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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

May 21, 1999

MEMORANDUM

EPA File Symbol: 241-GOE Chlorfenapyr (AC 303630 2 SC Termiticide-Insecticide)
DP Barcode: D255726
Case No: 061931
PC Code: 129093 Chlorfenapyr

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

Byron T. Backus
5/21/99

To: Ann Sibold/Arnold Layne, PM 03
Insecticide Branch
Registration Division (7505C)

Registrant: American Cyanamid Company

ACTION REQUESTED "Please review MRID 447635-01; "Acute Inhalation Toxicity Study with AC 303630 240g/L SC in Rats." Attached are copies of the label, CSF, previous acute tox reviews and administrative materials."

BACKGROUND: This acute inhalation toxicity study (MRID 44763501) was conducted at Huntingdon Life Sciences, Inc. (East Millstone, NJ). The registrant previously submitted acute oral LD50 (MRID 43268204), acute dermal LD50 (MRID 43268205), eye irritation (MRID 43268206) and dermal irritation (MRID 43268207) studies on this formulation; these studies have been reviewed in HED (Doc. No. 011245), and were all classified as acceptable.

COMMENTS AND RECOMMENDATIONS:

The inhalation toxicity study submitted for this product has been classified as acceptable.

The following is the acute toxicity profile for EPA File Symbol 241-GOE Chlorfenapyr, based on the results of the HED reviews for AC 303,630 2SC (21.24% a.i.; refer to Tox. Record No. 011245), as well as the findings in this inhalation study:

Acute Oral LD50	III	Acceptable
Acute Dermal LD50	III	Acceptable
Acute Inhalation LC50	III	Acceptable
Primary Eye Irritation	IV	Acceptable
Primary Dermal Irritation	IV	Acceptable
Dermal Sensitization	No	Cited[a]

[a]Data requirement satisfied by the results of studies on AC 303,630 3SC formulation (33.3% a.i.; in MRID 42770218) and on AC 303,630 technical (94.5% a.i.; in MRID 42770212).

Based on the acute toxicity profile indicated above, the following is the precautionary labeling for this product, as obtained from the label review system:

Date: 05/17/99 LABEL REVIEW SYSTEM

ID #: 000241-00392 CHLORFENAPYR (AC 303630 2SC) TERMITICIDE-INSECTICI

AGRICULTURAL USE REQUIREMENTS:

DIRECTIONS FOR USE:

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, wear: coveralls over long-sleeved shirt and long pants, socks and chemical resistant footwear and waterproof gloves.

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if swallowed or absorbed through skin or inhaled. Avoid contact with eyes, skin or clothing. Avoid breathing spray mist. Wear long-sleeved shirt and long pants, socks and shoes and waterproof gloves.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or if available by administering syrup of ipecac. If person is unconscious, do not give anything by mouth and do not induce vomiting.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

NOTE TO PHYSICIAN:

Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician." The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

[Note: This product is in toxicity category IV in terms of eye and dermal irritation potential, and so does not require the proposed statement "causes moderate eye irritation" or a Statement of Practical Treatment addressing eye exposure. However, we have no objections to toxicity category III labeling for a product which is in toxicity category IV in terms of a potential exposure hazard.]

The following statement should appear (or be included) under the heading USER SAFETY RECOMMENDATIONS:

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

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

Product Manager: 03
MRID No.: 44763501

Reviewer: Byron T. Backus, Ph.D.
Study Date: October 26, 1998
Laboratory Study No.: 98-5353

Testing Facility: Huntingdon Life Sciences, East Millstone, NJ 08875-2360
Author: Hoffman, G.M.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: AC 303630 240 g/L SC Batch No. AC 11694-2F, containing 21.88% w/w AC 303630; a beige liquid.

Species: Rat, albino (outbred) VAF/Plus®: CD® (Sprague-Dawley derived) [Crl: CD®(SD)IGS BR]; and (for one male exposure group) CD® (Sprague-Dawley derived) [Crl: CD®(SD)BR]

Age: 8-11 weeks at exposure
Weight: Males: 246-440 g; Females: 207-259 g
Source: Charles River Laboratories, Kingston, NY 12484 and Portage, Michigan

Conclusion:

1. **LC_{50} (mg/L):**
   Males: =0.571 mg/L
   Females: >2.43 mg/L (1/5 died following exposure to this concentration)
   Combined: n/a
2. **The estimated LC_{50} is** 0.571 mg/L (95% C.L. of 0.365 to 0.891 mg/L)
3. **Tox. Category:** III

Classification: Acceptable

Procedure (including deviations from 870.1300): "The test substance was mixed with distilled water. For groups that were exposed to 1.17 mg/L or more: "Approximately 100-200...mL of AC 303630 240 g/L SC water mixture were placed into a 125-250 mL Erlenmeyer flask and connected to fluid metering pump with a 1/8" piston. The test substance was fed from the pump directly into the liquid inlet of an air atomizing nozzle."

For groups that were exposed to 0.838 mg/L or less: "Approximately 55...mL of AC 303630 240 g/L SC water mixture were placed into a plastic syringe and mounted on a syringe pump. The test substance was fed from the syringe directly into the liquid inlet of an air atomizing nozzle..."

Exposure was nose-only.

Results:

Exposure Concentration (Gravimetrically Determined) mg/L	Number of Deaths/Number Tested		
	Males	Females	Combined
0.618	3/10[a]	-	-
0.820	3/5[a,b]	-	-
0.838	4/5[a]	-	-
1.17	4/5[a]	-	-
1.95	5/5[a]	-	-
2.13	4/5[a]	-	-
2.43	4/5	1/5	5/10

[a]Only males were tested at these exposure concentrations
[b]Non-IGS male rats were used; the mortality from this exposure level was not used in the LC_{50} computations.

Clinical Observations: "Labored breathing, noted in all exposure groups, and decreased activity, noted in the 2.43 mg/L group, were the only signs of toxicity noted during the exposure periods. During the fourth hour of exposure, animals were found dead in Group I [2.43 mg/L] (1), Group II [1.95 mg/L] (1), Group III [1.17 mg/L] (4), Group IV [2.13 mg/L] (1), Group VI [0.820 mg/L] (1) and Group VII [0.618 mg/L] (2).. Beige material on the fur was also frequently noted as an artifact of the exposure regimen."

"Four animals per group were found dead upon removal from the chamber of during the 2-hour post-exposure observation period, following the Group II (1.95 mg/L gravimetric), Group III (1.17 mg/L gravimetric) and Group IV (2.13 mg/L gravimetric) exposures. Three males per group were found dead upon removal from the chamber of during the 2-hour post-exposure observation period, following the Group I (2.43 mg/L gravimetric), Group V (0.838 mg/L gravimetric), Group VI (0.820 mg/L gravimetric) and Group VII (0.618 mg/L gravimetric) exposures. One female in the 2.43 mg/L (gravimetric) group was found dead upon removal from the chamber. Among survivors, signs of toxicity included respiratory responses (labored breathing and moist rales) and secretory responses (lacrimation, clear or red nasal discharge, excessive salivation, chromodacryorrhea and dried red material facial area). Prostration and poor condition generally preceded death in animals that were found dead following the exposures. Wet fur and beige material on fur were also noted but were considered artifacts of the nose-only exposure regimen."

"One male per group from Group I (2.43 mg/L gravimetric), Group II (1.95 mg/L gravimetric) and Group V (0.838 mg/L gravimetric) was found dead during the first day following the exposure. Among surviving animals, observations similar to those noted immediately following the exposure were seen up to 3 days after the exposure. The majority of clinical signs was resolved by 4 days following exposure."

Gross Necropsy Findings: "Abnormalities of the lungs and trachea, including red foci and/or fluid accumulation, were noted at necropsy for animals that died during the study. No treatment-

related macroscopic abnormalities were noted at necropsy for animals surviving to termination."

Chamber Atmosphere			
Av. Grav. Conc. (mg/L)	Nominal Conc. (Mg/L)	MMAD (µm)	GSD
0.618	5.3	4.0 ± 0.34	1.8
0.820	6.7	4.2 ± 0.29	1.8
0.838	6.4	4.5 ± 0.1	1.8
1.17	10	4.6 ± 1.0	1.9
1.95	13	4.9 ± 0.42	2.0
2.13	20	4.9 ± 0.1	1.7
2.43	14	4.6 ± 0.42	2.2

Particle Size Distribution (Percent of Particles)			
Av. Grav. Conc. (mg/L)	≤ 1.0 µm	≤ 4.0 µm	≤ 10 µm
0.618	1.1	49	95
0.820	0.61	46	94
0.838	0.55	42	92
1.17	2.9	39	90
1.95	1.5	38	86
2.13	0.08	34	92
2.43	2.8	43	84

Other Information:

Chamber Environment	
Chamber Volume	40 L
Airflow	25 LPM
Temperature	20-25°C
Relative Humidity	38-72%

Special Comments: The inhalation LC_{50} value for males is reported as 0.571 mg/L, with 95% C.L. of 0.365 to 0.891 mg/L. However, as 3/10 males died at following exposure to the lowest concentration (0.618 mg/L), then (using this observation alone) the probability that the LC_{50} value is ≥ 0.618 mg/L is 0.828.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D255726
2. **PC CODE:** 129093 Chlorfenapyr (proposed common name)
3. **CURRENT DATE:** May 21, 1999
4. **TEST MATERIAL:** EPA File Symbol: 241-GOE; Chlorfenapyr 2SC Termiticide-Insecticide; AC 303630 240 g/L SC Batch No. AC 11694-2F, containing 21.88% w/w AC 303630; a beige liquid.

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/American Cyanamid Company/T-0588/JUN-09-1994 [See HED Document 011245]	43268204	Decreased activity, salivation, writhing and abnormal posture. In mortalities, grossly, dark and mottled liver, pronounced striations of abdominal wall, salivation, pale intestinal tracts,dark lungs and diarrhea were observed. LD_{50}(95%C.I.)=560 (410-890) mg/kg for males; =567 (281-988) mg/kg for females.	III[a]	A[a]
Acute dermal toxicity/rabbit/American Cyanamid Company//T-0592/JUN-09-1994 [See HED Document 011245]	43268205	LD_{50} > 2000 mg/kg (no mortalities among 5M, 5F rabbits), symptoms included nasal discharge and lacrimation.	III[a]	A[a]
Acute inhalation toxicity/rat/Huntingdon Life Sciences/98-5353/OCT-26-1998	44763501	LC_{50}(female) >2.43 mg/L (1/5 died); LC_{50}(male) = 0.571 mg/L (95% C.I. 0.365-0.891 mg/L), with 3/10 males dying at 0.618 mg/L.	III	A
Primary eye irritation/rabbit/American Cyanamid Company/T-0593/MAR-12-1994 [See HED Document 011245]	43268206	Slight-to-moderate conjunctival redness and slight ocular discharge present at 1 hour. All signs of irritation had resolved by 24 hours.	IV[a]	A[a]
Primary dermal irritation/rabbit/ American Cyanamid Company/T-0594/MAY-12-1994 [See HED Document 011245]	43268207	Slightly irritating to rabbit skin. At 48 hr, 1/6 exhibited slight erythema which was gone at 72 hrs.	IV[a]	A[a]

[a]The acute oral, acute dermal, primary eye irritation, and dermal irritation studies were conducted on AC 303,630 2SC Lot #AC 8053-139 with 21.24% active ingredient. These studies were previously reviewed by HED; the toxicity categories and study classifications are taken from the summaries in the HED One-Liners.

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self-Validated**