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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 15, 1996

MEMORANDUM

SUBJECT: EFED's Chapters for the Registration of Chlorfenpyr (Pirate) (CASE 044966)

FROM: Karen Angulo
Science Analysis and Coordination Staff
Environmental Fate and Effects Division

THRU: Kathy Monk, Acting Chief
Science Integration Staff
Environmental Fate and Effects Division

TO: Meredith Johnson
Registration Division

Please find attached the EFED Branch Chapters for Pirate. The following provides an overview of our findings.

1. **Use Profile.** Chlorfenpyr is a new insecticide-miticide on cotton. Chlorfenpyr is the common name that is pending, and the trade names are PIRATE and ALERT. It can be applied by ground and air application. It is an emulsifiable concentrate that may be applied up to 1.05 lbs a.i. per acre per single cropping season.

2. **Environmental Fate Assessment.**

Chlorfenpyr is very persistent. Slow, long-term increase of structurally similar metabolites or degradates was observed (metabolites AC 312,094, AC 325,195, and others), which indicates that these compounds are also persistent. Mineralization is not appreciable.

Chlorfenpyr is not mobile in soil and does not leach, therefore, it is not likely to impact groundwater. However, its persistence, relatively high affinity for soil (but it is

not permanently bound), and ecotoxicity clearly indicate surface water and sediment concerns. Bioavailability in soil or sediment is an issue. As measures of potential bioavailability, parent and degradates are easily extractable in high yield from soil or sediment with simple organic solvents. Also, chlorfenpyr is dislodgeable from cotton foliage. A study on toxicity to organisms dwelling in sediments would provide critical insight on bioavailability.

Chlorfenpyr did not concentrate in bluegill sunfish. Instead, it was metabolized (AC 312,094). This metabolite concentrated up to 2300 times in whole fish, but was rapidly depurated.

Because of chlorfenpyr's very high ecotoxicity, currently reported analytical precision for water and plants is probably inadequate for the low concentrations that have caused ecological effects.

3. Ecological Effects Assessment.

a. Toxicology.

i. **Birds.** Chlorfenpyr is highly to very highly toxic on an oral and dietary acute basis to birds, and metabolites range from slightly to highly toxic (oral acute only). On chronic basis, chlorfenpyr affected critical reproductive endpoints, such as egg production and nestling survival (NOEL is 0.5).

ii. **Mammals.** Based on data available from HED, chlorfenpyr is slightly to highly toxic to mammals. Chronic concerns were identified at low concentrations.

iii. **Freshwater and Estuarine/Marine Fish and Invertebrates.** Chlorfenpyr is very highly toxic to freshwater and estuarine/marine fish and invertebrates on an acute basis (one freshwater fish species tested, Bluegill Sunfish, was highly toxic). Chronic effects to both estuarine/marine and freshwater fish and invertebrates, such as survival of young and decreased reproduction rate, were observed at very low concentrations.

iv. **Non-target Terrestrial Organisms.** Chlorfenpyr is highly toxic to honey bees on an acute contact basis.

b. **LOC Exceedances.**

i. **Birds.** All LOCs were exceeded for avian acute risk, and for avian chronic risk by as much 31-500 times.

ii. **Mammals.** In the majority of the mammal categories, LOCs were exceeded for both acute and chronic risk.

iii. **Freshwater and Estuarine/Marine Fish and Invertebrates.** All LOCs were exceeded for acute and chronic risk for freshwater and estuarine/marine fish and invertebrates (except the LOC for acute high risk for estuarine/marine fish was not exceeded).

c. **Risk Assessment.** The highly persistent nature of chlorfenpyr coupled with its very acute and chronic toxicity to almost all test species indicate significant environmental risks to aquatic and wildlife species. Many LOCs were exceeded at even the lowest recommended label rates. Application rates would have to be drastically lowered (approximately two orders of magnitude) in order to ensure protection of endangered species.

4. **Data gaps and Value of the Information.**

a. **Environmental Fate.** The environmental fate data requirements for chlorfenpyr on cotton are satisfied (even though field dissipation studies are not fully satisfactory), except for spray drift data and analytical methods validations.

Spray drift data [Droplet Size Spectrum (201-1) and Drift Field Evaluation (202-1)] data are requested for chlorfenpyr. The registrant is given the option to satisfy requirements in the near future through the Spray Drift Task Force according to PR Notice 90-3. Additionally, in the event of registration, the registrant should submit soil, plant, and water methods of analysis that are capable of detecting about one-tenth of the trace concentrations with observed ecological effects for EPA laboratory validation. Using this criterion, present procedures for water and plants may need to be improved by a factor of five or ten for sensitive species.

b. Ecological Effects.

i. **Terrestrial Field Study.** A Terrestrial Field Study (Guideline 71-5) is required. Several studies were submitted, but are not adequate to fulfill the requirement. While these studies did provide some information, chlorfenpyr is the first chemical in a new class of pesticides and the risks have not been sufficiently characterized. This study is needed to assess the potential ecological effects of chlorfenpyr under normal application.

ii. **Aquatic Studies.** The following studies are required:

- LC50 Rainbow Trout (72-1) on degradate.
- EC50 Oyster Shell Deposition Study (72-3).
- Sheepshead Minnow Early Life Stage (72-4).

Studies were submitted for these three guideline requirements, but they were found to be invalid. These studies need to be repeated in order to confirm our understanding of the aquatic toxicity of chlorfenpyr and its degradates, and complete the required data set.

- Sheepshead Minnow Life Cycle (72-5). This chronic study is triggered by the results of the Fish Early Life and Invertebrate Life Cycle studies. Chlorfenpyr is very highly acutely toxic to this species, and chronic effects are anticipated. This study would confirm our understanding of the chronic effects of chlorfenpyr, as shown in estuarine invertebrates.

- Sediment Toxicity Test. The registrant has agreed to conduct this study. This information will be useful in determining the toxicity of sediment-bound chlorfenpyr to benthic organisms. The guidelines for this study are being discussed between EFED and the registrant. Based on the sediment toxicity study, a mesocosm or other higher tiered tests may be required.

If you have questions, please call me at 305-5011.

cc: Denise Keehner, Kathy Monk, Hank Jacoby, Alex Clem, Akiva Abramovitch, Norm Cooke, Doug Urban, Ann Stavola, John Eisemann, Sharlene Matten

DP BARCODE: D211863

CASE: 044966 DATA PACKAGE RECORD DATE: 10/30/96
SUBMISSION: S481367 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REGISTRATION ACTION: 100 NC-FOOD/FEED USE
RANKING : 2 POINTS ()
CHEMICALS: 129093 Chlorfenapyr (proposed common name) 93.0000%

ID#: 000241-GAA AC 303,630 INSECTICIDE-MITICIDE TECHNICAL
COMPANY: 000241 AMERICAN CYANAMID COMPANY
PRODUCT MANAGER: 19 DENNIS EDWARDS, JR. 703-305-6386 ROOM: CM2 207
PM TEAM REVIEWER: MEREDITH JOHNSON 703-305-7080 ROOM: CM2 209
RECEIVED DATE: 02/08/95 DUE OUT DATE: 08/17/95

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 211863 EXPEDITE: N DATE SENT: 02/08/95 DATE RET.: 11/27/95
CHEMICAL: 129093 Chlorfenapyr (proposed common name)
DP TYPE: 001 Submission Related Data Package
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : EFED	02/13/95	11/27/95
BRAN: EEB	02/13/95	11/27/95
SECT: RS5	02/13/95	11/27/95
REVR : JEISEMAN	02/13/95	11/27/95
CONTR:	/ /	/ /

ADMIN DUE DATE: 06/08/95
NEGOT DATE: / /
PROJ DATE: 12/30/95

* * * DATA REVIEW INSTRUCTIONS * * *

This bean sheet serves to initiate the FULL REVIEW of all the data forwarded to you in support of the registration of the new chemical AC 303,630 = "Pirate." Note that there will be three products pending, a technical and two end-use products. Labels for these were included with the package sent for the screen. Please let me know if you need anything else. **A safer chemical expedite classification is pending. Thank you, Meredith

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
211860	EFGB/CRS3	02/08/95	06/08/95	Y	N	N
212117	OREB/RS-2	02/14/95	06/14/95	Y	N	Y
222690	EEB/RS5	02/06/96	06/05/96	Y	N	N
222694	EFGB/CRS3	02/06/96	06/05/96	Y	N	N

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NOV 15 1996

OFFICE OF
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TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Section 3 Ecological Risk Characterization of Chlorfenpyr (Pirate® AC 303,630 3SC) for Use on Cotton

FROM: John Eisemann and William Evans, Biologist
Ecological Effects Branch
Environmental Fate and Effects Division

THRU: Ann Stavola, Supervisory Biologist
Ecological Effects Branch
Environmental Fate and Effects Division (7507C)

THRU: Norman Cook, Acting Branch Chief
Ecological Effects Branch
Environmental Fate and Effects Division (7507C)

TO: Dennis Edwards, Branch Chief
Insecticide/Miticide Branch
Registration Division (7505C)

Attached please find the completed the Chlorfenpyr (Pirate® AC 303,630 3SC) Section 3 Ecological Risk Characterization in accordance with FIFRA 158 CFR for use on cotton. This action was transmitted to EEB under DP Barcode #:D211863.

If there are any questions concerning this review please contact John Eisemann on 305-6783 or Bill Evans on 305-6754.

A. **USE PROFILE - AC 303,630 Technical**
(4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile)

1. **Type of Use:** Insecticide-Miticide

2. **Use Site:** Cotton

3. **Target Pests:** Thrips spp, Tobacco Thrips, Soybeans Thrips, Onion Thrips, Western Flower Thrips, Two-spotted spider mite, Carmine spider mite, Pacific spider mite, Strawberry spider mite, Beet armyworm, Cabbage looper, Soybean looper, Fall armyworm, Yellowstriped armyworm, Cotton Leafperforator, Saltmarsh caterpillar, Cotton leafworm, Boll weevil, Silver whitefly, Tobacco budworm, and Cotton bollworm.

4. **Formulation Type:**

PIRATE™
One gallon contains 3.0 lbs of
Active ingredient = 3

FINAL !

ALERT™
One gallon contains 2
Active ingredient = 21

12/20/96

5. **Method and Rate of**

The recommended applic d aerial spray. The maximum applicat for a single cropping season is 1. the proposed label and outlines application timing and range of application rates.

Table 1. Recommended application rates and application periods of AC 303,630 formulations to control selected cotton pests. PIRATE™ 303,630 is for use in states east of the Rocky Mountains, ALERT™ is for use west of the Rocky Mountains.

Pest	PIRATE (lbs ai/acre)	ALERT (lbs ai/acre)	Remarks
Thrips spp. Tobacco Thrips Soybean Thrips Onion Thrips Western Flower Thrips (Pre-bloom)	0.09 - 0.16	0.09 - 0.16	Apply as required based on scouting.
Western Flower Thrips (Pre-bloom)	0.09 - 0.16	0.09 - 0.16	Aids in suppression.
Two-spotted spider mite Carmine spider mite Pacific spider mite Strawberry spider mite	0.12-0.19	Early cotton <12" 0.06 - 0.11 Late cotton >12" 0.12 - 0.20	Use adequate spray volume to insure thorough coverage. Treat when pest populations are in early stages of development. Repeat when necessary to maintain control.

Table 1. Recommended application rates and application periods of AC 303,630 formulations to control selected cotton pests. PIRATE™ 303,630 is for use in states east of the Rocky Mountains, ALERT™ is for use west of the Rocky Mountains.

Pest	PIRATE (lbs ai/acre)	ALERT (lbs ai/acre)	Remarks
Beet Armyworm Cabbage looper Soybean looper	0.12 - 0.21	0.11 - 0.20	Apply as required based on scouting
Fall armyworm Yellowstriped armyworm Cotton leafperforator Saltmarsh caterpillar Cotton leafworm	0.21 - 0.28	0.20 - 0.28	Apply as required based on scouting.
Boll weevil (Suppression)	0.21 - 0.35	0.20 - 0.34	Aids in suppression of light to moderate populations when applied on a 5-7 day interval.
Silver whitefly (Suppression)	0.2 - 0.25	0.20 -0.25	Aids in control when applied in combination with pyrethyroids.
Tobacco budworm Cotton bollworm	0.21 - 0.35	0.22 - 0.34	Rates of 0.22 - 0.25 lbs ai/acre (ALERT), 0.21 - 0.25 lbs ai/acre (PIRATE) should be used only in tank mixture combinations with pyrethyroids, carbamates, or organophosphates registered for use on cotton at their label recommended ovicide or lower larvicide rates. Rates of 0.27 - 0.35 lbs ai/acre (ALERT), 0.3 - 0.35 lbs ai/acre (PIRATE) have been shown to be effective when used alone. For best results, time applications to control small larvae. Apply on a 5-7 day schedule or as needed as determined by scouting. Use higher rate when pest pressure is heavy or large larvae (>1/4 inch) predominate. As pest pressure increases, it may be necessary to shorten spray interval. Use adequate spray volume to insure thorough coverage.

B. ENVIRONMENTAL ASSESSMENT

1. Ecological Toxicity Data

a. Toxicity to Terrestrial Animals

(1) Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient is required to establish the toxicity of a pesticide to birds. The preferred test species is either Mallard (a waterfowl species) or Northern Bobwhite (an upland gamebird). Results of these tests are listed in table 2.

Table 2. Acute oral toxicity of AC 303,630 Technical to avian species.

Species	% A.I.	End Point (mg ai/kg)	Toxicity Category	MRID No. Author/Year	Study Classification
Northern Bobwhite *(Colinus virginianus)*	94.5	LD_{50}= 34 NOEL (Wt., Feed) = 2	Highly Toxic	427702-28 Helsten, 1993	Core
Mallard *(Anas platyrhynchus)*	94.5	LD_{50} = 8.3 NOEL (Wt., Feed) = 1	Very Highly Toxic	427702-27 Helsten, 1993	Core
Red-winged Blackbird *(Agelaius phoeniceus)*	94.5	LD_{50} = 2.21 NOEL (Wt.)= 0.63	Very Highly Toxic	438870-04 Brewer, 1995	Supplemental[1]

[1] Not a required study.

All deaths reported for the Mallard and Northern Bobwhite occurred within the first 3 and 7 days, respectively. All Red-winged blackbird mortality occurred within the first two days following treatment.

Clinical signs of intoxication common to all three species included whole body and wing beat convulsions, lethargy and loose green or chalky excreta. In addition, dyspnea (labored breathing) and opisthotonos (head stretched over back) were reported for the Mallard. Lethargy was reported in the highest Red-winged blackbird dose group. Post-mortem exam showed no treatment related abnormalities other than firm pectoral muscles.

A significant reduction in body weight, as compared to the control animals, occurred in the Northern bobwhite at dose levels above 32 mg ai/kg during the first 3 days of the study. No body weight reduction was noted in the Mallards or Red-winged blackbirds.

A significant reduction in food consumption, as compared to the control animals, occurred in the Northern bobwhite at dose levels above 16 mg ai/kg during the first 3 days of the study. A similar response was observed in the Mallard at treatments higher than 4 mg ai/kg.

These results indicate that AC 303,630 is very highly toxic to waterfowl and passerine species and highly toxic to upland gamebirds on an acute oral basis. The guideline requirement (71-1) is fulfilled (MRID #427702-27 and 427702-28).

In addition to acute toxicity testing performed with the technical grade of the parent compound, acute testing was conducted with two metabolites which are produced under normal environmental conditions. Table 3 lists the results of those tests.

Table 3. Acute oral toxicity of two environmental metabolites of AC 303,630 Technical, AC 312,094 and AC 303,268.

Metabolite	Species	% A.I.	LD_{50} (mg ai/kg)	Toxicity Category	MRID No. Author/Year	Study Classification
AC 303,268	Northern Bobwhite (*Colinus virginianus*)	100.3	LD_{50} = 25 NOEL (wt.) = 3	Highly Toxic	434928-09 Campbell, 1993	Supplemental
	Mallard (*Anas plathryhnchus*)	100.3	LD_{50} = 77 NOEL (wt.) = 20	Moderately Toxic	434928-08 Campbell, 1993	Supplemental
AC 312,094	Northern Bobwhite (*Colinus virginianus*)	96.3	LD_{50} = 1685 NOEL (wt.) = 160	Slightly Toxic	438870-06 Brewer, 1995	Supplemental
	Mallard (*Anas platyrhynchus*)	96.3	LD_{50} = >2400 NOEL = >2400	Practically non-toxic	438870-05 Brewer, 1995	Supplemental

AC 312,094 was shown to kill slower than the parent compound and exhibit fewer negative impacts on the survivors. It is practically non-toxic to the Mallard. No Mallards died from the treatment nor were changes in behavior, weight or food consumption reported. However, it is considered slightly toxic to Northern Bobwhite. It killed Northern bobwhite slower than the parent (33% of total mortality occurred by day 6). Significant weight loss and decreased food consumption occurred in the highest treatment group (1200 mg ai/kg) on days 3 and 7. After 7 days the food consumption in the high treatment group increased to quantities higher than the controls, but weight remained significantly lower until the end of the study. Immediate symptoms of intoxication included rapid ventilation, esophageal fibrillation and ataxia. Longer lasting effects included unsteadiness, piloerection, inactivity and yellow-green feces.

AC 303,268, a soil photolytic degradate, was shown to kill nearly as quickly as the parent compound and was more toxic to Northern bobwhite. Deaths prior to day 4 accounted for 88% of the total mortality observed in Mallards and Northern Bobwhite. Weight loss coincided with decreased food consumption and was significant at day 3 at treatment groups 40 mg ai/kg and higher in the Mallard and at 25 mg ai/kg and higher in the Northern Bobwhite. Signs of intoxication common to both species included shallow rapid breathing, reduced reaction time, and loss of coordination. Necropsy showed small pale yellow spleens and stained vents.

These results indicate the metabolite AC 312,094 is practically non-toxic to waterfowl and slightly toxic to upland gamebirds. The metabolite AC 303,268 is moderately toxic to waterfowl and highly toxic to upland gamebirds

Two subacute dietary studies using the technical grade of the active ingredient are required to establish the toxicity of a pesticide to birds. The preferred test species are Mallard (a waterfowl species) and Northern Bobwhite (an upland gamebird). Results of these tests are listed in Table 4.

Table 4. Avian Subacute Dietary Toxicity Studies with AC 303,630 Technical.

Species	% A.I.	End Point (ppm)	Toxicity Category	MRID No. Author/Year	Study Classification
Northern Bobwhite *(Colinus virginianus)*	94.5	LC_{50} = 132 NOEL = 10 (clinical signs)	Highly Toxic	427702-30 Gange, 1993	Core
Mallard *(Anas platyrhynchus)*	94.5	LC_{50} = 8.6 NOEL (wt.) = <4	Very Highly Toxic	427702-29 Gange, 1993	Core

All deaths reported for the Northern Bobwhite and Mallard occurred within the first 4 and 5 days, respectively.

Clinical signs of intoxication observed in the Mallard included lethargy, dyspnea, loss of coordination, loss of righting reflex, circling backwards and unusual head posture. Northern Bobwhites exhibited no symptoms other than irregular excreta. Complete remission of all symptoms was achieved in survivors of both species by the beginning of the third day. Post-mortem exam showed no treatment related abnormalities in either species, other than green gizzards and enlarged gallbladders in Mallards.

Significant body weight reduction, as compared to the control animals, was noted throughout the entire study in Mallard at dose levels above 4 mg ai/kg and Northern Bobwhite at dose levels above 80 mg ai/kg.

Food consumption measurements showed only slight decreases at the two highest dose levels, as compared to the controls, for both species. Measurements taken after day 2 showed no significant difference.

These results indicate that AC 303,630 Technical is very highly toxic to waterfowl species and highly toxic to upland gamebirds on an acute dietary basis. The guideline requirement (71-2) is fulfilled (MRID # 427702-29 and 427702-30).

(2) Birds, Chronic

Avian reproduction studies using the technical grade of the active ingredient are required when any **one** of the following

conditions are met: (1) birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the breeding season; (2) the pesticide is stable in the environment to the extent that potentially toxic amounts may persist in animal feed; (3) the pesticide is stored or accumulated in plant or animal tissues; and/or (4) information derived from mammalian reproduction studies indicates reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the product. The preferred test species are Mallard and Northern Bobwhite. Avian reproduction studies were required for AC 303,630 Technical for the following reasons. Results of avian chronic tests are listed in table 5.

1) The proposed labeling and usage of both PIRATE™ and ALERT™ allow multiple applications during a growing season, totaling no more than 1 pound active ingredient per acre per year. Both products can be applied to control early season pests, such as Thrips, which coincide with breeding season.

2) AC 303,630 is slowly degraded under both aerobic and anaerobic laboratory conditions with a first-order half-life of approximately 4 to 2 years, respectively. First-order photolytic half-life on soil is approximately 5 months.

3) As stated in the American Cyanamid, Inc. publication "Summary of Data Submitted in Support of the Registration Application for AC 303,630, Insecticide-Miticide Technical" (Submission Date 12/1/94, Vol 11, Exhibit 8, p3), 'The AC 303,630 which settles onto the cotton plants is rapidly absorbed into the waxy cuticle and remains there because AC 303,630 is highly lipophilic and has no systemic activity. Most of the compound will remain bound to the leaf...'. However, a registrant's letter (dated 8 July 1996, no MRID assigned) correcting the study which examined foliar leaf wash (MRID #434928-14), contradicts this statement.

Table 5. Chronic Avian Toxicity Studies (Reproduction) with AC 303,630 Technical.

Species	% A.I.	NOEC/LOEC (ppm)	Endpoints Affected	MRID No. Author/Year	Study Classification
Northern Bobwhite *(Colinus virginianus)*	94.5	NOEL = 0.5 ppm LOEL = 1.5 ppm	14 day survivors at 4.5 ppm hatchling weight at 1.5 ppm	434928-11 Bryan/1994	Supplemental
Mallard *(Anas platyrhynchus)*	94.5	NOEL = 0.5 ppm LOEL = 1.5 ppm	adult female body weight at 1.5 ppm food consumption at 1.5 ppm reproductive parameters at 2.5 ppm	434928-13 Helsten/1994	Supplemental

Significant differences were observed during the Mallard experiment between the controls and treatment groups. Significant differences found in the 2.5 ppm treatment group include the total

number of eggs laid, the number of viable embryos (immediately after laying), the number of viable embryos at 21 days of age (just prior to hatch), the number of normal hatchlings, the number hatchlings surviving 14 days, and a decrease in body weight of adult males. At a treatment level of 1.5 ppm a significant decline was noted in the body weight of the adult females. Food consumption declined with increasing active ingredient concentrations and was found significant in the 2.5 ppm treatment group.

Significant differences were noted in the number of Northern Bobwhite hatchlings surviving 14 days at a treatment level of 4.5 ppm. Additionally, hatchling weight was significantly lower at the 1.5 ppm treatment level.

The two avian reproduction studies are supplemental. The Mallard study can be upgraded to core if the raw data for the environmental conditions are submitted. The quail study cannot be upgraded. However, the need for the new study is waived as the reported study has a very low NOEC, and a new study would not likely provide significantly different results. Therefore guideline requirement (71-4) is fulfilled for the Northern Bobwhite (MRID #434928-11) but not the Mallard (MRID #434928-13).

(3) Mammals, Acute and Chronic

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use pattern and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) substitute for wild mammal testing. These toxicity values are reported in the table 6.

Table 6. Mammalian Toxicity Tests conducted with AC 303,630 Technical and formulations 2SC (ALERT) and 3SC (PIRATE) and select metabolites.

Species	% A.I.	Test Type	Endpoint	Toxicity Category	MRID No.
AC 303,630 Technical					
laboratory rat	94.5	Acute Oral Toxicity (Technical)	LD_{50} (males) = 441 mg/kg LD_{50} (females) = 1152 mg/kg LD_{50} (both) = 626 mg/kg	Moderately to Slightly Toxic	427702-07 427702-01
laboratory mouse	94.5	Acute Oral Toxicity (Technical)	LD_{50} (males) = 45 mg/kg LD_{50} (females) = 78 mg/kg LD_{50} (both) = 55 mg/kg	Highly to Moderately Toxic	434928-28
laboratory mouse	94.5	Sub-chronic Feeding - 3 month	NOEL = 40 ppm (7.1 mg/kg/day) LOEL = 80 ppm (14.8 mg/kg/day)	n/a	434928-30

Table 6. Mammalian Toxicity Tests conducted with AC 303,630 Technical and formulations 2SC (ALERT) and 3SC (PIRATE) and select metabolites.

Species	% A.I.	Test Type	Endpoint	Toxicity Category	MRID No.
laboratory rat	94.5	Sub-chronic Feeding - 3 month	NOEL = 300 ppm (21 mg/kg/day) LOEL = 600 ppm (48.4 mg/kg/day)	n/a	427702-19
laboratory rat	94.5	2 Generation Reproduction	Systemic Toxicity NOEL = 60 ppm (5 mg ai/kg/day) LOEL = 300 ppm (22 mg ai/kg/day) Reproductive Toxicity NOEL = 60 ppm (5 mg ai/kg/day) LOEL = 300 ppm (22 mg ai/kg/day)	n/a	434928-36
AC 303,630 Formulations 2SC (ALERT) and 3SC (PIRATE)					
laboratory rat	21.44	Acute Oral Toxicity (AC 303,630 2SC)	LD_{50} (males) = 560 mg/kg LD_{50} (females) = 567 mg/kg	Slightly Toxic	432682-04
laboratory rat	33.3	Acute Oral Toxicity (AC 303,630 3SC)	LD_{50} (males) = 283 mg/kg LD_{50} (females) = 999 mg/kg LD_{50} (both) = 626 mg/kg	Moderately to Slightly Toxic	427702-14
Metabolites					
laboratory rat	100.3	Acute Oral Toxicity (AC 303,268)	LD_{50} (males) = 27.0 mg/kg LD_{50} (females) = 29.4 mg/kg LD_{50} (both) = 28.7 mg/kg	Highly Toxic	434928-24
laboratory rat	96.3	Acute Oral Toxicity (AC 303,094)	LD_{50} (males) = >5000 mg/kg LD_{50} (females) = >5000 mg/kg LD_{50} (both) = >5000 mg/kg	Practically Non-toxic	434928-25
laboratory rat	89.0	Acute Oral Toxicity (AC 312,250)	LD_{50} (males) = >5000 mg/kg LD_{50} (females) = 2500 mg/kg	Practically Non-toxic	434928-26
laboratory rat	89.0	Acute Oral Toxicity (AC 325,195)	LD_{50} (males) = 776 mg/kg LD_{50} (females) = 1367 mg/kg	Slightly Toxic	434928-27

Acute exposure to AC 303,630 Technical in mice resulted in 95% of the deaths occurring within 24 hours at a dose level of 140 mg/kg. No significant clinical or gross necropsy observations were reported.

Acute toxicity testing of formulated products is conducted with no correction for percent active ingredient. Consequently, a rat LD_{50} of approximately 565 mg/kg for the 2SC formulation (MRID #432682-04) contains only 121 mg active ingredient. On a unit of active ingredient basis, AC 303,630 is more toxic as a formulated product. It is unknown if the increased toxicity is due to a additional substance in the formulation or if there is a synergistic effect between the active ingredient and formulation ingredients. Ultimately, the quantity of either formulation or the active ingredient to result in mortality is approximately the same.

Symptoms of exposure to AC 303,630 2SC include decreased activity, salivation, writhing and abnormal posture. Necropsy was unremarkable in surviving animals, In dead animals, grossly dark and mottled livers, pronounced striations of abdominal wall, tetany, salivation, pale intestinal tracts, dark lungs and diarrhea were observed.

Symptoms of exposure to AC 303,630 3SC in rats include decreased activity, salivation, ataxia, hyperthermia, protruding testes, prostration and death. Grossly congested and mottled livers and pronounced striations of abdominal muscles were observed at necropsy. Weight gains of the survivors were not affected.

The acute toxicity of four metabolites to rats was determined. Of those tested only AC 303,268 resulted in higher toxicity than the parent compound. Of the 40 rats exposed to AC 303,268 at concentrations higher than 31.25 mg/kg, 39 died within 8 hours of dosing. Mortality occurred at a slower rate in tests with the other 3 metabolites but still most was observed within 3 days. Survivors of exposure to the metabolites exhibited no lasting clinical effects or notable findings during gross necropsy. No significant weight changes were reported for survivors. Clinical signs reported for exposure to the metabolites included decreased activity, prostration, ptosis, increased salivation and diuresis. Abnormalities found at necropsy included discolored livers and spleens, discolored and distended stomachs, and gas filled GI tracts. Striated muscle tissue was reported in animals killed by AC 303,268.

The sub-chronic LOEL (600 ppm) observed in rats (MRID No. 427702-19)is based on reduced body weight gain and increased relative liver weights in males, decreased percent hemoglobin and increased absolute/relative liver weights in females.

The sub-chronic LOEL (80 ppm for males and 160 for females) observed in mice (MRID # 434928-30) is based on hepatic cell hypertrophy in $\leq$20% of test animal.

In a two generation reproduction study with rats (MRID #434928-36) the LOEL for systemic toxicity was 300 ppm (22 mg ai/kg/day) and based on pre-mating effects on parental weight gain. The LOEL for reproductive toxicity was 300 ppm (22 mg ai/kg/day) and based upon decreased lactational weight gains. No effects were seen in reproductive performance at any dose (up to 600 ppm, 44 mg ai/kg/day).

The results indicate that based on the most sensitive species, AC 303,630 Technical is highly toxic to small mammals, AC 303,630 3SC is moderately toxic and AC 303,630 2SC is slightly toxic to small mammals on an acute oral basis. Male rats are 2.6X and 3.5X more sensitive than females when exposed to AC 303,630 Technical

3SC is moderately toxic and AC 303,630 2SC is slightly toxic to small mammals on an acute oral basis. Male rats are 2.6X and 3.5X more sensitive than females when exposed to AC 303,630 Technical and AC 303,630 3SC, respectively. When exposed to AC 303,630 2SC and the metabolites AC 303,268 and AC 312,094, no differences were noted between sexes. Male mice are 1.7X more sensitive than females when exposed to AC 303,630 Technical. Males were roughly 2X more sensitive to the metabolite AC 325,195 than females, while the reverse was seen with AC 312,250.

(4) Insects and Soil Organisms

A honey bee acute contact study using the technical grade of the active ingredient is required if the proposed use will result in honey bee exposure. A honey bee acute contact study is required for AC 303,630 Technical because multiple applications will be made throughout the growing season, including the period of flowering. Results of these tests are listed in table 7.

Table 7. Nontarget insect acute contact toxicity of AC 303,630 Technical and AC 303,630 3SC (PIRATE™).

Species	% A.I.	End Point	Toxicity Category	MRID No. Author/Year	Study Classification
Acute Contact Toxicity Honey Bee *(Apis mellifera)*	94.5	LD_{50} = 0.12 *ug*/bee	Highly Toxic	427702-33 Kirkland/1994	Core
Acute Foliar Toxicity Honey Bee *(Apis mellifera)*	33.3	No significant mortality at 0.34 and 0.43 lbs ai/acre	n/a	434928-45	Core

The results indicate that AC 303,630 Technical is highly toxic to bees on an acute contact basis. However, no mortality occurred after the formulation is allowed to dry on vegetation, at application rates up to 0.43 lbs ai/acre. The guideline requirements (141-1) are fulfilled (MRID # 427702-33 and 434928-45).

Two studies were submitted evaluating the toxicity of AC 303,630 Technical and AC 303,630 3SC on the earthworm *Eisenia fetida*. The results of these studies are listed in table 8.

Table 8. Nontarget Soil Organism Toxicity of AC 303,630 Technical and AC 303,630 3SC (PIRATE™).

Species	Product % A.I.	End Point	MRID No. Author/Year	Study Classification
Acute Toxicity Earthworm *(Eisenia fetida)*	Technical 94.5 %	LC_{50} = ≤22 ppm NOEL (wt) = 8.4 ppm	427702-33 England/1994	Supplemental[1]
Sublethal Toxicity Earthworm *(Eisenia fetida)*	AC 303,630 3SC 30.3 %	No adult mortality, adult body weight or reproductive effects at 0.26 and 1.3 lbs ai/acre.	438870-10 Canez/1995	Supplemental[1]

[1] Not required studies.

Earthworms in all treatment groups, including the control, lost weight in the acute toxicity study. Mortality was observed at treatment levels ≥17 mg/kg soil. The 14-day LC_{50} for survival was 22 mg ai/kg soil. The NOEC for both survival and weight was 8.4 mg ai/kg soil. No effect was observed on earthworm burrowing ability. Residue analysis was not conducted on earthworm tissue. A reference toxicant, 2-chloroacetamide, was used to validate the test methods. However, only 5% mortality was observed in the reference group instead of the expected 50%. The results of the reference treatment test indicate the experiment did not function properly and indicate that the actual toxicity of AC 303,630 is higher than predicted.

No mortality was reported in the adults from sublethal exposure to PIRATE 3SC at application rates up to 1.34 lbs ai/acre. Additionally, no significant differences were observed in either adult weight or the number of juveniles present at the end of the test. The positive control, Benomyl produced the expected results.

(5) Terrestrial Field Testing

A terrestrial field test using the active ingredient AC 303,630 was requested by EEB on November 4, 1994, because the active ingredient is in a new class of pesticides (pyrroles) and has an entirely new mode of action (uncouples oxidative phosphorylation in the mitochondria). The field study request specifically stated methods in the Guidance Document for Conducting Terrestrial Field Studies (1988)[1], and recommendations of the Avian Effects Dialogue Group[2] be used in designing the field test.

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[1] Fite, E.C., L.W. Turner, N.J. Cook, and C.Stunkard. 1988. Guidance document for conducting terrestrial field studies. USEPA. EPA 540/09-88-109.

[2] Avian Effects Dialogue Group. 1989. Pesticides and Birds: Improving impact assessment. The Conservation Foundation.

The registrant has submitted the following four studies towards fulfilling this requirement (Table 9): a simulated field (pen) test and a dermal toxicity test with the Northern Bobwhite; an avian census of southern cotton fields and a field dissipation study of a single dose (0.2 lbs ai/acre) on cotton. In addition, the registrant has submitted two proposed study protocols. One protocol outlined methods to be used in an avian census study and another protocol detailed methods to be used in a habitat utilization study of Red-winged blackbirds. Much of the information gained from the studies mentioned above can be used in this risk assessment. However, portions of some studies were rejected by EEB scientists due to unacceptable methods. None of the submitted studies meet the requirement of a field study.

Table 9. Nontarget Soil Organism Toxicity of AC 303,630 Technical.

Species	Formulation	End Point	MRID No. Author/Year	Study Classification
Food Choice Study Northern Bobwhite *(Colinus virginianus)*	Technical (94.5% ai)	NOEL - Adult Testing Survival = 250 ppm Weight = 250 ppm Food Consumption = 250 ppm NOEL - Juvenile Testing Survival = 140 ppm Weight = 140 ppm Food Consumption = 70 ppm	438870-07 Fairbrother 1995	Supplemental
Simulated Field(pen) Study Northern Bobwhite *(Colinus virginianus)*	AC 303,630 3SC (33.3% ai)	No mortality or morbidity at an application rate of 0.35 lb ai/acre. However, flawed study design limits usefulness of the data.	438870-07 434928-14 Ahmed/1995	Supplemental
Dermal Toxicity Northern Bobwhite *(Colinus virginianus)*	AC 303,630 3SC (33.3% ai)	No mortality or morbidity at an 1.4 lbs ai/acre. Study design limits interpretation to contact exposure to chemical after drying.	438870-07 434928-14 Driver/1995	Supplemental
Single application foliar residue and ecotoxicological study	AC 303,630 3SC (33.3% ai)	At 0.2 and 0.4 lbs ai/acre residues on cotton leaf 127% and 183% of Fletcher value. By day 28 residues on cotton leaf about 3 ppm. Residues in seeds collected from weeds in adjacent field border were below the method detection limit. Residues in live insects collected in the cotton field and in adjacent habitat had mean residue concentrations of 5.7 ppm through day 2 and below MDL, respecitvely.	434928-14 Sullivan/1994	Supplemental
Avian Census of Cottonfield Habitat	No active ingredient	Good preliminary census in preparation for a full-blown field study.	434928-14 Gagne/1995	Supplemental
Avian Census of Cottonfield Habitat (Proposed study protocol)	No active ingredient	Protocol would essentially repeat the above mentioned study.	N/A Sullivan 1995	N/A

Table 9. Nontarget Soil Organism Toxicity of AC 303,630 Technical.

Species	Formulation	End Point	MRID No. Author/Year	Study Classification
Monitoring technique of cotton field use by birds (Proposed study protocol)	No active ingredient	Design to document avian use of cotton by utilizing radio tagged Red-winged blackbirds and fixed-circular plot census methods.	N/A Gagne 1995	N/A

Simulated Field Pen Study. Results from the simulated field (pen) study (MRID #438870-07 and 434928-14) indicate the active ingredient was not available to Northern Bobwhite. However, most of this study was invalid. One application was made to a cotton field at 0.35 lbs ai/acre. The high dose pen contained half treated cotton and half untreated field edge plants. The low dose pen was located in the plant zone bordering the treated field. The control pen was located in untreated cotton. Test birds were de-beaked and provided clean feed *ad libitum*. One mortality occurred in the low dose pen and two in the high dose pen. Despite the observed mortality, most of this study was invalid for the following reasons: 1) birds were not placed in the pens until after the chemical had dried; 2) birds were provided clean feed during the entire study; 3) birds were debeaked prior to the experiment; 4) one-half of the high dose pen was located in habitat which received no direct pesticide application. An average of 83.7 ppm was reported on cotton foliage in the high dose treatment pens after one application. This value is 1.8X the concentration predicted by Fletcheret al. (1994)[3]. AC 303,630 residues were not detected on the sorghum in the high dose pen after the first application, indicating little deposition on adjacent vegetation from drift. Sorghum in the low dose pens, 25 feet from the treated field, received little detectable active ingredient.

Dermal Toxicity Study. A dermal toxicity study (MRID #438807-07 and 434928-14) with Northern bobwhite was conducted to assess the risk of exposure through contact via exposed skin, such as the feet, through the feather layers and by preening. The 16 birds per treatment level, birds were placed in 1.7 x 1.4 meter pens containing cotton treated at rates up to 4X the recommended application rate. The exposure period started after the chemical had dried. Following a 24 hour exposure period the birds were held for 27 days. Clean feed and water was provided *ad libitum*. No mortality or significant differences in body weight occurred in any treatment group. Residues on cotton leaf samples collected in the 1X treatment group were 0.8X the concentration predicted by Fletcher et al. (1994). Maximum residues found on cotton leaf samples were about 320 ppm after four applications at 0.35 lbs

[3] Fletcher, J.S. , J.E. Nellessen and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environ. Toxicol. Chem. 13(9):1383-1391.

ai/acre. This study was not designed to assess the affects of exposure to the wet chemical.

Avian Dietary Discriminatin Study. An avian dietary discrimination test (MRID #438870-07) was conducted with the Northern Bobwhite to determine the aversion qualities of AC 303,630. AC 303,630 Technical was mixed into a commercial diet at concentrations up to 250 ppm and each bird (male, female, adult and juvenile) was presented with both treated and clean feed. Changes in body weight, consumption of treated feed and mortality were the measured endpoints. No significant mortality, weight change, or food consumption changes were noted in the adults in any treatment group. However, five juveniles died at the 250 ppm treatment level. Significant weight loss was reported in the juvenile treatment groups 250 ppm by day 6 and in the 140 ppm and 250 ppm treatments by day 10. At the 250 ppm treatment level, consumption of treated feed by juveniles was significantly lower than the controls during the first 5 days of the test. It was reported that the Northern Bobwhite could not reliably discriminate feed treated with Methiocarb, a known avian repellent, concentrations less than or equal to 600 ppm. The adult quail tested for aversion to AC 303,630 did not alter their food consumption at concentrations up to 250 ppm. Since 250 ppm was the highest concentration tested it is not possible to determine if AC 303,630 has similar repellency properties to adult quail as methiocarb. However, no deleterious effects were observed in the adults at the highest concentration. Juveniles on the other hand were notably impacted at concentration above 70 ppm.

Foliar Residue Study. A single application of the AC 303,630 3SC formulation was made to cotton fields at 0.2 and 0.4 lbs ai/acre (MRID #434928-14). Residues reported on cotton leaf tissues five hours after the 0.4 lbs ai/acre application were 183% of residues predicted by Fletcher et al. (1994). By day 28 residues on cotton foliage were approximately 3 ppm. Residues were determined on live insects collected both within the treated field and in the adjacent field border. No AC 303,630 was detected in insects collected from the adjacent habitat. Residues in insects collected within the field averaged 5.7 ppm through day 2 and dropped to levels below the method detection limit between days 7 and 14. Seeds collected from weeds within the adjacent habitat had no detectable residues. Soil residues were 158 ppb immediately following application and peaked at 170 ppb on day 14. By day 28 residues in soil averaged 100 ppb. It was determined through foliar leaf was testing that nearly all AC 303,630 on foliage was easily removed with a mild surfactant and water solution, regardless of the sampling time.

Avian Census. A detailed census of the avian community in and around cotton fields was conducted in Arizona, Texas and Mississippi/Alabama, in 1993 (MRID #434928-14). The EEB views this study as a preliminary attempt to classify potential study

locations in terms of vegetative type and structure, avian community structure, and avian use patterns to better design a future field study during which PIRATE will be applied. Approximately 175 surveys were conducted in each state. These were subdivided into plots representing riparian, agricultural and scrub/forest communities. Results of the surveys included the total number of individuals and species observed, most abundant species, avian community diversity, avian use of cotton fields and incidental wildlife observations. The five most common species observed censuses are listed in table 10.

Table 10. Five most common avian species observed during the 1993 census of cotton fields and adjacent habitats (mean number observed per sampling period).

Arizona 51 total species	Texas 62 total species	Mississippi/Alabama 66 total species
Red-winged Blackbird (10.62)	Horned Lark (1.13)	Northern Cardinal (2.67)
Yellow-headed Blackbird (4.60)	Cliff Swallow (1.04)	Red-winged Blackbird (1.96)
Cliff Swallow (1.57)	Northern Mockingbird (0.84)	Horned Lark (1.73)
Abert's Towhee (1.29)	Red-winged Blackbird (0.63)	Indigo Bunting (1.66)
Gambel's Quail (1.25)	Lark Sparrow (0.60)	Blue Jay (1.08)

Generalizing over all three regions, avian abundance was greatest in Arizona, nearly twice that of Mississippi/Alabama and more than twice that of Texas. Avian abundance and use of cotton fields increased as the growing season progressed. Time periods immediately prior to harvest had the greatest avian use. Forest and riparian habitats had the greatest avian abundance and diversity with the exception of Arizona study sites. Among all habitat types, upland forest sites in the southeast were the most diverse. Sites in Arizona adjacent to agricultural habitats had low avian diversity but high abundance due to high numbers of Red-winged blackbirds. Species richness was highest in Arizona and Mississippi/Alabama

(6) Field Monitoring

Three reports (MRID #438870-01) have been submitted summarizing wildlife mortality associated with single field applications of up to 0.2 lbs ai/acre. These monitoring efforts are of varying intensity and quality, however none were extensive enough to refute the risk to terrestrial wildlife. No dead or debilitated animals were found in any monitoring effort.

Mississippi State wildlife personnel conducted surveys in a total of 33 treated fields. The surveys included 70.3 acres of habitat adjacent to treated fields. No surveys were conducted

within the treated fields. Thirty-six percent of the surveys were conducted within the first 24 hours after application, 33% between 24 and 48 hours post-application, the remaining surveys were conducted 2,3, and 4 days post-application. Twenty-six species were observed, of which 72% of all individuals were Mourning dove, sparrows, cowbirds or Red-winged blackbirds.

Alabama surveys were conducted by one individual and included 16 treated fields. The surveys encompasses 20.4 miles of treated field (30%) and adjacent habitat (70%) transects. One, 2, and 5 surveys was conducted within 24 hours, 48 and 72 hours of treatment, respectively. Twenty six species were observed within the treated field. The 4 most common species within the fields were the Indigo bunting, Cardinal, Red-winged blackbird and Mourning dove.

Georgia State wildlife personnel conducted 4 surveys. Elapsed time between treatment and surveys ranged from 3 to 15 days. The author of the report stated no general conclusions should be drawn from the surveys regarding the effect of AC 303,630 due to the excessive time between the application and survey.

b. Toxicity to Aquatic Animals

(1) Freshwater Fish, Acute

Two freshwater fish toxicity studies using the technical grade of the active ingredient are required to establish the toxicity of a pesticide to freshwater fish. One study should use a coldwater species (preferably the rainbow trout), and the other should use a warmwater species (preferably the bluegill sunfish). Results of these tests are listed in table 11.

Table 11. Freshwater Fish Acute Toxicity Findings for AC 303,630

Species	% A.I.	LC_{50} (ppb)	MRID No. Author/Year	Toxicity Category	Fulfills Guideline Requirement?
Rainbow trout	94.5	LC_{50} = 7.44	427702-31, 1991	Very Highly Toxic	Yes
Bluegill sunfish	94.5	LC_{50} = 11.6	428078-01, 1991	Very Highly Toxic	Yes

The results indicate that AC 303,630 is very highly toxic to fish on an acute basis. The guideline requirement (72-1) is fulfilled.

In addition, two freshwater fish toxicity tests were conducted on the major degradates. The results of the major degrade, CL 312,094 (the desbromo derivative of the parent compound) is in table 12.

Table 12. Freshwater Fish Acute Toxicity Findings for the metabolite CL 312,094

Species	% A.I.	LC_{50} (ppb)	MRID No. Author/Year	Toxicity Category	Fulfills Guideline Requirement?
Bluegill sunfish	93.6	$LC_{50} > 928$	428078-15, Davis, J.W., Youngerman, Wisk, J.D, 1994	Highly Toxic	Yes

The results indicate that the metabolite CL 312,094 LC_{50} is greater than the highest test concentration. Consequently, the toxicity cannot be characterized for freshwater fish. However, since this degradate is less toxic than the parent compound, additional data will not be required at this time. The guideline requirement (72-1) is fulfilled for this degradate.

The LC_{50} of 2.6 ppb for the rainbow trout acute toxicity test for CL 357,806, the degradate produced by photolysis in water, (MRID No. 438870-08) was classified invalid due to the failure to measure the test concentration as required. The purported LC_{50} would mean that this compound is more toxic than the parent and places it in the very highly toxic classification. Therefore, the guideline (72-1) is not fulfilled for this degradate. However, since photolysis in water is not expected to contribute significantly to exposure, the EEB is not requiring this study be repeated at this time.

(2) Freshwater Fish, Chronic

Data from a fish early life-stage test using the technical grade of the active ingredient are required if the product is applied directly to water or expected to be transported to water from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute LC_{50} or EC_{50} is less than 1 mg/L; (3) the EEC in water is equal to or greater than 0.01 of any acute EC_{50} or LC_{50} value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute EC_{50} or LC_{50} value and any one of the following conditions exist: studies of other organisms indicate the reproductive physiology of fish may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). The preferred test species is rainbow trout. All the conditions stated above apply for AC 303,630 except for condition (4). Results of this test is listed in table 13.

Table 13. Fish Early Life-Stage Toxicity Findings

Species	% A.I.	NOEC/LOEC (ppb)	MATC (ppb)	MRID No. Author/Year	Endpoints Affected	Fulfills Guideline Requirement?
Rainbow trout	94.5	NOEC = 3.68 LOEC = 7.64	5.3	434928-19, Ward, G. Scott, McElwee, C., Lintott, D., Wisk, Joseph D., 1993	Survival of juvenile rainbow	Yes

The results indicate that toxicological effects based on mortality first appeared at the 7.64 µg/L level. The guideline requirement (72-4) is fulfilled.

A fish life-cycle test using the technical grade of the active ingredient is required when an end-use product is intended to be applied directly to water or is expected to transport to water from the intended use site, and when any of the following conditions exist: (1) the EEC is equal to or greater than one-tenth of the NOEL in the fish early life-stage or invertebrate life-cycle test or; (2) studies of other organisms indicate the reproductive physiology of fish may be affected. The preferred test species is the fathead minnow. The EECs generated range from 6.35 ppb to 12.68 ppb for which the first condition stated above applies for AC 303,630. **This study has not been submitted.**

(3) Freshwater Invertebrates, Acute

A freshwater aquatic invertebrate toxicity test using the technical grade of the active ingredient is required to assess the toxicity of a pesticide to freshwater invertebrates. The preferred test organism is *Daphnia magna*, but early instar amphipods, stoneflies, mayflies, or midges may also be used. Results of this test is listed in table 14..

Table 14. Freshwater Invertebrate Toxicity Findings

Species	% A.I.	LC_{50}/ EC_{50} (ppb)	MRID No. Author/Year	Toxicity Category	Fulfills Guideline Requirement?
Daphnid *Daphnia magna*	94.5%	LC50 = 5.83	427702-32/1991	Very highly toxic	Yes

The results indicate that AC 303,630 is very highly toxic to aquatic invertebrates on an acute basis. The guideline requirement (72-2) is fulfilled.

In addition, a freshwater aquatic invertebrate test toxicity test was conducted on the major photolytic degradate in water, CL 357,806. The results of this study are listed in table 15.

Table 15. Freshwater Invertebrate Toxicity Findings with CL 357,806.

Species	% A.I.	LC_{50}/ EC_{50} (ppb)	MRID No. Author/Year	Toxicity Category	Pulfills Guideline Requirement?
Daphnid *Daphnia magna*	97%	LC_{50} = 18	438870-09, Davis, J.W., Dunham, H.R., Wisk, J.D., 1995.	Very highly toxic	Yes

The results indicate that CL 357,806 is highly toxic to freshwater aquatic invertebrates. Since the LC_{50} of 18 ppb is less toxic than the parent compound additional testing will not be required for this degradate at this time. However, no data was submitted for the major degrade, Cl 312,094 (the desbromo derivative of the parent compound), and the registrant does not explain the reason for the non-submission of data. Further acute testing for the desbromo compound will be considered after an explanation is submitted.

(4) Freshwater Invertebrate, Chronic

Data from an aquatic invertebrate life-cycle test using Daphnia magna are required if the product is applied directly to water or expected to be transported to water from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute LC_{50} or EC_{50} is less than 1 mg/L; or (3) the EEC in water is equal to or greater than 0.01 of any acute EC_{50} or LC_{50} value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute EC_{50} or LC_{50} value and any of the following conditions exist: studies of other organisms indicate the reproductive physiology of invertebrates may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). Daphnia magna is the preferred test species. All the conditions stated above apply for AC 303,630 except for condition (4). Results of this test are listed in table 16.

Table 16. Aquatic Invertebrate Life-Cycle Toxicity Findings

Species	% A.I.	NOEC/LOEC (ppb)	MATC (ppb)	MRID No. Author/Year	Endpoints Affected	Fulfills Guideline Requirement?
Daphnid *Daphnia magna*	94.3	NOEC = 3.57 LOEC = 7.7	5.24	434928-22, Davis, J.W., Wisk, J.D., 1994.	Survival, Reproduction, weight, and length	Yes

The results indicate that toxicological effects based on mortality first appeared at the 7.7 ug/L level. The guideline requirement (72-4) is fulfilled.

(5) Estuarine and Marine Animals, Acute

Acute toxicity testing with estuarine and marine organisms (fish, shrimp and oyster embryo-larvae or shell deposition) using the technical grade of the active ingredient is required when an end-use product is intended for direct application to the marine/estuarine environment or is expected to reach this environment in significant concentrations. The preferred test organisms are the sheepshead minnow, mysid shrimp and eastern oyster. Estuarine/marine acute toxicity testing is required for Pirate (AC 303,630) because the end-use product is expected to reach the marine/estuarine environment in significant concentrations. Results of these tests are listed in table 17.

Table 17. Estuarine/Marine Acute Toxicity Findings

Species	% A.I.	LC_{50}/EC_{50} (ppb)	MRID No. Author/Year	Toxicity Category	Fulfills Guideline Requirement?
Eastern Oyster shell deposition	-	-	-	-	No
Mysid shrimp	96.8	LC_{50} = 2.03	434928-10, Davis, J.W., Ward, 1994	Very highly toxic	Yes
Sheepshead minnow	94.5	LC_{50} = 60.2	434928-16, Ward, G.S., Wisk, J.D., 1993	Very highly toxic	Yes

The results indicate that AC 303,630 is very highly toxic to marine/esturine organisms on an acute basis. The oyster shell deposition study (MRID # 434928-17) was invalid due to inadequate growth in controls (< 2mm). Since an embryo-larvae study was not conducted, this study must be repeated. The guideline requirement (72-3) is not fulfilled.

(6) Estuarine and Marine Animals, Chronic

Data from estuarine/marine fish early life-stage and aquatic invertebrate life-cycle toxicity tests are required if the product is applied directly to the estuarine/marine environment or expected to be transported to this environment from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute LC_{50} or EC_{50} is less than 1 mg/L; (3) the EEC in water is equal to or greater than 0.01 of any acute EC_{50} or LC_{50} value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute EC_{50} or LC_{50} value and any of the following conditions exist: studies of other organisms indicate the reproductive physiology of fish and/or invertebrates may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). The preferred test organisms are the sheepshead minnow and mysid shrimp. All the conditions stated above apply for AC 303,630 except for condition (4). Results of this test are listed in table 18.

Table 18. Estuarine/Marine Chronic Toxicity Findings

Species	% A.I.	NOEC/LOEC (ppb)	MATC (ppb)	MRID No. Author/Year	Endpoints Affected	Fulfills Guideline Requirement?
Mysid	94.5	NOEC= 0.172 LOEC= 0.385	0.257	434928-21, Ward, G. Scott, Wisk, Joseph D., Davis, Jay W., 1994.	Survival	May be upgraded to core upon submission of missing data.
Sheepshead Minnow	94.5	-	-	434928-20, McElwee, Cindy, Ward, G. Scott, and Wisk, Joseph D. 1994.	N/A	Invalid

The results indicate that toxicological effects based on mysid shrimp mortality first appeared at the 0.385 µg/L level. The chronic sheepshead minnow study (MRID # 434928-20) was invalid due to low dissolved oxygen levels throughout the experiment. This study must be repeated. Therefore the guideline requirement (72-4) is not fulfilled.

An estuarine/marine fish life-cycle test using the technical grade of the active ingredient is required when an end-use product is intended to be applied directly to water or is expected to transport to water from the intended use site, and when any of the following conditions exist: (1) the EEC is equal to or greater than one-tenth of the NOEC in the fish early life-stage or

invertebrate life-cycle test or; (2) studies of other organisms indicate the reproductive physiology of fish may be affected. The preferred test species is the sheepshead minnow. In the case of AC 303,630, a determination of this requirement cannot be made until a valid fish early life cycle test is submitted.

(7) Aquatic Field Testing

Due to the aquatic concerns resulting from the use of AC 303,630 the registrant submitted a microcosm study "to develop an understanding of the potential impact of AC 303,630 on aquatic organisms under conditions more representative of an actual environmental application".

As explained in the abbreviated review, since EPA has no protocol or guidance documents for the review of microcosm studies, the results from this microcosm review can only be used as supplemental information only. It was noted in the review that 90% and 100% mortalities for fish (Bluegill sunfish) were observed at nominal concentration of 30 and 300 µg ai/L (11.33 and 221.32 µg ai/L measured concentrations), respectively.

c. Toxicity to Plants

(1) Terrestrial

Currently, terrestrial plant testing is not required for pesticides other than herbicides except on a case-by-case basis (e.g. labeling bears phytotoxicity warnings; incident data or literature which demonstrate phytotoxicity).

(2) Aquatic

As with terrestrial plants, currently, aquatic plant testing is not required for insecticides or other classes of pesticides, except on a case-by-case basis (e.g. labeling bears phytotoxicity warnings; incident data or literature which demonstrate phytotoxicity).

2. Exposure and Risk Characterization

a. Ecological Exposure and Risk Characterization

Risk Quotient (RQ) and the Levels of Concern (LOC):

Risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of integrating the results of exposure and ecotoxicity data is called the quotient method. For this method, risk quotients are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic.

$$\text{RISK QUOTIENT} = \frac{\text{EXPOSURE}}{\text{ECOTOXICITY}}$$

Risk quotients are then compared to OPP established levels of concern. These LOCs are criteria used by OPP to indicate potential risk to nontarget organisms and the need to consider regulatory action. More specifically, the criteria indicate that a pesticide, when used as directed, has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories:

- o **acute high risk** - potential for acute risk is high; regulatory action may be warranted in addition to restricted use classification
- o **acute restricted use** - the potential for acute risk is high, but this may be mitigated through restricted use classification
- o **acute endangered species** - the potential for acute risk to endangered species is high; regulatory action may be warranted

- o **chronic risk** - the potential for chronic risk is high; regulatory action may be warranted

Currently, EFED has no procedures for assessing chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to mammalian or avian species.

The ecotoxicity test values (i.e., measurement endpoints) used in the acute and chronic risk quotients are derived from the results of required studies. Examples of ecotoxicity values derived from the results of short-term laboratory studies which assess acute effects are:

- LC_{50} (fish and birds)
- LD_{50} (birds and mammals)
- EC_{50} (aquatic plants and invertebrates)
- EC_{25} (terrestrial plants)
- EC_{05} or NOEC (endangered plants)

Examples of toxicity test effect levels derived from the results of long-term laboratory studies which assess chronic effects are:

- LOEC (birds, fish, and aquatic invertebrates)
- NOEC (birds, fish and aquatic invertebrates)
- MATC (fish and aquatic invertebrates)

Generally, for birds and mammals, the NOEC value is used as the ecotoxicity test value in assessing chronic effects. Other values may be used when justified. Generally, the MATC (defined as

the geometric mean of the NOEC and LOEC) is used as the ecotoxicity test value in assessing chronic effects to fish and aquatic invertebrates. However, if the measurement end point is production or survivability then the NOEC is used.

Risk presumptions, along with the corresponding risk quotients and levels of concern, are listed in Table 19.

Table 19. Risk presumption, risk quotient derivation and risk threshold used for floral and faunal risk assessment.

RISK PRESUMPTION	RISK QUOTIENT	LEVEL OF CONCERN
Birds		
Acute High Risk	EEC[1]/LC_{50} or LD_{50}/sqft[2] or LD_{50}/day[3]	0.5
Acute Restricted Use	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day (or LD_{50} < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC_{50} or LD50/sqft LD_{50}/day	0.1
Chronic Risk	EEC/NOEC	1
Wild Mammals		
Acute High Risk	EEC/LC_{50} or LD50/sqft or LD_{50}/day	0.5
Acute Restricted Use	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day (or LD_{50} < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC_{50} or LD50/sqft or LD_{50}/day	0.1
Chronic Risk	EEC/NOEC	1

[1] abbreviation for Estimated Environmental Concentration; designated ppm in avian/mammalian food items

[2] $\frac{mg/ft^2}{LD_{50} * \text{wt. of bird}}$ [3] $\frac{\text{mg of toxicant consumed/day}}{LD_{50} * \text{wt. of bird}}$

Aquatic Animals		
RISK PRESUMPTION	RISK QUOTIENT	LEVEL OF CONCERN
Acute High Risk	EEC[1]/LC_{50} or EC_{50}	0.5
Acute Restricted Use	EEC/LC_{50} or EC_{50}	0.1
Acute Endangered Species	EEC/LC_{50} or EC_{50}	0.05
Chronic Risk	EEC/MATC or NOEC	1

[1] abbreviation for Estimated Environmental Concentration; designated ppb/ppm in water

RISK PRESUMPTION	RISK QUOTIENT	LEVEL OF CONCERN
Terrestrial and Semi-Aquatic Plants		
Acute High Risk	EEC[1]/EC_{25}	1
Acute Endangered Species	EEC/EC_{05} or NOEC	1
Aquatic Plants		
Acute High Risk	EEC[2]/EC_{50}	1
Acute Endangered Species	EEC/EC_{05} or NOEC	1

[1] abbreviation for Estimated Environmental Concentration; designated lb ai/A

[2] abbreviation for Estimated Environmental Concentration; designated ppb/ppm in water

At this time, EEB has no procedures for assessing chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to mammalian or avian species.

(b) Exposure and Risk to Nontarget Terrestrial Animals

For pesticides applied as a non-granular product (e.g. liquid, dust), the estimated environmental concentrations on food items following product application are compared to LC_{50} values to assess risk. The predicted 0-day maximum and mean residues of a pesticide that may be expected to occur on selected avian or mammalian food items immediately following a direct single application at 1 lb ai/A are given in table 20.

Table 20. Estimated maximum and mean Environmental Concentrations (EECs) on Avian and Mammalian Food Items (ppm) at an application rate of 1.0 lbs/acre.

Food Items	EEC (ppm) Predicted Maximum Residue[1]	EEC (ppm) Predicted Mean Residue[1]
Short Range Grass	240	85
Tall Range Grass	110	36
Broadleaf/Forage plants/Small Insects	135	45
Fruits/Pods/Seeds/Large Insects	15	7

[1] Predicted maximum and mean residues are based upon a 1 lb ai/acre application rate (Hoerger and Kenaga, 1973[4] as modified by Fletcher et al., 1994)[5].

[4] Hoeger, F. and E.E. Kenaga. 1972. Pesticide Residues on Plants: Correlation of representative data as a basis for estimation of their magnitude in the environment. *In:* F. Coulston and F. Korte, (*eds.*) Environmental Quality and Safety: Chemistry, Toxicology, and Technology. Georg Thieme Publishers, Stuttgart, West Germany, pp9-28.

[5] Fletcher, J.S., J.E. Nellessen and T.G. Pfleeger. 1994. Literature Review and Evaluation of the EPA Food-Chain (Kenega) Nomogram, an Instrument for Estimating Pesticide Residues on Plants, Environ. Toxicol. and Chem., 13(9):1383-1391.

(1) Birds

Non-granular Products- Acute and Chronic Risk

In this assessment risk quotients were calculated on predicted maximum residues on dietary items for both the maximum recommended application rate (0.35 lbs ai/acre) and minimum recommended application rate (0.09 lbs ai/acre). Maximum EECs, as predicted by Fletcher following multiple applications were also evaluated for chronic risk as well as acute risk because of the long estimated half-life of the active ingredient under aerobic soil metabolism, 1370 days, and applications can be made as little as 5 days apart. Under this application scenario, by the time the last application is made, little of the active ingredient from the previous applications would be degraded. To account for natural degradation of the chemical, the program FATE was used to compute EECs following multiple applications.

The EECs and acute risk quotients for both single and multiple broadcast applications of non-granular products are given in table 21.

Table 21. Avian Acute Risk Quotients for Single and Multiple Applications of Non-Granular Products (Broadcast) Based on a Mallard LC_{50} of 8.6 ppm.

Site	Application Rate (lbs a.i./A)	Food Items	Maximum EEC (ppm)		LC_{50} (ppm)	Acute RQ	
			1 App.	3 Apps.		1 App.	3 Apps.
Cotton	0.35 3 applications, 5 days apart at 0.35 lbs ai/acre	Short Range Grass	84	251	8.6	9.8	29.2
		Tall Range Grass	38.5	115	8.6	4.5	13.4
		Broadleaf plants /Forage/Small Insects	47.25	141	8.6	5.5	16.4
		Fruits/Seeds/Pods /Large Insects	5.25	15.7	8.6	0.61	1.8

EECs calculations made for multiple applications are based upon 3 applications at 0.35 lbs ai/acre at 7 day intervals, with an aerobic half-life of 1370 days.

The results indicate that for single and multiple broadcast applications of non-granular products, avian acute high risk, restricted use, and endangered species levels of concern are exceeded in all forage categories. EECs exceed LOCs for endangered species concerns by 6 to 98 times in fruits/seed/large insects and short range grass foraging categories, respectively. Multiple applications increase LOC concerns for the same categories to 292 and 18 times respectively.

Due to the rapid rate at which mortality occurs upon ingestion of contaminated food items and the relatively high toxicity of the chemical, potential hazard can be assessed by examining the LD_{50}s/day. This method of estimating potential hazard refines the calculated risk quotient by including the estimated daily quantity of food a bird will ingest in relation to body size. As outlined by Kenaga[6] (1973), three weight classes of birds, 20, 100 and 1000g, and estimated daily food consumption rates in relation to body weight, 18%, 9.2%, 3.6%, respectively, are examined in these calculations. The LD_{50}/day is a refined RQ and is compared to same scale as previously calculated RQs (see Table 9). The calculation used to determine LD_{50}s/day is:

$$LD_{50}s/Day = \frac{EEC * \frac{\text{Daily Food Consumption (g)}}{\text{Body Weight (g)}}}{LD_{50}}$$

With the acute toxicity information available it is possible to model two LD_{50}/day scenarios. The first utilizes the most sensitive species, the Red-winged blackbird, LD_{50} = 2.21 mg/kg, in calculation. While it is not representative of a bird weighing 1000 g, using it as the model allows for protection of smaller or larger birds which may be equally or more sensitive to the active ingredient. The second scenario utilizes LD_{50}s of birds which are similar in weight to the weight categories, namely the Mallard, Northern Bobwhite and Red-winged blackbird. This method is appropriate if it is assumed that in addition to weight class and daily dietary intake being better represented, the metabolic rates and toxicological response of the birds are also better represented. If to err on the side of safety is desirable, selection of an LD_{50} based on similar weight could potentially underestimate the actual risk. Despite the uncertainty associated with either method, RQs have been calculated using both methods and are presented in Table 22.

[6] Kenega, E.E. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. *In*: Environmental Quality, Global Aspects of Chemistry Toxicology and Technology as Applied to the Environment. Vol II. Coulston, F. and Korte, F. (eds.), Academic Press, NY, pp166-181.

Table 22. Avian acute risk based upon LD_{50}s/day. Calculated for a single application rate of 0.35 lbs a.i./acre. Multiple application EECs are based upon 3, 0.35 lbs ai/acre, applications made 5 days apart.

Forage Class	Bird Size Class (Forage Consumption Rate)	Maximum EEC[1]		RQ Calculation - representative weight class			RQ Calcualtion - Most Sensitive Species		
		1 App.	3 Apps.	LD^{50} [2]	1 App.	3 Apps.	LD^{50}	1 App.	3 Apps.
Small Insects/ Forage/ Broadleaf plants	20 g Bird (18%)	47.25	141	2.21	3.84	11.48	2.21	3.84	11.48
	100 g Bird (9.2%)	47.25	141	34	0.13	0.38	2.21	1.97	5.87
	1000 g Bird (3.6%)	47.25	141	8.1	0.20	0.59	2.21	0.77	2.30
Large Insects/ Seeds/ Fruits/ Pods	20 g Birds (18%)	5.25	15.7	2.21	0.43	1.21	2.21	0.43	1.23
	100 g Bird (9.2%)	5.25	15.7	34	0.01	0.04	2.21	0.22	0.65
	1000 g Bird (3.6%)	5.25	15.7	8.1	0.02	0.06	2.21	0.09	0.26
Tall Range Grass	20 g Birds (18%)	38.5	115.1	2.21	3.13	9.36	2.21	3.13	9.37
	100 g Birds (9.2%)	38.5	115.1	34	0.10	0.31	2.21	1.6	4.79
	1000 g Birds (3.6%)	38.5	115.1	8.1	0.16	0.51	2.21	0.63	1.87
Short Range Grass	20 g Bird (18%)	84	251	2.21	6.84	20.44	2.21	6.84	20.44
	100 g Bird (9.2%)	84	251	34	0.23	0.68	2.21	3.53	10.45
	1000 g Bird (3.6%)	84	251	8.1	0.35	1.05	2.21	1.37	4.09

[1] Expected Environmental Concentrations are based upon Fletcher et al., 1994.

[2] LD_{50}s are based upon the Red-winged Blackbird, 2.2 mg/kg; Northern Bobwhite, 34 mg/kg; and the Mallard 8.3 mg/kg which are used to represent 20, 100 and 1000 g birds, respectively

The first scenario in which the Red-winged blackbird LD_{50} is used, indicates that for broadcast applications of non-granular products, avian acute high risk, restricted use and endangered species LOCs are exceeded in many foraging categories. Acute high risk, restricted use and endangered species LOCs are exceeded after one application at 0.35 lbs a.i./acre for all weight classes in small insects/forage/broadleaf plant and both tall and short range grass foraging categories. Restricted use and endangered species LOCs are exceeded in the large insect/seeds/fruits/pods category for birds 20 and 100g in weight. RQs are essentially tripled when

the yearly allowable application is achieved. For birds foraging in the large insect/ seeds/fruit/pods category, the group with the lowest EEC's, acute high risk, restricted use and endangered species LOCs are exceeded after three 0.35 lb ai/acre applications for 20 and 100g animals. Restricted use and endangered species LOCs are exceeded after one 0.35 lb ai/acre application for 20 and 1000 g birds following 3 applications.

Analysis of LD_{50}s/day, under the assumption of utilizing the LD_{50} value for a bird of similar size to the appropriate weight class, indicates in nearly all scenarios, endangered species LOCs are exceeded. The exceptions are in the large insect/seeds/pods/fruit category where the 100 and 1000 g birds are considered safe. Acute high risk LOCs are exceeded after one application for a 20 g bird in all foraging categories except the large insect/seeds/pods/fruits where the restricted use LOC is exceeded. In addition, restricted use LOCs are exceeded after one application for 1000 g birds in the small insect/forage/broadleaf plant and short range grass categories. Three applications essentially triples the EECs and results in acute high risk LOCs being exceeded for 20 g birds in all categories, for 1000 g birds in all categories except for the large insect/seed/fruits/pods and for 100 g birds in the short range grass. Restricted use LOCs are exceeded for 100 g birds in the tall range grass and small insect/forage/broadleaf plant categories.

The chronic risk quotients for broadcast applications of non-granular products are listed in Table 23.

Table 23. Avian Chronic Risk Quotients for Non-Granular Products (Broadcast) Based on a Mallard NOEC of 0.5 ppm.

Site	Application Rate (lbs a.i./A)	Food Items	Maximum EEC (ppm)	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Cotton	0.35 3 applications, 5 days apart at 0.35 lbs ai/acre	Short Range Grass	251	0.5	502
		Tall Range Grass	115	0.5	230
		Broadleaf plants /Forage /Small Insects	141	0.5	282
		Fruits/Pods/Seeds /Large Insects	15.7	0.5	31.4

EECs calculations made for multiple applications are based upon 3 applications at 0.35 lbs ai/acre at 7 day intervals, with an aerobic half-life of 1370 days.

The above results indicate that for broadcast applications of non-granular products, the avian chronic level of concern is exceeded at a single application rate of 0.35 lbs/acre for endangered species, for all foraging categories.

(2) Mammals

Non-granular Products - Acute and Chronic Risk

Estimation of the potential for adverse effects to wild mammals is based upon EEB's draft 1995 SOP for mammalian risk assessment methods which is based on methods outlined by Hoerger and Kenaga (1972). The concentration of active ingredient in the diet which is expected to be acutely lethal to 50% of the test population (LC_{50}) is derived by dividing the LD_{50} value by the percent daily dietary intake in relation to body weight. A risk quotient is then determined by dividing the EEC by the derived LC_{50} value.

$$LC_{50} = \frac{\text{EEC (mg/kg)}}{LD_{50}\ \text{(mg/kg)}/\%\ \text{Body Weight Consumed}}$$

Risk quotients are calculated for three separate weight classes of mammals (15, 35, and 1000 g), each presumed to consume four different kinds of food (grass, forage, insects, and seeds). A small herbivorous mammal weighing 15g, is expected to ingest the equivalent of 95% of its body weight in food (short range grass) every day. This category of mammal is considered to be at the highest risk for experiencing the toxic effects of a chemical. The LD_{50} for the laboratory mouse was used to calculate the risk quotients.

The acute risk quotients for a single broadcast applications of non-granular products are listed in Table 24 and 25, respectively.

Table 24. Mammalian (Herbivore/Insectivore) acute risk quotients for single applications of non-granular products (broadcast) based on a laboratory mouse LD_{50} of 55 mg ai/kg.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Mouse LD_{50} (mg/kg)	EEC Short Range Grass	EEC Tall Range Grass	EEC Broadleaf plants/ Small Insects	Acute RQ Short Range Grass	Acute RQ Tall Range Grass	Acute RQ Broadleaf Plants/ Small Insects
Cotton 0.35	15	95	55	84	38.5	47.25	1.45	0.67	0.82
	35	66	55	84	38.5	47.25	1.01	0.46	0.57
	1000	15	55	84	38.5	47.25	0.23	0.12	0.13

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

Table 25. Mammalian (granivore) acute risk quotients for single application of non-granular products (broadcast) based on a laboratory mouse LD_{50} of 55 mg ai/kg.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Mouse LD_{50} (mg/kg)	EEC Seeds/ Large Insects	Acute RQ Seeds/ Large Insects
Cotton 0.35	15	21	55	5.25	0.02
	35	15	55	5.25	0.01
	1000	[illegible]	55	5.25	0.003

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

The results indicate that for a single broadcast application, at 0.35 lbs ai/acre, acute high risk, restricted use and endangered species LOCs are exceeded for 15g herbivore/insectivore mammals in short range grass, tall range grass and broadleaf plants/small insect forage categories and for 35g mammals in short grass and broadleaf plants/small insect foraging categories. Restricted use and endangered species LOCs are exceeded for 35g and 1000g herbivore/insectivore mammals in the both the tall range grass and short range grass forage categories, respectively. Endangered species LOCs are exceeded for 1000g mammals in the tall range grass and broadleaf plants/small insect foraging categories. No LOCs are exceeded for granivorous mammals.

The acute risk quotients for three broadcast applications, at 5 day intervals, at 0.35 lbs ai/acres are listed in table 26 and 27, respectively.

Table 26. Mammalian (Herbivore/Insectivore) acute risk quotients for multiple applications of non-granular products (broadcast) based on a laboratory mouse LD_{50} 55 mg ai/kg.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Mouse LD_{50} (mg/kg)	EEC Short Range Grass	EEC Tall Range Grass	EEC Broadleaf plants/ Small Insects	Acute RQ Short Range Grass	Acute RQ Tall Range Grass	Acute RQ Broadleaf Plants/ Small Insects
Cotton 0.35	15	95	55	251	115	141	4.34	1.99	2.43
	35	66	55	251	115	141	3.01	1.38	1.69
	1000	15	55	251	115	141	0.68	0.31	0.38

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

Table 27. Mammalian (granivore) acute risk quotients for multiple applications non-granular products (broadcast) based on a laboratory mouse LD_{50} 55 mg ai/kg.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Rat and Mouse LD_{50} (mg/kg)	EEC Seeds/ Large Insects	Acute RQ Seeds/ Large Insects
Cotton 0.35	15	21	55	15.7	0.06
	35	15	55	15.7	0.04
	1000	3	55	15.7	0.009

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

The results indicate that with multiple broadcast application, acute high risk, restricted use and endangered species LOCs are exceeded for 15g and 35g herbivore/insectivore mammals in short range grass, tall range grass and broadleaf plants/small insect forage categories and 1000g mammals in the short range grass foraging category. Restricted use and endangered species LOCs are exceeded for 1000g herbivore/ insectivore mammals in the tall grass and broadleaf plant/small insects foraging categories. No LOCs are exceeded for granivorous mammals.

The effects of chronic exposure can be assessed by comparing the NOEL from a mouse 90 day dietary study (MRID No. 434928-30) with the expected environmental concentrations after multiple applications. The results of this study show a strong dose dependent response expressed as hepatic cell hypertrophy, an early indication of liver damage, in both male and female rats. The selection of a NOEL of 40 ppm is also justified given the results reported in a one-year dietary neurotoxicity study on the rat (MRID #434928-33), a 2 generation reproduction study on the rat (MRID #434928-36), a chronic oncogenicity study with the mouse (MRID #434928-38) with NOELs of 60, 60 and 20 ppm, respectively. The results of this analysis are listed in table 28.

Table 28. Mammalian chronic risk quotients for non-granular products (broadcast) based on a mouse NOEL of 40 ppm in a 90 day feeding study.

Site	Application Rate (lbs ai/acre)	Food Items	Maximum EEC PPM	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Cotton	0.35 3 applications at 5 day intervals	Short Range Grass	251	40	6.3
		Tall Range Grass	115	40	2.9
		Broadleaf Plants/Forage/ Small Insects	141	40	3.5
		Seeds/Pods/Fruit/Large insects	15.7	40	0.4

The results indicate after 3 applications at a rate of 0.35 lbs a.i./acre, the chronic LOC for mammals, 1.0, is exceeded for all foraging categories except the large insect/seeds/pods/and fruit category.

(3) Avian and Mammalian Risk Quotients Based Upon Minimum Recommended Application Rates

Risk quotients can also be evaluated using the minimum recommended application rate. The lowest rate on the proposed label, 0.09 lbs ai/acre, is for controlling Thrips spp. and is to be used during the pre-bloom period. In this analysis a single application at a rate of 0.09 lbs ai/acre and multiple applications at the same rate (repeated 11 times at intervals of 5 days) are evaluated for both acute and chronic risk to birds. This model is assumed to be valid because later season applications, targeting a variety of pests, call for higher application rates (0.12 to 0.35 lbs ai/acre). Single application EEC's for this scenario based upon Fletcher et al. (1994) are 21.6, 9.9, 12.2 and 1.4 ppm for short range grass, tall range grass, broadleaf plants/forage/small insects, and fruits/pods/seed/large insects, respectively.

EECs and acute risk quotients for both single and multiple broadcast applications under the above scenario are listed in table 29.

Table 29. Avian Acute Risk Quotients based on a Mallard LD_{50} of 8.6 ppm. Single application EECs are based upon a rate of 0.09 lbs ai/acre, multiple application EECs are based upon 11 applications at 7 day intervals at a rate of 0.09 lbs ai/acre.

Site	Application Rate (lbs a.i./A)	Food Items	Maximum EEC (ppm)		LC_{50} (ppm)	Acute RQ	
			1 App.	11 Apps.		1 App.	11 Apps.
Cotton	0.09 11 applications, 5 days apart at 0.09 lbs ai/acre	Short Range Grass	21.6	233	8.6	2.51	27.09
		Tall Range Grass	9.9	107	8.6	1.15	12.44
		Broadleaf plants /Forage/Small Insects	12.2	131	8.6	1.42	15.23
		Fruits/Seeds/Pods /Large Insects	1.4	15	8.6	0.16	1.74

EECs calculations made for multiple applications are based upon 11 applications at 0.09 lbs ai/acre at 7 day intervals, with an aerobic half-life of 1370 days.

Acute avian RQs, at the lowest label recommended single application rate exceed acute high risk, restricted use and endangered species LOCs are exceeded in all categories but fruits/seeds/pods/large insects. Endangered species LOCs are exceeded in the latter category. After multiple applications, acute high risk LOCs are exceeded in all categories. A maximum single application rate below 0.0035 lbs ai/acre would be required to insure no LOCs are exceeded for acute hazard to birds.

Risk quotients based upon LD_{50}s/day calculated at the lowest recommended application rate are presented in table 30.

Table 30. Avian acute risk based upon LD_{50}/day for three bird size classes and forage types. Calculated for a single application rate of 0.09 lbs a.i./acre. Multiple application EECs are based upon 11, 0.09 lbs ai/acre, applications made 5 days apart.

Forage Class	Bird Size Class (Forage Consumption Rate)	Maximum EEC[1]		RQ Calculation - representative weight class			RQ Calcualtion - Most Sensitive Species		
		1 App.	11 Apps.	LD^{50}	1 App.	11 Apps.	LD^{50}	1 App.	11 Apps.
Small Insects, Forage, Broadleaf plants	20 g Bird (18%)	12.15	132	2.21	0.99	10.7	2.21	0.99	10.7
	100 g Bird (9.2%)	12.15	132	34	0.03	0.36	2.21	0.51	5.49
	1000 g Bird (3.6%)	12.15	132	8.1	0.05	0.59	2.21	0.2	2.41
Large Insects, Seeds, Fruits, Pods	20 g Birds (18%)	1.35	15	2.21	0.11	1.23	2.21	0.11	1.23
	100 g Bird (9.2%)	1.35	15	34	0.004	0.04	2.21	0.06	0.63
	1000 g Bird (3.6%)	1.35	15	8.1	0.006	0.07	2.21	0.02	0.25
Tall Range Grass	20 g Birds (18%)	9.9	107	2.21	3.81	8.71	2.21	0.81	8.71
	100 g Birds (9.2%)	9.9	107	34	0.03	0.29	2.21	0.42	4.45
	1000 g Birds (3.6%)	9.9	107	8.1	0.04	0.48	2.21	0.16	1.74
Short Range Grass	20 g Bird (18%)	21.6	233	2.21	1.76	19.01	2.21	1.76	19.01
	100 g Bird (9.2%)	21.6	233	34	0.06	0.63	2.21	0.9	9.71
	1000 g Bird (3.6%)	21.6	233	8.1	0.1	1.04	2.21	0.35	3.8

[1] Expected Environmental Concentrations are based upon Fletcher et al., 1994.

[2] LD_{50}s are based upon the Red-winged Blackbird, 2.2 mg/kg; Northern Bobwhite, 34 mg/kg; and the Mallard 8.3 mg/kg which are used to represent 20, 100 and 1000 g birds, respectively

Avian acute RQs for a single application of 0.09 lbs ai/acre are essentially 4 times lower than those calculated at the highest rate. Under this application scenario and utilizing the LD_{50} value for the Red-winged Blackbird, acute high risk LOCs are exceeded for 20 g birds in the short and tall range grass and small insect/forage/broadleaf plant categories and 100 g birds in the short range grass and small insect/forage/broadleaf plant categories. Restricted use LOCs are exceeded for 1000 g birds in the tall range grass and small insect/forage/broadleaf plant categories. Endangered species LOC is exceeded for 1000 gg bird in

the tall range grass category. Following 11 applications acute high risk LOCs are exceeded in all categories with all weight classes of birds, with the exception of the 1000 g bird in the large insect/seeds/pods/fruits category.

RQ calculations conducted when LD_{50}/day values represent birds based on size class, show acute high risk LOCs exceeded for 20 g birds in the short and tall range grass and small insect/forage/broadleaf plant categories. Endangered species LOCs are exceeded for 20 and 1000 g birds in the large insects/seeds/pods/fruit and short range grass categories, respectively. Following 11 applications acute high risk LOCs are exceeded for 20 g birds in all categories and for 1000 g birds in the short range grass and small insect/seeds/pods/fruit categories. Additionally, restricted use LOCs are exceeded for a 1000 g bird in the tall range grass category and 100 birds in tall range grass and small insect/forage/broadleaf plant categories.

Chronic avian RQs based upon this model are very similar to those calculated on the maximum application rate. The program FATE is also used to predict the maximum EEC after repeated applications. The maximum allowable amount of active ingredient in either scenario is 1.05 lbs ai/acre. The main difference between the two scenarios is the amount of time required to reach the maximum EEC's. Predictions based upon multiple applications of 0.35 lbs ai/acre (5 day application intervals) reach a maximum of 251 ppm on short grass, in 21 days. Predictions based upon multiple applications of 0.09 lbs ai/acre (5 day application intervals) reach a maximum of 233 ppm in 70 days. Table 31 lists the EECs and RQs for the chronic analysis.

Table 31. Avian Chronic Risk Quotients for Non-Granular Products (Broadcast) Based on a Mallard NOEC of 0.5 ppm.

Site	Application Rate (lbs a.i./A)	Food Items	Maximum EEC (ppm)	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Cotton	0.09 11 applications, 5 days apart at 0.09 lbs ai/acre	Short Range Grass	233	0.5	466
		Tall Range Grass	107	0.5	214
		Broadleaf plants /Forage /Small Insects	132	0.5	264
		Fruits/Pods/Seeds /Large Insects	15	0.5	30

EECs calculations made for multiple applications are based upon 11 applications at 0.09 lbs ai/acre at 7 day intervals, with an aerobic half-life of 1370 days.

Based upon the Mallard and Northern Bobwhite NOEL (0.5 ppm) for adverse reproductive effects, chronic RQs are exceeded in all foraging categories. A maximum application rate of 0.003 lbs ai/acre would be required to ensure no LOCs are exceeded for chronic hazard to birds.

Mammalian risk quotients at the lowest application rate 0.09 lbs ai/acre are presented in table 32 and 33.

Table 32. Mammalian (Herbivore/Insectivore) acute risk quotients for single applications of non-granular products (broadcast) based on a laboratory mouse LD_{50} of 55 mg ai/kg and an application rate of 0.09 lbs ai/acre.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Mouse LD_{50} (mg/kg)	EEC Short Range Grass	EEC Tall Range Grass	EEC Broadleaf plants/ Small Insects	Acute RQ Short Range Grass	Acute RQ Tall Range Grass	Acute RQ Broadleaf Plants/ Small Insects
Cotton 0.35	15	95	55	21.6	9.9	12.15	0.37	0.17	0.2
	35	66	55	21.6	9.9	12.15	0.25	0.12	0.15
	1000	15	55	21.6	9.9	15.15	0.06	0.03	0.03

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

Table 33. Mammalian (granivore) acute risk quotients for a single 0.09 lbs ai/acre application of non-granular products (broadcast) based on a laboratory mouse LD_{50} of 55 mg ai/kg.

Site/ Application Rate (lbs ai/A)	Body Weight (g)	% Body Weight Consumed	Mouse LD_{50} (mg/kg)	EEC Seeds/ Large Insects	Acute RQ Seeds/ Large Insects
Cotton 0.35	15	21	55	1.35	0.005
	35	15	55	1.35	0.004
	1000	3	55	1.35	0.0007

[1] the equation for the RQ is:

$$\frac{\text{EEC (mg/kg)}}{\text{LD50 (mg/kg)/ \% Body Weight Consumed}}$$

Restricted use and endangered species LOCs are exceeded or met for 15 g mammals (herbivore/insectivore) in the short range grass and broadleaf plant/forage/small insect categories and for 35 g (herbivore/insectivore) mammals consuming short grass. Additionally, endangered species LOCs are exceeded for tall grass habitats for 15 and 35 g mammals (herbviore/insectivore) and for 35 g mammals in the broadleaf plant/forage/small insect category.

Following multiple applications as outlined in the previous section, acute high risk, restricted use and endangered species

LOCs are exceeded for 15 and 35 g herbivore/insectivores short and tall range grass and broadleaf plant/forage/small insect forage categories. RQs for 1000 g herbivores exceed the acute high risk LOC in short grass and restricted use LOCs in tall range grass and broadleaf plant/small insect categories. No acute LOCs are exceeded for granivores of any size in any of the forage groups.

Results of mammalian chronic risk quotient analysis at minimum recommended rates are essentially the same as those at the highest rate. The primary difference is the time required to reach the maximum allowable rate. Table 34 lists the RQs.

Table 34. Mammalian chronic risk quotients for non-granular products (broadcast) based on a mouse NOEL of 40 ppm in a 90 day feeding study.

Site	Application Rate (lbs ai/acre)	Food Items	Maximum EEC PPM	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Cotton	0.09 11 applications at 5 day intervals	Short Range Grass	233	40	5.8
		Tall Range Grass	107	40	2.7
		Broadleaf Plants/Forage/ Small Insects	132	40	3.3
		Seeds/Pods/Fruit/Large insects	15	40	0.4

Chronic LOCs are exceeded for mammals in the short and tall range grass and broadleaf plant/forage/small insect categories. Due to the persistence of AC 303,630, any application above 0.17 lbs ai/acre or multiple applications totaling more than this amount will exceed the LOCs for mammalian risk.

(4) Insects

Currently, EFED has no procedure for assessing risk to nontarget insects. Results of acceptable studies are used for recommending appropriate label precautions.

(c) Exposure and Risk to Nontarget Aquatic Animals

As explained in the EFGWB assessment, AC 303,630 has been characterized as extremely persistent with an aerobic soil metabolic half-life of 3.8 years and a strong tendency to adsorb to soil (Kd_{ads} = 32-155, Kd_{des} = 67-362) and pond sediment. For these reasons, the EEB requested the Surface Water Section of the Environmental Fate and Ground Water Branch to use environmental fate and transport computer models to calculate more refined EECs. The Pesticide Root Zone Model (PRIZM2, version 2.3) was used to simulate pesticides in field runoff. The Exposure Analysis

Modeling System (EXAM II) was used to simulate pesticide fate and transport in an aquatic environment (1-hectare body of water six feet deep receiving runoff from 10 hectare field).

Some of the environmental fate parameters used in the model for this pesticide were:

Parameter	Value
Soil K_{oc}	11,500 L/Kg
Aerobic Soil metabolism half-life	3.8 years
Anaerobic Soil metabolism half-life	2.0 years
Solubility	0.13 mg/L
Photolysis	15 days

The EECs generated from the EXAM II/PRIZM2 runoff model are presented in table 35. Two scenarios were chosen for modeling. The Mississippi site was chosen because it presented a high potential for runoff, while the Texas site was chosen because of the significant cotton production in the state.

Table 35. Estimated Environmental Concentrations (EECs) For Aquatic Exposure

Crop, Site (Spray drift)	Soil Surface Texture	Application Method	Applic. Rate lbs a.i./A (Number of Applications)	Maximum Initial EEC (ppb)	21-day EEC (ppb)	56-day EEC (ppb)	90-day EEC (ppb)
PRIZM1/EXAM II							
Cotton, Texas (1% spray drift)	Fine Sandy Loam	Ground	0.40(1) 0.40(1) 0.25(1)	7.01	3.58	3.24	3.16
Cotton, Texas (5% spray drift)	Fine Sandy Loam	Aerial	0.40(1) 0.40(1) 0.25(1)	6.35	3.84	3.58	3.51
Cotton, Mississippi (1% spray drift)	Silt Loam	Ground	0.40(1) 0.40(1) 0.25(1)	12.68	9.89	9.55	9.47
Cotton, Mississippi (5% spray drift)	Silt Loam	Aerial	0.40(1) 0.40(1) 0.25(1)	10.98	8.99	8.63	8.59

(1) Freshwater Fish

Acute and chronic risk quotients for freshwater fish are listed in tables 36 and 37.

Table 36. Risk Quotients (RQs) for Freshwater Fish Based On a Rainbow trout LC_{50} of 7.44 ppb and a Rainbow trout NOEC/MATC of 3.68/5.3 ppb in the State of Mississippi

Site/ Application Method and Rate (lb ai/a)	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 56-Day (ppb)	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/aerial 0.4	7.44	3.68/5.3	10.98	8.63	1.48	2.35/1.64
Cotton/ground 0.4	7.44	3.68/5.3	12.68	9.55	1.70	2.60/1.80

Table 37. Risk Quotients (RQs) for Freshwater Fish Based On a Rainbow trout LC_{50} of 7.44 ppb and a Rainbow trout NOEC/MATC of 3.68/5.3 ppb in the State of Texas

Site/ Application Method and Rate (lb ai/a)	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 56-Day (ppb)	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/aerial 0.4	7.44	3.68/5.3	6.35	3.58	0.85	0.97
Cotton/ground 0.4	7.44	3.68/5.3	7.01	3.24	0.94	0.88

The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for freshwater fish for aerial applications by a magnitude of 2.96X, 14.8X, and 29.6X, respectively for Mississippi. Risks posed by ground applications are exceeded by magnitudes of 3.4X, 17X, and 34X, respectively. The Mississippi chronic risk LOC is exceeded for freshwater fish by a magnitude of 1.6X for aerial applications and 1.8X for ground applications.

For the Texas scenario the results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for freshwater fish for aerial applications, by magnitudes of 1.7X, 8.5X, and 17X. Ground applications exceed acute risk, restricted use, and endangered species LOCs by 1.9X, 9.4X, and 19X respectively. Chronic risk LOC is not exceeded for freshwater fish for aerial and ground applications.

(2) Freshwater Invertebrates

The acute and chronic risk quotients for freshwater invertebrates are listed in tables 38 and 39.

Table 38. Risk Quotients (RQs) for Freshwater Invertebrates Based On a *Daphnia magna* EC_{50}/LC_{50} of 5.83 and a *Daphnia magna* NOEC/MATC of 3.57/5.24 in the State of for Mississippi

Site/ Application Method and Rate (lb ai/a)	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 21-Day Average	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/aerial 0.4	5.83	3.57/5.24	10.98	8.99	1.88	2.52/1.72
Cotton/ground 0.4	5.83	3.57/5.24	12.68	9.89	2.18	2.77/1.89

Table 39 . : Risk Quotients (RQs) for Freshwater Invertebrates Based On a *Daphnia magna* EC_{50}/LC_{50} of 5.83 and a *Daphnia magna* NOEC/MATC of 3.57/5.24 in the State of Texas

Site/ Application Method and Rate (lb ai/a)	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 21-Day Average	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/aerial 0.4	5.83	3.57/5.24	6.35	3.84	1.09	1.08/0.73
Cotton/ground 0.4	5.83	3.57/5.24	7.01	3.58	1.20	1.00/0.68

The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for freshwater invertebrates for aerial applications by a magnitude of 3.76X, 18.8X, and 37.6X, respectively for Mississippi. Risks posed by ground applications are exceeded by magnitudes of 4.3X, 21.8X, and 43X, respectively. The Mississippi chronic risk LOC is exceeded for freshwater invertebrates by a magnitude of 1.7X for aerial applications and 1.9X for ground applications.

For the Texas scenario the results indicate that acute risk, restricted use, and endangered species LOCs are exceeded for freshwater invertebrates by magnitudes of 2.18X, 10.9X, and 21.8X respectively for aerial applications. Risks posed by ground applications exceed acute risk, restricted use, and endangered species LOCs by 2.4X, 12X, and 24X respectively. Chronic risk LOC is <u>not</u> exceeded for freshwater invertebrates for aerial and ground applications in Texas.

(3) Estuarine and Marine Animals

The acute and chronic risk quotients for two estuarine and marine organisms are listed in table 40 and 41.

Table 40. Risk Quotients (RQs) for Estuarine/Marine Organisms in the State of Mississippi

Site/ Application Method and Rate (lb ai/a)	Species	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 21-Day Average	EEC 56-Day Average	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/ aerial 0.4	Mysid	2.03	0.172	10.98	8.99	8.63	5.41	52.27
	Sheepshead Minnow	60.2	-	10.98	8.99	8.63	0.18	-
Cotton/ ground 0.4	Mysid	2.03	0.172	12.68	9.89	9.55	6.25	57.50
	Sheepshead Minnow	60.2	-	12.68	9.89	9.55	0.21	-

Table 41. Risk Quotients (RQs) for Estuarine/Marine Organisms in the State of Texas

Site/ Application Method and Rate (lb ai/a)	Species	LC_{50} (ppb)	NOEC/ MATC (ppb)	EEC Initial (ppb)	EEC 21-Day Average	EEC 56-Day Average	Acute RQ (EEC/LC_{50})	Chronic RQ (EEC/NOEC or MATC)
Cotton/ aerial 0.4	Mysid	2.03	0.172	6.35	3.84	3.58	3.13	22.33
	Sheepshead Minnow	60.2	-	6.35	3.84	3.58	0.11	-
Cotton/ ground 0.4	Mysid	2.03	0.172	7.01	3.58	3.24	3.45	20.81
	Sheepshead Minnow	60.2	-	7.01	3.58	3.24	0.12	-

The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for marine/estuarine invertebrates for ground applications by a magnitude of 12.5X, 62.5X, and 125X, respectively for Mississippi. Risks posed by aerial applications are exceeded by magnitudes of 10.8X, 54.1X, and 108.2X, respectively. Restricted use and endangered species LOCs are exceeded for marine/estuarine fish for ground applications by magnitudes of 2.1X and 4.2X, respectively. Risks posed by aerial applications are exceeded by magnitudes of 1.8X and 3.6X, respectively. The Mississippi chronic risk LOC is exceeded for marine/estuarine invertebrates by a magnitude of 52.27X for aerial applications and 57.5X for ground applications.

The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for estuarine shrimp for ground applications by magnitudes of 6.9X, 34.5X, 69X, respectively. Aerial application LOCs for shrimp are exceeded by magnitudes of 6.26X, 31.3X, and 62.6X, respectively. The restricted use and endangered species LOCs are exceeded for estuarine fish by magnitudes of 1.2X and 2.4X, respectively for ground and aerial applications. The chronic risk LOC is exceeded for estuarine shrimp by magnitudes of 22.8X and 22.3X for ground and aerial applications, respectively.

(d) Exposure and Risk to Nontarget Plants

As explained under Section 2.7.c. above currently, terrestrial and aquatic plant testing is not required for insecticides or other classes of pesticides, except on a case-by-case basis (e.g. labeling bears phytotoxicity warnings; incident data or literature which demonstrate phytotoxicity). Hence, terrestrial and aquatic plant risk assessments will not be accomplished at this time.

(e) Endangered Species

Endangered species LOCs are exceeded for acute risk to avian species in short and tall range grass, broadleaf plants/forage/ small insects and seeds/fruits/pods/large insects at both single and multiple applications at 0.35 lbs ai/acre. When evaluating acute risk using the LD_{50}/day model, endangered species LOCs are exceeded in all foraging categories at 3 applications of 0.35 lbs ai/acre. When a single 0.35 lbs ai/acre application is made endangered species LOCs are exceeded in all categories except for a 1000g bird foraging on large insects, seeds, pods and fruit. Endangered species LOCs are exceeded for acute risk to mammalian species in all size and foraging categories except for granivorous mammals at both singe and multiple applications of 0.35 lbs ai/acre.

At the lowest label recommended single application rate of 0.09 lbs ai/acre endangered species LOCs are exceeded for avian species, when based upon the Mallard LC_{50} in all forage categories.

At the lowest lable recommended single application rate of 0.09 lbs ai/acre endangered species LOCs are exceeded for 13 and 35 g mammalian herbivores and insectivores in all forage groups except the large insect/seeds/pods/fruits category. Multiple applications enlarges the group to inclued 1000 g mammals in the same groups. No LOCs are exceeded for insectivorous mammals when either single or multiple applications are made at 0.09 lbs ai/acre.

Endangered species LOCs are exceeded for both aerial and ground application methods for freshwater aquatic vertebrate and invertebrate species, and estuarine and marine species at application rates of 0.4 lbs ai/acre.

The Endangered Species Protection Program is expected to become final in the future. Limitations in the use of AC 303,630 will be required to protect endangered and threatened species, but these limitations have not been defined and may be formulation specific. EPA anticipates that a consultation with the Fish and Wildlife Service will be conducted in accordance with the species-based priority approach described in the Program. After completion of consultation, registrants will be informed if any required label modifications are necessary. Such modifications would most likely consist of the generic label statement referring pesticide users to use limitations contained in county Bulletins.

(f) Major Data Gaps

Terrestrial. Because no definitive terrestrial field study has been submitted, the registrant is still required to submit a terrestrial field test using the active ingredient AC 303,630. The EEB requested a field study November 4, 1994, because the active ingredient is in a new class of pesticides (pyrroles) and has a reported new mode of action (uncouples oxidative phosphorylation in the mitochondria).

Contradictory data make the submission of a well designed and conducted field study critical to evaluating potential ecological effects. Because of the persistence in natural environments, long term accumulation in soils and sediment make chronic toxicity to birds and other wildlife probable. The effects observed in laboratory avian reproductive tests, i.e. reduced egg production, hatchability and nestling survival, make it highly probable population effects will occur. For this reason, a field study should emphasize avian reproductive effects.

Aquatic. A major unanswered question is the bioavailabililty of AC 303,630 to benthic organisms. In order to answer this vital question, sediment toxicity testing is required. Additional higher tier testing, such as a mesocosm study may be required after the results of the sediment study are analyzed. The purpose of such a study would be to clarify the long-term effects from the use of a highly persistent chemical when it reaches the aquatic environment.

Invalid acute and/or chronic aquatic tests which need to be repeated are listed in the table below.

GUIDELINE #	STUDY	REASON
72-1	LC_{50} Rainbow trout	**Optional.** To be repeated at the discretion of the registrant (see study description) . Invalid test due to failure to measure test concentration on photolytic degradate (CI 357,806). The purported LC_{50} of 2.6 ppb implies that this compound is more toxic than the parent.
72-3	EC_{50} Oyster Shell Deposition Study	Invalid study due to inadequate shell growth in controls (MRID 438870-08) Since an embryo-larvae study was not conducted, this study must be repeated.
72-4	Sheepshead minnow Early life (marine/estuarine)	Invalid study due to low Dissolved Oxygen level throughout the experiment. The required fish full life-cyle study listed directly below would satisfy this requirement.
72-5	Sheephead minnow Life-cycle Study	The EEC is greater than 0.1 of the NOEL in the fish early life and invertebrate Life-Cycle study.

It should be noted that limited tests were performed on two different degradates of AC 303,630. The major degradate CL 312,094 (the desbromo derivative of AC 303,630), was tested only on bluegill sunfish. The photolytic degradate in water, CL 357,806, however, was tested on rainbow trout and *Daphnia magna*. The purpose of testing these two degradates on different species was not revealed in any of the material submitted. The registrant should explain this selectivity before the EEB considers additional testing on degradates.

The acute LC_{50} of the major degradate CL 312,094 was greater than 928 ug/L, the highest concentration tested. Since the toxicity of this degradate is much lower than the parent compound, additional data will not be required at this time.

(g) Environmental Risk Characterization and Summary of Ecological Concerns

Serious environmental concerns are raised with the proposed registration of AC 303,630. All indications are that at maximum application rates both acute and chronic effects will occur in the faunal communities associated with cotton fields and adjacent habitats. It is imperative the registrant submit a well designed and conducted terrestrial field study and sediment toxicity study.

(1) General

Numerous core environmental fate and ecological effects studies clearly raise serious concerns about the proposed reg yistration of AC 303,630. Comparisons with other classes of chemicals must be made judiciously and in the proper context.

** As the first of a new class of pesticides, any comparisons of effects with other classes of insecticides with an established history of use (e.g. organophosphates, carbamates, pyrethyroids, organochlorines) are tenuous and require careful interpretation based on all environmental fate (exposure) and toxicological characteristics.

** At a time when the Agency is actively soliciting "safer" pesticides, AC 303,630 exhibits 1) persistence characteristics not seen since the introduction of organochlorine compounds, and 2) a high degree of acute and chronic toxicity to terrestrial and aquatic organisms. Because of its persistence, the probability of some environmental build-up and significant levels of continous exposure in soil, surface water and sediments is high. Compounding these characteristics, structurally similar metabolites or degradates are also persistent (mineralization is not appreciable) and variably toxic, in some cases more so than parent.

(2) Terrestrial Risks

The application pattern for the proposed registration of AC 303,630 on cotton is conducive to both acute and chronic exposure. The projected use would allow applications during most of the growing season. Earliest applications have the lowest application rates, ranging from 0.09 to 0.16 lbs ai/acre to control seedling pests such as thrips. Mid-season applications range from 0.12 to 0.28 lbs ai/acre and target spider mites, armyworms and bollworms. Late season pests which affect the boll receive the highest concentrations of insecticide, from 0.2 to 0.35 lbs ai/acre. This gradual increase in active ingredient as the growing season progresses may be the most important factor in characterizing the risk associated with AC 303,630.

Early season applications are made with the lowest application rates and coincide with peak nesting activity. Although lower application rates will not eliminate the long term risks, it should lower the potential for avian reproductive effects. The highest application rates occur after the majority of nesting activity has ceased. **However, even the lowest application rate exceeds the threshold for anticipated chronic effects by 3 to 43 times.** Prolonged exposure to dietary concentrations slightly greater than 0.5 ppm could result in reproductive effects.

AC 303,630 appears to be a rapid killer in acute exposure situations. The majority of deaths reported in acute studies occurred within 3 days. At the maximum recommended application rates the probability of lethal response is high. Evaluation of acute risk quotients indicates a single application could not exceed 0.0035 lbs/acre if the goal was to protect the most

sensitive endangered avian species from acute exposure. Considering the long half-life of the chemical, protection of endangered species from acute toxicity in a multiple application situation would require reducing the application another 3 times.

Long term exposure leads to reduced egg production, reduced hatching success and reduced nestling survival in the avian species tested. **The fact that these effects occur at test doses above 0.5 ppm (NOEL) active ingredient in the diet make AC 303,630 one of the most chronically toxic pesticides to avian species that EEB has evaluated.** Given the persistence of the compound and multiple applications, the probability of chronic exposure is great and concentrations could remain at toxic levels indefinitely.

The registrant submitted estimates of residues on avian food items (MRID #434928-14). Within 24 hours post application AC 303,630 concentrations of 5.7 ppm were found in live insects collected within the cotton fields. **Risk qoutients (based upon both the mallard LC_{50} and LD_{50}s/day for 20 g birds) calculated on residues levels of this magnitude exceed the LOCs for acute high risk, restricted use and endangered species. Foraging adults could be killed outright. Mortality of young reared near treated fields may occur by death of the parent and subsequent starvation of the nestlings or by nestlings being fed contaminated insects.** It should be noted that in this study the registrant collected only live insects, those which did not receive a lethal dose of AC 303,630. It is not unreasonable to assume foraging birds would select for moribund or dead insects, those with higher AC 303,630 concentrations.

The registrant also submitted a study demonstrating repellency of AC 303,630 treated feed to the Northern Bobwhite (MRID #438870-07). Although not stated, the conditioned aversion the quail showed to treated feed might have been related to the sickness the birds experienced after ingestion. It not uncommon for birds foraging for nestling food items to simply take invertebrates into their beak, never swallowing the insect, and returning to the nest. In this instance, repellency may not reduce the amount of contaminated forage an adult will collect. Nestlings may be forced to eat contaminated items by the parent or may consume them due to a lack of anything else to eat. As shown in the repellency study, juveniles were more sensitive to AC 303,630.

The registrant has demonstrated the low potential for ill effects via dermal exposure to the chemical after it has dried on vegetation. No signs of toxicity were observed in quail which were held in cages containing treated cotton plants. The low potential for dermal exposure is also shown for rabbits in studies submitted for the EPA Health Effects Division. This however does not eliminate the possibility of animals in treated fields becoming intoxicated through other routes of exposure such as oral. The

impact to animals receiving the compound during the application process in unknown.

The cotton plant itself is not known to be used for food by wildlife. However, Gusey and Maturgo (1973)[7] listed a wide variey of birds and mammals using cotton fields for feed, nesting, cover, brood-rearing, and loafing. The registrant submitted the results of an avian census in and near cotton fields in Arizona, Texas and Mississippi/Lousiana. The most common species observed were the blackbirds, swallows and other passerines. Fields adjacent to riparian zones had the highest diversity and total number of birds. The highest avian use of cotton fields occurred during boll development and prior to harvest. Other censuses submitted by the registrant have shown the Mourning dove to be a frequent visitor to cotton fields. Early season applications occur when the cotton canopy is sparse, which would allow more of the chemical to settle directly on the soil. Because the dove is one of the earliest birds to nest in the spring and they gleen food items from the ground, it may be very susceptible to exposure even at early season application rates.

(3) Aquatic Risks

Cotton is grown as a major cash crop near aquatic habitats along all the Gulf coast states as well as the bayou regions and all the tributaries of the Mississippi River. To a lesser extent, cotton is grown in the riparian regions of the Southwest and California. The use of a pesticide with toxicity and risk profiles like AC 303,630 (chlorfenapyr) on cotton is predicted to cause significant adverse effects in aquatic communities.

The exposure models predicted maximum initial residues of AC 303,630 to be as high as 13 ppb (ug/L) in the water column after off-target entry from spray drift and surface runoff. Due to the high persistence of the chemical, the models predict that significant amounts of residues will remain in the water column for a long time. It is also persistent in sediments. In a microcosm study fish exposed to directs sprays of at least 11.3 ug/L were killed within a few days. Also, decreased abundances of several invertebrate taxa, which are a food source for fish, were also observed. **The data and risk profiles taken together indicate a high potential for fish kills and depletion of invertebrate communities to occur in waterways near fields treated with AC 303,630. Depletion of invertebrates in field studies with other insecticides caused decreased growth in fish. This effect is also likely to occur in aquatic habitats from use of AC 303,630.**

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[7] Gusey W. F. and Z. D. Maturgo. 1974. Wildlife utilization of Croplands. Environmental Affairs, Shell Oil Company, Houston, TX

Additionally, economically important organisms such as shrimp can be expected to be affected in estuaries near to where cotton is cultivated. These shrimp breed offshore and may be particularly at risk because they migrate for miles up the streams that feed the estuaries. As AC 303,630 can typically be applied at any time during the cotton growing season, it is likely that shrimp migrations will coincide with applications of AC 303,630.

A major unanswered question is the bioavailabililty of AC 303,630 to benthic organisms. In order to answer this vital question, sediment toxicity testing is required. Additional higher tier testing, such as a mesocosm study may be required after the results of the sediment study are analyzed. The purpose of such a study would be to clarify the long-term effects from the use of a highly persistent chemical when it reaches the aquatic environment.