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

JAN 23 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

Subject: EPA ID#: 5G04523 - Alert®/AC 303,630 2SC Insecticide-Miticide: Application for Experimental Use Permit and a Temporary Tolerance for Use on Head Lettuce

P.C.#: 129093
Submission #: S487533
Project No. D215978

From: Guruva B. Reddy, D.V.M., Ph. D. 12/12/95
Section 4
Toxicology Branch I
Health Effects Division (7509C)

To: Dennis Edwards/Meredith Johnson
Project Manager 19
Registration Division (7505C)

Thru: Marion P. Copley, D.V.M., D.A.B.T. Marion Copley 1/19/96
Section Head
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Health Effects Division (7509C)

I. **CONCLUSIONS:**

The data base supports the requested EUP for use of Alert®/AC 303,630 2SC on head lettuce with a temporary tolerance.

Attachment I addresses the toxicity data base for this product and pesticide.

cc: RCAB (Madden), OREB (Dorsey)

I **ACTION REQUESTED:**

American Cyanamid Company, has submitted an application for an Experimental Use Permit for Alert™/AC 303,630 2SC Insecticide-Miticide on head lettuce. No new data were submitted with this application.

The experimental use program proposes to evaluate product efficacy against target pests on head lettuce. The petitioner is requesting an authorization for the use of 2,976 lbs of active ingredient on 4,990 acres in the states of Arizona, California, Colorado, Florida and Texas during the next two years. The rate of application is 0.06 - 0.18 lbs/acre and does not exceed 1.0 lbs. a.i. per crop.

The proposed residue tolerance for head lettuce 5 ppm.

III. **COMMENTS:**

1. The toxicity data base for Alert®/AC 303,630 2SC Insecticide-Miticide used to support this EUP program and temporary tolerance is described in Attachment I.

2. Under Section IV of the attachment, the 90-day rat subchronic and rat teratology studies were inadvertently omitted. The studies are acceptable and will be made part of the updated Toxicology Profile.

3. We are reevaluating the chromosomal aberration assay study in the light of additional information submitted by the registrant. The review findings will be conveyed under a separate memo.

IV. **DATA REQUIREMENTS:**

Technical: Data requirements have been satisfied (see HED Doc. 010651)

Formulation: Alert™ Insecticide-Miticide/AC 303,630 2SC Formulation

Data requirements on AC 303,630 2SC formulation have been satisfied (see HED Doc. 011245; Attachment I).

Attachment

ATTACHMENT I

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

SEP 27 1994 011915

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

Subject: AC 303,630 2SC Insecticide-Miticide: Application for Experimental Use Permit for Use on Greenhouse and Shadehouse Ornamentals

P.C.#: 129093
Submission #s: S468291
Project No. D204626
EPA ID#: 000241-EUP-REI

From: Guruva B. Reddy, D.V.M., Ph. D.
Section 4
Toxicology Branch I
Health Effects Division (7509C)

9/21/94

To: Dennis Edwards/Meredith Johnson
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Thru: Marion P. Copley, D.V.M., D.A.B.T.
Section Head
Section 4, Toxicology Branch I
Health Effects Division (7509C)

9/21/94

9/23/94

I. CONCLUSIONS:

The data base supports the requested EUP for use on greenhouse and shadehouse ornamentals. All reviewed studies are acceptable. The cross reference to inhalation toxicity (81-3, MRID 427702-15) and dermal sensitization study (81-6, MRID 427702-18) in support of AC 303,630 2SC Formulation is appropriate and acceptable, since the active and inactive ingredients were same, except for minor changes in the concentrations. However, it should be noted that HED files remain incomplete for the chromosomal aberration assay which was a NON-TEST.

A copy of the DERs are attached.

cc: CCB, OREB (Dorsey)

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There is no acute toxicity endpoint of concern based on current data. Based on the Toxicity Category of the technical the restricted entry interval (REI) of 12 hours is adequate.

II. ACTION REQUESTED:

American Cyanamid Company, has submitted an application for an Experimental Use Permit for AC 303,630 2SC Insecticide-Miticide. The studies included in this package are listed below and the * by the studies indicate that the DERs are attached.

Technical:

Data requirements on the Technical AC 303,630 have been satisfied (see HED Doc. 010651).

Formulation: AC 303,630 2SC Insecticide-Miticide

Guideline #	Study Type	MRID #
81-1*	Acute Oral Toxicity	432682-04
81-2*	Acute Dermal Toxicity	432682-05
81-3	Acute Inhalation Toxicity	Satisfied by study using 3SC Formulation - MRID 427702-15
81-4*	Primary Eye Irritation	432682-06
81-5*	Primary Dermal Irritation	432682-07
81-6	Dermal Sensitization	Satisfied by studies using Technical and 3SC Formulations (MRID #s 427702-12 and 427702-18, respectively)

The sponsor's preliminary data indicate that AC 303,630 2SC is effective when applied (0.02 to 0.32 lb ai/100 gallons) as foliar spray against a number of problem insects and mites on greenhouse and shadehouse ornamentals. The experimental use program proposes to evaluate product efficacy against target pests, when applied to larger plots, shadehouses and entire greenhouse buildings. The petitioner is requesting an authorization for the use of 300 lbs of active ingredient to treat a maximum of 150 acres (about 100 acres in greenhouses and 50 acres in shadehouses) during the next two years. The objective of this EUP is to fine tune the rates of AC 303,630 2SC against the target pests.

The proposed EUP is for nonfood use; no residue tolerance is required.

Registrant has requested use of 81-3 and 81-6 studies on 3SC Formulation to be used instead of studies on the 2SC Formulation. This appears reasonable because the active and inactive ingredients are same, except for minor changes in the

concentrations.

III. DATA REQUIREMENTS:

For nonfood EUP. Updated: 8/18/94

Technical: AC 303,630 (Pirate® Insecticide-Miticide, MP)
Use Pattern: Domestic outdoor and Indoor
Action Type: Experimental Use Permit

Guideline #	Study	Required	Satisfied
81-1	Acute Oral Toxicity	Yes	Yes
81-2	Acute Dermal Toxicity	Yes	Yes
81-3	Acute Inhalation Toxicity	Yes	Yes
81-4	Primary Eye Irritation	Yes	Yes
81-5	Primary Dermal Irritation	Yes	Yes
81-6	Dermal Sensitization	Yes	Yes
82-1(b)	Subchronic Oral (non-rodent)	Yes	Yes
83-3	Teratology (non-rodent)	Yes	Yes
84-2	Gene mutation (Ames)	Yes	Yes
84-2	Gene mutation (mammalian)	Yes	Yes
84-2	Structural chromosomal aberration	Yes	No

Formulation: AC 303,630 2SC Insecticide-Miticide

Guideline #	Study Type	Required	Satisfied
81-1	Acute Oral Toxicity	Yes	Yes
81-2	Acute Dermal Toxicity	Yes	Yes
81-3	Acute Inhalation Toxicity	Yes	Yes
81-4	Primary Eye Irritation	Yes	Yes
81-5	Primary Dermal Irritation	Yes	Yes
81-6	Primary Dermal Sensitization	Yes	Yes

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IV. TOXICOLOGY PROFILE Updated: 8/18/94

Guideline #	Study Identification and Classification	Results
Technical		
81-1	Acute Oral Toxicity in Rats MRID 427702-07/428842-01 Study #:T-0417 7/20/1992 Acceptable	LD_{50} (95% C.I.) = 441 (195 - 832) mg/kg, males LD_{50} (95% C.I.) = 1152 mg/kg, females LD_{50} (95% C.I.) = 626 (274 - 1085) mg/kg, combined TOXICITY CATEGORY: II, based on most sensitive sex
81-2	Acute Dermal Toxicity in Rabbits MRID 427702-08 Study #:T-0406 7/20/1992 Acceptable	LD_{50} > 2000 mg/kg (Limit Dose) TOXICITY CATEGORY: III
81-3	Acute Inhalation Toxicity in Rats MRID 427702-09 Study (american Cyanamid) #:91-8351 3/25/1993 Acceptable	Doses 0, 0.34, 0.71, 1.8 or 2.7 mg/l in SD rats. LC_{50} (95% C.I.) = 0.83 (0.48 - 1.4) mg/l, (males) LC_{50} (95% C.I.) = > 2.7 mg/l, females) LC_{50} (95% C.I.) = 1.9 (1.1 - 3.3) mg/l, combined TOXICITY CATEGORY: III, based on most sensitive sex
81-4	Primary Eye Irritation in Rabbits MRID 427702-10 Study #:T-0404 7/20/1992 Acceptable	Corneal opacity (4/6), iritis (2/6) and conjunctivitis (6/6) present at 48 hours. At 72 hours iritis was resolved. All rabbits were normal by Day-7. TOXICITY CATEGORY: III
81-5	Primary Dermal Irritation in Rabbits MRID 427702-11 Study #:T-0405 7/20/1992 Acceptable	Non-irritating. TOXICITY CATEGORY: IV
81-6	Dermal Sensitization in Guinea Pigs MRID 427702-12 Study #:T-0439 3/26/1993 Acceptable	Not a skin sensitizer (Closed-Patch Repeated Insult)

82-1(b)	Subchronic Feeding in Dogs (90-Day) MRID 427702-20 Study (American Cyanamid)#:971-92-118 4/8/1993 Minimum	Doses is beagles: 0, 60, 120 or 247 ppm (0, 2.16, 4.23 or 6.1 mg/kg/day) in feed. The 247 ppm was based on concentration of AC 303,630 in the diet of 300 ppm from Day 1 - 14, 240 ppm from Day 15 - 25 and 200 ppm from Day 25 - 93 (5.2, 5.9 and 7.2 mg/kg/day, respectively). NOEL = 120 ppm (4.23 mg/kg/day) LOEL = 247 ppm (6.1 mg/kg/day), based on reduced body weight gain and feed efficiency and emaciation.
83-3(b)	Teratology Study in Rabbits MRID 427702-22 Study (American Cyanamid)#:971-90-179 3/2/1993 Minimum	Doses of 0, 5, 15 or 30 mg/kg/day administered by gavage in 0.5% carboxymethylcellulose to pregnant New Zealand White rabbits from Days 7 to 19 of gestation, inclusive. Maternal NOEL: 5 mg/kg/day and LOEL: 15 mg/kg/day, based upon reduced body weight gain during treatment. Developmental NOEL: > 30 mg/kg/day.
84-2(a)	Gene Mutation-Ames MRID#: 427702-23 American Cyanamid # 91-02-001; 03/24/93 Acceptable	Negative for reverse mutation in S. typhimurium strains TA 98, TA 100, TA 1535, TA 1537, TA 1538 and E. coli strain WP2 uvrA- exposed up to cytotoxicity (50 µg/plate, +/- S9)
84-2(a)	Gene Mutation - in mammalian cells (CHO/HGPRT) MRID#: 427702-24 American Cyanamid # 91-05-001; 03/25/93 Not Acceptable	Repeatedly negative at doses up to 250 µg/ml +/- S9, which were not cytotoxic to Guideline levels.
84-2(b)	Structural chromosome aberration - in vivo mouse MRID # 427702-25 American Cyanamid #: 91-18-001; 03/17/93 Non test	Although reportedly negative for micronucleus induction in mice treated orally up to 20 or 30 mg/kg, the highest dose was lethal without causing cytotoxicity to target tissue.
84-4	Repair in vitro (UDS) MRID #: 427702-26 Microbiological#: T9775.380026 02/23/93 Acceptable	Negative for inducing unscheduled DNA synthesis in primary rat hepatocyte cultures exposed up to severely toxic concentrations (≥ 30 µg/ml).