MEMORANDUM:

Subject: EPA ID#: SG04523 - 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.
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.
Section Head
Section 4, Toxicology Branch I
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).
MEMORANDUM:

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

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

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

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

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 (81-5, MRID 427703-18) in support of AC 303,630 2SC Formulation is appropriate and acceptable, since the active and inactive ingredients were the 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)
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. 010551).

**Formulation: AC 303,630 2SC Insecticide-Miticide**

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

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

<table>
<thead>
<tr>
<th>Guideline #</th>
<th>Study</th>
<th>Required</th>
<th>Satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>81-1</td>
<td>Acute Oral Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-2</td>
<td>Acute Dermal Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-3</td>
<td>Acute Inhalation Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-4</td>
<td>Primary Eye Irritation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-5</td>
<td>Primary Dermal Irritation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-6</td>
<td>Dermal Sensitization</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>82-1(i)</td>
<td>Subchronic Oral (non-rodent)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>83-3</td>
<td>Teratology (non-rodent)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>84-2</td>
<td>Genetic mutation (Ames)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>84-2</td>
<td>Genetic mutation (mammalian)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Structural chromosomal aberration</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Formulation: AC 303,630 2SC Insecticide-Miticide

<table>
<thead>
<tr>
<th>Guideline #</th>
<th>Study Type</th>
<th>Required</th>
<th>Satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>81-1</td>
<td>Acute Oral Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-2</td>
<td>Acute Dermal Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-3</td>
<td>Acute Inhalation Toxicity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-4</td>
<td>Primary Eye Irritation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-5</td>
<td>Primary Dermal Irritation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>81-6</td>
<td>Primary Dermal Sensitization</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
### IV. TOXICOLOGY PROFILE Updated: 8/18/94

<table>
<thead>
<tr>
<th>Guideline #</th>
<th>Study Identification and Classification</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Technical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>81-1</td>
<td>Acute Oral Toxicity in Rats MRID 427702-07/428842-01 Study #:T-0417 7/20/1992</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = 441 (196 - 832) mg/kg, males&lt;br&gt;LD&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = 1152 mg/kg, females&lt;br&gt;LD&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = 628 (274 - 1085) mg/kg, combined&lt;br&gt;TOXICITY CATEGORY: II, based on most sensitive sex</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
<tr>
<td>81-2</td>
<td>Acute Dermal Toxicity in Rabbits MRID 427702-08 Study #:T-0409 7/20/1992</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt; &gt; 2000 mg/kg (Limit Dose)&lt;br&gt;TOXICITY CATEGORY: III</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
<tr>
<td>81-3</td>
<td>Acute Inhalation Toxicity in Rats MRID 427702-09 Study (american Cyanamid):#91-8361 3/25/1993</td>
<td>Dose: 0, 0.34, 0.71, 1.8 or 2.7 mg/l in SD rats.&lt;br&gt;LC&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = 0.83 (0.48 - 1.4) mg/l, (males)&lt;br&gt;LC&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = &gt; 2.7 mg/l, females&lt;br&gt;LC&lt;sub&gt;50&lt;/sub&gt; (95% C.I.) = 1.6 (1.1 - 3.3) mg/l, combined&lt;br&gt;TOXICITY CATEGORY: III, based on most sensitive sex</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
<tr>
<td>81-4</td>
<td>Primary Eye Irritation in Rabbits MRID 427702-10 Study #:T-0404 7/20/1992</td>
<td>Corneal opacity (4/6), iridts (2/6) and conjunctivitis (5/6) present at 48 hours. At 72 hours iridts was resolved. All rabbits were normal by Day 7.&lt;br&gt;TOXICITY CATEGORY: III</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
<tr>
<td>81-5</td>
<td>Primary Dermal Irritation in Rabbits MRID 427702-11 Study #:T-0406 7/20/1992</td>
<td>Non-irritating&lt;br&gt;TOXICITY CATEGORY: IV</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
<tr>
<td>81-6</td>
<td>Dermal Sensitization in Guinea Pigs MRID 427702-12 Study #:T-0439 3/28/1993</td>
<td>Not a skin sensitizer (Closed-Patch Repeated Insult)</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td></td>
</tr>
</tbody>
</table>
| 82-1(b) | Subchronic Feeding in Dogs (90-Day)  
MRID: 427702-20  
Study (American Cyanamid#971-92-118)  
4/8/1993  
Minimum | Doses is beesies: 0, 50, 120 or 247 ppm (0, 2.16, 4.23 or 8.1  
mg/kg/day) in feed. The 247 ppm was based on concentration of AC  
302 ppm in the diet of 300 ppm from Day 1 - 14, 240 ppm from Day 15  
- 25 and 200 ppm from Day 25 - 33 (5.2, 5.9 and 7.2 mg/kg/day,  
respectively).  
NOEL = 120 ppm (4.23 mg/kg/day)  
LOEL = 247 ppm (8.1 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  
Not 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#:  
T8777.380026  
02/22/83  
Acceptable | Negative for inducing unscheduled DNA synthesis in primary rat  
hepatocyte cultures exposed up to severely toxic concentrations (≥ 30  
μg/ml). |