DP Barcode: D259132
Case No.: 0271

From: Marianne Lewis, Biologist
Product Reregistration Branch
Special Review and Reregistration Division (7508C)

Marianne Lewis 3/21/00

To: Venus Eagle-Kunst, CRM
Product Reregistration Branch
Special Review and Reregistration Division (7508C)

Applicant: Aceto Agricultural Chemicals Corporation
One Hollow Lane
Lake Success, NY 11042-1215

FORMULATION FROM EPA Reg. No. 2749-517 LABEL:

	% by wt.
Active Ingredient(s):	
*Chlorpropham	78.5%
Inert Ingredient(s):	21.5%
Total	100.0%

*Isopropyl N-(3-chlorophenyl) carbamate
Contains 7 pounds active ingredient per gallon. Contains methanol.

BACKGROUND: In the 8 month response to the Chlorpropham RED, the registrant has submitted acute toxicity studies to support the reregistration of their product, EPA Reg. No. 2749-517. The MRID's were as follows: 443304-01 (81-1), 443304-02 (81-2), 443304-03 (81-3), 443304-04 (81-4), 443304-05 (81-5), and 443304-06 (81-6). These studies were conducted by Product Safety Labs and the material used in the studies was CIPC 7A, EPA Reg. No. 2749-517.

RECOMMENDATIONS:

- The acute toxicity studies submitted are acceptable to support the reregistration of EPA Reg. No. 2749-517.

The acute toxicity profile for EPA Reg. No. 2749-517 is currently:

Acute Oral	III	Acceptable
Acute Dermal	III	Acceptable
Acute Inhalation	IV	Acceptable
Primary Eye	III	Acceptable
Primary Dermal	IV	Acceptable
Skin Sensitization	non sensitizer	Acceptable

The acute toxicity requirements have been satisfied for the subject product.

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

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

Reviewer: Marianne Lewis
Study Completion Date: 6/12/97
Report No.: 5171

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386

Species: Sprague-Dawley derived albino rat
Age: young adult
Weight: males = 184 - 230 g; females = 162 - 191 g
Source: Ace Animals, Inc.

Conclusion:

1. **LD_{50} (mg/kg):**
   Males : 3610 mg/kg (2990 - 4620 mg/kg)
   Females: 3730 mg/kg (3090 - 4920 mg/kg)
   Combined: 3670 mg/kg (2900 - 5260 mg/kg)

2. **Tox. Category:** III

Classification: Acceptable

Procedure (Deviations from §81-1): none

Results:

Dosage (mg/kg)	Number Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10
3500	2/5	1/5	3/10
5000	5/5	5/5	10/10

Observations:

Dose mg/kg	Time of Death	Observations
2000	N/A	The following clinical signs were observed: piloerection, irregular respiration, hypoactivity, hunched posture, and prone. All animals appeared to be healthy and active from day 3 until the end of the study.
3500	1/10 on day 1 2/10 on day 3	The following clinical signs were observed: hunched posture, hypoactivity, and prone. The survivors appeared to be healthy and active from day 3 until the end of the study.
5000	1/10 on day 1 9/10 on day 2	The following clinical signs were observed: hunched posture, prone, hypoactivity, prostrate, irregular respiration, and tremors.

Gross Necropsy:

Dose mg/kg	Gross Necropsy Observations
2000	All lungs were moderately red (customarily seen with CO_2 inhalation, euthanasia procedure).
3500	Lungs slightly to moderately red, 1/10 had an extremely red G.I. tract, 1/10 had black/red G.I. tract, and 1/10 had red intestines.
5000	Lungs slightly to moderately red, 5/10 liver discolored, and 9/10 intestines extremely red/black.

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

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

Reviewer: Marianne Lewis
Study Completion Date: 6/13/97
Report No.: 5172

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386

Species: Sprague-Dawley derived albino rat
Weight: males = 238 - 254 g; females = 215 - 240 g
Age: young adult
Source: Ace Animals, Inc.

Summary:

1. **LD_{50} (mg/kg):** >2000 mg/kg

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

Procedure (Deviations From §81-2): none

Results: **Reported Mortality**

DOSAGE (mg/kg)	(number deaths/number tested)		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: Twenty four hours prior to application, the dorsal area and trunks of the test animals were clipped and examined for health and any abnormalities. The test material was applied evenly over the test site (approx. 2 x 3 inches) and covered with a 2 x 3 inch 4-ply gauze pad. This was wrapped with a 3 inch Durapore tape. After 24 hours, the pads and wrappings were removed and the test sites were wiped with water, ethanol, and a clean towel to remvoe any residual test substance.

All test animals survived, gained weight, and appeared active & healthly. On days 1 and 2 erythema and edema were present at each test site.

Gross Necropsy Findings: All lungs were slightly to moderately red (customarily seen with CO_2 inhalation, euthanasia procedure).

5

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

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

Reviewer: Marianne Lewis
Study Completion Date: 6/17/97
Report No.: 5176

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386

Species: Sprague-Dawley derived albino rat
Weight: males = 214 - 231 g; females = 185 - 222 g
Age: young adult
Source: Ace Animals, Inc.

Summary:

1. LC_{50} **(mg/L):** >2.03 mg/L
2. **MMAD:** 2.4 μm **GSD:** 1.84
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Deviation From §81-3): none

Results: **Reported Mortality**

Exposure Concentration	(Number Deaths/Number Tested)		
	Males	Females	Combined
2.03 mg/L	0/5	0/5	0/10

Chamber Atmosphere		
Dose Level	MMAD	GSD
2.03 mg/L	2.4 μm	1.84

Chamber Environment	Dose levels
	2.03 mg/L
Chamber Volume	150 L
Airflow Lpm	45.5 - 45.7
Temperature (°F)	71 - 73
Relative Humidity (%)	49 - 60

Clinical Observations: At 1 hour, all test animals had test substance on fur. Upon removal from the exposure chamber until the end of the study, all test animals were active and healthy.

Gross Necropsy Findings: All lungs were moderately red (customarily seen with CO_2 inhalation, euthanasia procedure).

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

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

Reviewer: Marianne Lewis
Study Completion Date: 6/13/97
Report No.: 5173

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386

Dosage: 0.1 ml
Species: New Zealand Albino rabbit
Sex: 3 females, 3 males
Weight: not given
Age: adult
Source: Davidson's Mill Farm

Summary:

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

Procedure (Deviations From §81-4): none

Results:

OBSERVATIONS	(number "positive"/number tested)			
	Hours			
	1	24	48	72
Corneal Opacity	0/6	0/6	0/6	0/6
Iris	0/6	0/6	0/6	0/6
Conjunctivae				
Redness	6/6	3/6	1/6	0/6
Chemosis	2/6	0/6	0/6	0/6
Discharge	6/6	0/6	0/6	0/6

At 1 hour, 6/6 had diffuse crimson red to beefy red conjunctivae, 2/6 had obvious swelling with partial eversion of the lids, and 6/6 had discharge with moistening of lids/hairs just

adjacent to and a considerable area around the eye. By 24 hours, 3/6 had diffuse crimson red conjunctivae. At 48 hours, only one test animal had diffuse crimson red conjunctivae. By 72 hours all eye irritation had cleared.

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

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

Reviewer: Marianne Lewis
Study Completion Date: 6/13/97
Report No.: 5174

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386

Dosage: 0.5 ml
Species: New Zealand albino rabbit
Age: adult
Sex: 3 females, 3 males
Weight: not given
Source: Davidson's Mill Farm

Summary:

1. **Toxicity Category:** IV

2. **Classification:** Acceptable

Procedure (Deviations From §81-5): none

Results: Twenty four hours prior to application, the dorsal area and trunks of the test animals were clipped and examined for health and any abnormalities. The test material was applied evenly over the 6 cm^2 intact dose site and covered with a 1x1 inch 4-ply gauze pad. The pad and the trunk of the animals were then wrapped with 3" Micropore tape. After 4 hours, the pads and wrappings were removed and the test sites were wiped with 95 % ethanol, then water, and then wiped dry.

At 1 hour and at 24 hours, 6/6 had very slight erythema and 1/6 had very slight edema. By 48 hours, all skin irritation had cleared.

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

Product Manager: Jim Tompkins, 25
MRID No.: 443304-06

Reviewer: Marianne Lewis
Study Completion Date: 6/18/97
Report No.: 5175

Testing Facility: Product Safety Labs
Author: G.Wnorowski

Quality Assurance (40 CFR §160.12): Included

Test Material: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386
Positive Control Material: DNCB

Species: Hartley albino guinea pig (males only)
Weight: males = 298 - 377 g
Age: young adult
Source: Davidson's Mill Farms

Method: Buehler

Summary:

1. **This Product is a non sensitizer**

2. **Classification:** Acceptable

Procedure (Deviation From §81-6): none

Procedure: A group of animals were used to determine the highest non-irritating concentration (HNIC) of the test substance and the positive control material prior to the challenge dose. The HNIC for the test substance was determined to be 100% and the HNIC for the positive control was determined to be 0.04% w/w solution in acetone.

The test animals were induced with 0.4 ml of 100% test material once a week for three weeks using a 25 mm Hill Top Chamber. Twenty four and 48 hours after each induction dose the animals were scored for irritation. Thirteen days after the last induction dose, 0.4 ml of 100% test material was used to challenge the test animals. Twenty four and 48 hours after the challenge the animals were evaluated for sensitization.

The positive control animals were induced with 0.4 ml of 0.08% DNCB in 80% aqueous alcohol using a 25 mm Hill Top Chamber. Twenty four and 48 hours after each induction dose the animals were scored for irritation. Thirteen days after the last induction dose, 0.4 ml of 0.04% w/w DNCB in acetone was used to challenge the test animals. Twenty four and 48 hours after the challenge the animals were evaluated for sensitization.

//

ACUTE TOX ONE-LINER

1. PC CODE: 018301
2. CURRENT DATE: March 21, 2000
3. TEST MATERIAL: CIPC 7A, EPA Reg. No. 2749-517, Batch #04C126386
   Chlorpropham:78.5%

Study/Species/ Lab/Study#/Date	MRID #	Results	Tox. Cat.	Core Grade
acute oral toxicity/rat/Product Safety Labs/5171/6-12-97	44330401	LD_{50} males = 3610 mg/kg females = 3730 mg/kg combined = 3670 mg/kg	III	A
acute dermal toxicity/rat/ Product Safety Labs/5172/ 6-13-97	44330402	LD_{50} >2000 mg/kg	III	A
acute inhalation toxicity/rat/ Product Safety Labs/5176/ 6-17-97	44330403	LC_{50} >2.03 mg/L MMAD = 2.4 μm; GSD = 1.84	IV	A
primary eye irritation/rabbit/ Product Safety Labs/5173/ 6-13-97	44330404	At 1 hr, 6/6 had diffuse crimson red to beefy red conjunctivae, 2/6 had obvious swelling with partial eversion of the lids, & 6/6 had discharge with moistening of lids/hairs just adjacent to & a considerable area around the eye. By 24 hrs, 3/6 had diffuse crimson red conjunctivae. At 48 hrs, only one test animal had diffuse crimson red conjunctivae. By 72 hrs all eye irritation had cleared.	III	A
primary dermal irritation/ rabbit/Product Safety Labs/ 5174/6-13-97	44330405	At 1 hr & at 24 hrs, 6/6 had very slight erythema & 1/6 had very slight edema. By 48 hrs, all skin irritation had cleared.	IV	A
skin sensitization/guinea pig/ Product Safety Labs/5175/ 6-18-97	44330406	Product is a non sensitizer.	--	A

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

LABELING:

ID #: 002749-00517 CIPC 7A

INGREDIENT LABELING:

Contains Methanol.

SIGNAL WORD: **DANGER** **PELIGRO**

POISON **SKULL & CROSSBONES** symbol

HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

Harmful if swallowed or absorbed through 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 rubber, nitrile rubber, neoprene rubber, polyvinyl chloride, or viton; Category C). Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.

FIRST AID:

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.

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 a poison control center or doctor for treatment advice.

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

Have the product container or label with you when calling a poison control center or doctor or going for treatment.