Calculating Avian and Mammalian Dietary Exposure Levels

In preparation of their own risk assessment (MRID 444779-01), the registrant presented field and literature data on the species of birds that occur in cotton fields. The species selected for the risk assessment include Carolina wren, white-eyed vireo, northern cardinal, blue grosbeak, mourning dove, red-winged blackbird, and mallard duck. The first six species listed were selected from an exhaustive list of species known from the literature and empirical observation data of bird species in cotton fields and for which there existed published data on dietary characteristics. The mallard duck was considered a migratory transient, stopping to rest but not necessarily feeding in cotton fields. For the purposes of this risk assessment, EFED used the same species (with the exception of the mallard duck) as surrogates for birds using cotton fields. The mallard duck was excluded from the surrogate species list as it is expected that exposure for non-feeding birds in cotton fields would be minimal.

With respect to mammalian receptors, no intensive census of species use of cotton fields has been submitted by the registrant. However, trapping and carcass data from MRID 444526-16 indicate that a number of rodent species occur in cotton fields. Trapping data from MRID 444526-16 revealed that *Peromyscus* species accounted for 7 of 11 small mammals recovered. From the data in MRID 444525-16, and the availability of biological data on the closely-related deer mouse (*Peromyscus maniculatus*), EFED selected the white-footed mouse (*Peromyscus leucopus*) as a surrogate for small mammals known to occur in cotton fields.

Pastorok et al. (1996)[1] has summarized a basic chemical intake model for wildlife species to calculate a dietary exposure dose for a given chemical of concern and a given receptor species. The general formula for this basic chemical intake model is as follows:

$$IR_{chemical} = \sum (C_i)(M_i)(A_i)/W$$

where:

$IR_{chemical}$ is the species-specific total rate of intake of chemical by ingestion (mg/kg-bw/day)

C_i is the chemical concentration in medium I (mg/kg) (soil and dietary components)

M_i is the rate of ingestion of medium I (kg/day)

A_i is the gastrointestinal absorption efficiency of the chemical in medium I relative to absorption in laboratory toxicity tests

W is the body weight of the receptor species (kg)

This basic model was used to estimate oral dose exposures for the six surrogate avian species and one mammalian species selected for risk assessment. Because of a lack of data regarding gastrointestinal absorption efficiencies both in the available toxicity studies and for free-living receptors, the absorption efficiency (A_i) for all species was conservatively assumed to be 100%

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[1]Pastorok, R.A., M.K. Butcher, R.D. Nielsen. 1996. Modeling wildlife exposure to toxic chemical; trends and recent advances. Human and Ecological Risk Assessment 2:444-480.

or 1.0. The registrant has presented a kinetics-based argument that chlorfenapyr in soils is essentially non-bioavailable as compared to chlorfenapyr associated with dietary items (MRID 444779-01). In addition, supplemental information (Ahmed 1998b)[2] has been submitted by the registrant that suggests that aged chlorfenapyr residues are of low extraction efficiency under acidic conditions approximating the avian gut. However, the soil extractions for this supplemental study were performed on samples collected from the field 180 days post-treatment and stored for almost 4 years. The registrant has cited a number of studies in the above submissions that suggest that the sorption affinity of organic compounds to soils increases as residues age. Therefore, the 180-day sample extractions on samples collected almost 4 years earlier have little applicability to the question of the bioavailability of chlorfenapyr from soil within the comparatively short 4-week post-application exposure period modeled in this risk assessment. While there exists the possibility for differential bioavailability between diet and soils, there are insufficient data relative to chlorfenapyr absorption efficiency by avian and mammalian species in any medium to develop a quantitative relationship between media. For soil exposure, EFED has assumed 100% bioavailability but has chosen a very low incidental soil ingestion rate for each receptor species assessed.

The model used for estimating oral dose exposure for each species was based on a simple four-component model that considered incidental ingestion of soil and consumption of invertebrates (i.e., larval armyworms), seeds, and fruit or vegetative fodder. The equation describing this model is as follows:

exposure mg/kg-bw/day =

$$\frac{(C_{insect}\ \text{mg/kg})(\text{kg insect/day}) + (C_{seed}\ \text{mg/kg})(\text{kg seed/day}) + (C_{fruit\ or\ plant}\ \text{mg/kg})(\text{kg fruit or plant/day}) + (C_{ss}\ \text{mg/kg})(\text{kg soil/day})}{\text{kg body weight}}$$

where: C_{insect}, C_{seed}, and C_{ss} are the estimated concentration in insects, seeds, and soils (0-3 cm) as reported in Tables 28, 29, 31. C_{fruit} is the concentration of chlorfenapyr residue in fruit of non-target plants of treated fields. No data have been submitted for concentrations in non-target fruits, therefore C_{fruit} is estimated by the corresponding C_{seed} value from Table 28. C_{plant} is the concentration of chlorfenapyr in other vegetative forage for small mammal receptors as estimated by the cotton plant vegetative residue data from Table 30.

kg insect, seed, fruit, or plant is the mass in daily diet attributable to the component for each species as a function of allometric relationships for field metabolic rate, food item gross energy, and assimilation efficiency from USEPA (1993)[3] (See Tables 32 and 33)

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[2]Ahmed, Z. 1998b. Memorandum (with attachments) from Zareen Ahmed, Product Registrations Manager, American Cyanamid to Ann Sibold, Registration Division, USEPA/OPP, May 15, 1998.

[3]USEPA. 1993. Wildlife Exposure Factors Handbook. Chapter 4. EPA/600/R-93/187b, Office of Research and Development, United States Environmental Protection Agency.

kg soil is the product of the total dietary intake of the organism (Tables 32 and 33) and an assumption of incidental soil ingestion at a rate of 2% of dietary intake. This function is based on the lowest fraction of diet recorded by Beyer et al. (1993)[4] for avian species and for the meadow vole and is not conservative.

kg body weight is the average body weight of adult birds from Dunning (1984)[5] or average adult bodyweights of mammals (EPA 1993)[6]

Table 32 presents the bodyweights, and feeding characteristics for each of the six surrogate avian species. Table 33 presents similar data for the white-footed mouse.

Tables 34 through 40 present the daily oral dose estimates for each avian and mammalian species for all potential application senarios.

Aquatic Organism Exposure Assessment

In an earlier EFGWB assessment, chlorfenapyr was 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. 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 (PRZM2, version 2.3) was used to simulate pesticides in field runoff. The Exposure Analysis Modeling System (EXAMS II) was used to simulate pesticide fate and transport in an aquatic environment (1-hectare body of water 2-meters deep receiving runoff from 10-hectare field).

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

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 half-life	15 days

The EECs generated from the EXAMSII/PRZM2 runoff model were presented in earlier risk assessments and are not presented here. 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 high level of cotton production in the state.

Subsequent to this early EXAMS/PRZM2 assessment, additional environmental fate data have

[4]Beyer, W.N., E.E. Connor, S. Gerould. 1994. Estimates of soil ingestion by wildlife. J. Wildl. Manage. 58:375-382.

[5]Dunning, J.B. 1984. Bodyweights of 686 Species of North American Birds. Western Bird Banding Association Monograph 1.

been made available to EFED and significant updates to the PRZM model have been completed. Review of these new data and the advent of concerns regarding potential effects on sediment organisms prompted EFED to re-evaluate the potential for chlorfenapyr to enter and persist in surface water and sediments. To further refine the chlorfenapyr exposure assessment, the Multiple Scenario Risk Assessment Tool (MUSCRAT) was used. MUSCRAT is designed to give a spatial and temporal distribution of EEC's for each of the predominant USDA Census of Agriculture regions (4, 6, 7, 11) in which cotton is grown and utilizes the updated version of the PRZM model. (Note: MUSCRAT more precisely quantifies the upper 90th percentile confidence bound previously assumed by the PRZM model, but does not change *individual* PRZM model outputs. However, MUSCRAT has not been adopted as standard practice for EFED risk assessment. MUSCRAT was used in this case to compare results with the modeling submitted by the registrant in MRID 444526-02). The EEC's presented graphically by the MUSCRAT program are the one-in-ten year return period concentration values for all of the cotton capable acreage in the four main growing regions.

The process used for using the MUSCRAT program was as follows:

1. Four USDA agricultural regions were selected for modeling, that represented more than 99 percent of cotton grown in the United States.

2. A series of cotton-growing sites were selected from each region to encompass the distribution of erosion and run-off vulnerabilities.

3. A PRZM/EXAMS modeling run (36-year) was performed on each selected site.

4. A 1-in-10 year exceedance probability set of concentrations (water column and sediment) was calculated from the PRZM/EXAMS run on each site.

5. These 1-in-10 year exceedance probability values were then combined for each site and region and the 90th percentile of that distribution of values was selected to represent the EECs for this assessment.

MUSCRAT inputs selected for this simulation by EFED are as follows:

Aerobic Soil Metabolic Half-life	496 Days
Aerobic Aquatic Metabolic Half-life	278 Days
Anaerobic Aquatic Metabolic Half-life	412 Days
K_{oc}	11,950
Solubility	0.12 mg/L
Molecular Weight	407.6
Vapor Pressure	4.0E-8
PRBEN	default (0.5)

Sediment input values were normalized for sediment Total Organic Carbon (TOC). Since the acute sediment toxicity study submitted did not report the TOC, a 6% value was used. This was derived under the assumption that the standard organic carbon in organic matter is about 58.8%. Since the organic matter content of the spagnum peat was 10%, the resulting TOC was calculated to be 6%.

The concentrations for the interstitial water (pore water) were not modeled because the moisture content of the sediment was not reported in the sediment toxicity study and therefore comparisons for the purposes of risk assessment were not possible.

The values for the MUSCRAT-predicted concentrations in the water column and sediment are summarized in Table 41. Also included in the table, for reference purposes, are water column concentrations calculated using EFED's standard cotton modeling scenario and PRZM3.2/EXAMS. As can be seen from this table, chlorfenapyr concentrations estimated for water and sediment are higher using the MUSCRAT program than those estimated with PRZM 3.1.2/EXAMS for USDA regions 4,6, and 7. Only in USDA Region 11 (California) are the MUSCRAT concentrations lower than the PRZM 3.1.2/EXAMS, though the difference is not great. Therefore, the MUSCRAT concentrations were selected as the generally more conservative concentrations for risk assessment purposes and represent a general methodology consistent with that used by the registrant in MRID 444526-02.

RISK ASSESSMENT and 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.

$$\text{risk quotient} = \frac{\text{exposure level}}{\text{toxicological endpoint}}$$

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. For the purposes of this risk assessment the NOEC is used as the ecotoxicity test value in assessing chronic effects to fish and aquatic invertebrates.

Risk presumptions, along with the corresponding risk quotients and levels of concern, are listed in Table 42.

Risk Assessment for Nontarget Terrestrial Animals

Avian Acute and Chronic Risks

In this risk assessment, risk quotients were calculated on predicted daily oral exposures to parent chlorfenapyr, which were based on measured ("real") residue data for avian food items. In order to provide the reader with an idea of the relative risks for all application scenarios, risk quotients were calculated for each scenario.

Daily risk quotients reflect the ratio of daily oral dose to toxicological endpoint. For the purposes of this risk assesment all units (both oral dose and toxicological endpoint) have been normalized in terms of mass of chlorfenapyr per receptor organism body mass. This normalization process is important to note because it differs from the dietary concentration-based risk assesment practice employed in previous EFED risk assessments for chlorfenapyr and currently used in the registrant's avian risk assessment. The approach is intended to account for the effect of metabolic requirements on the ingestion of food per unit body mass. The proportion of body mass ingested as food increases as the mass of the bird species decreases. The net effect is that for any given dietary concentration of a pesticide, smaller birds will receive higher oral doses than larger birds per unit of bodyweight. It should be noted that this normalization process does not take into account the potential for higher metabolic rates to influence the sensitivity of a given avian species. In cases where metabolic activation is required for toxic action (i.e., the mixed function oxidase activation of chlorfenapyr to a toxic degradate), higher metabolism rates may result in increased sensitivity. Finally, this risk assessment does not consider potential interactions with other pesticidal chemicals used on cotton fields. Both the labels for Pirate and Alert products allow for tank mixes, and the Alert label indicates that repeated uses of the product should be interspersed with other pesticides of different modes of action. The lack of data concerning what other chemicals could be included in tank mixes or interspersed with chlorfenapyr applications and the paucity of toxicity data concerning the effects of mixtures precludes a quantitative assessment of increased risk associated with multiple-chemical exposures.

Because of the large number of risk quotients calculated for this risk asessment, Tables 43 through 45 present all risk quotients in tabular form by receptor species. To facilitate a more rapid evaluation of this information, Figures 4 through 9 present a comparison of toxicological endpoints with exposure for each of the six selected avian species known to occur in cotton fields and each basic chlorfenapyr application scenario. For the Figures 4 through 9, the single oral dose and the subacute dietary toxicity endpoints were multiplied by a factor of 0.5 to be consistent with the EFED high risk level of concern (RQ=0.5). From these figures it can be seen that all application scenarios result in daily oral dose level that exceed the chronic avian reproduction endpoint of 0.059 mg/kg/d (based on the NOEC 0.5 mg/kg diet for mallard ducks) for at least 14 days. If more than two applications of chlorfenapyr are made, the exposure models suggest that dietary exposure may exceed the chronic avian reproduction endpoint for a minimum of another 14 days (the duration of the exposure model was 28 days total, residue data permitting). In addition, the subacute lethal oral dose endpoint and/or the acute single oral dose lethal endpoint, adjusted for a high risk level of concern, are exceeded by the oral dose estimates for multiple days for all application rates for every modelled avian species.

In all modelled species for all application scenarios, for all time periods, exposures exceed chronic risk level of concern (1.0) by factors exceeding an order of magnitude. In addition, exposures exceeding acute endpoints result in RQs that exceed the high acute risk (0.5), restricted use (0.2), and endangered species (0.1) levels of concern. Tables 43 through 45 indicate that the high acute risk level of concern is exceeded for multiple days for every application scenario in all species but the mourning dove. For this species the lowest application scenario 0.075 lb ai/A does not trigger the acute high risk level of concern, but does trigger the restricted use level of concern at times of application.

These findings suggest that chlorfenapyr applications to cotton, consistent with labeled rates, number of applications, and non-conservative application intervals (7 days versus a minimum label of 5 days) pose acute and chronic risks to avian species known to utilize cotton fields. Based on the very high RQs encountered for reproductive effects throughout the modelled 28-day period, there appears to a be an extensive opportunity for avian species to be exposed to chlorfenapyr in the diet for sufficiently long periods of time and at more than sufficient dose levels to cause reproductive effects. In all application scenarios, exposures may be considered to represent high acute risks for most avian species modelled.

Mammalian Acute and Chronic Risks

In this risk assessment risk quotients for the mamalian receptor organism were calculated and are presented in a manner consistent with the avian receptors.

Table 46 presents the RQs for the selected mammalian receptor (white-footed mouse) for all treatment scenarios. Figure 10 presents a comparison of the estimated oral exposure levels with mammalian toxicity endpoints. For the purposes of Figure 9, the single oral dose and subchronic toxicity endpoints have been multiplied by a factor of 0.5 to be consistent with the EFED high risk level of concern (RQ=0.5).

Estimated oral exposures exceeded the chronic toxicity threshold at all application rates for multiple days. The acute single oral dose toxicity endpoint was not exceeded by the exposure estimates. The restricted use level of concern (0.2) is exceeded by exposures immediately following application for the 0.25 and 0.3 lb ai/A application rates. The endangered species acute level of concern (0.1) is exceeded by single oral doses for one or more days at all application rates. The subchronic oral dose toxicity endpoint is exceeded by oral dose estimates for all application scenarios for one or more days, and the restricted use (0.2) and endangered species (0.1) levels of concern are exceeded frequently over the 28-day modelling period for all application scenarios.

These results suggest that small mammals using cotton fields as sources of dietary materials are at risk for reproductive impairment and mortality**.**

Risks to Beneficial Insects

Currently, EFED has no procedure for assessing risk to nontarget insects. Results of acceptable studies are used for recommending appropriate label precautions. The high toxicity of chlorfenapyr to honeybees suggests a concern that chlorfenapyr will adversely impact beneficial insects. In particular, early applications of chlorfenapyr (i.e., mite control) at times of cotton inflorescence may adversely affect populations of pollinators.

Risk to Nontarget Aquatic Animals

The non-target aquatic risk assessment considers MUSCRAT-calculated EECs derived for the USDA Agricultural Regions 3,4,7, and 11.

Freshwater Fish

Acute and chronic risk quotients for freshwater fish are listed in Table 47. The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for freshwater fish for aerial applications in regions 3, 4, and 7. The chronic risk LOC is not exceeded for freshwater fish when the 60-day EEC is employed. However, the finding that chronic risks are not anticipated is of low confidence because of the limited availability of chronic effects testing data in freshwater fish, and the persistence of the compound.

Freshwater Invertebrates

The acute and chronic risk quotients for freshwater invertebrates are listed in Table 48. The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for freshwater invertebrates for aerial and ground applications in Regions 4, 6, and 7. Acute restricted use and endangered species LOCs are exceeded for Region 11. Chronic risk LOC are not exceeded for freshwater invertebrates.

Estuarine and Marine Animals

The acute and chronic risk quotients for two estuarine and marine organisms are listed in Table 49. The results indicate that acute high risk, restricted use, and endangered species LOCs are exceeded for marine/estuarine invertebrates for aerial and ground applications for all Regions. Only endangered species LOCs are exceeded for marine/estuarine fish. Chronic LOCs for marine/estuarine invertebrates are exceeded by factors ranging from 6.8X to 15.9X. Chronic LOCs for marine fish can not yet be determined since the fish life-cycle study (MRID 443648-02) has been determined to be Invalid and must be repeated.

Sediment-Dwelling Organisms

Acute risk quotients for the freshwater amphipod *Hyalellea azteca* are listed in Table 50. The results indicate that acute high risk, restricted use, and endangered species LOCs are not exceeded for freshwater amphipods for aerial and ground applications in Regions 4,6,7, and 11.

Although the marine amphipod study has yet to be reviewed and validated, the preliminary toxicity results (not fully reviewed by EFED) submitted by the registrant show a measured 10-day acute LC_{50} of 0.18 mg/kg for the marine amphipod *Leptocheirus plumulosus*.

Table 52 presents preliminary Risk Quotients for sediment-dwelling marine amphipods. The results submitted by the registrant suggest that acute high risk, restricted use, and endangered species LOCs are exceeded. The acute high risk level of concern is exceeded by factors ranging from 4.7 to 10.8 for aerial and ground applications in Regions 4, 6,7, and 11.

Risk to Nontarget Plants

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.

Endangered Species

Assessment of potential risks to avian and mammalian endangered species is limited by the receptor species selection process incorporated into this risk assessment. Direct application of the risk quotients calculated for avian receptors should be limited to endangered species of similar bodyweights and similar dietary habits. To this end, the calculated risk quotients suggest a potential for acute and chronic risks to endangered avian species that may (if any) utilize cotton fields. Similarly, aquatic EECs exceeding the endangered aquatic organisms levels of concern suggests the potential for run-off from cotton fields treated with chlorfenapyr to adversely affect endangered aquatic organisms. A listing of endangered animals potentially at risk from chlorfenapyr exposure in the cotton-growing areas is listed in Appendix A.

The Endangered Species Protection Program is expected to become final in the future. Limitations in the use of chlorfenapyr 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.

Avian Risk Characterization

This risk assessment has expanded upon the estimates of dietary exposure for avian and mammalian receptor organisms through the incorporation of measured field residues not used in previous assessments of the risks of chlorfenapyr use on cotton. In addition, the risk assessment has moved from using generalized avian receptors to a consideration of avian census data and subsequent inclusion of avian species demonstrated to occur in and around cotton fields. Biological information for these identified representative avian species was considered in the construction of species-specific models of dietary exposure. Both dietary exposures and toxicological endpoints were expressed in terms of daily oral doses (mg/kg-bw/day) so that comparisons of exposure and toxicity could account for differences between food intake for receptor species and laboratory test species.

The results of the avian risk assessment strongly suggest that mortality of a number of bird species, with varying feeding strategies, can occur at numerous time periods over the course of cotton field treatment. In addition, the reproductive toxicity at very low exposure levels compared to measured residues in avian food items suggests that exposure opportunities within cotton fields are of sufficient magnitude and duration to pose important toxicological risks to the reproductive success of avian species.

Mortality and reproductive impairment of survivors pose important risk to the maintenance of viable populations of the avian species assessed in this risk assessment. Because these species are representative of the more than 50 avian species known to occur in and around cotton fields, the potential for adverse population impacts to many avian species from chlorfenapyr exposure is great. Table 51 presents the present trends in breeding bird populations of the avian species used in this risk assessment. These data originate from National Biological Service (Sauer et al. 1997)[6]. All the species included in this risk assessment exhibit downward trends in population in three or more cotton states since 1966. Four of the species (white-eyed vireo, mourning dove, northern cardinal, and red-winged blackbird) showed population declines that were highly statistically significant ($p<0.05$) in three or more states. While these data do not establish causality for population declines (a variety of factors are likely to contribute to population declines), they do suggest that populations of many bird species at a state-wide level of resolution could be sensitive to additional reproductive impairment and reduced survival rates from exposure to chlorfenapyr.

EFED risk concerns are further magnified by the potential to impact single representatives of threatened or endangered avian wildlife. In the case of these stressed populations, mortality and reproductive impairment of individuals could pose threats to the continued survival of a species.

However, EFED recognizes that there are a number of important issues, not addressed in the assessment above, that must be considered in order to further understand the terrestrial risk picture. These include information related to (1) the opportunity for avian species to use dietary resources from treated cotton fields; (2) the timing of application with respect to important life-history periods; (3) the geographical extent of treated cotton; (4) the importance of degradates to exposure and toxicity; (5) the stability of chlorfenapyr in treated fields; (6) application interval effects; (7) the importance of other routes of exposure; (8) species-specific toxicity; and (9) daily dose versus cumulative dose as a predictor of subacute lethal effects. These items are addressed below.

<u>The Impact of Data Concerning Avian Use of Cotton Fields Upon Risk Assessment Outcome</u>

Based on the information summarized in Figures 4 through 9 and Tables 43 through 45, chlorfenapyr poses serious risks for reproduction and acute toxic effects when avian receptors utilize cotton fields as a sole source of diet (i.e., an assumption of 100% diet from cotton fields). It is recognized that an assumption of total dietary resources originating from treated fields is likely to be conservative for long-term exposures associated with observed reproductive efects. However, for acute effects associated with a single oral dose or a few days of dietary exposure, an assumption of 100 percent of the short-term diet originating from a cotton field is not unreasonable.

In the registrant's avian risk assesment, dietary exposures are modified through consideration of

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[6]Sauer, J.R., J.E. Hines, G. Gough, I. Thomas, B.G. Peterjohn. 1997. The North American Breeding Bird Survey results and Analyses. Version 96.4. Patuxent Wildlife Research center, Laurel, MD.

the potential for avian species to use cotton fields as a dietary source. The registrant calculated RQ values for acute, subacute, and reproduction effects based on a high (100% treated field use), medium (50% treated field use), and low (0% treated field use) exposure scenarios. In this approach, exposures to dietary items from treated fields were diluted by corresponding exposures from dietary items foraged from untreated areas surrounding cotton fields. These exposure estimates considered drift-associated contamination. The registrant maintains that avian exposures are closest to the low (0% field use) exposure scenario.

The avian census data of cotton fields in MRID 444642-02 show a total of 54 bird species were identified in Arizona fields; 47 species in Texas fields; and 54 species in Alabama and Mississippi fields. Avian use of Arizona fields ranged from 60% to 69% of observations. In Texas, avian use ranged from 21% to 27% of observations. Use of Alabama and Mississippi fields ranged from 11% to 24% of observations. These avian census data primarily are concerned with presence or absence of species within fields and surrounding buffer. However, there are data for 72 hours of in-field observation of activities within cotton fields. In both Arizona and southeastern cotton field sites, perching and foraging accounted for over 50% of the observations. In Texas, foraging activities comprised 35% of the observations.

In a field study performed to investigate the acute effects of chlrofenapyr treatment of cotton on birds (MRID 444526-16), birds occurred in chlorfenapyr-treated and untreated cotton fields for a total of 13% of the observations made. Chlorfenapyr treatment had no impact on the degree to which cotton fields were used by birds. Observations from this study indicated that cardinals and morning doves were actively seeking patches of weeds within the cotton crop and the authors concluded that the birds were feeding on johnson grass seed dropped on the soil.

In addition to data submitted by the registrant, Gusey and Maturo (1972)[7] report avian foraging (listed as medium and high levels of feeding activity) in cotton fields in Arizona, Arkansas, Georgia, South Carolina, and Texas.

Clearly, a large variety of avian species use cotton fields with appreciable frequency and the uses include a substantial number of foraging behavior observations. However, the available avian census data do not provide sufficient information on the actual proportions of avian diet that originate in cotton fields. It is possible that cotton fields may contribute to avian diets out of proportion to the time birds have been observed in the fields. It is also possible that pest outbreaks in cotton fields may result in higher foraging rates in cotton fields. However, for the purposes of evaluating the impact of data concerning avian use of fields on the outcome of the risk asessment, an assumed minimum proportion of the avian diet of 10% from treated cotton fields was used to test the impacts on calculations of avian chronic RQs. This assumption of 10% is lower than the minimum number of observations of birds in cotton fields (11% reported in MRID 444642-02 and 13% in MRID 44526-16). To simplify the evaluation of avian use effects on risk assessment, no contribution of chlorfenapyr residues from off-field food sources contaminated by drift were included in the re-calculation of avian RQs

[7]Gusey, W.F. and Z.D. Maturo. 1972. Wildlife Utilization of Croplands. Environmental Conservation department, Shell Oil Company, Houston, TX.

Reducing intake of food from treated fields to 10% of the total diet and assuming all off-field dietary residues are zero, effectively reduces all avian reproduction RQ values to 10% of the values listed in this assessment. Even with such a reduction, reproduction effects-based RQs for all but one species (mourning dove) still exceed the chronic level of concern (1) over most, if not all exposure periods modelled, and for all application scenarios except the lowest (0.075 lb ai/A). At the lowest application rate only a few modelled exposure periods exceeded the chronic level of concern for all species except the mourning dove, with no modelled exposure above the chronic level of concern.

It must be stressed that an assumed 10% use factor is lower than all avian census data reported by the registrant and does not account for the presence of chlorfenapyr residues in avian food resources in off-field habitat (the off-field residues are roughly 10% of on-field residues as reported in 444779-01). Actual avian uses of cotton fields and corresponding dietary exposures are likely to be higher.

Based on this analysis, EFED believes that, even with a very limited assumption for dietary exposure (10% avian diet from treated fields and no inclusion of chlorfenapyr contamination from field buffer areas) there remains a high potential for avian reproduction impairment for all application rates. It should be emphasized that, because of considerations of dietary exposures only, the actual exposure of a given bird in a treated cotton field could be higher than estimated in this risk assessment. Although there are limited test data to suggest that dermal exposure, by itself, may not result in toxic body burdens in birds, the combined burdens associated with dermal, inhalation, and drinking water exposures may be important contributions to the daily exposure of birds to chlorfenapyr.

<u>Application Patterns and Corresponding Reproduction Periods for Avian Species</u>

The most sensitive endpoint used in this avian risk assessment is the reproduction NOEC.

Long-term exposure to chlorfenapyr leads to reduced egg production, reduced hatching success and reduced nestling survival in the avian species tested. **The fact that these effects occur at a chlorfenapyr doses above 0.059 mg/kg-bw/day (NOEL) active ingredient in the diet make chlorfenapyr one of the most reproductively toxic pesticides to avian species that EFED has evaluated.**

In an oral presentation by registrant representatives before EPA (April 1998), RQ values above the level of concern for reproduction effects were dismissed by the registrant because the application dates for chlorfenapyr were said to occur after reproduction periods of birds using cotton fields. However, MRID 444779-01 presents information on the reproduction periods of all avian species reported to occur in cotton fields. These reproduction periods are compared to windows of likely chlorfenapyr application to cotton fields. For southern cotton fields (Texas and eastward), 37 species are profiled, with 33 species (89%) exhibiting egg laying and/or nestling periods overlapping with the chlorfenapyr application window. For southern United States cotton areas and windows for application to control mites, 33 species are profiled, with all species' egg-laying and/or nestling periods overlapping the mite-control application window. For western cotton fields, 34 species were profiled, with all species' egg-laying and/or nestling periods overlapping the mite-control application window, and 31 species (91%) with egg-laying and/or nestling periods overlapping the armyworm-control application window.

The registrant, in the April 1998 oral presentation, argued that much of this overlap of reproductive periods with chlorfenapyr application periods is for second and third clutching attempts by birds, and suggested that effects at these periods may not be ecologically important. However, MRID 444779-01 states that standard cotton agricultural practices in the early season (i.e., early cultivation for weed control) are likely to cause a large number of nest failures or abandonment. It is therefore logical to expect that second and third clutch attempts at reproduction would be ecologically significant in the face of early reproduction disruption.

Based on this evaluation of registrant information, there appears to be substantial opportunity for chlorfenapyr applications to occur during critical reproduction events sensitive to chlorfenapyr intoxication. Contrary to the registrant opinion, EFED believes that impairment of second or third reproduction attempts would be of particular ecological importance for avian species adversely affected by early season standard agricultural practices.

Geographical Consideration of Cotton Acreage and Potentially Treated Areas

MRID 444779-01 presents an analysis of the total cotton acreage in the United States and the acreage potentially treated with chlorfenapyr. The registrant estimates that the cotton acres treated will average 6.7 million for budworm and bollworm, 0.88 million for beet armyworm, 0.38 million for fall armyworm, and 1.1 million for mites. This estimate is based on an assumption that chlorfenapyr will only be used in areas of outbreaks of pests resistant to other insecticidal treatments.

What remains an uncertainty associated with the treated acreage is the geographical distribution of treatments in a given year. Cotton production covers approximately 16 states. However, according to MRID 444779-01, predictions of exactly where within these states lepidopteran outbreaks will occur in any given year is quite problematic. If outbreaks of lepidopteran pests of cotton are regional, as suggested by past Section 18 requests, rather than throughout the entire cotton belt in scope, then chlorfenapyr treated acres would be concentrated within infested pockets within a particular region or region(s). Therefore, impacts to avian populations from year-to-year would not be dispersed throughout the cotton belt, but would be concentrated within more limited geographical areas and would enhance the potential adverse impacts of avian reproduction impairment to more localized populations.

Analysis for Parent Chlorfenapyr and Not for Potentially Toxic Degradates In Avian Food Items

MRID 444779-01 states that the chlorfenapyr metabolite AC 303268 is responsible for the parent compound toxicity. MRID 444779-01 also indicates that AC 303268 has been has been identified in chlorfenapyr-exposed tobacco budworms. However, the insect residue data submitted by the registrant (MRID 444642-01) are for analysis of parent chlorfenapyr only.

Available acute avian toxicity data indicate that AC 303268 is of comparable toxicity to parent chlorfenapyr. This risk assessment, based on parent chlorfenapyr residues alone, represents an underestimate of the total toxicological risk associated with chlorfenapyr and toxic metabolites. The lack of information on the concentration of AC 303268 residues in insects precludes an assessment of the extent to which this risk assessment underestimates exposure to important toxic metabolites.

<u>Chlorfenapyr Stability in Soil and Its Implications for Risks From Repeated Annual Use</u>

Laboratory aerobic soil and field dissipation studies for chlorfenapyr show that the compound is very stable. Indeed, chlorfenapyr's persistence in soil from annual treatment to annual treatment would contribute to increasing soil residues with time. Multiple-year applications of chlorfenapyr to cotton fields would therefore result in asymptotic increases in soil concentrations.

As discussed for multiple-year uniform applications in the environmental fate section, the 90 percent upper bound for aerobic soil metabolism half-life (1.4 years, approximately the same as the 1.3 year field disipation half-life), yields a calculated asymptotic first-order value approaching 2.5 times the annual application amount (1.5 leftover from previous applications plus 1.0 from the current year application). Using the average aerobic soil half-life of 0.96 year, rather than the upper 90% limit of 1.4 years, the asymptotic value becomes 2.0 times the annual amount (1.0 residual plus 1.0 current).

Under the assumption of minimal incidental soil ingestion, the effects of chlorfenapyr accumulation in soil to approximately 1.7 to 2.5 times the first year soil residue are essentially negligible, and do not alter the outcome of the risk assessment. However, if higher incidental soil ingestion rates are assumed (e.g., Bier et al. (1994) suggests soil incidental ingestion rates as high as 30% for some probing birds), then accumulation in soil may influence the outcome of the risk assessment to a greater extent. In addition, if other routes of exposure were to be considered (e.g., dermal), accumulation of chlorfenapyr from multiple years of use would serve to increase the exposure of chlorfenapyr in birds in any given year.

<u>The Effect of Application Interval Upon Exposure Estimates</u>

It should be noted that multiple application scenario risk quotients are based on oral doses (from diet) calculated using a 7-day application interval. The use of the 7-day application interval was predicated upon the available avian food item residue data and may not reflect maximum possible oral doses if the minimum labeled treatment interval of 5 days is considered. The stability of chlorfenapyr in soil, at first analysis, would suggest that interval differences of a few days would not be important. However, the dissipation of chlorfenapyr residues in plants and insects is more rapid than degradation of chlorfenapyr in soil, and reduction of the application interval from 7 to 5 days could produce higher residues in plants and insects.

<u>The Importance of Other Routes of Exposure</u>

As stated in the exposure assessment of this document, the risk assessment does not account quantitatively account for a number of additional exposure routes, including respiration of chlorfenapyr vapors or particulate-associated chlorfenapyr, dermal absorption of chlorfenapyr, and ingestion of chlorfenapyr during preening. Furthermore, bioconcentration of chlorfenapyr residues in fish (BCF 2,300), while less toxic than parent, have the potential for additional, but unquantified, toxic risks to piscivorous wildlife. Finally, there remains an unquantified concern regarding the potential for chlorfenapyr to accumulate in aquatic invertebrates (e.g. molluscs), which may not have the biochemical capability to degrade the parent compound. These accumulators may be additional dietary sources of chlorfenapyr for wildlife.

Interspecies Sensitivity Issues

This risk assessment has relied on the most sensitive measured toxicological endpoints for birds and mammals for generating deterministic risk quotients. Because of the departure from the usual EFED approach, which is based on estimated residues immediately post-application (Fletcher et al., 1994), this risk assessment does not incorporate EFED's usual conservative safety factors used to mitigate for uncertainties regarding interspecies sensitivity. However, consideration of the high risk level of concern (RQ values greater than or equal to 0.5 trigger the concern) accounts for uncertainties regarding *intraspecies* extrapolation.

Daily Dose Versus Cumulative Dose as a Predictor of Subacute Lethal Effects

The daily RQs calculated for subacute lethal dietary risk should be evaluated with some care. There is considerable uncertainty as to the minimum exposure duration required before test organisms exhibit a lethal response to chlorfenapyr. The role of pharmacodynamics and kinetics in the expression of the lethal response is uncertain. It is not clearly known whether mortality in birds occurs once a threshold cumulative internal dose is achieved or once a certain level of cellular injury occurs. In the case of chlorfenapyr in the passerine red-winged blackbird (MRID 444526-13), birds exposed to dietary concentrations as low as 10 ppm, exhibited all observed mortality before the end of the 5-day exposure period. For example, mortality of 50 percent of the treatment group occurred at the 10 ppm treatment level (1.52 mg/kg-bw/d) after 3 days of exposure for a total accumulated exposure of 4.56 mg/kg-bw (1.52 mg/kg-bw/d X 3 days = 4.56 mg/kg-bw). Assuming that the pharmacodynamics and kinetics for the calculated study LC50 of 10.75 ppm (1.63 mg/kg-bw/d) are similar to the 10 ppm (1.52 mg/kg-bw/d) treatment level, one could expect that the necessary exposure to result in 50 percent mortality would occur well before a full five days of exposure are completed. The accumulated dose could be similar to the 10 ppm treatment group such that the required period of exposure could be as little as three days, with an accumulated dose of approximately 4.89 mg/kg-bw (1.63 mg/kg-bw/d X 3 days = 4.89 mg/kg/d).

If accumulated dose is a controlling factor in chlorfenapyr subacute mortality, then daily RQs based on single-day dose predictions may not fully account for the risk of subacute mortality. Indeed, a single dose above the toxicity endpoint (1.63 mg/kg-bw/d) followed by a series of daily doses below the endpoint sufficient to achieve the cumulative dose on concern, or *vice versa,* could still result in sufficient exposure to chlorfenapyr to result in lethality equivalent to the present toxicity endpoint. Therefore, concern for lethal effects of chlorfenapyr in birds may not be limited to the days for which exposure is expected to be above the subacute toxicity endpoint.

Aquatic Risk Characterization

Cotton is grown as a major cash crop near aquatic habitats along all the Gulf coast states as well as the bayou regions and tributaries of the lower 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 chlorfenapyr on cotton is predicted to cause important adverse effects in aquatic communities. The likely adverse impacts in freshwater communities would be associated with acute short-term exposures. Freshwater acute RQ values exceed the acute high (0.5), restricted use (0.1), and endangered species (0.05) levels of concern. No freshwater chronic levels of concern were exceeded by the estimated MUSCRAT exposure values. However, the confidence in this finding regarding chronic effects is low because of the limited chronic freshwater toxicity data, the persistence of the chemical in aquatic systems. For estuarine/marine receptor species, there are high levels of exceedance of the chronic level of concern (over an order of magnitude), suggest that impacts to invertebrates may be severe. It should be noted that the invalid sheepshead minnow toxicity study precluded assessment of chronic risks to fish in estuarine/marine systems.

The exposure models predicted maximum initial residues of chlorfenapyr to be as high as 13 ppb (μg/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 toxicologically 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 direct sprays of at least 11.3 μg/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 chlorfenapyr. 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 chlorfenapyr.

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.

DATA GAPS

Appendix B is a table summarizing the data requirements relative to the use of chlorfenapyr as an insecticide/miticide on cotton.

Terrestrial

Because no definitive avian terrestrial field study has been submitted, the registrant is still required to submit a terrestrial field test using the active ingredient chlorfenapyr. 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). The registrant has submitted a field study to only assess the potential for avian acute lethal effects in cotton fields treated with chlorfenapyr (MRID 444526-16). However, EFED requests for field testing of chlorfenapyr effects in birds (e.g., DP Barcode 210808) have stressed that an appropriate field study should emphasize an investigation of avian **reproductive** effects. The results of this risk assessment, incorporating biological data specific to a number of species found in cotton fields and measured residues in avian food items has (1) allowed EFED to reduce some uncertainties relative to exposure of avian wildlife and (2) increased EFED confidence in concluding that avian wildlife would be at risk for reproduction impairment. Therefore, EFED does not require a field study incorporating reproduction endpoints at this time.

In an April 1998 oral presentation before the Agency, the registrant presented preliminary results of an avian reproduction toxicity test that utilized a modified exposure regime. This study used variable dietary concentrations to simulate the decreasing concentrations of chlorfenapyr observed for weed seed head, cotton plant, and insect residues. The oral presentation of the resultant data suggested that some information from the study may be applicable to assessing the risks of field residues of chlorfenapyr to avian reproduction. However, written presentation of these data has not been made available to EFED at the time of preparation of this risk assessment. In the absence of data to the contrary, the existing avian toxicity data set, when combined with residue data, is sufficient to suggest that there exists a substantial risk to avian reproduction for the species evaluated for this risk assessment.

Aquatic

A major unanswered question in the last risk assessment for chlorfenapyr is the bioavailabililty of chlorfenapyr to benthic organisms. In order to answer this vital question, sediment toxicity testing was required. To address the question of sediment toxicity an acute sediment toxicity test was conducted using the EPA test protocols. The freshwater organisms tested was the amphipod *Hyallea azteca*. Although this study has been classified as supplemental, it can still be upgraded to core status with the submission of additional data. In addition, the data from this study can be utilized in a risk assessment. On the other hand, the marine amphipod study has only just recently been submitted to the Ecological Hazard Branch/EFED for review.

At the time EPA requested sediment toxicity testing, the only protocol which had been fully developed was a 10-day acute sediment toxicity test. However, at this time EPA has developed a *provisional* guideline protocol for a 28-day chronic sediment test. Although specific criteria for requiring a chronic toxicity test have yet to be published, one criterion will include the persistence of the compound. Since chlorfenapyr has been characterized as a persistent compound, EFED will require a chronic sediment toxicity test. In the case of marine sediment toxicity, a chronic test is clearly justified because the LOCs appear to be exceeded by the results of the acute study submitted by the registrant. Because of the recent development of protocols for chronic sediment toxicity testing, EFED recommends that any study protocols (including the selection of test species) developed by the registrant to address these data requirements be submitted to the Agency for approval prior to test initiation.

Upon review of all sediment toxicity data (including the studies listed above), additional higher tier information may be necessary to clarify the long-term effects from the use of a highly persistent chemical when it reaches the aquatic environment. These higher tier needs may include studies to determine the community-level effects of persistent chlorfenapyr in sediments.

Invalid acute and/or chronic aquatic tests which need to be repeated at this time are listed in Table 53.

It should be noted that limited tests were performed on two different degradates of chlorfenapyr. The major degradate CL 312,094 (the desbromo derivative of chlorfenapyr), 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 EFED considers additional testing on degradates.

The acute LC_{50} of the major degradate CL 312,094 was greater than 928 μg/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.

LABELING AND MITIGATION

Chlorfenapyr meets the criteria for classification as a **Restricted Use Pesticide** with regard to risks to aquatic organisms and birds (40 CFR 152.170 (c)(1)(iii)). EFED therefore recommends that chlorfenapyr be classified as a Restricted Use Pesticide. This recommendation is consistent with the proposed product labels.

The following language found on the proposed product labels is consistent with EFED conclusions:

> This pesticide is toxic to fish and wildlife.
>
> Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate.
>
> This product is toxic to bees exposed to direct treatment on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area.

> This product must not be used in areas where impact on threatened or endangered species is likely. Notify state and/o Federal authorities and American Cyanamid Company immediately if you observe any adverse environmental effects due to the use of Alert Insecticide-Miticide (or Pirate Cotton Insecticide).

There is an important inconsistency between the Pirate and Alert product labels. The Alert label contains the following statement, which does not appear on the Pirate label:

> **Do not make more than two consecutive applications of Alert;** then rotate to another product from a different class based on mode of action. Alert has a unique mode of action and can be an important component of a resistance management program in cotton.

EFED recommends that the above language be incorporated into the Pirate label. This recommendation is not based on a pest resistance concern, but on the available avian food item residue data and stability of the compound that suggest repeated applications of chlorfenapyr to a field result in increasing residues in environmental compartments. By limiting applications to two consecutive treatments followed by a treatment period using another pesticide, the Pirate label-listed low application rate scenario 0.15 lb ai/A would be limited to two consecutive instead of three consecutive applications. This would allow some time for reduction in avian food item residues before a third (and still label consistent) application would be made. However, the stability of chlorfenapyr in soil would preclude this strategy from reducing residues available to runoff and erosion.

Both the Pirate and Alert proposed labels have language regarding spray drift precautions. EFED recommends that this language be compared to current spray drift best management practices and any required modifications be made to the labels to achieve consistency with current spray drift management practices.