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EXECUTIVE SUMMARY

An avian ecological risk assessment was carried out for the use of chlorfenapyr (AC 303630) in cotton. The assessment employed the terminology and followed the procedures set out in the United States Environmental Protection Agency's (EPA's) *Framework for Ecological Risk Assessment* (1992). This document defines ecological risk assessment as "a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors." It also notes that an ecological risk assessment may evaluate one or many stressors and one or many ecological components. In the present assessment, a single stressor, chlorfenapyr, was evaluated for many ecological components. The assessment followed the procedures specified in the *Framework* in that the **Problem Formulation, Analysis**, and **Risk Characterization** phases were all performed.

This assessment was carried out to provide EPA with a higher tier evaluation for chlorfenapyr. EPA's Environmental Fate and Effects Division (EFED) previously reviewed the data on chlorfenapyr and performed a Tier 1-type assessment using Risk Quotients, or RQs. EFED's assessment concluded that chlorfenapyr poses unacceptable acute and chronic risks to birds because RQs deemed acceptable by EPA were exceeded. The Tier 1-type RQ assessment is a screening evaluation which relies on laboratory toxicity studies and published theoretical values for residues in avian food items, which are not necessarily representative or valid for all chemicals[1]. An important issue to registrants is, if a Tier 1 assessment indicates unacceptable risk, what can be done to provide a valid "higher tier" characterization of actual ecological risk? American Cyanamid Company is unaware of any guidance as to the scope of studies, or procedures, needed to perform such an assessment. We elected to follow the formalism of the *Framework* document closely in the hope that the resulting higher tier assessment will be useful to EPA.

Cyanamid's higher tier assessment focused on developing better estimates of potential avian exposure to chlorfenapyr. In the context of the higher tier assessment, avian exposure has three related, but distinct components. The first component is the potential for contact with residues of chlorfenapyr, as gauged by measured residue levels in relevant matrices. The second component is the potential for bird species to come into contact with residues of chlorfenapyr as gauged by the degree to which these species use cotton fields. The third component is the potential for regional bird populations to come into contact with chlorfenapyr, as gauged by the proportion of a region that might be treated. Consideration of three different components of exposure is a major difference from a Tier 1-type RQ assessment that relies solely on published point estimates of residues, and assumes exposure to that level of residues 100% of the time.

The higher tier assessment relied on an extensive set of guideline and non-guideline studies for chlorfenapyr, including studies that were not available when EFED completed its Tier 1-type assessment. The extensive database was supplemented with information on the mode of action of chlorfenapyr, the fate and partitioning of chlorfenapyr in the environment, cotton insects and pest management, and cotton production in a regional context. Risk was evaluated at three levels of biological organization (i.e., ecological components) - the individual bird, the "local" bird population, and the "regional" bird population. The risk to threatened and endangered species was also considered. Highlights of the significant outcomes or conclusions of each of the three phases of the assessment follow.

[1] Issues pertaining to the validity and representativeness of the RQ as an indicator of acute and chronic risk are discussed in the Analysis and Risk Characterization sections.

In the **Problem Formulation** phase, the valued ecological entity was identified as bird species associated with cotton fields and their borders. This spatial unit was termed the "cotton agroenvironment". Assessment endpoints were established for the individual bird, the "local" population (i.e., birds associated with a single cotton field and its borders), and the "regional" population (i.e., birds associated with the cotton agroenvironments in a county, state, or ecoregion). Based on toxicity information, the assessment endpoints for individual birds and endangered species were survival and reproduction. For the local population, the assessment endpoint was change in population size due to changes in survival and reproduction. For the regional population, the assessment endpoint was also change in population size due to changes in survival and reproduction. For each assessment endpoint, a suite of measurement endpoints was used, as appropriate to individuals, local, and regional populations and the components of exposure described above. A detailed conceptual model was developed in narrative and in tabular form to evaluate the relative significance of the various possible exposure pathways and routes.

The **Analysis** phase summarized and synthesized the extensive study database and related information. Based on the key cotton pests, cultural practices, and the timing of chlorfenapyr applications, the Cotton Belt was divided into two parts for the purposes of the assessment: (1) "Western Cotton" was defined as West Texas, Arizona and California; and (2) "Southern Cotton" was defined as Texas High Plains and east to North Carolina. These regions roughly correspond to the use patterns specified in the ALERT® and PIRATE® labels. Bird species using cotton were identified using census data and scientific literature, and focal species were selected for purposes of risk characterization. The results of the Analysis included a refined conceptual model which identified dietary exposure for birds that eat insects and seeds as the most likely and most significant exposure and risk scenario. In addition, exposures via ingestion of earthworms, soil and sediment were quantitatively estimated using available information and worst-case assumptions. Additional data are currently being gathered on residues in, and populations of, earthworms in cotton fields to validate these exposure estimates for birds that eat worms. The cotton agroenvironment was qualitatively and quantitatively described in detail, using Geographical Information System (GIS) data. Exposure and effects profiles were established and key assumptions of the analysis were supported.

The **Risk Characterization** phase incorporated information on ecological effects, residues, bird species using cotton, and nature and extent of cotton as measurement endpoints. A weight-of-the-evidence approach, relying on suites of endpoints and expert judgment, was used for all levels of biological organization. For risk to individual birds, toxicity information, information about the food base in cotton agroenvironments, timing of usage, and field study results were considered. This information was supplemented with survey and species occurrence data for endangered species. Section 18 monitoring program results were considered supportive. Uncertainties were explicitly evaluated.

Risks to local and regional bird populations were estimated when risks to individual birds were considered possible, even if improbable. For local populations, measured or estimated residue levels in relevant avian food items, laboratory toxicity test results, and information on bird food habits and behavior were used to develop refined Risk Quotients (RQs). Uncertainties in the RQs that might bias estimates of risk were explicitly evaluated. Finally, for regional populations, historical information on cotton planting in counties, states and ecoregions, along with insect infestation information and habitat classifications, were used. Again, uncertainties were explicitly evaluated.

At the level of the individual bird, it was concluded that there is a low to very low likelihood for adverse impacts on survival or reproduction in either Southern or Western Cotton. There is temporal overlap of bird breeding and early season applications of chlorfenapyr for mites in Western Cotton. However, incremental risks to reproduction are not likely, due to the low application rates, the limited degree to which most bird species use cotton fields and the background of existing cultural practices. Risk to endangered species was considered low because data indicated their very low usage of the cotton agroenvironment. At the level of the local population, RQs calculated for what are considered typical exposure scenarios were within, or very close to, values deemed acceptable by EPA. Certain highly conservative worst-case scenario RQ calculations somewhat exceeded EPA's levels of concern; however, when these RQs were refined using exposure estimates representative of typical exposures they were within, or much closer to, EPA acceptable values. Additionally, the estimated residues in fruit and insects off the field may likely be up to 10-fold less than the levels used in the analysis. Therefore, RQs may have been overestimated. It was concluded that there is very low likelihood of impacts on population size of a species. Likewise risks to regional populations was also considered to be low or very low. The absence of risk at the regional population level corresponds not only to the absence of significant risk to the individual and the local population, but also to the relatively low proportion of the landscape that is planted to cotton, and the limited area within cotton that will be treated with chlorfenapyr according to the proposed label. A highly conservative overestimate assumes 19% of the total acres planted to cotton may receive a chlorfenapyr application. This is based on a historical average of 6.8M acres of cotton requiring treatment for the control of tobacco budworm/cotton bollworm. From state resistance monitoring results, it can be conservatively estimated that resistant tobacco budworm/cotton bollworm infest approximately 20%, or 1.4M acres, of the 6.8M acres. Cotton acreages requiring insecticide applications for mite and beet armyworm infestations, historically average 1.1M and 0.8M acres, respectively. Based on a high market estimates, a maximum of 50% of these acreages (0.6M for mites and 0.4M for beet armyworm) may receive chlorfenapyr applications.

The mitigation measures included in the proposed chlorfenapyr label were evaluated with respect to the risk factors identified in the assessment. These measures provide effective and adequate protection.

This higher tier assessment concludes that the risk of chlorfenapyr to birds is low to very low. The conclusion applies to individual birds, threatened and endangered species, local populations, and regional populations. This deterministic risk assessment, which is based on the recommendations specified in the EPA's *Framework* document, represents a significant expansion of the Tier 1 Risk Quotient-based screening level assessment typically conducted by EFED. Furthermore, EFED's assessment relies on default assumptions to estimate concentrations in the environment, while this higher tier refined assessment utilizes measured field concentrations to define realistic exposures. This assessment identifies potential problems, offers effective mitigation measures and provides a thorough scientific evaluation which demonstrates that the use of chlorfenapyr on cotton does not pose any unreasonable risk to avian species.

BACKGROUND, FEATURES, AND ORGANIZATION OF THE ASSESSMENT

Background -- Ecological Risk Assessment in General

This is an avian ecological risk assessment of chlorfenapyr (AC 303630) for the control of budworm, bollworm, the armyworm complex, and mites in cotton. It is based on the Environmental Protection Agency's (EPA) *Framework for Ecological Risk Assessment* (EPA 1992). The *Framework* defines ecological risk assessment as: *"... a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors. A risk does not exist unless (1) the stressor has the inherent ability to cause one or more adverse effects and (2) it co-occurs with or contacts an ecological component (i.e., organisms, populations, communities, or ecosystems) long enough and at sufficient intensity to elicit the identified adverse effect. Ecological risk assessment may evaluate one or many stressors and ecological components."* In the present assessment, a single stressor, chlorfenapyr, is evaluated. Many ecological components are considered.

There are three major phases to the ecological risk assessment process as set forth by the *Framework*. The first phase, **Problem Formulation**, includes preliminary characterization of exposure and effects, examination of scientific data and data needs, policy and regulatory issues, and site-specific factors to define the feasibility, scope, and objectives of the risk assessment (EPA 1992). Successful completion of this phase will result in: assessment endpoints that adequately reflect management goals and the ecosystem they represent; conceptual models that describe key relationships between a stressor and assessment endpoint; and an analysis plan (EPA 1996).

The second phase of ecological risk assessment is termed **Analysis**. It consists of two components, characterization of exposure and characterization of effects. Characterization of exposure aims to predict or measure the spatial and temporal distribution of a stressor and its co-occurrence or contact with ecological components of concern. Characterization of effects aims to identify and quantify the adverse effects elicited by the stressor, and, if possible, evaluate cause and effect relationships.

The third phase of ecological risk assessment is termed **Risk Characterization**. In this phase, the results of the exposure and ecological effects analyses are used to evaluate the likelihood of adverse effects occurring, in this case when chlorfenapyr is applied to cotton. Risk characterization includes a summary of the assumptions used, the scientific uncertainties, and the strengths and weaknesses of the analyses. Also, the ecological significance of the risks is discussed, with consideration of the types and magnitudes of the effects, their spatial and temporal patterns, and the likelihood of recovery.

The output of the ecological risk assessment process is a key product for the decision-makers' deliberations. Depending on the potential adverse effect and the regulatory context, the risk manager may also weigh the ecological risks against likely benefits; this exercise falls outside the scope of ecological risk assessment. Because chlorfenapyr will be regulated under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), weighing of its benefits against its risk is permissible.

Background -- *Chlorfenapyr*

In the standard laboratory tests required under FIFRA, chlorfenapyr has exhibited high or very high oral toxicity to birds. It has also been shown to be relatively persistent in soil (according to EPA criteria), with an average field half-life of about 9 months. This combination of high toxicity and relative persistence in soil has raised concerns about the risk the compound may pose to birds, as indicated by the standard Tier 1-type assessment done for chlorfenapyr by the EPA Ecological Fate and Effects Division (EFED). In this screening level assessment, the main tool used is the Risk Quotient (RQ), the ratio of estimated environmental concentration (EEC) to toxicity (LD_{50} or LC_{50} test results). EFED concluded that chlorfenapyr poses unacceptable acute and chronic risks to birds (DP Barcode D211863).

Features of this Ecological Risk Assessment

An initial objective of the present assessment is to identify the major ecological factors to be considered and their regulatory context. The valued ecological entity is bird species associated with cotton fields and their borders ("the cotton agroenvironment"). The regulatory context is pesticide registration as governed by federal law (FIFRA) and EPA regulations. One very important aspect of this context is the Tier 1-type assessment. Specifically, if the Tier 1-type assessment indicates unacceptable risk, what can be done to provide EPA with a refined (higher tier) assessment? There appears to be little guidance or agreement on the scope, data requirements, and procedures necessary to produce an acceptable higher tier assessment, with the exception of the general guidance of the EPA *Framework Document*. American Cyanamid Company hopes that by closely following the formalism of the ecological risk assessment process as set forth in the *Framework*, and by providing additional data and analyses, we can produce a useful higher tier assessment.

There are four main differences between the present higher tier assessment and a standard Tier 1 assessment. First, as mentioned above, the present assessment follows the formalism outlined in the EPA's Framework for Ecological Risk Assessment (1992). There will be explicit statements and discussions of assessment and measurement endpoints, of assumptions, and of uncertainties.

The assessment considers multiple endpoints -- risk to individual birds, "local" populations, and "regional" populations. "Local" populations are defined as the birds that frequent a cotton field and the area within a 50 meter border around the cotton field – the "cotton agroenvironment". This operational definition is suggested because the cotton field is the basic management unit.

Second, the present assessment draws on many guideline and non-guideline laboratory tests as well as a variety of field tests. It also draws on information about the cotton crop and its environs, insects and pest management in cotton, and published information about avian phenology, behavior, and environmental exposures. Results from monitoring programs conducted by the States to support Section 18 Emergency Exemptions are also considered, as ancillary information. One unique feature of the field information is a Geographical Information System (GIS) analysis of habitats and avian species associated with cotton. This array of information produces greatly improved estimates of exposure compared to a Tier 1 assessment because it allows key variables that affect avian exposure to chlorfenapyr in cotton to be considered. Such key variables include, for example, the specific bird species using cotton fields, the prevalence of food items and distribution of residues, and the geographic relationship between the cotton agroenvironment and other features of the landscape. It should be noted that co-occurrence, as an indicator of potential for exposure, is given as an important element in ecological risk by EPA (see the *Framework* definition). Detailed consideration of exposure is clearly desirable.

The third major difference between the present assessment and a standard Tier 1 assessment is that the EPA approach essentially assumes every individual bird will be exposed all the time. The present assessment explicitly addresses the uncertainties (in this case, conservatisms) in this approach. The assessment also focuses explicitly on the two major parts of the Cotton Belt, based on geography and cultural practices. These areas are termed "Western Cotton" (West Texas, Arizona and California) and "Southern Cotton" (Texas High Plains and East). By looking at multiple endpoints and different cotton cultural practices in this manner, the assessment not only provides a valid and reliable characterization of risks, but also provides information that supports the incorporation of practical, effective risk mitigation measures on the label.

Finally, the fourth major difference between the present assessment and a Tier 1 assessment relates to reliance on the Risk Quotient (RQ) to characterize risk. In the Tier 1 assessments currently done under FIFRA, the major tool used is the RQ. It is perhaps unfortunate that the term Risk Quotient implies that the RQ is a measure of risk. The RQ is a screening tool that does not specifically address, or incorporate information relating to, the likelihood that adverse effects will occur. Nonetheless, the RQ is the measure used by EPA in its assessments and Cyanamid is unaware of any other index that is accepted by EPA for regulatory evaluations. Therefore, this assessment improves the RQ approach by using an array of data and information to produce refined or improved estimates of realistic worst-case and typical-case exposures. The RQ is used here as a component of an overall weight-of-the-evidence approach to produce a realistic characterization of avian risk with a high degree of confidence.

This assessment also considered the potential exposure to threatened and endangered species from chlorfenapyr use on cotton. Only one endangered species, the Brown Pelican *(Pelicanus occidentalis)* was observed in any of Cyanamid's avian censuses or field studies. This species is not likely to use cotton or be exposed to chlorfenapyr. The major focus of the present assessment is therefore on non-threatened, non-endangered avian species as found in cotton by the avian census studies or indicated by a detailed review of available literature. However, the new information that has been gathered on measured residue levels of chlorfenapyr in food items, bird usage of cotton fields, and factors that mitigate exposure potential, is also germane to threatened and endangered species. As EPA is aware, a substantial effort for protecting endangered species is underway by an Industry group termed the FIFRA Endangered Species Task Force (FESTF). Cyanamid is a founding member of that Task Force, which will help provide EPA with additional information and approaches to protect threatened and endangered species from potential effects of pesticides.

Organization of the Ecological Risk Assessment

This assessment follows the organization set forth in EPA's *Framework* document. That organization necessitates repetition of some information in each phase of the assessment. Attempts will be made to keep this repetition to a minimum. Definitions of key terms unique to this assessment will be provided in the text as soon as possible after a term has been used or as footnotes. Because of the extensive database on chlorfenapyr, study-specific information will be provided in Appendices and will only be summarized in the body of the assessment. Finally, because of the multiple assessment endpoints, multiple measurement endpoints, and the different techniques used to assess risk, the reader is urged to peruse the Analysis Plan carefully. That section will provide a road map and illustrate how the data and assumptions are used to assess risk.

PROBLEM FORMULATION

The Problem Formulation phase includes a preliminary characterization of exposure and effects, examination of scientific data and data needs, policy and regulatory issues, and site-specific factors to define the feasibility, scope, and objectives of the risk assessment. According to the EPA *Framework*, successful completion of this phase will result in assessment endpoints that adequately reflect management goals and the ecosystem they represent; conceptual models that describe key relationships between a stressor and assessment endpoint(s); and an analysis plan.

Table of Contents for the Problem Formulation Phase		
Stressor Characteristics	Summary of Physical and Chemical Characteristics of Chlorfenapyr	*Summary Table*
	General Information on Use Pattern	*Application Information for Southern and Western Cotton*
	Physical and Chemical Properties and Fate in the Environment	*Dissipation and degradation*
	Biological/Mode of Insecticidal Action	*Description*
	Overview of Toxicity	*Acute toxicity of chlorfenapyr and major soil degradates to birds, fish and mammals*
	Metabolism in and Excretion from Biological Systems: Potential for Biomagnification and Bioaccumulation	*Cattle feeding study, fish bioaccumulation, rat and hen metabolism studies*
Ecosystem Potentially at Risk	The Cotton Agroenvironment	*Southern and Western Cotton; PIRATE® and ALERT® use pattern*
	Cultural Practices in the Cotton Agroenvironment	*Southern and Western Cotton; PIRATE® and ALERT® use pattern*
	Field Borders	*Estimated number of acres in borders based on field size*
Assessment Endpoints for Avian Risk		*Direct effects on survival and reproduction; changes in population size*
Measurements Endpoints for Avian Risk	Individual Birds	*General toxicity of chlorfenapyr; partitioning and degradation; bird species associated with cotton; field study results*
	Local Bird Populations	*Results of standard laboratory tests for acute, dietary and reproductive effects; numerous field studies (residue levels and decline)*

Table of Contents for the Problem Formulation Phase

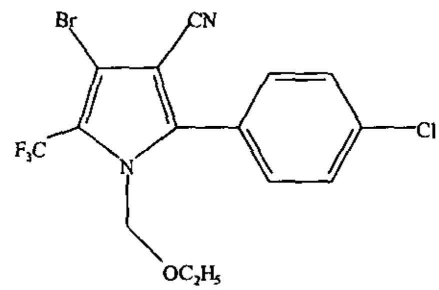
Stressor Characteristics

The stressor being evaluated in this risk assessment is the novel pyrrole chlorfenapyr (also referred to as AC 303630), an insecticide-miticide being developed by Cyanamid for foliar applications in cotton. Below is a summary of some of the physical and chemical and environmental characteristics of chlorfenapyr, which are important in assessing the expected concentrations in the environment and the potential for exposure of birds to chlorfenapyr.

According to EPA (1992), exposure to a stressor is determined by the following factors:

- Persistence and compartmentalization in the environment;
- Duration and frequency of residue pulses;
- Kinetics of accumulation and depuration;
- Seasonality of use and ecological relevance.

Summary of Physical and Chemical Characteristics of Chlorfenapyr.

Structure	
Chemical name	
UPAC	4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile
CAS	4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile
CAS Number	122453-73-0
Molecular weight	407.6
Molecular formula	$C_{15}H_{11}BrClF_3N_2O$
Water solubility	0.12, 0.13, 0.14, and 0.12 ppm in deionized water, at pH 4, 7, and 10 buffers, respectively
Vapor pressure	4.05 x 10^{-8} torr at 25°C
K_{ow}	67670 (Log K_{ow} = 4.83)
Hydrolysis	Stable to hydrolysis over 30 days in pH 5, 7 and 9 buffers
Aqueous photolysis	Half-life 5-7 days in pH 5, 7 and 9 buffers
Soil photolysis	Half-life 130 ± 40 days

Aerobic Soil	
Lab	Half-life 230 days - alluvial clay loam (Japan) 250 days - volcanic ash light clay (Japan) 241 days - clay soil (TX) 349-415 days - sandy loam (CA, MS, NC,NJ)
Anaerobic Soil - Lab	Half-life 670 days - sandy loam (NJ)
Field Dissipation Half-lives	175-418 days (CA, FL, MS, TX), average 275 days
Kd_{ads}	32 - 155
Kd_{des}	67 - 362
K_{oc}	
AC 303630	11500 (median)
CL 312094	3060

General Information on Use Pattern

Chlorfenapyr will be used primarily to control the budworm, bollworm, and armyworm complex in cotton across Southern Cotton, and to control mites and worm pests in Western Cotton. The proposed labels are provided in Appendix 1. In Southern Cotton, applications will generally begin about July 1, for budworm and bollworm. From August 16 to boll maturation, applications may be made for budworm and bollworm and for the armyworm complex. In Western Cotton, applications for early season mite control could start as early as May 1. Applications for mid-season mite control would be possible starting June 15. Applications for the budworm and bollworm and the armyworm complex could begin by July 1 and continue until boll maturation. In all areas of the Cotton Belt, the budworm, bollworm, and armyworm moths must find and colonize the fields, and this colonization depends on many factors that are difficult to predict. Although it may be necessary to treat for budworm and bollworm several times during the season, the current labels allow a maximum single application of 0.3 lb. a.i./A and a maximum total of 0.5 lb. a.i./A per season, with a minimum interval of five days between applications. Due to the variable nature of insect infestations in cotton, and the nature and scope of Integrated Pest Management (IPM) programs for resistance management in cotton, it is difficult to predict which fields will need a chlorfenapyr treatment or whether a particular field will be treated once or more often.

Details of product use relevant to avian exposure and risk are discussed below, under **Ecosystems Potentially at Risk** (see page 23).

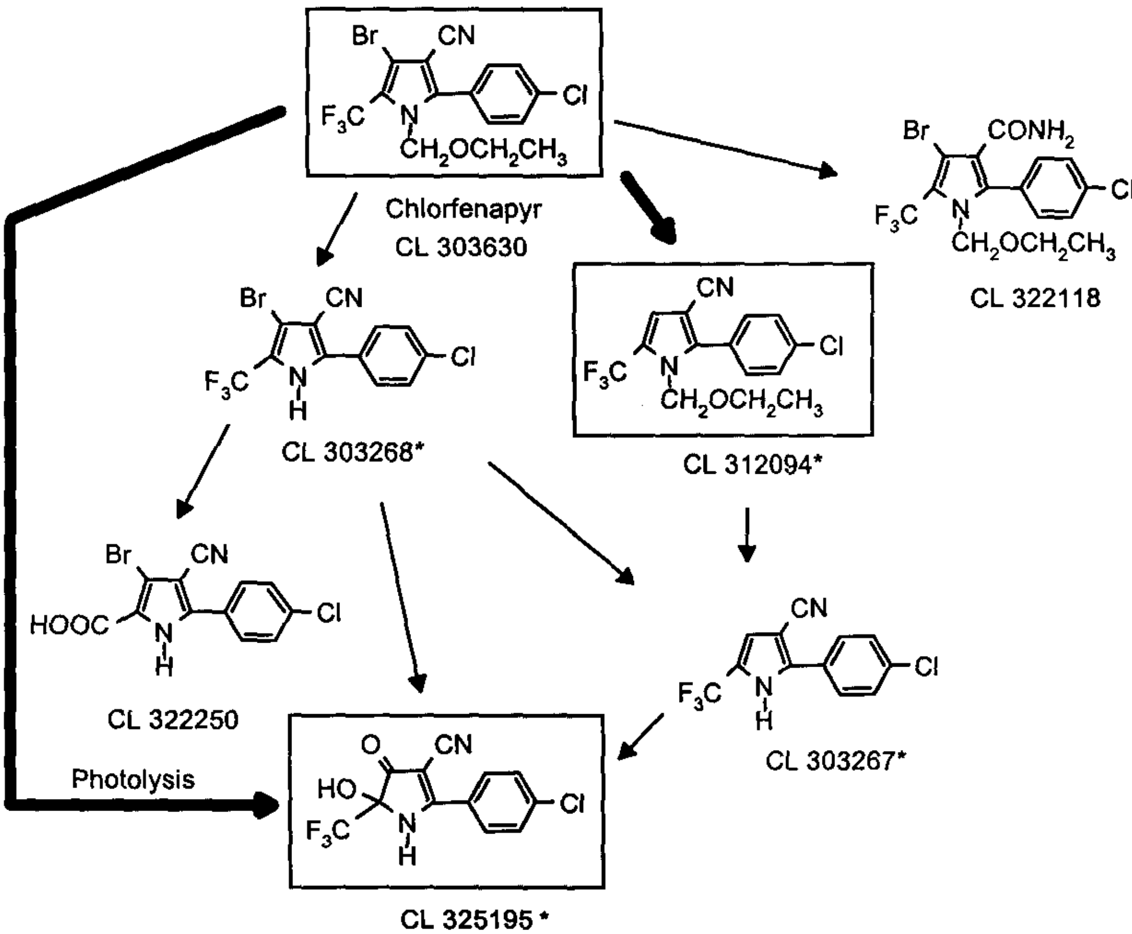
Physical and Chemical Properties and Fate in the Environment

The dissipation and compartmentalization of chlorfenapyr in different environmental matrices is influenced by several factors. The three physical and chemical properties of chlorfenapyr that have the greatest impact on this distribution are its very low volatility, extremely low water solubility, and strong binding to soil.

Chlorfenapyr and CL 312094 (its major metabolite in soil, sediment, and fish), are strongly adsorbed to soils, with K_{oc}s of 11500 and 3060, respectively. The large soil/water adsorption coefficients and the low water solubility of chlorfenapyr (0.12 ppm) and CL 312094 (0.36 ppm) indicates that the compounds are immobile in soil and leaching would not be expected to occur. In the laboratory, chlorfenapyr is degraded in soil under aerobic conditions with half-lives of 230-250 days in an alluvial clay loam and a volcanic ash light clay from Japan, in 241 days in clay soil from Texas and in 349-415 days in sandy loam soils from California, Mississippi, North Carolina and New Jersey. Several metabolites, most of which are considerably less toxic than parent (see page 21), were identified and include CL 312094, CL 303267, CL 303268 and CL 325195. Chlorfenapyr slowly degraded in soil under anaerobic conditions, with a half-life of 670 days. As in the aerobic soil studies, the major compound produced is CL 312094. A soil photolysis study showed that chlorfenapyr degrades more rapidly in the presence of light than in an aerobic soil metabolism study. Half-lives on soil are estimated to be about 75 days of continuous irradiation or 130 ± 40 days for a 14-hour photoperiod, which would represent approximately 225 days in the field. Two compounds, CL 303268 and CL 325195, were formed over 30 days, but they each accounted for only 5% of the applied dose. Half-lives in five field dissipation studies range from 175-418 days. The study on a sandy soil in Florida clearly demonstrates that there should be no concerns about the leaching potential for this compound since there was no movement of the compound through the soil profile on a sand (92% sand, 4% silt, 4% clay, 1.5% O.M.) which received 60 inches of rainfall in the year after application, and 95 inches of rainfall over the 540 days of the study (MRID Nos. 43492850 and 44452622).

The dissipation and degradation of chlorfenapyr, observed in the laboratory and in five field dissipation studies, are corroborated by the results of a related outdoor cotton field dissipation study conducted with [^{14}C] chlorfenapyr (MRID No. 44452623). In this latter study, [*Phenyl-U-*^{14}C] and [2-*Pyrrole*-^{14}C] chlorfenapyr were separately applied to cotton fields of sandy loam soil at a nominal use rate of 0.40 lb. a.i./A in a single application. The radioactivity was largely confined to the top 0-3 inch soil profile, with a steady decline in the concentration of [^{14}C] chlorfenapyr over time. Highly acidic solvents (pH 0.18) were required to extract the bound radioactivity; this indicates that these bound radioactive residues are not likely to be biologically available (MRID No. 44452623). The pathway for degradation included debromination to CL 312094, N-dealkylation to CL 303268 and CL 303267 and oxidation to CL 325195, along with other minor metabolites (Figure 1). A degradation half-life of 275 days was calculated by curve fitting the time-course decline of the normalized percent of the total recovered radioactivity (TRR) that is present to a first order regression model. The microbial and photolytic degradation of chlorfenapyr in arable soils contributes significantly to its dissipation under agricultural use conditions.

Figure 1: Degradation Pathway for Chlorfenapyr in Field Soil



* These degradates were also identified in laboratory soil under aerobic conditions

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Biological/Mode of Insecticidal Action

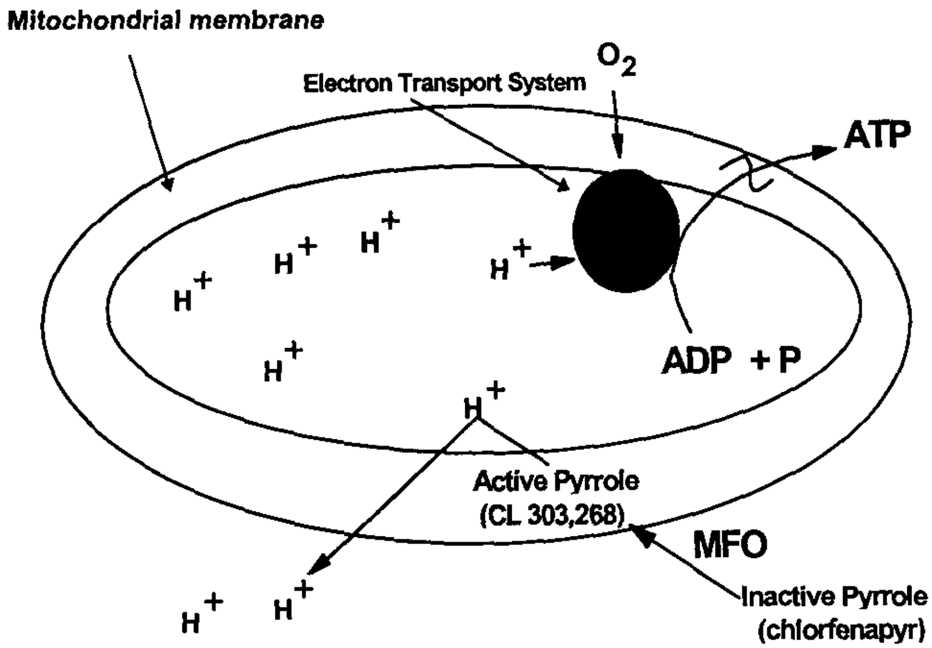
Chlorfenapyr is a member of a novel class of insecticide-miticides called pyrroles. *In vitro* studies have shown that chlorfenapyr can be converted by mixed function oxidases (MFOs) to CL 303268, which targets the mitochondria, and that the fatal biochemical effect is due primarily to uncoupling of oxidative phosphorylation. The proton (H+) gradient across mitochondrial membranes is disrupted and the ability of the mitochondria to produce ATP from ADP is impeded. The impediment leads to cell death and may ultimately lead to the death of the target pest (Treacy *et al.* 1994).

This mode of action (Figure 2) is supported by the following information. First, herbivorous insects generally are known to be able to oxidize xenobiotics (Hung *et al.* 1990). Second, CL 303268 has been identified in tobacco budworm (*Heliothis virescens*) larvae (Treacy *et al.* 1994). Third, Colorado potato beetles (*Leptinotarsa decemlineata*), exposed to the microsomal mono-oxygenase inhibitor piperonyl butoxide, were significantly less sensitive to chlorfenapyr than beetles that were not exposed to piperonyl butoxide (R. M. Hollingworth, unpublished). Piperonyl butoxide would inhibit oxidative metabolism and the biotransformation of chlorfenapyr to CL 303268, in this particular case. And fourth, CL 303268 has been shown to be a potent uncoupler of oxidative phosphorylation in mouse liver mitochondria. CL 303268 stimulated state-4 respiration and decreased respiratory control in mouse liver mitochondria. Stimulation of state-4 respiration continued until oxygen was depleted. The UC_{50} is the concentration which causes 50% uncoupling of oxidative phosphorylation in the bioassay. The UC_{50} for CL 303268 in this system was 2.4 nM (nanoMolar), whereas the UC_{50} for chlorfenapyr in the same system was >1000 nM (Treacy *et al.* 1994).

One very important result from the laboratory evaluations was the relative toxicity of the compound to target pests by the oral and the dermal routes of exposure. Screening work had shown that the compound is toxic to insects by both routes of exposure (Lovell *et al.* 1990). Treacy *et al.* (1990) evaluated the toxicity of chlorfenapyr to 5th instar tobacco budworm larvae by oral gavage and by topical application. The 48 hour oral LD_{50} was 5.7μg/gram, whereas the 48 hour dermal LD_{50} was greater than 450 μg/gram. For tobacco budworm larvae, it is not clear if the difference between oral and dermal toxicity is due to biochemical activation of the chlorfenapyr to CL 303268 in the hindgut, or to limited adsorption to, and/or adsorption through, the cuticle, or to some combination of these factors (Treacy *et al.* 1990). The work by Treacy *et al.* (1990) also provides a working level for concentrations in dying insects. This value, 5.7 μg chlorfenapyr/gram insect wet weight, was obtained in tobacco budworm larvae that averaged 212 mg in weight.

Additional detail on the mode of action of chlorfenapyr is provided in Appendix 2.

Figure 2. Uncoupling of Oxidative Phosphorylation in the Mitochondrion by CL 303268



Overview of Toxicity

Chlorfenapyr is a "pro-insecticide" that must be metabolically converted to an active form, CL 303268, by mixed function oxidases (MFOs). The active form is a potent uncoupler of oxidative phosphorylation in mitochondria. Mammals have a lower titer of MFOs and chlorfenapyr is metabolized via different pathways to other metabolites without significant accumulation of CL 303268. This metabolic selectivity is thought to account for the relative level of safety in mammals. The following table gives an overview of the comparative toxicity of chlorfenapyr and its major soil degradates.

Compound	Bird LD_{50} (mg/kg b.w.)	Fish LC_{50} (μg/L)[a]	Aquatic Invert EC_{50}[a] (μg/L)	Mammals[a] (mg/kg b.w.)
Chlorfenapyr AC 303630	Bobwhite: 34 Mallard: 10.3 Red-winged Blackbird: 2.2	Bluegill: 11.6 Rainbow: 7.44 (dynamic)	Daphnia: 6.11 (dynamic)	Rat: 441/1152 (M, F) Mouse: 45/78 (M, F)
CL 312094	Bobwhite: >1600 Mallard: >2400	Bluegill: >928 (dynamic)	Daphnia: 600 (static)	Rat: >5000 (M, F)
CL 325195	Bobwhite: 741 Mallard: >2250	Bluegill: 2100 (static)	Daphnia: 1700 (static)	Rat: 776/1367 (M, F)
CL 303268	Bobwhite: 25 Mallard: 77	Environmental Concentrations Insignificant[b]	Environmental Concentrations Insignificant[b]	Rat: 27/29 (M, F)
CL 303267	Bobwhite: >2250 Mallard: >2250	Bluegill: 70 (static)	Daphnia: 107 (static)	Rat: >5000 (M, F)

a MRID Nos. 42884201, 4349282, 443493825, 43492826, 43492827, 43492828, 44452620, 42770227, 42770228, 43887004, 43492809, 43492810, 43887005, 43887606, 44452611, 44452612, 42770231, 42807801, 42770232, 43492815, 44452617, 44452618.

b Because CL 303268 accounted for less than 1% of the soil total recovered radioactivity (TRR) in both laboratory aerobic as well as field dissipation studies, the environmental concentrations of this metabolite are not of ecotoxicological relevance.

Metabolism in and Excretion from Biological Systems: Potential for Biomagnification and Bioaccumulation

Based on metabolism studies in several species, chlorfenapyr is rapidly eliminated following oral administration to the rat, goat, cattle, hen and also following exposure to fish, and accordingly, is not expected to bioaccumulate in these systems.

Although highly lipophilic, chlorfenapyr does not accumulate in the rat; over 85% was excreted within two days (MRID No. 43492844). Chlorfenapyr quickly establishes a low level equilibrium in the fat, as demonstrated by the fact that the residue levels remained virtually constant, irrespective of whether the animals received a single low dose, multiple low doses, or a single high dose. This pattern of deposition and depletion of chlorfenapyr in fat tissues in the rat is also observed in poultry, goats (MRID No. 43492855) and cattle.

The metabolic fate of chlorfenapyr was investigated in domestic hens (MRID No. 43492852). Hens were dosed daily with ^{14}C-chlorfenapyr in gelatin capsules for seven days. High-dose groups received 1.82 - 1.86 mg/day and low-dose groups received 0.36 - 0.39 mg/day. Results showed that chlorfenapyr is rapidly eliminated in excreta (78% to 93%) in laying hens dosed daily for seven consecutive days.

In addition, parent chlorfenapyr comprised only 5% of the total residue in the bluegill in a fish bioaccumulation study (MRID No. 43492852). Based on the actual concentration of chlorfenapyr in the fish and aquarium water, the calculated bioconcentration factor (BCF) for chlorfenapyr in whole fish was 74. The only metabolite, the desbromo-derivative CL 312094, accounted for the remaining residue. This metabolite is less toxic to bluegill than the parent (LC_{50} >928 ppb), practically nontoxic to mammals (Rat Oral LD_{50} >5000 mg/kg) and slightly toxic to birds (Mallard/Quail Oral LD_{50} >1600/2400 mg/kg). The half-life for depuration in bluegill was 3-4 days.

The pattern of deposition in and depletion from the fat of chlorfenapyr in cattle, observed in a 28-day feeding study, provides strong evidence that bioaccumulation does not occur in mammals (MRID No. 43492859). In cattle, after 28 days of dosing at 150 mg/day (approximately 0.25 mg/kg b.w./day by capsule) the level of chlorfenapyr in the fat was less than 0.6 ppm. The low level of chlorfenapyr in the fat after a 28-day repeated exposure suggests that bioaccumulation in mammals is unlikely to occur. The level in fat decreased further to less than 0.06 ppm after a 14 day withdrawal period. This supports the conclusion that mammalian species are capable of depleting residues of chlorfenapyr and that this material is not bioaccumulated in the fat. It is noteworthy that residues in milk fall below detectable limits (LOQ = 10 ppb) within 24 hours of the cessation of dosing.

Depletion of Residues of chlorfenapyr in Bovine Fat

Treatment Group and Animal No.	Average Dose of AC 303630 in mg/kg b.w./day	Wt. of Fat Sample (kg)	Measured Concentration in the Fat (ppm)
Group A[1]			
663	0.270	1.108	0.597
670	0.249	1.075	0.026
675	0.288	0.747	0.153
Group B[2]			
668	0.250	0.927	0.053
669	0.220	1.268	0.010

[1]Group A was treated for 28 days then evaluated for content of chlorfenapyr.

[2]Group B was treated for 28 days then was withdrawn from treatment for 14 days prior to evaluation for content of chlorfenapyr.

The above studies in mammals, poultry and fish demonstrate rapid metabolism and excretion of chlorfenapyr residues and indicate that bioaccumulation in animals, or biomagnification of chlorfenapyr in the food chain, is highly unlikely.

Ecosystems Potentially at Risk

The Cotton Agroenvironment

Meaningful definitions of ecosystems are elusive because it is difficult to precisely define their spatial and temporal scales. In an attempt to circumvent this difficulty, the term ecosystem will therefore be replaced by "cotton agroenvironment" which we define as the agricultural land that is capable of supporting commercial cotton production and a border area of 50 meters surrounding each field. This definition is suggested because it describes the area that will receive the vast majority of residues of chlorfenapyr by direct application or drift, and is therefore the area where risk could occur (see **Analysis** for supporting data, pages 46 and 59). Operationally, the individual cotton field is the basic spatial unit for pest management; recommendations for treatments will be made at the field level. The temporal scale for the cotton agroenvironment is suggested to be 20 years; this value is based on what historically would be twice the use-life for an insecticide for control of budworm and bollworm in cotton (Herzog *et al.* 1996).

Cultural Practices in the Cotton Agroenvironment

In general, the cotton agroenvironment is a tilled annual monoculture surrounded by the 50 meter border. Across the Cotton Belt, the cropped areas generally have similar edaphic characteristics, allowing them to support cotton production. They are tilled and maintained in a generally similar fashion within a locale. A key part of this maintenance is control of insects, frequently with insecticides, and control of weeds, either mechanically or with herbicides. From the standpoint of the cotton portion of the system, crop protection chemical treatments are used to reduce competition from other plants and limit plant damage by insects. The parts of the cotton plant that are critical to protect from insects are the squares (buds), bolls, and the leaves. We will show that from the standpoint of birds, the cotton portion of the system is a relatively poor habitat to forage for food. Weed and insect populations will be low in properly managed fields. Soil invertebrate populations are also likely to be low due to tillage practices. The cotton plants themselves are not typically eaten by birds. There is variability in production practices across the Cotton Belt, which we will address by discussing Western Cotton (West Texas, Arizona, and California) and Southern Cotton (Texas High Plains east to North Carolina) separately. Chlorfenapyr will be used in two different ways, as shown in the PIRATE® and ALERT® labels, and the use patterns roughly correspond to Southern and Western Cotton. Following is a description of cultural practices in the these two portions of the Cotton Belt. (See also Figure 3, page 26.)

Land preparation is intensive in most cotton production areas. Cotton has an average crop production time of 240 days. Weather permitting, cotton land is disced and rows are formed in the fall following crop harvest. In the spring, the rows are reformed in preparation for planting.

Southern Cotton

Annual Pattern - In Southern Cotton (from Texas High Plains to the Carolinas), planting typically takes place from mid-April through May. Seedling cotton will emerge one to two weeks after planting if weather is optimal. Pinhead square stage begins in late-May to early-June with first bloom occurring in July. Peak bloom begins in mid-July and continues for 4 - 6 weeks at which point boll maturation begins. Harvest typically begins in September and can run through November. Southern Cotton produces moderate to high average yields of 1½ to 2½ five hundred pound bales per acre. The High Plains region of Texas (low input) can have low yields of about ½ bale per acre.

Irrigation - In general, there is adequate soil moisture until July. In July, dry periods may occur and supplemental irrigation is required. Approximately 30% of the Southern Cotton acreage receives supplemental overhead irrigation, usually through center pivot systems. Most of this acreage is concentrated in the Mississippi Delta and the High Plains of Texas. Irrigation, if required, is provided through August.

Weed Management - After crop emergence, the crop is typically cultivated 2 - 3 times to control weeds and to aerate the soil for better crop growth. Weed control in cotton is critical to reduce not only competition from weeds for nutrients and water, but also to reduce contamination of the cotton lint with weed parts during harvest. Weed control is accomplished with a combination of cultivation, preplant, preemergent, and multiple postemergent herbicide applications.

Pest Management - From crop emergence to the pinhead square stage, the crop should be protected from arthropod pests such as thrips and aphids. In general, crop protection is provided by an at-planting application of a granular soil insecticide. At pinhead square (late-May to June), overwintering boll weevils, plant bugs, and the 1st *Heliothis* generation can be serious pests causing significant square loss. Pre-bloom stage is Phase I of the Southern States Resistance Management Plan. The primary objective in Phase I is to preserve the efficacy of the pyrethroids and the organophosphates. The guidelines recommend that pre-bloom crop protection products should be selected based on consideration of all insect pests in the field to be treated, impact on beneficial arthropods, and risk of control failures due to pesticide resistance in subsequent *Heliothis* generations.

Phase II is the post-bloom stage of cotton. By early- to mid-July, *Heliothis* moths of the June infestation emerge and begin laying eggs in cotton. Pest population levels typically exceed treatment thresholds and require control. Selection of pest control materials during this stage is particularly critical because all pests can multiply through the remainder of the season. In late-July through September, moths of the July infestation emerge and begin laying eggs in cotton. However, *Heliothis* generations become less distinct as the season progresses due to varying developmental time and extended egglay by individual moths. These circumstances result in overlapping generations and the occurrence of all growth stages (eggs, larvae, and moths) simultaneously in the field. From July through September, aphids, armyworms and loopers can be important pests that require control measures. Boll weevil infestations may also require control measures until harvest.

PIRATE® Use Pattern

Mite Control on Mid- to Late-season Cotton - PIRATE applications at rates ranging from 0.15 to 0.2 lb. a.i./A provide effective control of mites on cotton.

Worm Control on Mid- to Late -season Cotton - PIRATE applications at 0.2 lb. a.i./A will provide effective control of beet armyworm. Rates of 0.3 lb. a.i./A alone, or 0.2 to 0.25 in a tank-mixture with labeled larvicides, will provide effective control of tobacco budworm and cotton bollworm. The unique mode of action of PIRATE provides control of budworm and bollworms resistant to other chemistries. In addition, these rates will also control other armyworms and loopers present in the field at time of application.

Input costs - In general, input costs to produce a good cotton crop are moderate to high. For example, a grower could expect to spend, at a minimum, $450 per acre for land preparation, planting, cultivation, weed and insect control, harvest preparation, and harvest. Insect control treatments are highly dependent on pest pressure and can further increase costs.

Western Cotton

Annual Pattern - In Western Cotton (West Texas to California), planting typically takes place in April through mid-May. However, in some areas, such as the Lower Rio Grande Valley of Texas, planting may occur as early as February. Seedling cotton will emerge about one to two weeks after planting if weather is optimal. In general, pinhead square stage begins in June with first bloom occurring in July. Peak bloom begins in late-July and continues for 4 - 6 weeks, at which point boll maturation begins. Generally, harvest begins in September and runs into December. However, in the Lower Rio Grande Valley of Texas, harvest may begin as early as late-July for cotton planted in February. Western Cotton can produce high average yields of 2½ to 3 five hundred pound bales per acre. Stalk destruction shortly after harvest is a common practice in Western Cotton to reduce overwintering insect populations, especially boll weevil and pink bollworm.

Irrigation - Irrigation is used on the vast majority of Western Cotton acreage. Typically irrigation starts after crop emergence (March through April) and continues until crop maturity (mid-August through September). Irrigation is provided primarily via furrow irrigation with some overhead irrigation. It is provided on a 10 day schedule or as needed.

Weed Management - After crop emergence, the crop is typically cultivated 2 - 3 times to control weeds and to aerate the soil for better crop growth. Weed control in cotton is critical to reduce not only competition from weeds for nutrients and water, but also to reduce contamination of the cotton lint with weed parts during harvest. Weed control is accomplished with a combination of cultivation, preplant, preemergent, and multiple postemergent herbicide applications.

Pest Management - From crop emergence and until pinhead square, the crop should be protected from arthropod pests such as mites and thrips. In general, crop protection is provided by an at-planting application of a granular soil insecticide. Early season mite infestations are typically controlled by thrips; however, insecticide applications may be warranted. At this stage of cotton growth, thrips can be a beneficial insect that keeps mite numbers low, or it can be a pest causing damage to the cotton. Lygus (plant bugs) become important pests at the pinhead square stage. Once applications are initiated for lygus control, there is little control of mites by natural enemies. Mites continue to be a problem on cotton until September, with peak squaring (mid-July) as the most critical period for control. Pink bollworm is the major worm pest in Arizona and California cotton. First generations begin feeding on small squares, with later generations feeding on bolls. Pink bollworm populations peak in August and September. During peak bloom, worm pests, such as budworm/bollworm and armyworms, may cause significant damage to the crop.

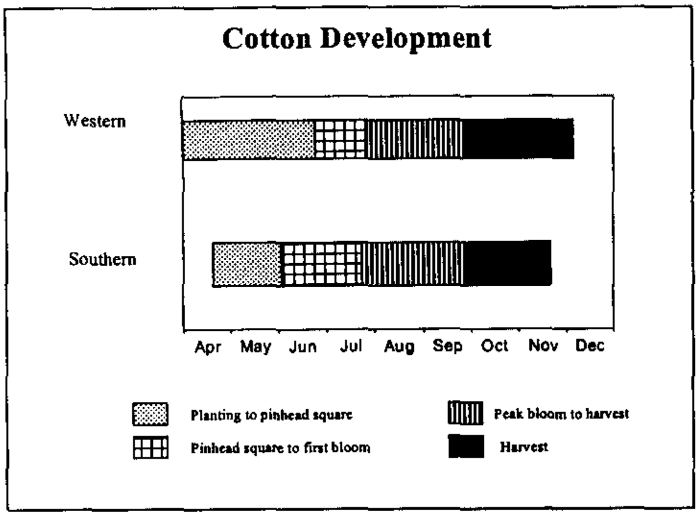
ALERT® Use Patterns

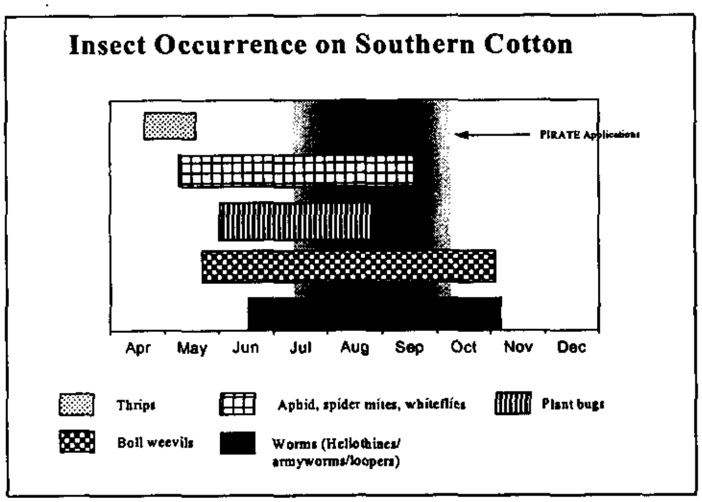
Mite Control on Seedling Cotton (May to early-June) - ALERT used at low use rates (0.075 - 0.15 lb. a.i./A) provides effective control of mites infesting seedling cotton (< 12" in height).

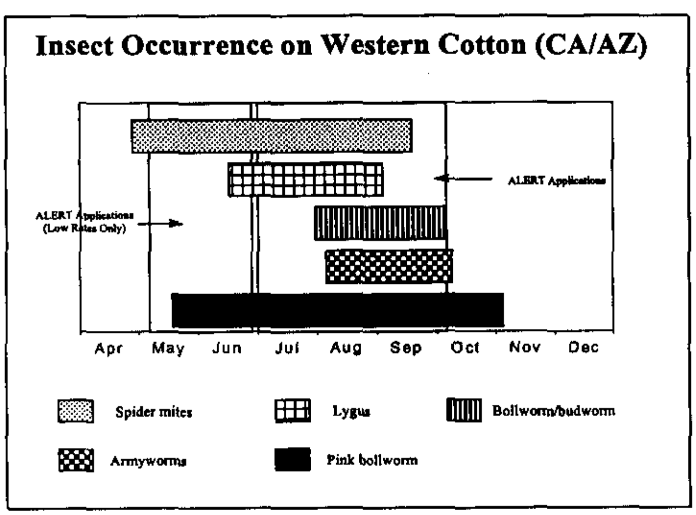
Mite/Budworm/Bollworm/Armyworm Control on Mid- to Late-season Cotton (July to September) - ALERT applications at rates ranging from 0.15 to 0.25 lb. a.i./A for mites and 0.2 to 0.3 lb. a.i./A for worms are the effective for control of these pests on mid- to late-season cotton.

Input costs - In general, monetary input costs to produce a good cotton crop are moderate to high. Water and insect control costs can be very high. For example, a grower could expect to spend typically $590 per acre for land preparation, planting, cultivation, weed and insect control, harvest preparation, and harvest. Insect control treatments are highly dependent on pest pressure and can further increase costs.

Figure 3. Cotton Development and Insect Occurrence in U.S. Cotton.







Field Borders

The border area surrounding the cotton field is potentially a more suitable habitat for birds than the treated field itself. This border comprise a wide variety of vegetation types and associated ecotones grading into the cotton field. The types include, *inter alia,* desert scrub, riparian, hardwood forest, pine forest, bottomland forest, grassland, and other cotton or agricultural fields. More detail will be provided about these habitat types in the Analysis.

As mentioned earlier the border area was defined as 50 meters for purposes of this assessment, since drift could deposit residues in this area. (See **Analysis** for supporting data, pages 46 and 59.)

It is possible to derive estimates for the maximum acreages of cotton field borders that have potential to contain residues. First, there are about 12,425,000 acres (range 7,926,300 to 16,931,400 acres) of cotton routinely planted in 16 states of the US Cotton Belt annually (AL, AR, AZ, CA, FL, GA, LA, MO, MS, NM, OK, NC, SC, TN, TX, VA). These numbers represent the averages and minima and maxima for the period of 1965 through 1996. (USDA Agricultural Statistics, 1980, 1986, and 1997). The numbers are not expected to change significantly due to the edaphic and climatic requirements of commercial cotton production. Second, a representative commercial field size might range from 10 to 200 acres. Third, assume the fields are square. Given these assumptions, the following table shows ranges for acreages of the 50 meter borders around cotton fields.

Cotton Acres	Field Size (Acres)	Number of Fields	Acres in the Border
12,425,000	10	1,242,500	15,410,000
12,425,000	50	248,500	6,138,000
12,425,000	100	124,250	4,212,000
12,425,000	200	62,125	2,914,000

These values represent conservative estimates of the non-crop acreages potentially exposed to chlorfenapyr, if all cotton acreage were to be treated. Not all cotton acres will be treated with chlorfenapyr; most of the market is in AL, AR, CA, FL, GA, LA, MS, and TX based on Section 18 Emergency Exemption applications for 1994, 1995, 1996, and 1997. Furthermore, not all the acres in these states will be treated in any given year. For example, a highly conservative overestimate assumes 19% of the total acres planted to cotton may receive a chlorfenapyr application. This is based on a historical average of 6.8M acres of cotton requiring treatment for the control of tobacco budworm/cotton bollworm. From state resistance monitoring results, it can be conservatively estimated that resistant tobacco budworm/cotton bollworm infest approximately 20%, or 1.4M acres, of the 6.8M acres. Cotton acreages requiring insecticide applications for mite and beet armyworm infestations, historically average 1.1M and 0.8M acres, respectively. Based on a high market estimates, maximum of 50% of these acreages (0.6M for mites and 0.4M for beet armyworm) may receive chlorfenapyr applications. Another consideration is that not all of the border will be non-crop – often agricultural fields are adjacent to other agricultural fields. Finally, the body of data on drift indicates that the levels of chlorfenapyr residues in the border will be much lower than the residue levels in the treated fields.

Assessment Endpoints For Avian Risk

According to the EPA *Framework*, assessment endpoints are explicit expressions of the actual environmental value that is to be protected (EPA 1992). There are several criteria for selecting assessment endpoints. These criteria include ecological relevance, susceptibility to the stressor, and the relationship of the assessment endpoints to management goals. Also, it would be ideal if assessment endpoints could be measured directly and thereby serve also as measurement endpoints (EPA 1996). Such a direct relationship would reduce the uncertainty in the assessment.

Each assessment endpoint must contain two elements: the valued ecological entity and the characteristic of that entity which is potentially at risk and which is important to protect (EPA 1996). For this assessment, the valued ecological entity is the bird species associated with the cotton agroenvironment defined above. Endpoints are established for three levels of biological organization of the valued ecological entity: the individual, the local population (i.e., birds associated with a single cotton agroenvironment – see Footnote [2]), and the regional population (i.e., birds in a county or larger unit).

At the individual level, reductions in survival and reproduction due to direct effects of chlorfenapyr have been selected as endpoints, based on the toxicity characteristics observed in laboratory tests. At the local population level, change in population size due to changes in survival or reproduction has been selected. At the regional population level, change in population size due to changes in survival or reproduction has also been selected as the endpoint. The assessment endpoints selected are for direct effects, not secondary or "cascading" effects (EPA 1996). The rationale for focusing on direct effects is that use of chlorfenapyr is not expected to alter the insect or plant food bases compared to the food bases that currently exist. These food bases have come about due to current and historical management of insects and weeds in cotton and other cultural practices.

The assessment endpoints selected clearly have ecological relevance, and have the potential to be susceptible to chlorfenapyr. Furthermore, both the valued ecological entity and the characteristic to be protected are identified. The major shortcoming of the assessment endpoints selected is that they are not measured directly under the current FIFRA Pesticide Assessment Guideline requirements for testing. Therefore, it will be necessary to use measurement endpoints that are different from the assessment endpoints. Although some uncertainty may be introduced into the assessment because of this difference, it will likely be small, because the assessment endpoints can be represented by variables that it is possible to measure, monitor, or model with reasonable confidence.

Measurement Endpoints for Avian Risk

Measurement endpoints are measurable responses to a stressor that are related to the valued characteristics identified by the assessment endpoints (EPA 1992). There are several considerations for selecting measurement endpoints. These considerations include: relevance to the assessment endpoint; consideration of indirect effects; sensitivity and response time;

[2] It is clear that this use of the term "population" could be debated. It is clearly debatable whether the 2 or 3 pairs of songbirds inhabiting the border around a cotton field are a population in the strictest sense. Such a small number of pairs of birds would be highly subject to the vagaries of weather and predators, and might easily become "extinct". Nonetheless, because the field is the basic management unit, as well as the likely experimental unit, some term needs to be used to describe the birds associated with individual units of the agroenvironment.

signal-to-noise ratio; consistency with assessment endpoint exposure scenarios; diagnostic ability, and practicality (EPA 1992).

Since the 1992 *Framework* document, EPA has issued a draft guidance document for ecological risk assessment (1996). In the guidance document, the term "measurement endpoints" was replaced with three terms. These terms are "measures of effect", "measures of exposure" and "measures of ecosystem and receptor characteristics". Measures of effect are measures used to evaluate the response of the assessment endpoint when exposed to the stressor. Measures of exposure are measures of how exposure may be occurring, including how a stressor moves through the environment and how it may co-occur with an assessment endpoint. Measures of ecosystem and receptor characteristics include ecosystem characteristics that influence the behavior and location of assessment endpoints, the distribution of a stressor, and life history characteristics of the assessment endpoint that may affect exposure or response to a stressor. In fact, all of these measures are inter-related to some extent.

Some general observations about the approach taken in deciding upon the measures used in this assessment are in order. The assessment endpoints selected are not measured in the standard testing battery required by the current Pesticide Assessment Guidelines. Nor can some of these assessment endpoints be readily estimated from the results of standard tests. Therefore, we decided to rely on a suite of measures and a weight-of-the-evidence approach rather than relying on a single index or measure. An advantage of endpoints at different levels of biological organization is that the likelihood of effects at one level can be inferred from the likelihood of effects at lower levels. The use of a suite of measures at different levels of biological organization can build greater confidence in the conclusions of the assessment (EPA 1992). While this approach may not make regulatory decisionmaking easy, because it does not necessarily provide point estimates that indicate risk or lack of risk, it does provide the risk manager with a wealth of information with which to evaluate relative risks and to recommend effective risk mitigation measures.

As noted above, the various measures – effects, exposure, ecosystem and receptor characteristics – are, by their nature, inter-related. The same statement holds true for the three levels of biological organization selected. It is somewhat artificial to draw a sharp distinction between survival and reproduction of individual birds versus survival and reproduction of local or regional populations of birds. Nonetheless, it is also clear that risk managers have questions about potential effects of a stressor at the different levels of biological organization. In an attempt to address these questions, the various parts of the chlorfenapyr data base will be relied on differentially for the different levels of biological organization. Again, this is a somewhat artificial distinction, because in a sense the entire data base relates to all three levels of biological organization.

Although the distinctions being drawn are somewhat artificial, they provide a major advantage in this higher tier assessment compared to a Tier 1-type assessment. In a Tier 1-type assessment, which relies primarily on Risk Quotients and published residue levels, it is difficult to integrate information on other measures, such as measures of ecosystem and receptor characteristics.

Individual Birds

Protection of individual birds is a valid risk management objective, especially for threatened or endangered species. However, neither the standard laboratory toxicity tests under

Subdivision E nor the standard "Hoerger and Kenaga" (1972) estimates of residues on certain bird food items are useful for assessing risk to individual birds. Toxicity information in and of itself may be an indicator of effects if a bird receives a dose. Day of application, worst case residue levels on certain bird food items are not reliable estimators of dose, because of the vagaries of bird feeding behavior.

The measure of effect used for individual birds will be the general toxicity profile for chlorfenapyr. The measure of exposure used will be the general partitioning and degradation of chlorfenapyr in the environment. Measures of ecosystem and receptor characteristics will include: state lists of birds in cotton-growing regions, along with information on their habitat preferences, seasonal occurrence, and feeding and breeding habits; data from avian censuses in and around cotton fields across the Cotton Belt; Section 18 Emergency Exemption monitoring efforts by the States; avian field study information, and estimates of the food base for birds in cotton fields and associated non-cotton habitats. This latter estimate can be made from the entomological literature and the cotton scouting guides published by state Extension Services.

Local Bird Populations

In the context of this assessment, local bird populations are defined as those populations inhabiting individual cotton agroenvironments. It should be clear that the information used to assess risk to individual birds is also applicable at this higher level of biological organization. The information for individual birds helps to focus the assessment on the birds most likely to be exposed and identifies species at risk. Also, the conclusions for risk to individual birds will be important in evaluating risk to local bird populations.

The measures of effect used for local populations will be the numerical results of the standard laboratory toxicity tests under Subdivision E, i.e., LD_{50}, LC_{50}, 28-day feeding, and avian reproduction study results, and similar non-guideline toxicity studies. The measures of exposure used will be the results of the numerous field studies that provide residue levels, and their decline over time, in relevant avian food items. The measures of ecosystem and receptor characteristics will be incorporated by selecting bird species that are likely to be exposed to residues of chlorfenapyr due to their feeding habits and the times they use the cotton agroenvironment.

Regional Bird Populations

In the context of this assessment, regional bird populations are defined as those populations inhabiting the cotton agroenvironments in convenient politically-based units such as counties and states, or biologically-based ecoregions. It should be clear that the information used to assess risk to individual birds and local populations is also applicable to this level of biological organization. Also, the conclusions for risk to local bird populations will be important in evaluating risk to regional bird populations.

At the regional population level of organization, the measure of effect will again be the general toxicity profile for chlorfenapyr. The measure of exposure will be the general partitioning and degradation of chlorfenapyr in the environment. Measures of ecosystem and receptor characteristics will include information on the borders of the cotton agroenvironment, information on the extensiveness of applications of chlorfenapyr, and information on the extensiveness of cotton production.

The suites of measures selected and the different levels of biological organization assume applicable exposure scenarios, are likely to be susceptible to chlorfenapyr on the same time scale as the assessment endpoints, and are practical to measure. It is assumed that they have acceptable signal-to-noise ratios. Many of the measures do not possess diagnostic ability specific to chlorfenapyr; hence inferences about effects will be biased towards overestimates (i.e., based on laboratory toxicity information, mortalities observed in field studies may be inferred to be due to chlorfenapyr). The measures do not relate particularly well to indirect effects, but as explained above, chlorfenapyr is not expected to alter the insect or weed food bases, given the existing need to manage insects and weeds in commercial cotton fields.

Ecological Effects

As mentioned in the **Background**, there is a large database of guideline and non-guideline studies of chlorfenapyr in the laboratory and in the field. There is also considerable information available on cotton pest management practices, the numbers of acres treated, and the cotton production system in a spatial context. The ecological effects that could arise from exposure to chlorfenapyr are intoxication, mortality, or reduced egg production. As developed in the **Conceptual Model** below, and the **Refined Conceptual Model** (page 81), it is expected that the most important route of exposure will be ingestion of the compound on food items. The potential for secondary (indirect) effects is likely to be low. The application of chlorfenapyr will reduce insect populations in the treated cotton fields, but these fields are already managed to control insects (chlorfenapyr will substitute for application of some other chemistry). There may be some reductions of the insect populations in the border areas of fields as well, but we will show that these reductions will be transient and will only occur very close to the treated field. Chlorfenapyr has no toxicity to plants, so there is no reason to expect effects on the plant food base.

Conceptual Model

According to the *Framework* for Ecological Risk Assessment (EPA 1992), summarization of the information obtained from the problem formulation process is developed into a conceptual model. The conceptual model allows for the development of working hypotheses about how the stressor might affect components of the natural environment (NRC 1986). The conceptual model is used to define possible exposure scenarios. These are qualitative descriptions of how the ecological components contact the stressor (EPA 1992). The conceptual model also includes descriptions of the ecosystem at risk and the relationship between the measurement and assessment endpoints (EPA 1992). Finally, the conceptual model describes the types of data and analytical tools to be used in the analysis phase. The general risk scenario to be evaluated is as follows:

- Foliar applications of chlorfenapyr on cotton may result in residues in different *environmental compartments;*
- If levels of residues are sufficiently high and durations of exposure are sufficiently long, there may be acute or chronic effects on avian species.

Potential Pathways and Routes of Avian Exposure

Table 1 summarizes the conceptual direct and indirect pathways and routes of exposure of an individual bird to an insecticide applied to cotton. These are discussed in more detail below. This table is based on a generalized schematic of possible exposures developed by R. Bennett, ecological planning & toxicology, inc. Note that spatial aspects of treated fields, which are important in estimating risk to the local and the regional population, will be incorporated into the refined conceptual model later, during the **Analysis** phase.

TABLE 1. *Conceptual Direct and Indirect Pathways and Routes of Avian Exposure for an Insecticide Sprayed on Cotton*[1]

Potential Pathway	Potential Route
1. Spray Droplets a. Contacting bird b. Contacting insects/invertebrates	 Direct[2]: dermal, inhalation, ingestion Indirect[3] ingestion
2. Sprayed plants a. *(Revolatilized in air)* b. Residues on plant surfaces c. Residues in plant tissue	 (Direct: inhalation) Direct & indirect: dermal, ingestion Direct & indirect: ingestion
3. Water (overspray or resulting from runoff) a. Surface water, wet soil, etc. b. (Revolatilized in air) c. Residues in aquatic organisms	 Direct & indirect: dermal, ingestion (Direct: inhalation) Indirect: ingestion
4. Soil (overspray or from runoff or tillage) a. *(Revolatilized in air)* b. Adsorbed to soil c. Adsorbed to sediment d. Residues in aquatic organisms	 *(Direct: inhalation)* Direct & indirect: dermal, ingestion Direct & indirect: dermal, ingestion Indirect: ingestion

[1]Pathways in parentheses are considered insignificant contributors to overall avian risk in the case of chlorfenapyr due to its negligible volatility.
[2]Birds may be exposed directly to residue.
[3]Birds may be exposed indirectly via another organism or object that has been directly exposed.

General Partitioning of Chlorfenapyr into Air, Soil, Plants and Other Possible Food Items, and Water

In this section, we discuss the potential ways that exposure to chlorfenapyr might theoretically occur. These theoretically plausible scenarios are evaluated in the **Analysis** phase.

Chlorfenapyr is applied as a water-based spray of a Suspension Concentrate (SC) formulation. Applications will be made either with ground or aerial equipment. The general partitioning of the compound in the environment should be substantially similar for the two types of application equipment, although the potential for off-site movement, via drift, will likely be greater for the aerial application method.

As the application equipment moves over the cotton crop, chlorfenapyr is released as a "medium spray" based on a volume mean diameter (vmd) of 201-300 microns. As these droplets settle, they may be intercepted by the cotton plants, hit the ground in the cotton field, or move off-site. Before the droplets settle, birds can only inhale them if they are of sufficiently small diameter. Droplets which settle onto birds may be absorbed through the skin or ingested as a result of preening or grooming activities. These would be "primary" routes of exposure in the first moments after application before droplets settle. Another potential "secondary" route of exposure would be by ingestion of organisms that have themselves come into contact with the spray.

Droplets which settle onto cotton plants will come into contact with the waxy cuticle and remain there; chlorfenapyr exhibits translaminar movement, but no systemic activity. Theoretically, the compound on the cuticle could volatilize off with time, be washed off the cuticle by rainfall, dew, or irrigation water, remain in place bound to the cuticle, or degrade to other compounds. In cotton culture, the leaves are typically removed from the plants using a defoliant prior to harvest. These desiccated leaves may remain on the soil surface in the cotton field, or they may be turned under in preparation for planting the next crop. Therefore, any chlorfenapyr that is bound to cotton leaves could theoretically become incorporated into the upper tilled layer of soil. From this analysis, considering the treated plant, primary exposure of birds to chlorfenapyr might occur as follows: by ingestion of the treated cotton plant; by contact with treated surfaces of the plant; or by ingestion or contact with water that contains chlorfenapyr and has run off plant surfaces. Because of chlorfenapyr's low volatility, inhalation exposure from treated surfaces is unlikely. Soil-inhabiting organisms could also be exposed to chlorfenapyr that remains in cotton leaves that are turned under into the soil. Secondary exposure could occur as a result of ingesting organisms that come into contact with chlorfenapyr via the primary routes just listed.

Droplets which settle onto the soil will tend to bind to it and remain there; as will be developed in more detail later, chlorfenapyr has a very strong tendency to bind to (adsorb to) soil and will therefore not tend to desorb from it. In a laboratory study, less than 1.5% of the compound was extractable into water from flooded soil (MRID No. 43492847) during two months under anaerobic conditions.

The behavior on the soil is analogous to that which theoretically could occur on the leaves. Because of chlorfenapyr's low volatility and low water solubility, volatilization from the soil surface or dissolution in dew, rainfall, or irrigation water is unlikely. Residues will either remain bound in place on the soil, or degrade to other compounds. Residues are unlikely to volatilize from solutions. Thus, primary exposure of organisms to chlorfenapyr might occur as follows: by ingesting or burrowing through the treated soil; by contact with the treated soil surface; or by contact with water that contains dissolved chlorfenapyr. The secondary route of exposure mentioned above, i.e. by ingestion of organisms that have come into contact with chlorfenapyr by the primary routes, also applies here.

The general partitioning and potential routes of exposure described above, will also hold for any chlorfenapyr that moves off the treated field and settles onto vegetation or bare soil. The major compartment that could come into play as a result of off-site movement would be a pond or other body of water adjacent to a treated area. Chlorfenapyr which settles onto a body of water would either go into solution in the water column, bind to suspended matter in the water, or to the bottom sediments. Exposure of aquatic organisms could be by immersion or ingestion of the contaminated water, suspended particles, and sediment.

A considerable body of evidence suggests there will be a significant difference in the amount and nature of exposure that arises from ground and from aerial applications. In general, it is known that the potential for drift is less from ground applications as compared to air. This fact implies that the magnitude of residues in the various compartments on the treated field will be higher after ground application than after aerial application. Conversely, the likely magnitude of residues in off-site compartments will likely be greater after aerial application.

Physical and Chemical Properties

The theoretical exposure scenarios described above can be refined based on chemical-specific properties. The physical and chemical characteristics of chlorfenapyr determine how it will partition in the cotton agroenvironment and therefore what exposures may be significant. Exposures via the inhalation route can be expected to make a negligible contribution, if any, to overall risk. Chlorfenapyr has a very low vapor pressure (4.05×10^{-8} torr @25°C) and is considered to be non-volatile according to results of EPA required tests. In light of chlorfenapyr's low vapor pressure and its lipophilicity, it is highly unlikely to revolatilize from solution on the waxy cuticle of plants or on soil or other environmental surfaces. While there is theoretically some potential for direct avian inhalation exposure during periods of spray application, this is unlikely due to the size of droplets produced by typical nozzles. (See page 55 for additional supporting information.)

Because chlorfenapyr's water solubility is very low (0.12 ppm) and because it and its major soil metabolite have a high affinity for organic matter (K_{oc} of AC 303630 = 11500, K_{oc} of CL 312094 = 3060), avian exposure pathways involving soil and/or sediment may reasonably be expected to dominate any direct avian exposure to chlorfenapyr via water. Direct and indirect ingestion of water will therefore not be specifically evaluated in the assessment.

Table 2 presents a summary of the potentially significant avian exposure pathways for chlorfenapyr in cotton. These pathways will be examined in the **Analysis** (see page 81). A weight-of-the-evidence approach will be employed, using a suite of measurement endpoints as well as qualitative information, to characterize exposures and risks. This conceptualization will be further refined in the **Analysis**.

TABLE 2. Avian Exposure Assessment for Chlorfenapyr on Cotton: Potentially Significant Pathways

Route of Exposure	Potentially Significant Pathway
Dermal	Spray droplets Plant surfaces Bare soil Sediment
Ingestion	Spray droplets In/on insect/invertebrate diet items In/on plant material diet items On sediment In aquatic organism diet items In vertebrate diet items

Spatial and Temporal Aspects of Exposure

Maximum potential for exposure to chlorfenapyr exists during the period of application (July - September in Southern Cotton and May - August in Western Cotton). Exposure potential drops *off after application according to the degradation/metabolism rates in various media. This will be* discussed in detail in the **Analysis**.

At the local and regional population level, the potential for exposure is dependent on the percent of local/regional acreage planted to cotton, the use of cotton fields by birds, and the percent of cotton acreage treated with chlorfenapyr in any given year. We will consider these factors in the **Analysis**.

Analysis Plan for this Risk Assessment

The database on chlorfenapyr is very extensive and will be used to assess risk at multiple levels of biological organization. It is possible to present only the highlights of the key studies in the assessment. The discussion of the studies is keyed to detailed summaries in the appendices that the reader may refer to for more information. The **Analysis** phase will provide the data, assumptions, and justification for the **Risk Characterization** phase.

The **Analysis** *will provide the following information to be used during risk estimation and* characterization.

Analysis Plan Outline – Data to be Considered and How they will be Used

Level of Biological Organization	*Southern Cotton*	*Western Cotton*	*Type of Risk Estimate*
Individuals and Threatened and Endangered Species	**Measure of Effect** – Toxicological data in general **Measure of Exposure** – General partitioning and degradation in the environment **Measures of Ecosystem and Receptor Characteristics** – Birds in the Cotton Belt, birds *actually using cotton (censuses)*, timing of applications, suitability of cotton as bird habitat (insect biomass in managed cotton and environs), field study results, Section 18 results	**Measure of Effect** – Toxicological data in general **Measure of Exposure** – General partitioning and degradation in the environment **Measures of Ecosystem and Receptor Characteristics** – Birds in the Cotton Belt, birds *actually using cotton (censuses)*, timing of applications, suitability of cotton as bird habitat (insect biomass in managed cotton and environs), field study results, Section 18 results (these are primarily for Southern Cotton, but will be considered for Western Cotton)	Qualitative Deterministic
Local Populations	**Measures of Effects** – Laboratory toxicity test results **Measures of Exposure** – Measured levels of residues of *chlorfenapyr and their decline in* avian food items **Measures of Ecosystem and Receptor Characteristics** – Bird species likely to be exposed to chlorfenapyr	**Measures of Effects** – Laboratory toxicity test results **Measures of Exposure** – Measured levels of residues of *chlorfenapyr and their decline in* avian food items **Measures of Ecosystem and Receptor Characteristics** – Bird species likely to be exposed to chlorfenapyr	Quantitative (RQs) Multiple scenarios for Southern and Western Cotton *Deterministic*
Regional Populations	**Measure of Effect** – Toxicological data in general **Measure of Exposure** – General partitioning and degradation in the environment **Measures of Ecosystem and *Receptor Characteristics*** – Cotton agroenvironment borders, extent of area treated, extent of area in cotton	**Measure of Effect** – Toxicological data in general **Measure of Exposure** – General partitioning and degradation in the environment **Measures of Ecosystem and *Receptor Characteristics*** – Cotton agroenvironment borders, extent of area treated, extent of area in cotton	Semi-quantitative Deterministic

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Comments on the Problem Formulation Phase for Chlorfenapyr in Cotton

Efforts have been made to perform a comprehensive scoping during **Problem Formulation**. Three levels of biological organization have been identified, assessment endpoints and suites of measurement endpoints have been selected, and a generic conceptual model has been set forth and refined. The conceptual model attempts to identify all potentially significant exposure scenarios. A source of uncertainty that has been identified is the indirect relationships between the assessment and measurement endpoints. This is an issue common to virtually all ecological risk assessments. A weight-of-the-evidence approach, which uses a suite of measurement endpoints, is the best approach to minimize this uncertainty.