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Office of Pesticide Programs

Reregistration Eligibility Decision (RED) for Chlorflurenol

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Reregistration Eligibility Decision for Chlorflurenol Methyl Ester

Reregistration Eligibility Decision (RED) Document for
Chlorflurenol Methyl Ester

List B

Case Number 2095

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Glossary of Terms and Abbreviations

ai	Active Ingredient
aPAD	Acute Population Adjusted Dose
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formulation
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
GLN	Guideline Number
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of a substance per weight or volume of water, air, or feed, e.g., mg/l, mg/kg, or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligram Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification Number. EPA 's system for recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NOAEL	No Observed Adverse Effect Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides, and Toxic Substances
PAD	Population Adjusted Dose
PHED	Pesticide Handler's Exposure Data
PHI	Pre-harvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
ROW	Rights-of-way
RQ	Risk Quotient
TGAI	Technical Grade Active Ingredient
UV	Ultraviolet
WPS	Worker Protection Standard

Abstract

This document presents the Environmental Protection Agency's (hereafter referred to as EPA or the Agency) decision regarding the reregistration eligibility of the registered uses of chlorflurenol methyl ester (hereafter referred to as chlorflurenol). The Agency has determined that chlorflurenol-containing products are eligible for reregistration provided that: (1) current data gaps are addressed; (2) the risk mitigation measures identified in this document are adopted; and (3) labels are amended to implement these measures.

Chlorflurenol is an herbicide and a plant growth regulator registered for use in agricultural, commercial, and residential settings. As chlorflurenol has no food/feed uses and no U.S. tolerances associated with its use, it is not subject to the Food Quality Protection Act of 1996. The Agency has conducted human health and environmental fate and ecological effect risk assessments for chlorflurenol. The risk conclusions of these assessments are summarized below.

Overall Risk Summary

The Agency's human health assessment identifies potential chronic risks to infants from the consumption of drinking water from groundwater sources containing chlorflurenol residues. The reduction in turf rates and limit on number of applications reduces chronic drinking water risks below the Agency's level of concern (LOC).

While potential residential handler risks for all use scenarios are below the LOC, EPA's assessment identifies potential residential postapplication risks to adults and toddlers (including dermal and incidental oral exposure to toddlers). However, the turf mitigation measures lower these risks below the LOC.

Occupational handlers may be exposed to chlorflurenol while mixing, loading, or applying chlorflurenol products. The Agency's assessment identifies potential occupational handler risks for many use scenarios. In order to mitigate risks below the Agency's LOC [margin of exposure (MOE) above 100], this RED requires reduced application rates and the addition of a single layer of personal protective equipment (PPE) plus gloves for all use patterns, with the exception of nonagricultural rights-of-way (ROW), such as utility lines, fence/hedge rows, culverts, ditches, and median strips. In order to mitigate potential risk to handlers for ROW scenarios, this RED requires that handlers wear a double layer of PPE, plus gloves, when handling chlorflurenol for nonagricultural ROW applications.

EPA's assessment identifies potential risk to golf course workers through exposure to postapplication residues of chlorflurenol. The required reduced application rate for commercial use on turf (e.g., golf courses) reduces potential postapplication risks to these workers below the LOC.

The Agency's ecological fate and effects assessment identifies potential chronic risk to mammals from the use of chlorflurenol. However, the required reduced application rates for turf, ROW, and forestry management areas lower the chronic mammalian risk quotients (RQ) below the Agency's LOC; therefore, chronic risk to

mammals (including listed species) is not expected.

While the Agency cannot determine definitive, acute RQ values for birds and mammals, acute effects data demonstrate that chlorflurenol is practically nontoxic to these taxa on an acute basis (avian LD_{50} >10,000 mg ai/kg body weight; mammalian LD_{50}>5,000 mg ai/kg body weight). In addition, the required rate reductions for turf, ROW, and forestry management areas result in a decrease in terrestrial estimated environmental concentrations (EECs) to less than 500 ppm. As these EECs are below the no-effect levels established at the highest doses tested for these taxa, the Agency does not expect acute risk to birds and mammals (including listed species) from the use of chlorflurenol.

The chlorflurenol database is insufficient to preclude risk to the following taxa: birds (chronic), invertebrates, aquatic organisms, and nontarget plants. However, given the current limited use patterns, the low volume of use, and the low acute toxicity to birds and mammals, risk to these organisms is presumed to be low for nonlisted species. For listed species of invertebrates, aquatic organisms, nontarget plants, and birds, the Agency cannot preclude risk to these organisms given the lack of toxicity data.

As there is uncertainty in the ecological fate and effects assessment, the Agency is calling in data to confirm that there is no unreasonable adverse effect to the environment from the use of chlorflurenol. In addition, the Agency is requiring the registrant to place a cap on the sale and distribution of chlorflurenol.

Risk Mitigation

To mitigate potential dietary, residential, and occupational risks from the use of chlorflurenol and to reduce potential exposure to nontarget plants and animals, the Agency is requiring and the registrant has agreed to:

- place a cap on the sale and distribution of chlorflurenol;
- prohibit the use on sod farms and greenhouses;
- prohibit aerial application;
- amend labeling for residential turf by lowering application rates from 3.0 lbs ai/A to 0.25 lb ai/A and a maximum of two applications per year, with a minimum application interval of 45 days;
- amend labeling for commercial use on turf (e.g., golf courses/parks/ornamental turf/weed turf in ditches, etc.) by lowering the application rate from 3.0 lbs ai/A to 0.5 lb ai./A (liquid formulation) and 0.25 lb ai./A (granular formulation), with a limit of one application per year;
- amend labeling for nonagricultural ROW by lowering the application rate from 3.0 lbs ai/A to 1.0 lbs ai/A and one application per year;
- amend labeling for forestry management uses by lowering the application rate from 4.0 lbs ai/A to 2.0 lbs ai/A, with a limit of one application per year;
- amend labeling for ornamental/shade trees uses by lowering the application rate from 4.5 lbs ai/A to 1.0 lb ai/A, with a limit of one application per year; and,
- limit all uses, except for pineapples and residential turf, to one application per year (number of applications currently unspecified on labels).

Next Steps

The Agency is issuing this Reregistration Eligibility Decision (RED) document for chlorflurenol as announced in a Notice of Availability published in the *Federal Register*. In the future, EPA will issue a generic Data Call-In (DCI) for additional data necessary to confirm the conclusions of this RED for the active ingredient chlorflurenol. EPA will also issue a product specific DCI for data necessary to complete product reregistration for products containing chlorflurenol.

I. Introduction

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all submitted data by the EPA. Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential risks arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

This document summarizes the Agency's revised human health and ecological risk assessments and the reregistration eligibility decision for chlorflurenol. The document consists of six sections. Section I contains the regulatory framework for reregistration. Section II provides a profile of the use and usage of the chemical. Section III provides links to the chlorflurenol human health and ecological risk assessments. Section IV presents the Agency's reregistration eligibility and risk management decisions. Section V summarizes label changes necessary to implement the risk mitigation measures outlined in Section IV. Section VI provides information on how to access related documents and contains the appendices that list related information and supporting documents. The chlorflurenol risk assessments are available in the Public Docket, under docket number EPA-HQ-OPP-2006-0874 on the web page, http://www.regulations.gov.

II. Chemical Overview

Chlorflurenol is a plant growth regulator and an herbicide. As an herbicide, chlorflurenol is used for the postemergent control of broadleaf weeds in turf. While chlorflurenol has inherent herbicidal properties, it is typically combined with other herbicides, such as dicamba, to enhance their activity. As a plant growth regulator, chlorflurenol is used to retard the growth of grasses, broadleaf weeds, trees, shrubs, and vines. It penetrates into herbaceous plants, via foliage and/or roots, and moves freely inside the plant (acro and basipetal transport). Chlorflurenol blocks or slows down the growth and development of growing tips and buds of herbaceous plants.

Chlorflurenol is also used to stimulate the growth of pineapple planting material or sliplets. The Agency does not consider this use on pineapples to be a food use, as the

first harvest from chlorflurenol-treated planting material occurs well over one year after planting. Thus, no finite chlorflurenol residues are expected to remain at harvest and no tolerance for pineapples is necessary.

A. Regulatory History

The first chlorflurenol registration was issued to the U.S. Borax Corporation by the U.S. Department of Agriculture in 1970. In response to the 1989 GDCI, the registrants, EM Industries and Shell International, decided to voluntarily cancel all chlorflurenol registrations. Nita Industries, Inc. (subsequently Repar Corporation) committed to support the reregistration of chlorflurenol through three end-use products. The Pineapple Growers Association of Hawaii acquired a fourth end-use product, which was eventually transferred to Repar Corporation in 1995.

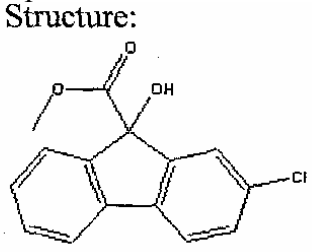
In its 1991 Phase 2 reregistration response, Nita Industries, Inc. requested that the Agency waive a number of data requirements due to the limited production of chlorflurenol and to the "low volume/minor use" of the chemical. The registrant provided the Agency with production and sales data for the principal chlorflurenol product, and anticipated that future sales of the product would stay within a projected low volume. As a result, the Agency waived or put in reserve several studies required in the 1989 GDCI.

B. Chemical Identification of Chlorflurenol

Chlorflurenol consists of three components. The major component (65% to70%) is methyl 2-chloro-9-hydroxyfluorene-9-carboxylate (PC code 098801). The minor components are methyl 2,7-dichloro-9-hydroxyfluorene-9-carboxylate (10% to 15%; PC code 098803) and methyl 9-hydroxyfluorene-9-carboxylate (15% to 20%; PC code 098802). Since the chemical structures for the two minor components are very similar to that of the major component, it is reasonable to believe that they all have herbicidal activity. According to the registrant, these three components are inseparable and are synthesized in a relatively constant ratio.

Tables 1 and 2 provide an overview of chlorflurenol's structure and properties.

Table 1. Nomenclature for Chlorflurenol

Chemical structure	Major product Structure: 
Common name	chlorflurenol-methyl, flurenol
Molecular formula	C15H11ClO3

Molecular weight	274.07 g/mol
IUPAC name	Methyl (*RS*)-2-chloro-9-hydroxyfluorene-9-carboxylate
CAS name	Methyl 2-chloro-9-hydroxy-9*H*-fluorene-9-carboxylate
CAS number	2536-31-4
PC Code	098801

Table 2. Physicochemical Properties of Chlorflurenol

Parameter	**Value**
Melting point/range	136-142 degrees Celsius
pH	Not Applicable, Crystalline material
Density	-1.5 g/L
Water solubility	18 mg/L
Solvent solubility at: 25 degrees Celsius	Cyclohexane 0.24 g/ 100 ml Isopropanol 2.4 g/100 ml Benzene 7.0 g/100 ml Ethanol 8.0 g/100 ml Methanol 15 g/100 ml Acetone 26 g/100 ml
Vapor pressure	5 - 10^{-5} Torr at 25 degrees Celsius
Dissociation constant, pK_a	None
Octanol/water partition coefficient	Estimated Log P 2.86 Estimate from fate data on water 65 or log P=1.81
UV/visible absorption spectrum	None provided

C. Use Sites:

- Chlorflurenol is an herbicide and a plant growth regulator with no registered food/feed uses. As an herbicide, it is registered for the postemergent control of broadleaf weeds in turf. While chlorflurenol has inherent herbicidal properties, it is typically combined with other herbicides, such as dicamba, to enhance their activity.

- As a plant growth regulator, chlorflurenol is used to retard growth of grasses, broadleaf weeds, trees, shrubs and vines. It can be applied to hedge and fence rows, ornamental turf, golf courses, recreational areas, nonagricultural rights-of-way, and forestry management areas.

- Chlorflurenol is also used as a plant growth regulator to produce pineapple planting material (sliplets), which is the only agricultural use of this herbicide. The Agency does not consider this use on pineapples to be a food use, as the first harvest from chlorflurenol-treated planting material occurs well over one year after planting. Thus, no finite chlorflurenol residues are expected to remain at harvest and no tolerances in pineapples

are necessary.

- The only registered residential use of chlorflurenol is for the postemergent control of broadleaf weeds on lawns.

- While chlorflurenol is registered for use on a variety of sites, it is currently being marketed only for the control of pollen and fruit on ornamental olives/citrus in Arizona, Nevada and California, and for the production of pineapple planting material in Hawaii.

D. Formulations:

- Chlorflurenol is formulated as an emulsifiable concentrate and a granular.

E. Methods of Application:

- Chlorflurenol can be applied with several types of application equipment, including airblast sprayers, ground boom sprayers, low pressure handwand sprayers, handgun sprayers, rights-of-way sprayers, tractor-drawn spreaders, push-type spreaders, and belly grinders.

F. Use rates:

- Application rates of chlorflurenol range from 0.25 pounds active ingredient per acre on residential turf to 4.5 pounds active ingredient per acre on ornamental/shade trees.

G. Annual usage:

- As there is only one chlorflurenol registrant, annual usage data cannot be disclosed for confidential business reasons. However, chlorflurenol is considered a low volume use chemical.

H. Technical Registrant:

- Repar Corporation is the sole registrant.

III. Links to the Chlorflurenol Risk Assessments

For details on the risks associated with the use of chlorflurenol, please refer to the Human Health and Ecological Risk Assessments for chlorflurenol located respectively in Appendices J and K. These documents are also available in the public docket EPA-HQ-OPP-2006-0874, located on-line in the Federal Docket Management System (FDMS) at http://www.regulations.gov.

IV. Risk Management and Reregistration Decision

A. Determination of Reregistration Eligibility

Section 4(g)(2)(A) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether pesticides containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic (i.e., active ingredient specific) data required to support reregistration of products containing chlorflurenol.

The Agency has completed its assessment of the dietary (water), residential, occupational, and ecological risks associated with the use of pesticides containing the active ingredient chlorflurenol. Dietary (food) risks are not assessed because there are no food/feed uses of chlorflurenol. Based on a review of the chlorflurenol data base and public comments on the Agency's assessments for the active ingredient chlorflurenol, the Agency has sufficient information on the human health and ecological effects of chlorflurenol to make decisions as part of the reregistration process under FIFRA. The Agency has determined that currently registered uses of chlorflurenol will not pose unreasonable risks or adverse effects to humans or the environment provided that the risk mitigation measures and label changes outlined in this RED are implemented; therefore, products containing chlorflurenol are eligible for reregistration.

Products containing chlorflurenol are eligible for reregistration provided that: (i) required generic and product-specific data are submitted; (ii) the risk mitigation measures outlined in the document are adopted; and, (iii) label amendments are made to implement these measures. Label changes are described in Section V of this document. Appendix B identifies the generic data that the Agency reviewed as part of its determination of reregistration eligibility of chlorflurenol and lists the submitted studies that the Agency found acceptable.

Based on its evaluation of chlorflurenol, the Agency has determined that chlorflurenol products, unless labeled and used as specified in this document, would present risks inconsistent with FIFRA. Accordingly, should a registrant fail to implement any of the risk mitigation measures identified in this document, the Agency may take regulatory action to address the risk concerns from the use of chlorflurenol. If all changes outlined in this document are incorporated into the product labels, then current risks for chlorflurenol will be adequately mitigated for the purposes of this determination under FIFRA. Once a comprehensive endangered species assessment is completed, further changes to these registrations may be necessary.

B. Public Comments and Responses

The Agency solicited comments from the public regarding the reregistration of chlorflurenol through a 60-day comment period, which opened on November 1, 2006 and closed on January 2, 2007. During the public comment period, the Agency received comments from Repar Corporation, the Maui Pineapple Company, Target Specialty

Products, and several university researchers. The Maui Pineapple Company stated that the loss of chlorflurenol, the only registered growth regulator for the production of pineapple planting materials in Hawaii, will result in severe economic hardship for the Hawaiian pineapple industry. Target Specialty Products attested to the important niche that chlorflurenol plays in reducing the production of pollen and fruit in ornamental trees, thus minimizing allergy-related effects and injuries from slipping on fallen fruit. Several university researchers commented on chlorflurenol's ability to enhance the activity of other herbicides, such as dicamba and picloram, when used at low rates in combination with these herbicides. To view the complete set of public comments and the Agency's responses to these comments, please refer to the public docket at http://www.regulations.gov, EPA-HQ-OPP-2006-0874.

C. Regulatory Position

1. Regulatory Rationale

The Agency has determined that chlorflurenol is eligible for reregistration provided the risk mitigation measures outlined in this document are adopted and label amendments are made to reflect these measures. This decision considers the risk assessments conducted by the Agency and the significance of the use of chlorflurenol.

To mitigate identified human health risk concerns from the use of chlorflurenol and to reduce potential exposure to nontarget plants and animals, the Agency is requiring and the registrant has agreed to:

- place a cap on the sale and distribution of chlorflurenol;
- prohibit the use on sod farms and greenhouses;
- prohibit aerial application;
- amend labeling for residential turf by lowering application rates from 3.0 lbs ai/A to 0.25 lb ai/A and a maximum of two applications per year, with a minimum application interval of 45 days;
- amend labeling for commercial use on turf (e.g., golf courses/parks/ornamental turf) by lowering the application rate from 3.0 lbs ai/A to 0.5 lb ai/A (liquid formulation) and from 1.1 lbs ai/A to 0.25 lb ai/A (granular formulation), with a limit of one application per year;
- amend labeling for vegetation (e.g., weed turf, trees, vines and hedges) in nonagricultural ROW and other difficult to access areas by lowering the application rate from 3.0 lbs ai/A to 1.0 lb ai/A and one application per year;
- amend labeling for forestry management uses by lowering the application rate from 4.0 lbs ai/A to 2.0 lbs ai/A, with a limit of one application per year;
- amend labeling for ornamental/shade trees uses by lowering the application rate from 4.5 lbs ai/A to 1.0 lb ai/A, with a limit of one application per year; and,
- All limit all uses, except for pineapples and residential turf, to one application per year (number of applications currently unspecified on labels).

The following is a summary of the rationale for managing risks associated with the use of chlorflurenol. Where labeling revisions are warranted, specific language is set

forth in the summary table in Section V of this document.

a. Human Health Risk Management

For additional details on the chlorflurenol human health risk assessment, please refer to the Human Health Risk Assessments for chlorflurenol located in Appendix J. This document is also available in the public docket EPA-HQ-OPP-2006-0874, located on-line in the Federal Docket Management System (FDMS) at http://www.regulations.gov.

1) Drinking Water Risk Mitigation

The Agency's human health assessment identifies potential chronic risks to infants [142%-176% of the reference dose (RfD)] from the consumption of drinking water from groundwater sources containing chlorflurenol residues. This potential risk is based on eight applications (with 28 day intervals) to turf at 3 lbs ai/A. To mitigate potential drinking water risks, the Agency is requiring that the registrant reduce the turf application rates from a maximum of 3.0 lbs ai/A to 0.5 lb ai/A for liquid formulations and 0.25 lb ai/A for granular formulations. In addition, chlorflurenol labels must specify that only one application may be made per year (number of applications not currently specified). These mitigation measures reduce chronic drinking water risks (3%-3.7% of the RfD for infants) below the Agency's LOC (100% RfD).

2) Residential Postapplication Risk Mitigation

The Agency assessment considers several residential postapplication scenarios for chlorflurenol, including dermal exposure from residue on lawns and turf (adult, youth and toddler), hand-to-mouth transfer of residues on lawns (toddler), ingestion of pesticide residue on treated grass (toddler), and incidental ingestion of soil from pesticide-treated residential areas (toddler). Potential dermal risks to adults (MOE of 44) and toddlers (MOE of 27) from high contact activity on lawns exceed the LOC (MOE of 100) at the 3 lbs ai/A rate. Calculated combined risks to toddlers (i.e., dermal high contact activity plus hand to mouth activity plus object to mouth activity on treated turf plus incidental soil ingestion of pesticide residue from treated turf areas) are, therefore, also of concern.

To mitigate potential residential risks, the Agency is requiring that the registrant lower the application rate for residential turf to 0.25 lb ai/A, with a maximum of two applications per year and 45 days between treatments. These measures reduce the potential residential postapplication risks below the Agency's LOC.

3) Occupational Handler Risk Mitigation

Occupational handlers may be exposed to chlorflurenol while mixing, loading, or applying chlorflurenol products. The Agency's assessment identifies potential occupational handler risks for many use scenarios. In order to mitigate risks below the LOC (MOE above 100), the Agency requires, through this RED, reduced application rates for turf, forestry management, and ornamental/shade trees and the addition of a single layer of personal protective equipment (PPE) plus gloves for these use patterns.

For nonagricultural ROW, in addition to reduced application rates (from 3 lbs ai/A to 1 lb ai/A), this RED requires that handlers wear a double layer of PPE, plus gloves, when handling chlorflurenol. While the MOE for this ROW scenario (MOE=92) is slightly below the target MOE (100), this potential risk is based on the very conservative assumption that handlers absorb 100% of chlorflurenol residues through the dermal route. Because of this conservative assumption, the Agency has determined that the potential risk for the ROW scenario is below the LOC.

While the Registrant indicates that gymnosperm growth can be retarded at a rate of 0.25 lb ai/A, for sake of label simplicity, the Agency is requiring a maximum rate of 1.0 lb ai/A for all vegetation (e.g., deciduous/evergreen trees, hedges, vines, turf) to be controlled in ROW. The Agency does not expect the LOC to be exceeded for chlorflurenol handlers at this rate, as the MOE at 0.25 lb/A is 5,100 (with single layer PPE plus gloves).

4) Occupational Postapplication Risk Mitigation

There are potential postapplication exposures to occupational workers during the typical use patterns associated with chlorflurenol. EPA's assessment identifies potential risk to golf course workers through postapplication exposure to chlorflurenol residues. At the 3.0 lbs ai/A rate for liquid and granular applications, risks are not a concern for hand weeding and transplanting tasks at day 14 and for mowing at day 8. In order to mitigate potential risk to golf course workers, the Agency is requiring that the turf rate be reduced to 0.5 lb ai/A for liquid applications and 0.25 lb ai/A for granular applications. These mitigation measures reduce the potential postapplication risks to golf course workers below the Agency's LOC (MOE of greater than 100 on the day of application).

b. Environmental Risk Management

For additional details on the chlorflurenol ecological fate and effects risk assessment, please refer to the Ecological Risk Assessment for chlorflurenol located in Appendix K. This document is also available in the public docket EPA-HQ-OPP-2006-0874, located on-line in the Federal Docket Management System (FDMS) at http://www.regulations.gov.

Typical use of chlorflurenol may result in exposures to nontarget plants and animals. The Agency's assessment identifies potential chronic risk to mammals from the use of chlorflurenol. The risk quotients (RQs) range from 0.2 to 2.90, the upper bound of which is above the target chronic LOC of 1.0. However, the reduced application rates required in this reregistration decision lower the chronic mammalian risk quotients (RQs from 0 to 0.83) below the LOC; therefore, chronic risk to mammals is not expected.

While the Agency cannot determine definitive, acute RQ values for birds and mammals, acute effects data show that chlorflurenol is practically nontoxic to these taxa on an acute basis (avian LD_{50} >10,000 mg ai/kg body weight; mammalian LD_{50}>5,000 mg ai/kg body weight). In addition, the required rate reductions for turf (from 3.0 lbs ai/A to 0.5 lb ai/A for liquid applications and 0.25 lb ai/A for granular applications), ROW (from 3.0 lbs ai/A to 1 lb ai/A), and forestry management areas (from 4.0 lbs ai/A

to 2.0 lbs ai/A) result in a decrease in terrestrial estimated environmental concentrations (EECs) to less than 500 ppm. As these EECs are below the no-effect levels established at the highest doses tested for these taxa, the Agency does not expect acute risk to birds and mammals from the use of chlorflurenol. The Agency also believes that potential chronic risk to birds is unlikely due to the low acute toxicity to birds and mammals and the low EECs.

The chlorflurenol database is insufficient to preclude risk to the following taxa: birds (chronic), terrestrial invertebrates, aquatic organisms, and nontarget plants. However, given the current limited use patterns, the low volume of use, and the low toxicity to birds and mammals, risk to these organisms is presumed to be low. The Agency is requiring a cap on the sale and distribution of chlorflurenol to maintain its low volume use until additional data are submitted and reviewed by the Agency. These data will be used to confirm the Agency's belief that there is no unreasonable adverse effect to the environment from the use of chlorflurenol.

2. Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide actives and other ingredients) *"may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate."* Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, chlorflurenol may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

3. Endangered Species Considerations

Based upon the screening-level assessment conducted for chlorflurenol, the Agency has identified exceedances of endangered species LOCs for direct chronic effects mammals. However, reduced application rates for turf, ROW, and forestry management areas lower the chronic mammalian RQs below the LOC of 1.0 (RQs from 0 to 0.83); therefore, chronic risk to listed mammals is not expected.

While definitive acute toxicity endpoints could not be determined for birds and mammals, acute risk to listed birds and mammals is not expected as chlorflurenol is considered to be practically nontoxic to these taxa on an acute basis. In addition, the rate reductions required by this RED for turf, ROW, and forestry management areas result in a decrease in terrestrial estimated environmental concentrations (EECs) to less than 500 ppm. As these EECs are below the no-effect levels established at the highest doses tested for these taxa, the Agency does not expect acute risk to listed birds and mammals from the use of chlorflurenol.

The Agency believes that potential chronic risk to birds is unlikely due to the low acute toxicity to birds and mammals and the low EECs. However, given the lack of chronic toxicity data, the Agency cannot completely preclude chronic risk to listed birds at this time.

The chlorflurenol database is insufficient to determine the potential acute/chronic risk to the following listed taxa: nontarget plants, aquatic organisms, and invertebrates. The Agency believes that potential risk to these taxa is unlikely given the current limited use patterns, the low volume of use, and the low acute toxicity to birds and mammals. However, given the lack of toxicity data, the Agency cannot preclude risk to these organisms.

The Agency considers a potential for not only direct effects, but also adverse indirect effects to listed species that rely on other affected organisms. There may be a potential concern for indirect effects to the following groups of organisms from the use of chlorflurenol: terrestrial plants, aquatic plants, birds, mammals, reptiles, aquatic invertebrates, fish, amphibians, and terrestrial insects.

Table 3 summarizes the potential risk to listed species associated with the application of chlorflurenol for turf use.

Table 3. Listed Species Risks Associated with Direct or Indirect Effects Due to Applications of Chlorflurenol for Turf Use.

Listed Taxon	Direct Effects	Indirect Effects
Terrestrial and semi-aquatic plants – monocots	Yes [a]	Yes
Terrestrial and semi-aquatic plants – dicots	Yes [a]	Yes
Insects	Yes [a]	Yes
Birds	Acute – No [b]; Chronic – Yes [a]	Yes
Terrestrial phase amphibians	Acute – No [b]; Chronic – Yes [a]	Yes
Reptiles	Acute – No [b]; Chronic – Yes [a]	Yes
Mammals	Acute – No [b]; Chronic – No [c]	Yes
Aquatic vascular plants	Yes [a]	Yes
Freshwater fish	Yes [a]	Yes
Aquatic phase amphibians	Yes [a]	Yes

Freshwater crustaceans	Yes [a]	Yes
Mollusks	Yes [a]	Yes
Marine/estuarine fish	Yes [a]	Yes
Marine/estuarine crustaceans	Yes [a]	Yes

[a] We cannot preclude risk due to lack of data.
[b] RQs were not calculated because toxicity endpoints were not definite values; however, since the amount estimated to occur in the environment falls below 500 ppm, RQs will not likely exceed the LOC for endangered species.
c Based on calculations using a developmental study showing evidence of delayed skull ossification and cleft palates in young rats.

a. The Endangered Species Program

The Endangered Species Act requires federal agencies to ensure that their actions are not likely to jeopardize listed species or adversely modify designated critical habitat. The Agency has developed the Endangered Species Protection Program to identify pesticides whose use may cause adverse impacts on threatened and endangered species, and to implement mitigation measures that address these impacts. To analyze the potential of registered pesticide uses that may affect any particular species, the Agency uses basic toxicity and exposure data developed for the REDs and then considers ecological parameters, pesticide use information, geographic relationship between specific pesticide uses and species locations, and biological requirements and behavioral aspects of the particular species. When conducted, this species-specific analysis will also consider the risk mitigation measures that are being implemented as a result of this RED.

Following this future species-specific analysis, a determination that there is a likelihood of potential effects to a listed species may result in limitations on use of the pesticide, other measures to mitigate any potential effects, or consultations with the Fish and Wildlife Service and/or the National Marine Fisheries as appropriate. If the Agency determines use of chlorflurenol "may affect" listed species or their designated critical habitat, the Agency will employ the provisions in the Services' regulations (50 CFR Part 402). Until the species-specific analysis is completed, the risk mitigation measures being implemented through this RED will reduce the likelihood that endangered and threatened species may be exposed to chlorflurenol at levels of concern. The Agency is not requiring specific chlorflurenol label language at the present time relative to threatened and endangered species. If, in the future, specific measures are necessary for the protection of listed species, the Agency will implement them through the Endangered Species Program.

4. Other Labeling Requirements

In order to be eligible for reregistration, various use and safety information will be included in the labeling of all end-use products containing chlorflurenol. For the specific labeling statements and a list of outstanding data, refer to Section V of this document.

V. What Registrants Need to Do

The Agency has determined that chlorflurenol is eligible for reregistration provided that the risk mitigation measures identified in this document are adopted and label amendments are made to reflect these measures; however, additional data are required to confirm this decision. In the near future, the Agency intends to issue Data Call-In Notices (DCIs) requiring product specific data and generic (technical grade) data. Generally, registrants will have 90 days from receipt of a DCI to complete and submit response forms or request time extension and/or waiver requests with a full written justification. For product specific data, the registrant will have 8 months to submit data and amend labels. For generic data, due dates can vary depending on the specific studies being required. Below are tables of additional generic data that the Agency intends to require for chlorflurenol to be eligible for reregistration.

A. Manufacturing Use Products

1. Additional Generic Data Requirements

The generic database supporting the reregistration of chlorflurenol has been reviewed and determined to be adequate for this reregistration assessment. However, the following studies would reduce the uncertainty in the ecological risk assessment and will be considered in the development of the generic DCI for chlorflurenol.

Table 5. Confirmatory Data Requirements for Reregistration

New Guideline Number	Old Guideline Number	Study/Requirements
830.7050	none	UV/Visible Absorption
835.2120	161-1	Hydrolysis
835.2240	161-2	Aqueous photolysis
835.2410	161-3	Soil photolysis
835.4100	162-1	Aerobic soil metabolism
835.4200	162-2	Anaerobic soil metabolism
835.4400	162-3	Anaerobic aquatic metabolism
835.1230	163-1	Adsorption/desorption
835.6100	164-1	Terrestrial field dissipation
850.1730	165-4	Fish bioaccumulation
840.1100	201-1	Droplet size spectrum
840.1200	202-1	Droplet Field Evaluation
850.1075	72-1	Acute freshwater and estuarine/marine fish
850.1010	72-2	Acute freshwater invertebrate
850.1035	72-3	Acute estuarine/marine invertebrate
850.1400 850.1300 850.1350	72-4	Chronic fish and invertebrate
850.2300	71-4	Avian reproduction

New Guideline Number	Old Guideline Number	Study/Requirements
850.4225 850.4250	123-1	Terrestrial plant seedling emergence and vegetative vigor
850.4400 850.5400	123-2	Aquatic plant growth
850.3020	141-1	Honey bee acute contact toxicity

2. Labeling for Technical and Manufacturing Use Products

To ensure compliance with FIFRA, technical and manufacturing use products (MP) labeling should be revised to comply with all current EPA regulations, PR Notices and applicable policies. In order to be eligible for reregistration, the technical registrants should amend all product labels to incorporate the risk mitigation measures outlined in Section IV. The technical and MP labeling should also bear the labeling statements contained in Table 6, the Label Changes Summary Table.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g) (2) (B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticides after a determination of eligibility has been made. The registrant must review previous data submissions to ensure they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then the study MRID numbers should be cited according to the instructions in the Requirement Status and Registrations Response Form provided for each product.

A product-specific data call-in, outlining specific data requirements will be issued in the near future.

2. Labeling for End-Use Products

Labeling changes are necessary to implement measures outlined in Section IV above. Specific language to incorporate these changes is specified in the Label Changes Summary Table below.

a. Label Changes Summary Table

In order to be eligible for reregistration, registrants must amend all product labels to incorporate the risk mitigation measures outlined in Section IV. The following table describes how language on the labels should be amended.

Table 6: Summary of Labeling Changes for Chlorflurenol

Description	Amended Labeling Language	Placement on Label
Manufacturing Use Products		
For all Manufacturing Use Products	"Only for formulation into a plant growth regulator or herbicide for the following use(s) [fill blank only with those uses that are being supported by MP registrant]." "Not to be formulated into end-use products with directions for use on sod farms."	Directions for Use
One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user	"This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)." "This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)."	Directions for Use

Environmental Hazards Statements Required by the RED and Agency Label Policies	"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."	Precautionary Statements

End Use Products Intended for Occupational Use		
PPE Requirements Established by the RED[1] For Liquid Formulations	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are" (*registrant inserts correct chemical-resistant material*). "If you want more options, follow the instructions for category" *[registrant inserts A,B,C,D,E,F,G,or H]* "on an EPA chemical-resistance category selection chart." "All mixers, loaders, applicators, and other handlers, except for rights-of-way applicators, must wear: long sleeve shirt, long pants, shoes plus socks, and chemical-resistant gloves." "Rights-of-way applicators must wear: coveralls over long-sleeved shirt and long pants, chemical-resistant footwear plus socks, chemical-resistant gloves, and chemical-resistant headgear if overhead exposure."	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

1 PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

PPE Requirements Established by the RED2 For Granular Formulations	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are" (*registrant inserts correct chemical-resistant material*). "If you want more options, follow the instructions for category" *[registrant inserts A,B,C,D,E,F,G,or H]* "on an EPA chemical-resistance category selection chart." "All loaders, applicators and other handlers must wear: long sleeve shirt, long pants, shoes plus socks, and chemical-resistant gloves."	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals
User Safety Requirements	"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry."	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements
User Safety Recommendations	"User Safety Recommendations Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing. Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Precautionary Statements under: Hazards to Humans and Domestic Animals immediately following Engineering Controls (Must be placed in a box.)

2 PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Environmental Hazards	"Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate."	Precautionary Statements immediately following the User Safety Recommendations
Restricted-Entry Interval for products with directions for use within scope of the Worker Protection Standard for Agricultural Pesticides (WPS)	"Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 12 hours.	Directions for Use, Under Agricultural Use Requirements Box
Entry Restrictions for products having occupational uses on the label not subject to the WPS	***Entry Restriction for non-WPS uses applied as a spray:*** "Do not enter or allow others to enter the treated area until sprays have dried." ***Entry Restriction for non-WPS uses applied as a solid (i.e. granular) and watered-in:*** "Do not enter or allow others to enter the treated area until dusts have settled." **If watering in is required, then add this statement:** "If soil incorporation is required after the application, do not enter or allow others to enter the treated area (except those persons involved in the incorporation) until the incorporation is complete. If the incorporation is accomplished by watering-in, do not enter or allow others to enter the treated area until the surface is dry after the watering-in."	If no WPS uses on the product label, place the appropriate statement in the Directions for Use Under General Precautions and Restrictions. If the product also contains WPS uses, then create a Non-Agricultural Use Requirements box as directed in PR Notice 93-7 and place the appropriate statement inside that box.

Early Entry Personal Protective Equipment for products with directions for use within the scope of the WPS	"PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: * coveralls, * shoes plus socks, * chemical-resistant gloves made of any waterproof material."	Direction for Use Agricultural Use Requirements box
General Application Restrictions	"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."	Place in the Direction for Use directly above the Agricultural Use Box.

Other Application Restrictions for Liquid Formulations (Note: Except for tree bark banding, the maximum allowable application rate and maximum allowable rate per year must be listed as pounds or gallons of formulated product per acre, not just as pounds active ingredient per acre.)	"For Pineapple Plants (for production of planting material): maximum application rate of 1 lb ai/acre, maximum of two applications/year; a 2nd application may only be made after an interval of 10 days." "Not for use on sod farms." "Aerial applications are prohibited." "Not for use in greenhouses." "For Turf (lawns, ornamental, golf courses, parks): maximum application rate of 0.5 lb ai/acre; one application per year." "For Nonagricultural Rights-of-way (e.g., adjacent to highways, culverts, ditches, under fences/utility lines, not to include residential use): maximum application rate of 1 lb ai/acre; one application per year." "For Ornamental/Shade Trees: maximum application rate of 1 lb ai/acre; one application per year." "For Tree bark banding: 0.083 lb ai/gallon; one application per year." "For Forestry management areas (e.g., conifer release, forest/shelterbelts): maximum application rate of 2.0 lbs ai/acre; one application per year."	Directions for Use

Other Application Restrictions for Granular Formulations (Note: the maximum allowable application rate and maximum allowable rate per year must be listed as pounds or gallons of formulated product per acre, not just as pounds active ingredient per acre.)	Turf (lawns): maximum application rate of 0.25 lb ai/acre; one application per year. "Not for use on sod farms." "Aerial applications are prohibited." "Not for use in greenhouses."	
Spray Drift	"Avoid spray drift (coarse sprays are less likely to drift)." "Apply in a manner which confines spray to target area." "Leave an adequate buffer zone between sensitive plants and spray area."	Directions for Use
End Use Products Intended for Residential Use		
Application Restrictions	"Do not apply this product in a way that will contact any person, pet, either directly or through drift. Keep people and pets out of the area during application."	Directions for Use under General Precautions and Restrictions

Entry Restrictions	"Do not allow people or pets to enter the treated area until dusts have settled. [If watering in is required after the application, do not enter or allow others to enter the treated areas (except those involved in the watering) until the watering-in is complete and the surface is dry.]"	Directions for use under General Precautions and Restrictions
Environmental Hazards	"Do not apply directly to water. Do not contaminate water when disposing of equipment washwaters or rinsate."	Precautionary Statements immediately following the User Safety Recommendations
Other Application Restrictions (Note: the maximum allowable application rate and maximum allowable rate per year must be listed as pounds or gallons of formulated product per acre, not just as pounds active ingredient per acre.)	Turf: lawns: maximum application rate of 0.25 lb ai/acre; maximum 2 applications per year; a 2nd application may be made after an interval of 45 days.	Directions for Use

[1] PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

VI. Appendices

Appendix A. Chlorflurenol Uses and Use-Patterns Eligible for Reregistration

Appendix A. Use Patterns Subject to Reregistration for Chlorflurenol							
Application Timing Application Type Application Equipment	**Formulation EPA Reg. No.**	**Maximum Single Application Rate[1]**	**Maximum No. of Applications per Year**	**Maximum Seasonal Rate**	**Application Interval (days)**	**Reentry Interval**	**Limitations**
Pineapples (for production of planting material, not a food use)							
Forcing Spray Groundboom, Airblast	69361-6 HI-980007	1 lb ai/A	2	2 lbs ai/A	10 days	12 hours	
Turf (lawns and ornamental turf, including golf courses and parks)							
Foliar Spray Handgun, Low Pressure Handwand, Groundboom	69361-1	0.5 lb ai/A	1	0.5 lb ai/A	N/A	N/A	
Granular Tractor-drawn spreader, Push-type Spreader, belly grinder	69361-2	0.25 lb ai/A	1	0.25 lb ai/A	N/A	N/A	
Turf (residential use on lawns)							
Granular Push-type spreader Belly grinder	69361-3	0.25 lb ai/A	2	0.5 lb ai/A	45 days	N/A	

Nonagricultural Rights-of-Way (e.g., adjacent to highways, culverts, ditches, under fences/utility lines, not to include residential areas)							
Foliar Spray Rights-of-way Sprayer Handgun Low-Pressure Handwand	69361-6	1.0 lb ai/A	1	1 lb ai/A	N/A	N/A	
Forestry Management Areas (conifer release, forest/shelterbelt)							
Spray Low Pressure Handwand	69361-6	2.0 lb ai/A	1	2 lb ai/A	N/A	N/A	
Ornamental/Shade Trees							
Foliar Spray Handgun, Low-Pressure Handwand	69361-6	1.0 lb ai/A	1	1 lb ai/A	N/A	N/A	
Trees							
Bark banding Low-Pressure Handwand	69361-6	0.083 lb ai/gallon	1	N/A	N/A	N/A	

[1]Maximum application rate identified from product label review.

Appendix B. Table of Generic Data Requirements and Studies Used to Make the Reregistration Decision for Chlorflurenol

Guide to Appendix B

Appendix B contains the list of data requirements which support the reregistration for active ingredients within case #2095 (chlorflurenol) covered by this RED. It contains generic data requirements that apply to chlorflurenol in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following formats:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR Part 158. The reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidance, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (703) 487-4650.

2. Use Pattern (Column 2). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns.

    A. Terrestrial food
    B. Terrestrial feed
    C. Terrestrial non-food
    D. Aquatic food
    E. Aquatic non-food outdoor
    F. Aquatic non-food industrial
    G. Aquatic non-food residential
    H. Greenhouse food
    I. Greenhouse non-food
    J. Forestry
    K. Residential
    L. Indoor food
    M. Indoor non-food
    N. Indoor medical
    O. Indoor residential

3. Bibliographic Citation (Column 3). If the Agency has acceptable data in its files, this column list the identify number of each study. This normally is the Master Record Identification (MRID) number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography appendix (Appendix D) for a complete citation of the study.

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographic Citation(s)
Product Chemistry				
830.7000	63-12	pH	C,J,K	43154901
830.7050	N/A	UV/Visible absorption	C,J,K	**Data Gap**
830.7200	63-5	Melting point/melting range	C,J,K	43154903
830.7300	63-7	Density	C,J,K	43154903
830.7370	63-10	Dissociation Constants in Water	C,J,K	43154903
830.7840	63-8	Water Solubility	C,J,K	43154903
830.7950	63-9	Vapor Pressure	C,J,K	43154903
Environmental Fate				
35.2120	161-1	Hydrolysis	C,J,K	43496201, **Additional Data Required**
835.2240	161-2	Photodegradation Water	C,J,K	**Data Gap**
835.2410	161-3	Photodegradation Soil and Air	C,J,K	**Data Gap**
835.4100	162-1	Aerobic Soil Metabolism	C,J,K	43595403, **Additional Data Required**
835.4300	162-3	Anaerobic Aquatic Metabolism	C,J,K	**Data Gap**
835.4400	162-4	Aerobic Aquatic Metabolism	C,J,K	**Data Gap**
835.1240	163-1	Leaching/Adsorption/Desorption	C,J,K	43496202, **Additional Data Required**
835.6100	164-1	Terrestrial Field Dissipation	C,J,K	**Data Gap**
835.6300	164-3	Forestry	C,J,K	**Waived**
850.1730	165-4	Fish Bioaccumulation	C,J,K	**Data Gap**
860.1400	165-5	Aquatic Non-Target Organism	C,J,K	**Waived**
835.2100	166-1	Small Scale Prospective Groundwater Study	C,J,K	**Reserved**
Spray Drift				
840.1100	201-1	Droplet Size Spectrum	C,J,K	**Data Gap**
840.1200	202-1	Drift Field Evaluation	C,J,K	**Data Gap**

Ecological Effects				
850.2100	71-1a	Avian Oral LD50 Quail/Duck	C,J,K	43595401
850.2200	71-2	Avian Dietary LC50 Quail	C,J,K	43623601, 43623602
850.2300	71-4	Avian Reproduction	C,J,K	**Data Gap**
850.1075	72-1	Freshwater Fish LC50	C,J,K	120852/00047185, 140979, 45137401, 45242602, 45242601, 45137402, 90289, 119925/120889, 120870, **Additional Data Required**
850.1010	72-2	Freshwater Invertebrate LC50	C,J,K	45137403, 45242603
850.1045	72-3a	Estuarine/Marine Fish LC50	C,J,K	**Data Gap**
850.1025	72-3b	Estuarine/Marine Mollusk EC50	C,J,K	**Data Gap**
850.1035	72-3c	Estuarine/Marine Shrimp EC50	C,J,K	**Data Gap**
850.1400	72-4a	Fish Early Life-Stage (freshwater)	C,J,K	**Data Gap**
850.1400	72-4a	Fish Early Life-Stage (estuarine/marine)	C,J,K	**Data Gap**
850.1300	72-4b	Aquatic Invertebrate Life-Cycle (freshwater)	C,J,K	**Data Gap**
850.1350	72-4c	Aquatic Invertebrate Life-Cycle (estuarine/marine)	C,J,K	**Data Gap**
850.1500	72-5	Fish Full Life-Cycle	C,J,K	**Data Gap**
850.4225	123-1a	Seedling Emergence (Tier II)	C,J,K	**Data Gap**
850.4250	123-1b	Vegetative Vigor (Tier II)	C,J,K	**Data Gap**
850.4400	123-2	Aquatic Plant Growth (Tier II)	C,J,K	**Data Gap**
850.5400	123-2	Algal Toxicity (Tiers I and II)	C,J,K	**Data Gap**
850.3020	141-1	Honey Bee Acute Contact LD50	C,J,K	**Data Gap**
850.3030	141-2	Honey Bee Residue on Foliage	C,J,K	**Waived**
Toxicology				
870.1100	81-1	Acute Oral Toxicity Rat	C,J,K	43355402
870.1200	81-2	Acute Dermal Toxicity Rabbit	C,J,K	43355403
870.1300	81-3	Acute Inhalation Toxicity Rat	C,J,K	45147201
870.2400	81-4	Primary Eye Irritation Rabbit	C,J,K	43355404
870.2500	81-5	Primary Skin Irritation Rabbit	C,J,K	43355405
870.2600	81-6	Dermal Sensitization Guinea pig	C,J,K	43361701
870.3100	82-1a	90-Day Oral Toxicity SD Rat	C,J,K	45441001 [2001]
870.3100	82-1a	90-Day Oral Toxicity Wistar rat	C,J,K	00120854 & 00120867 [1968]
870.3150	82-1b	90-Day Oral Toxicity Dog	C,J,K	00120868 [1968]

870.3150	82-1b	21-Day Dermal Toxicity Rabbit	C,J,K	00120883 [1970]
870.3700a	N/A	Developmental Toxicity SD Rat	C,J,K	4510901 [2000]
870.3700b	N/A	Developmental Toxicity NZW Rabbit	C,J,K	00120862 [1969]
870.3800	N/A	3-Generation Reproduction Charles River Rat	C,J,K	00082867 [1973]
870.4100a	83-1	Chronic Toxicity Rat	C,J,K	00082864 [1971]
870.4100b	83-1	Chronic Toxicity Dog	C,J,K	00082863 [1975]
870.4200b	83-2	Carcinogenicity Mouse	C,J,K	00082865 [1976]
870.4300a	83-3a	Prenatal Developmental Toxicity Study - Rat	C,J,K	45190901
870.5100	N/A	Ames, *S typhimurium*	C,J,K	43562802 [1995]
870-5300	N/A	*In vitro* Cell (CHO) Chromosomal Aberration	C,J,K	43562801 [1995]
870.5300	84-2	*In vitro* Mammalian Cell HGPRT Test	C,J,K	45137405 [1988]
N/A	N/A	Non GDL Metabolism & Pharmacokinetics Unacceptable/NG	C,J,K	00082868 [1972]
N/A	N/A	Non GDL Carcinogenicity Rats	C,J,K	0082866 [1969]

Appendix C. Technical Support Documents

Additional documentation in support of this RED is maintained in the OPP docket EPA-HQ-OPP-2006-0874. This docket may be accessed in the OPP docket room located at Room S-4900, One Potomac Yard, 2777 S. Crystal Drive, Arlington, VA. It is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m. All documents may be viewed in the OPP docket room or downloaded or viewed via the Internet at the following site: http://www.regulations.gov.

The docket initially contained preliminary risk assessments, supporting documents, and technical (or manufacturing-use) registrant error comments for chlorflurenol as of November 1, 2006. After a sixty-day public comment period, EPA considered the public comments that were submitted to the docket and revised the risk assessments as necessary. The revised risk assessments, any supporting documents that needed to be revised, and memos describing the Health Effects Division (HED), the Ecological Fate and Effects Division (EFED), and the Biological and Economic Assessment Division (BEAD) response to public comments will be added to the docket in April 2007.

The Agency documents in the docket include:

1. Federal Register Notice: Chlorflurenol Risk Assessment; Notice of Availability, and Risk Reduction Options
2. Reader's Guide to the Chlorflurenol E-docket # EPA-HQ-OPP-2006-0874
3. Request for Additional Information and Risk Management Suggestions for the Reregistration of Chlorflurenol, Phase 3 Public Comment Period (October 25, 2006)
4. Chlorflurenol Methyl Ester. HED Chapter of the Reregistration Eligibility Decision Document (RED)
5. Chlorflurenol Methyl Ester: Occupational and Residential Exposure Assessment for the Reregistration Eligibility Decision Document
6. Response to Phase I comments from Mandava Associates (HED)
7. Chlorflurenol RED Chapter: Environmental fate and ecological risk assessment for re-registration of chlorflurenol methyl ester (ME), an herbicide/plant growth regulator for use on ornamentals, hedge and fence rows, turf, shade trees, woody shrubs and vines, and to produce planting material for pineapple production (EFED memo)

8. Environmental Fate and Ecological Risk Assessment for Chlorflurenol Methyl Ester Reregistration

9. EFED RED Chapter Appendices

10. Water Assessment for Chlorflurenol Growth Regulator and Herbicide

11. Review of Registrant Error Correction Comments on EFED Reregistration Chapter for Chlorflurenol

12. Addendum to EFED RED Chapter for Chlorflurenol Methyl Ester Accounting for Updated Label Rates

13. Revised Drinking Water Assessment for Chlorflurenol Growth Regulator and Herbicide

14. Chlorflurenol: Human Health Risk Assessment Addendum for the Reregistration Eligibility Decision Document

15. Chlorflurenol Methyl Ester: Chronic Drinking Water Exposure and Risk Assessment for the Section 3 Reregistration Eligibility Decision

16. Chlorflurenol: Revised Occupational and Residential Exposure Assessment for the Reregistration Eligibility Decision Document

17. EFED's Responses to Phase 3 Comments for Chlorflurenol

18. Chlorflurenol: Response to comments from Maui Pineapple Company, Ltd. (HED)

19. Response to Comments to Docket # EPA-HQ-2006-0874 during the Phase 3 Comment Period for Chlorflurenol (BEAD)

Appendix D. Citations Considered to be Part of the Database Supporting the Reregistration Decision (Bibliography)

Guide to Appendix D

1. Contents of Bibliography. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Reregistration Eligibility Document. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, are included.

2. Units of Entry. The unit of entry in this bibliography is called a "study." In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review and can be described with a conventional bibliographic citation. The Agency has also attempted to unite basic documents and commentaries upon them, treating them as a single study.

3. Identification of Entry. The entries in this bibliography are sorted numerically by Master Record Identifier, or "MRID" number. This number is unique to the citation, and should be used whenever a specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies (see paragraph 4(d)(4) below for further explanation). In a few cases, entries added to the bibliography late in the review may be preceded by a nine character temporary identifier. These entries are listed after all MRID entries. This temporary identifying number is also to be used whenever specific reference is needed.

4. Form of Entry. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standard of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

    a. Author. Whenever the author could confidently be identified, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as the author. When no author or laboratory could be identified, the Agency has shown the first submitter as the author.

b. Document date. The date of the study is taken directly from the document. When the date is followed by a question mark, the bibliographer has deduced the date from the evidence contained in the document. When the date appears as (1999), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative number. The next element immediately following the word "under" is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter. When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," which stands for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume.

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Appendix E. Generic Data Call-In (GDCI)

Note that a complete generic DCI, with all pertinent instructions, will be sent to registrants under separate cover.

Appendix F. Product-Specific Data Call-In (PDCI)

Note that a complete product-specific DCI, with all pertinent instructions, will be sent to registrants under separate cover.

Appendix G. EPA'S Batching of Chlorflurenol Products for Meeting Acute Toxicity Data Requirements for Reregistration

The Agency has determined that no batching of chlorflurenol products is necessary given the small number of registered products.

Appendix H. List of Registrants to be Sent this Data Call-in

1) Repar Corporation

Appendix I. List of Available Related Documents and Electronically Available Forms

Pesticide Registration Forms are available at the following EPA internet site: http://www.epa.gov/opprd001/forms/.

Pesticide Registration Forms (These forms are in PDF format and require the Acrobat reader)

Instructions:

1. Print out and complete the forms. (Note: Form numbers that are bolded can be filled out on your computer then printed.)

2. The completed form(s) should be submitted in hardcopy in accord with the existing policy.

3. Mail the forms, along with any additional documents necessary to comply with EPA regulations covering your request, to the following address for the Document Processing Desk.:

   Document Processing Desk (distribution code)*
   Office of Pesticide Programs (7504P)
   Environmental Protection Agency
   1200 Pennsylvania Ave, NW
   Washington, DC 20460-0001

   * Distribution Codes are as follows:
   (APPL) Application for product registration
   (AMEND) Amendment to existing registration
   (CAN) Voluntary Cancellation
   (EUP) Experimental Use Permit
   (DIST) Supplemental Distributor Registration
   (SLN) Special Local Need
   (NEWCO) Request for new company number
   (NOTIF) Notification
   (PETN) Petition for Tolerance
   (XFER) Product Transfer

DO NOT fax or e-mail any form containing "Confidential Business Information" or "Sensitive Information."

If you have any problems accessing these forms, please contact Nicole Williams at (703) 308-5551 or by e-mail at *williams.nicole@epamail.epa.gov*. If you want these forms mailed or faxed to you, please contact Lois White, *white.lois@epa.gov* or Floyd Gayles, *gayles.floyd@epa.gov*.

If you have any questions concerning how to complete these forms, please contact OPP's ombudsperson for conventional pesticide products: Linda Arrington, (703) 305-5446

The following Agency Pesticide Registration Forms are currently available via the Internet at the following locations:

8570-1	Application for Pesticide Registration/Amendment	http://www.epa.gov/opprd001/forms/8570-1.pdf
8570-4	Confidential Statement of Formula	http://www.epa.gov/opprd001/forms/8570-4.pdf
8570-5	Notice of Supplemental Registration of Distribution of a Registered Pesticide Product	http://www.epa.gov/opprd001/forms/8570-5.pdf
8570-17	Application for an Experimental Use Permit	http://www.epa.gov/opprd001/forms/8570-17.pdf
8570-25	Application for/Notification of State Registration of a Pesticide To Meet a Special Local Need	http://www.epa.gov/opprd001/forms/8570-25.pdf
8570-27	Formulator's Exemption Statement	http://www.epa.gov/opprd001/forms/8570-27.pdf
8570-28	Certification of Compliance with Data Gap Procedures	http://www.epa.gov/opprd001/forms/8570-28.pdf
8570-30	Pesticide Registration Maintenance Fee Filing	http://www.epa.gov/opprd001/forms/8570-30.pdf
8570-32	Certification of Attempt to Enter into an Agreement with other Registrants for Development of Data	http://www.epa.gov/opprd001/forms/8570-32.pdf
8570-34	Certification with Respect to Citations of Data (in PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf
8570-35	Data Matrix (in PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf
8570-36	Summary of the Physical/Chemical Properties (in PR Notice 98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf
8570-37	Self-Certification Statement for the Physical/Chemical Properties (in PR Notice 98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf

Pesticide Registration Kit http://www.epa.gov/pesticides/registrationkit/

Dear Registrant:

For your convenience, we have assembled an on-line registration kit which contains the following pertinent forms and information needed to register a pesticide product with the U.S. Environmental Protection Agency's Office of Pesticide Programs (OPP):

1. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA) as Amended by the Food Quality Protection Act (FQPA) of 1996.

2. Pesticide Registration (PR) Notices

    a. 83-3 Label Improvement Program-Storage and Disposal Statements
    b. 84-1 Clarification of Label Improvement Program
    c. 86-5 Standard Format for Data Submitted under FIFRA
    d. 87-1 Label Improvement Program for Pesticides Applied through Irrigation Systems (Chemigation)
    e. 87-6 Inert Ingredients in Pesticide Products Policy Statement
    f. 90-1 Inert Ingredients in Pesticide Products; Revised Policy Statement
    g. 95-2 Notifications, Non-notifications, and Minor Formulation Amendments
    h. 98-1 Self Certification of Product Chemistry Data with Attachments (This document is in PDF format and requires the Acrobat reader.)

    Other PR Notices can be found at http://www.epa.gov/opppmsd1/PR_Notices.

3. Pesticide Product Registration Application Forms (These forms are in PDF format and will require the Acrobat reader.)

    a. EPA Form No. 8570-1, Application for Pesticide Registration/Amendment
    b. EPA Form No. 8570-4, Confidential Statement of Formula
    c. EPA Form No. 8570-27, Formulator's Exemption Statement
    d. EPA Form No. 8570-34, Certification with Respect to Citations of Data
    e. EPA Form No. 8570-35, Data Matrix

4. General Pesticide Information (Some of these forms are in PDF format and will require the Acrobat reader.)

    a. Registration Division Personnel Contact List
    b. Biopesticides and Pollution Prevention Division (BPPD) Contacts
    c. Antimicrobials Division Organizational Structure/Contact List
    d. 53 F.R. 15952, Pesticide Registration Procedures; Pesticide Data Requirements (PDF format)
    e. 40 CFR Part 156, Labeling Requirements for Pesticides and Devices (PDF format)
    f. 40 CFR Part 158, Data Requirements for Registration (PDF format)
    g. 50 F.R. 48833, Disclosure of Reviews of Pesticide Data (November 27, 1985)

Before submitting your application for registration, you may wish to consult some additional sources of information. These include:

1. The Office of Pesticide Programs' Web Site

2. The booklet "General Information on Applying for Registration of Pesticides in the United States", PB92-221811, available through the National Technical Information Service (NTIS) at the following address:

   National Technical Information Service (NTIS)
   5285 Port Royal Road
   Springfield, VA 22161

   The telephone number for NTIS is (703) 605-6000. Please note that EPA is currently in the process of updating this booklet to reflect the changes in the registration program resulting from the passage of the FQPA and the reorganization of the Office of Pesticide Programs. We anticipate that this publication will become available during the Fall of 1998.

3. The National Pesticide Information Retrieval System (NPIRS) of Purdue University's Center for Environmental and Regulatory Information Systems. This service does charge a fee for subscriptions and custom searches. You can contact NPIRS by telephone at (765) 494-6614 or through their website.

4. The National Pesticide Telecommunications Network (NPTN) can provide information on active ingredients, uses, toxicology, and chemistry of pesticides. You can contact NPTN by telephone at (800) 858-7378 or through their website: http://npic.orst.edu

   The Agency will return a notice of receipt of an application for registration or amended registration, experimental use permit, or amendment to a petition if the applicant or petitioner encloses with his submission a stamped, self-addressed postcard. The postcard must contain the following entries to be completed by OPP:

   - Date of receipt
   - EPA identifying number
   - Product Manager assignment

   Other identifying information may be included by the applicant to link the acknowledgment of receipt to the specific application submitted. EPA will stamp the date of receipt and provide the EPA identifying File Symbol or petition number for the new submission. The identifying number should be used whenever you contact the Agency concerning an application for registration, experimental use permit, or tolerance petition.

To assist us in ensuring that all data you have submitted for the chemical are properly coded and assigned to your company, please include a list of all synonyms, common and trade names, company experimental codes, and other names which identify the chemical (including "blind" codes used when a sample was submitted for testing by commercial or academic facilities). Please provide a CAS number if one has been assigned.

Appendix J: Chlorflurenol Human Health Risk Assessment

Date: July 10, 2006
MEMORANDUM

SUBJECT: Chlorflurenol Methyl Ester. HED Chapter of the Reregistration Eligibility Decision Document (RED).

PC Code:	098801
Decision #:	362457
DP Barcode:	D323832.
Risk Assessment Type:	Single Chemical Aggregate

FROM: David G Anderson, Risk Assessor and Toxicologist
Shanna Recore, Occupational/Residential Risk Assessor
Yvonne Barnes, Product Chemist
Reregistration Branch II
Health Effects Division (7509P)

THROUGH: Alan Nielsen, Branch Senior Scientist
William Hazel, Chief
Reregistration Branch II
Health Effects Division (7509P)

TO: Tawanda Spears, Chemical Review Manager
Reregistration Branch III
Special Review and Reregistration Division

Attached is the HED risk assessment for chlorflurenol methyl ester.

Table of Contents

1.0 EXECUTIVE SUMMARY

This assessment provides the evidence for reregistration of chlorflurenol methyl ester. The reregistration process provides re-review of previously registered pesticides under the Federal Insecticide, Fungicide and Rodenticide Act [FIFRA] to assure scientific reliability and conformity to the data standards established under the Food Quality Protection Act [FQPA] of 1996.

Chlorflurenol methyl ester is a nonfood use herbicide, plant growth retardant and plant growth regulator. As a herbicide and plant growth retardant it is used for the postemergent control of annual grasses, broadleaf weeds, trees, shrubs and vines. As a plant growth regulator, chlorflurenol is used to produce pineapple planting material [sliplets] well over one year before the pineapples are harvested. As this use is not expected to result in finite residues in pineapples, this is considered to be a nonfood use and no tolerances are necessary in pineapples.

Chlorflurenol methyl ester [technical] is greater than 96% total ester and is composed of three related chemicals chlorflurenol methyl ester [65% to70%], dichlorflurenol methyl ester [10% to 15%] and deschlorflurenol methyl ester [15% to 20%].

Chlorflurenol methyl ester shows low acute toxicity by the oral, dermal and inhalation routes [toxicity is category IV]. Clorflurenol methyl ester was essentially non-irritating to the eye and skin, respectively [toxicity category III and IV]. It is not a skin sensitizer in a Guinea pig study.

The acceptable and unacceptable studies with chlorflurenol methyl ester show no severe toxicity. The most sensitive species is the dog showing slight red blood cell destruction at 4 weeks after the start of the study and only at the highest dose tested. A 13-week subchronic study in rats showed toxicity, but did not confirm the hematological effects. The female body weight decrement was seen in rats at higher dose levels than in the dog study at month 13 or the effects on hematology at week 4. A 21-day dermal study in rabbits with a formulation of chlorflurenol methyl ester showed no systemic effects, but showed destruction of the hair follicles and edema in the treated skin. The skin effects were dose related. These effects were considered due to skin irritation from the formulation containing 87.5% inerts, most of which are known skin irritants. Potential systemic effects of the technical grade could not be definitively evaluated due to these inerts; however, systemic effects are not likely to be seen at lower dose levels than those of the active ingredient tested in the 21-day dermal study in rabbits. Potential reproductive effects were not tested in the 21-day dermal study.

A carcinogenicity study in mice showed no evidence of carcinogenicity at lower doses or above a limit dose of 1 g/kg/day. A battery of mutagenicity studies was all

negative.

Unacceptable kinetic/distribution studies suggest that each of the three radiolabeled components comprising chlorflurenol methyl ester were barely detectable in the rat mammary glands or in nursing pups. Since the studies used only one female/treatment, the findings could not be verified. However, this study showed that each of the three components in chlorflurenol methyl ester is probably rapidly excreted mostly in the urine within 24 hours. Radiolabel in the mammary gland and the nursing pups was not quantified in the treated animals.

Prenatal studies in the rat and rabbit show no increased fetal susceptibility. At the highest dose tested, rats showed delayed ossification at higher incidence than control incidence. Maternal toxicity in the form of body weight decrement was seen at mid- and highest dose tested. The rabbit showed no effects in fetuses or mothers at the highest dose tested. Post-natal studies were not required, but a 1973 three-generation reproduction study previously submitted for other purposes showed equivocal litter size and pup weight decrement at birth and subfertility in adult offspring, but showed a poor dose response.

Due to these ambiguous findings in the reproduction study, an additional uncertainty factor of 3X was used when calculating human oral risk. The additional 3X factor may be removed by another acceptable reproduction study showing a more definitive NOAEL for effects on the litters and fertility.

Exposures to the pesticide were calculated assuming maximum application rates from both labels and from a March 14, 2006 memorandum from the Biological and Economic Analysis Division [BEAD] of the USEPA [BEAD memo]. No dermal absorption studies are available. This resulted in the assumption of 100% dermal absorption from an oral study endpoint for dermal exposure.

When levels of exposure were above the Level of Concern [LOC], suggesting an unacceptable exposure, the exposures to granular formulations were recalculated using 10% dermal absorption for comparison.

There is opportunity for adult residential handler exposure from the application to lawns and ornamentals. A Margin of Exposure [MOE] less than 100 exceeds OPP's LOC and suggests unacceptable risk. All residential handler activities showed MOE greater than 100, suggesting acceptable risk. Attire for residential handlers is assumed to be short-sleeved shirts, short pants, shoes and socks.

Several residential postapplication scenarios were identified for chlorflurenol methyl ester, including dermal exposure from residue on lawns and turf (adult, youth and toddler), hand-to-mouth transfer of residues on lawns (toddler), ingestion of pesticide residue on treated grass (toddler), and incidental ingestion of soil from pesticide-treated

residential areas (toddler).

For the adult populations, all postapplication risks were below HED's level of concern, except for the 3.0 lb ai/A (BEAD) application rates where MOEs are 44 on day 0. For the youth populations, all postapplication noncancer risks were below HED's level of concern. For toddlers, postapplication noncancer risks are not of concern for the oral route. For the dermal route, risks to toddlers from high contact activity on lawns exceed HED's level of concern at the 1.0/1.1 lb ai/A (Label) and 3.0 lb ai/A (BEAD) application rates, except when 10% dermal absorption is assumed for the granular formulations. Calculated combined risks to toddlers (i.e., dermal high contact activity plus hand to mouth activity plus object to mouth activity on treated turf plus incidental soil ingestion of pesticide residue from treated turf areas) are therefore, also of concern, except when 10 percent dermal absorption is assumed for the granular formulations.

There are potential exposures to occupational mixers, loaders, applicators, and other handlers during the usual use-patterns associated with chlorflurenol methyl ester. These risks were calculated assuming maximum application rates from both the product labels and from the BEAD memo. For all occupational scenarios, the inhalation risks were below HED's level of concern at the baseline level.

The dermal risks were below HED's level of concern at some level of mitigation for all occupational scenarios, except applying liquid sprays using rights-of-way equipment:

- to turf growing in culverts, rights of way, median strips, ditches, and/or under security fences at the 3 lb ai/A rate (Label & BEAD);
- to non-agricultural rights-of-ways/fence rows and hedge rows at the 3 lb ai/A rate (Label & BEAD);
- to gymnosperms and hardwoods at the 5 lb ai/A rate;
- to shrubs, shade trees and vines at the 4.5 lb ai/A rate (BEAD); and
- to high density forestry management at the 4.0 lb ai/A rate (BEAD).

Risks remain a concern at maximum personal protective equipment and no engineering controls are available for rights-of-way application equipment.

Using ORETF data, the dermal risks were a concern at baseline for handlers mixing/loading/applying liquids with an overhead directed low pressure handwand equipment for the scenarios where BEAD application rates are assessed. No ORETF data currently are available to assess the corresponding personal protective equipment exposures for these scenarios. However, using PHED data, the dermal risks were not a concern with the addition of chemical-resistant gloves to baseline attire.

There are potential postapplication exposures to occupational workers during the usual use-patterns associated with chlorflurenol. Specifically, there is concerned about postapplication exposures from treatment of pineapples and golf course turf. In agricultural crop settings, a Restricted Entry Interval or REI – is used to mitigate

postapplication risks following applications to crops. The REI is time period following a pesticide application during which entry into the treated area is restricted. To establish REIs, EPA considers postapplication risks on varying days after application. For pineapple applications, the MOEs are greater than 100 on day 0 (REI = 12 hours) for all of the exposure levels.

For the golf course turf using the 1.0 and 1.1 lb ai/A (Label) rates for sprays and granular applications respectively and assuming hand weeding and transplanting tasks are performed and assuming 100% dermal absorption, risks are not a concern at day 4 for liquid formulations and at day 5 for granular formulations. Assuming golf course mowing tasks are performed, risks are not a concern on day 0 (12 hours following application) for liquid or granular applications using these application rates and assuming 100 percent absorption. Risks are not a concern at day 0 (12 hours following application) for granular applications for any postapplication tasks using the 1.1 lb ai/A application rate and assuming 10% dermal absorption.

For the golf course turf using the 3.0 lb ai/A (BEAD) rates for sprays and granular applications and assuming 100% dermal absorption, risks are not a concern for hand weeding and transplanting tasks at day 14 and for mowing at day 8. For the golf course turf using the 3.0 lb ai/A (BEAD) rates for granular applications and assuming 10% dermal absorption, risks are not a concern for any tasks at day 0 (REI = 12 hours).

See Sections 6.0 through 7.2.6 for Residential Exposure and Occupational Exposure for mixed exposure scenarios of concern.

Potential contamination of surface water and ground water were modeled by Tier II PRZM/EXAMS and Tier I SCIGROW. Risk was assessed by DEEM for chronic exposure to drinking water using modeled surface water estimated concentrations and modeled groundwater estimated concentrations. Using surface water estimates, exposures to all groups were below the chronic RfD and OPP's LOC. The highest exposure groups were non-nursing infants at 20% of the chronic oral RfD and all infants (< one year) at 16% of the chronic oral RfD. However, using ground water estimated concentrations two groups were above the chronic RfD and above OPP's LOC. The assessment by DEEM for ground water showed that the highest estimated exposure was 176% of the chronic RfD for non-nursing infants and 142% of the chronic RfD for all infants (< 1 year). The next highest estimated exposure was to children 1-2 years at 64% of the chronic RfD. These exposures were not combined with infants and children exposured to lawns treated with sprays or granulated cholorflurenol. It should be noted that since toddler exposure from treated lawns was above OPP's LOC, and any additional exposure from drinking water would result in additional concern.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

At this time, there are four products containing chlorflurenol that are intended for occupational and/or residential uses. All products are registered by Repar Corporation. Two of the products (Maintain CF 125 and Reap Thru Herbicide) are emulsifiable concentrates and contain 12.5 and 15.9 percent active ingredient, respectively. Maintain CF 125 is also registered as a special local needs product under EPA SLN No. HI-980007. The other two products (Repar Broad Spectrum Weed and Feed and Repar Weed and Feed 28-3-3) are granulars and contain 0.17 and 0.70 percent active ingredient, respectively.

2.2 Registered Use Categories and Use Sites

An analysis of the current labeling and available use information was incomplete, in that frequency of application and number of applications per season is not stated. Chlorflurenol is registered for use in a variety of agricultural, commercial, and residential scenarios and thus these populations are potentially exposed while performing handling tasks, including mixing/loading, applying, and flagging tasks. It is also possible for these populations to be exposed to chlorflurenol during postapplication time periods. Tables 1a, 1b, and 1c provided the maximum application rates for the registered scenarios based on information from the product labels. Table 2 provides the maximum application rates from a March 14, 2006 memo from the Biological and Economic Analysis Division (BEAD) of USEPA (BEAD memo).

Table 1a: Summary of Maximum Application Rates for Registered Chlorflurenol Methyl Ester Agricultural Uses – Label				
Crop Site	Target of Application	Maximum Application Rate	Application Equipment	Area Treated or Amount Handled Per Day
Liquid Formulations				
Pineapple plants: for plant material production (non food use)	Plant growth regulator	1 lb a.i./A (Label)	Groundboom	80 acres
			Airblast	40 acres

Table 1b: Summary of Maximum Application Rates for Registered Chlorflurenol Methyl Ester Commercial Uses – Label				
Crop Site	Target of Application	Maximum Application Rate	Application Equipment	Area Treated or Amount Handled Per Day
Liquid Formulations				
Turf: Lawns and Ornamental Turf (including golf course and parks)	Broadleaf weeds and plant growth retardant	1.0 lb a.i./A	low pressure handwand	40 gallons
			Handgun	5 acres for A and M/L/A 100 acres for M/L (for 20 LCOs)
			Groundboom	40 acres
Gymnosperms	Plant growth retardant	0.25 lb ai/100 gallons	low pressure handwand	40 gallons
			Handgun	1,000 gallons
			rights-of-way sprayer	1,000 gallons
Hardwoods: growing under utility lines, as screens or ground cover, adjacent to highways	Plant growth retardant	1.0 lb ai/100 gallons	handgun	1,000 gallons
			rights-of-way sprayer	1,000 gallons
			low-pressure handwand	40 gallons
Hedges: growing under	Plant growth retardant	1.0 lb ai/100 gallons	handgun	1,000 gallons
			rights-of-way sprayer	1,000 gallons

Table 1b: Summary of Maximum Application Rates for Registered Chlorflurenol Methyl Ester Commercial Uses – Label				
Crop Site	Target of Application	Maximum Application Rate	Application Equipment	Area Treated or Amount Handled Per Day
utility lines, as screen			low-pressure handwand	40 gallons
Vines growing under utility lines, as screens or ground cover, rights-of-way, hedgerows	Plant growth retardant	1.0 lb ai/100 gal	handgun	1,000 gallons
			rights-of-way sprayer	1,000 gallons
			low-pressure handwand	40 gallons
Turf: growing in culverts, rights-of-way, median strips, ditches, under security fences	Plant growth regulator	3.0 lb a.i./acre	rights-of-way sprayer	80 acres
			handgun	5 acres
			low-pressure handwand	5 acres
Trees: bark banding	Plant growth retardant	0.083 lb a.i./gal	low-pressure handwand	40 gallons
Granular Formulations				
Turf: Lawns and Ornamental Turf (including golf course and parks)	Broadleaf weeds	1.1 lb a.i./acre	tractor-drawn spreader	40 acres
			push-type spreader	5 acres
			belly grinder	1 acre

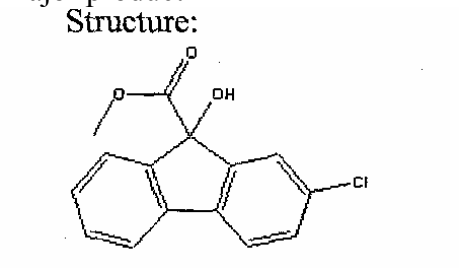
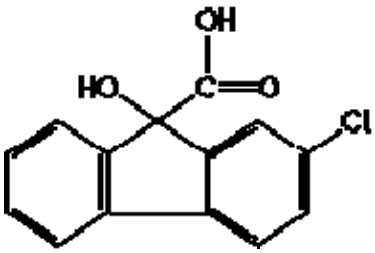
Table 1c: Summary of Maximum Application Rates for Registered Chlorflurenol Methyl Ester Residential Uses – Label				
Crop Site	Target of Application	Maximum Application Rate	Application Equipment	Area Treated or Amount Handled Per Day
Granular Formulations				
Turf: lawns	Broadleaf weeds	0.25 lb a.i./A	push-type spreader	0.5 acre
			belly grinder	1,000 ft^2

Table 2. Summary of Maximum Application Rates for Registered Chlorflurenol Methyl Ester Uses – BEAD		
Use Site	Treatment Type	Maximum Application Rate (a.i. lb/acre)
Pineapple	Growth regulator	1.0
Ornamental trees	Growth regulator	2.5
Non-agricultural rights-of-ways/fence rows and hedge rows	Weed control & growth retardant	3 .0
Established turf	Weed control & turf growth retardant	3.0
High density forestry vegetation management (plant density >1500 stems per acre; plant height > 8 ft)	Weed control	4.0
Shrubs, shade trees and vines	Growth regulator	4.5
Hardwood and gymnosperm trees	Height control	5.0

2.3 Application Methods

Chlorflurenol is applied with several types of application equipment, including airblast sprayers, ground boom sprayers, low pressure handwand sprayers, handgun sprayers, rights-of-way sprayers, tractor-drawn spreaders, push-type spreaders, and belly grinders. For information on the Occupational Handler assumptions and variables used in the calculation of exposure, see [Section 7.1 Occupational Handler Exposures and Risk Estimates].

2.4 Structure and Nomenclature

Table 3. Nomenclature for Chlorflurenol Methyl Ester	
Chemical structure	Major product Structure:  Hydrolysis product 
Common name	chlorflurenol-methyl, flurenol
Molecular formula	C15H11ClO3
Molecular weight	274.07 g/mol
IUPAC name	Methyl (*RS*)-2-chloro-9-hydroxyfluorene-9-carboxylate
CAS name	Methyl 2-chloro-9-hydroxy-9*H*-fluorene-9-carboxylate
CAS number	2536-31-4
PC Code	098801

2.5 Physical and Chemical Properties

Table 4 Physicochemical Properties of Chlorflurenol Methyl Ester		
Parameter	Value	Reference
Melting point/range	136-142 degrees Celsius	MRID 434549-03
pH	Not Applicable, Crystalline material	MRID 43154901
Density	-1.5	MRID 431549-03
Water solubility	18mg/L	MRID 431549-03
Solvent solubility at: 25 degrees Celsius	Cyclohexane 0.24 g/ 100 ml Isopropanol 2.4 g/100 ml Benzene 7.0 g/100 ml Ethanol 8.0 g/100 ml Methanol 15 g/100 ml Acetone 26 g/100 ml	MRID 431549-02

Table 4 Physicochemical Properties of Chlorflurenol Methyl Ester		
Parameter	Value	Reference
Vapor pressure	5 - 10^{-5} Torr at 25 degrees Celsius	MRID 431549-03
Dissociation constant, pK_a	None	MRID 431549-03
Octanol/water partition coefficient	Estimated Log P 2.86 Estimate from fate data on water 65 or log P=1.81	MRID 433554-01 MRID 43496202
UV/visible absorption spectrum	None provided	Data Gap

3.0 Hazard/Dose-Response Characterization/Assessment

3.1 Hazard and Dose-Response Characterization

3.1.1 Database Summary:

Chlorflurenol methyl ester shows low acute toxicity by the oral, dermal and inhalation routes [toxicity is category IV]. Eye and skin irritation were mild and essentially non-irritating, respectively [toxicity category III and IV]. It is not a skin sensitizer in a Guinea pig study.

The acceptable and unacceptable studies with chlorflurenol methyl ester show no severe toxicity. The most sensitive species is the dog showing slight red blood cell destruction at 4 weeks after the start of the study and only at the highest dose tested [NOAEL/LOAEL = 31/94 mg/kg/day]. This red blood cell destruction was supported by hemosiderin deposits in the liver at the 2-year termination. No studies were seen that confirmed the hematological findings in the chronic dog study. At month 13, the study showed decreased body weight in males and females, but not in females at termination. An unacceptable 13 week study in 3 dogs/sex/group at comparable dose levels showed inconsistent nominally decreased red blood cells, but no hemosiderin deposits at termination. A 13-week subchronic study in rats showed a dose related decreased body weight in females accompanied by decreased food efficiency and at the mid dose tested and at the highest dose tested decreased male body weight gain . The female body weight decrement was seen in rats at higher dose levels than in the dog study at month 13 or the effects on hematology at week 4. A 21-day dermal study in rabbits with a formulation of chlorflurenol methyl ester showed no systemic effects, but showed destruction of the hair follicles and edema in the treated skin. The skin effects were dose related. These effects were considered due to skin irritation from the formulation containing 87.5% inerts, most of which are known skin irritants. Potential systemic effects of the technical grade could not be definitively evaluated due to these inerts; however, systemic effects are not likely to be seen at lower dose levels than those of the active ingredient tested in the 21-day dermal study in rabbits. Potential reproductive effects were not tested in the 21-day dermal study.

A carcinogenicity study in mice showed no evidence of carcinogenicity at lower

doses or above a limit dose of 1 g/kg/day. A battery of mutagenicity studies was all negative.

Unacceptable kinetic/distribution studies showed that each of the three radiolabeled components comprising chlorflurenol methyl ester were barely detectable in the rat mammary glands or in nursing pups. Since the studies used only one female/treatment, the findings could not be verified. However, this study showed that each of the three components in chlorflurenol methyl ester is probably rapidly excreted mostly in the urine within 24 hours. Radiolabel in the mammary gland and the nursing pups was not quantified.

Prenatal studies in the rat and rabbit show no increased fetal susceptibility. The rat showed delayed ossification at higher incidence than control values. This delayed ossification was shown at the highest dose tested and maternal toxicity was seen at the mid- and highest dose tested. The rabbit showed no effects in fetuses or mothers at the highest dose tested. Postnatal studies were not required, but a 1973 three-generation reproduction study previously submitted for other purposes showed equivocal litter size and pup weight decrement at birth and subfertility in adult offspring. The potential effects were more variable than usual for a study on reproduction. The reproducibility of these effects can be questioned. In addition, the study showed an excessive number of pregnancies in female rats that showed no sperm during the period of cohabitation, i.e., no evidence that mating had occurred. Although, this finding could raise questions about the conduct of the study, there was no suggestion in the data of a dose related response among the generations of females that showed no sperm. However, when all these females from all 6 groups of matings among the 3 generations in the study were added together, there was a suggestion of a treatment related response. Due to these ambiguous findings in the reproduction study, an additional uncertainty factor of 3X was used when calculating human oral risk. The additional 3X factor may be removed by another acceptable reproduction study showing a more definitive NOAEL for effects on the litters and fertility.

3.1.2 Studies available and considered (animal, human, general literature)

No animal or human toxicity studies with chlorflurenol methyl ester were found in the literature. The toxicity studies available and considered in the assessment of chlorflurenol methyl ester were:

1. Acute – Oral LD50, Dermal LD50, Inhalation LC50, Eye and skin irritation and dermal sensitization

2. Subchronic - An acceptable/nonguideline 21-day dermal study in rabbits. An acceptable 90-day subchronic study in rats

3. Chronic - An acceptable chronic 2-year feeding study in dogs A carcinogenicity study in mice.

4. Developmental - An acceptable developmental toxicity study in rats and an unacceptable developmental toxicity study in rabbits

5. Reproduction - An unacceptable 3-generation reproduction study in rats

6 Mutagenicity - A study on reverse mutation in *S. typhimurium;* A study on chromosomal aberration in CHO cells; An *in vitro* study for rat hepatocyte unscheduled DNA synthesis; An *in vitro* mammalian cell HGPRT test. The battery of guideline mutagenicity studies was acceptable.

7. Kinetics/distribution - An unacceptable/non-guideline study of kinetics and distribution, including radiolabel in rat milk.

3.1.3 Mode of action, metabolism, toxicokinetic data

There was no data on a mode of action. However, general information about suggested distribution and kinetic data has been submitted. The data suggest that chlorflurenol methyl ester is circulated enterohepatically and excreted in the feces and mostly in urine all within 24 hours, resulting in no accumulation.

3.1.4 Sufficiency of studies/data

The toxicity data base for chlorflurenol methyl ester is adequate for risk assessment. The toxicity data requirements for a nonfood use pesticide depend on exposure and toxicity. In the case of chlorflurenol methyl ester which shows both low toxicity and moderate exposure, the requirements are the 6 acute studies, a subchronic study, a developmental toxicity study and a battery of mutagenicity studies. These data requirements have been satisfied by acceptable studies. However, a 1973 reproduction study submitted for other purposes shows equivocal effects that add uncertainty to the data base.

3.1.5 Toxicological Effects

Toxicological effects of concern are found in a chronic study in dogs at 4 weeks. Chlorflurenol methyl ester administered to dogs resulted in treatment-related red blood cell destruction at the highest dose tested within 4 weeks with a NOAEL/LOAEL of 31/94 mg/kg/day. No other study showed a lower NOAEL.

3.1.6 Dose-response

The acceptable and unacceptable subchronic studies in the rat and dog showed treatment related effects at the highest dose tested [HDT] in the dog.. The chronic dog study showed marginal hematological effects within 4 weeks at the HDT. The only

studies showing a dose related response were the rat subchronic and developmental toxicity studies in the form of a body weight decrement in female rats and maternal rats, respectively at the middle and high dose.

An old reproduction study (1973)[See section A.3.3 in Appendix A], that was not required showed possible, but inconsistent subfertility in rats. This unacceptable reproduction study may have shown equivocal effects on fertility, litter size at birth and pup weight decrement at the HDT. The fertility of P0 parents was unaffected; the next generation apparently showed effects at all dose levels, but showed no dose-related response and in the last generation there was statistically significant dose-related decrease in fertility at the two top dose levels. The study also showed a peculiar effect at mating. An unusual number of pregnant females showed no sperm during cohabitation. This effect is rarely seen in studies on reproduction. However, the method for identification of sperm at mating was not described and may have been inadequate. Older studies show more variation in fertility than current studies, raising the question that the potential decreased fertility may not be reproducible. The study was unacceptable largely due the variable fertility. For these reasons an extra 3X database uncertainty factor will be used in the Risk assessment for chlorflurenol methyl ester, unless another study on reproduction is submitted that shows a more definitive NOAEL for reproductive effects.

3.2 Absorption, Distribution, Metabolism, Excretion (ADME)

Chlorflurenol methyl ester is rapidly absorbed and excreted mostly in the urine within 24 hours, with minor additional excretion between 24 and 72 hours. In the study in one female rat/treatment, the report authors claimed that very small amounts of radiolabel were retained in the mammary gland and barely detectable amounts in nursing pups. The amount of label retained in the mammary gland and nursing pups was not quantified, and is thus unknown.

The kinetic data submitted suggest that chlorflurenol in the rat was circulated enterohepaticaly. Although the data also suggested that chlorflurenol was not secreted in rat milk, these data were not replicated or quantified and the sensitivity of the radio-autography/radiological methods used were not described, the absence in the milk supply was not proven.

3.3 FQPA Considerations

As there are no uses of chlorflurenol methyl ester that qualify as food uses, no tolerance has been established and the requirements of FQPA are not applicable.

3.4 Hazard Identification and Toxicity Endpoint Selection

3.4.1 Acute Reference Dose (aRfD) - Females age 13-49, Children of the General Population.

There is no study with a single dose suitable.

Comment: An acute RfD is used to assess acute food exposure. Since exposure to chlorflurenol methyl ester does not occur through food, addressing this endpoint is unnecessary.

3.4.3 Chronic Reference Dose (cRfD)

Selected Study: Chronic Feeding study in Dogs [MRID# 0082863] GDL 870.4100

EXECUTIVE SUMMARY: In a chronic toxicity study (MRID 00082863) IT 3456 [Chlorflurenol, technical (96% a.i., batch/lot # 5/69)] was administered to 4 Beagle dogs/sex/group in the diet at dose levels of 0, 300, 1000 or 3000 ppm (for male/female equivalent to 0, 8.7/8.8, 30.6/29.9 or 94.0/94.4 mg/kg bw/day, calculated from test material consumption) for 104 weeks. One extra dog/sex/group was treated with test material for 104 weeks, after which the dogs were untreated for 8 weeks. Hematology and clinical chemistry evaluation was performed at 6 intervals during the study. Animals were subjected to gross pathology and microscopic examination.

Body weight appeared to be slightly reduced by month 13 at the highest dose tested [HDT]. Dogs showed this body weight decrement at month 13 when compared with initial body weights for males [the HDT gained 0% vs. 22.3% for control weight] and for females [the HDT gained 6.6% vs. 20.3% for control body weight]. Male body weight gain appeared to be reduced for the remainder of the study. Male body weight gain was decreased at 104 weeks [body weight gain was 0.8 kg at the HDT and 2.5 kg for controls]. At the end of the study female body weight gain was the same as control weight gain. Food consumption was unaffected in both sexes.

Erythrocytes [ERY], hemoglobin concentration [Hb] and hematocrit [Ht] values appeared to be slightly decreased at the HDT in males and females starting at week 4 [the first time period evaluated] and male dogs maintained a decrease through out the study. Some of the values in the HDT were statistically significantly reduced, but were still within the normal range for dogs. The □ERY, □Hb and □Ht values [difference between measured values and week -2 values] appeared to decrease in males and females at the HDT starting at week 4 and male dogs maintained the decrease through out the study. This decrease is consistent with the slightly higher incidence and/or severity of siderous in the spleen, liver and Kupffer cells at the HDT. Hemosiderin in the 1000 ppm group was not considered sufficiently consistent to show that the mid dose group was affected. In addition the values for ERY, Hb and Ht from the 1000 ppm group of animals did not show consistent effects. From week 26-52 to termination, the values for ERY, Hb and Ht for treated female dogs did not appear to differ from control.

Clinical chemistry values showed no consistent treatment related effects. Organ weights were unchanged from control values.

On microscopic examination increased hemosiderin in liver and liver Kupffer cells and possibly in the spleen at the HDT seemed to confirm the hematological effects. In addition, the highest dose group showed higher incidence of gastritis and possible stomach lymphatic hyperplasia.

A single dog/sex was allowed to recover for 2 months and although the hemosiderin appeared to decrease, effects in one dog are difficult to interpret.

The NOAEL was 30.6/29.9 mg/kg/day for males/females. The LOAEL was 94.0/94.4 mg/kg/day for male/females based on decreased erythrocytes, hemoglobin and hematocrit by week 4 in males and females, supported by hemosiderin deposits in liver and increased incidence of gastritis and possible decreased body weight in males and females by month 13 of the study, but not in females by study termination at 24 months.

This study is **ACCEPTABLE/GUIDELINE** and satisfies the guideline requirement [870.4100b] for a dog chronic study. This DER takes precedence over previous conclusions.

Dose and Endpoint for Establishing cRfD: NOAEL is 31 mg/kg/day. The LOAEL is 94 mg/kg/day based on male and females decreased erythrocyte, hemoglobin and hematocrit by week 4 of the study and supported by hemosiderin deposits in the liver at termination. At this same dose body weight decrement was seen in male and females at month 13, but not in females by the end of the study.

Uncertainty Factor: 300x [10 for interspecies extrapolation, 10 for intraspecies variation and 3X for database uncertainty in the NOAEL in a reproduction study].

Comments about the Study/Endpoint/Uncertainty Factor: The hematological effects occurred at 4 weeks and remained until termination where hemosiderin deposits confirmed the red blood cell destruction. This endpoint will be unnecessary for current uses, since there are no food uses. However, this endpoint may be necessary at a later date and/or handler exposures.

3.4.4 Incidental Oral Exposure (Short- and Intermediate-Term)

Selected Study: Chronic Feeding study in Dogs [MRID 00082863] GDL 870.4100
[See Section 3.5.3 for the executive Summary of MRID 00082863]

Dose for Establishing an Endpoint: NOAEL is 31 mg/kg/day. The LOAEL is 94 mg/kg/day based on male and females decreased erythrocyte, hemoglobin and hematocrit by week 4 of the study and supported by hemosiderin deposits in the liver at termination. At this same dose body weight decrement was seen in male and females at month 13, but not in females by the end of the study.

Uncertainty Factor: 300x [10 for interspecies extrapolation, 10 for intraspecies variation and 3X for database uncertainty in the NOAEL in a reproduction study].

Comments about the Study/Endpoint/Uncertainty Factor: The hematological effects occurred at 4 weeks and remained until termination with hemosiderin deposits confirming the red blood cell destruction.

3.4.5 Dermal Absorption

There are no dermal absorption studies. Therefore, 100% dermal absorption will be assumed; exposure will also be calculated assuming 10% dermal absorption for comparitive purposes

3.4.6 Dermal Exposure (Short-, Intermediate- and Long-Term)

Selected Study: Chronic Feeding study in Dogs [MRID 00082863] GDL 870.4100
[See Section 3.5.3 for the executive Summary of MRID 00082863]

Dose for Establishing an Endpoint: NOAEL is 31 mg/kg/day. The LOAEL is 94 mg/kg/day based on male and females decreased erythrocyte, hemoglobin and hematocrit by week 4 of the study and supported by hemosiderin deposits in the liver at termination. At this same dose body weight decrement was seen in males and females at month 13, but not in females by the end of the study.

Uncertainty Factor: 100x [10 for interspecies extrapolation, 10 for intraspecies variation].

Comments about the Study/Endpoint/Uncertainty Factor: The hematological effects occurred at 4 weeks and remained until termination with hemosiderin deposits confirming the red blood cell destruction. The 3x uncertainty factor is dropped for dermal exposure, since an endpoint from an oral study is used. In addition, since there is no dermal absorption study, the default assumption is 100% dermal absorption, which is excessive. This built in extra safety factor is adequate, especially since a non-guideline 21-day dermal study on a formulation showed no systemic toxicity.

3.4.7 Inhalation Exposure (Short-, Intermediate- and Long-Term)

Selected Study: Chronic Feeding study in Dogs [MRID 00082863] GDL 870.4100
[See Section 3.5.3 for the executive Summary of MRID 00082863]

Dose for Establishing an Endpoint: NOAEL is 31 mg/kg/day. The LOAEL is 94 mg/kg/day based on male and females decreased erythrocyte, hemoglobin and hematocrit by week 4 of the study and supported by hemosiderin deposits in the liver at termination. At this same dose body weight decrement was seen in male and females at month 13, but not in females by the end of the study.

Uncertainty Factor: 100x [10 for interspecies extraploationvariation, 10 for intraspecies variation].

Comments about the Study/Endpoint/Uncertainty Factor: The hematological effects occurred at 4 weeks and remained until termination with hemosiderin deposits confirming the red blood cell destruction. This endpoint maybe unnecessary for current uses, since chlorflurenol methyl ester is not irritating and shows low toxicity by the oral route and effects from inhalation exposure are unlikely.

3.4.8 Level of Concern for Margin of Exposure

Table 5 Summary of Levels of Concern for Risk Assessment.

Route	Short-Term (1 - 30 Days)	Intermediate-Term (1 - 6 Months)	Long-Term (> 6 Months)
Occupational (Worker) Exposure			
Dermal	100	100	NA
Inhalation	100	100	NA
Residential Exposure			
Dermal	100	100	NA
Inhalation	NA	NA	NA
Incidental Oral	300	300	300

Occupational exposure: Since oral studies are used for dermal and inhalation endpoints, there is a built in safety factor associated with absorption which is assumed to be 100%, but may be much lower.

Residential exposure: Since the potential exists for incidental oral exposure to infants and children, a 3X database factor is applied when infants or children are exposed.

3.4.9 Recommendation for Combining Exposure Risk Assessments

Since all endpoints are oral, all routes of exposure may be combined, including incidental oral, dermal and inhalation. However, a combined risk index must be

used when combining dermal and oral risk because the uncertainty factors associated with the two types of exposures differ.

3.4.10 Classification of Carcinogenic Potential

There is no indication of dose related or treatment related carcinogenic effects in males or
females in an acceptable carcinogenicity study in mice below or above the limit dose of 1 g/kg/day [MRID 00082865].

3.4.11 Mutagenicity Studies

A battery of acceptable mutagenicity studies were all negative.

3.4.12 Summary of Toxicological Doses and Endpoints for chlorflurenol methyl ester for Use in Human Risk Assessments

No studies in humans have been submitted.

Table 6. Summary of Toxicological Doses and Endpoints for Chlorflurenol methyl ester for Use in Human Health Risk Assessments.

Exposure/ Scenario	Dose Used in Risk Assessment	Level of Concern [LOC] for Risk Assessment and contributing factors	Study and Toxicological Effects
Acute Dietary (Females 13-49 years of age)	No studies reflecting a single dose are appropriate or available from which to select this endpoint.		
Acute Dietary (General population including infants and children)	No studies reflecting a single dose are appropriate or available from which to select this endpoint.		
Chronic Dietary (All populations)	NOAEL = [31] mg/kg/day Chronic RfD = 0.10 mg/kg/day	LOC = 100% of the cRfD. Total UF=300 Interspecies10X Intraspecies 10X Database 3X	Chronic 2-year feeding study in dogs LOAEL = 94 mg/kg/day based on decreased erythrocyte, hemoglobin and hematocrit at 4 weeks.
Incidental Oral Short-Term (1 - 30 days) and Intermediate-Term (1-6 moths)	NOAEL = 31 mg/kg/day	LOC for MOE = 300	Chronic 2-year feeding study in dogs LOAEL = 94 mg/kg/day based on decreased erythrocyte, hemoglobin and hematocrit at 4 weeks.

Table 6. Summary of Toxicological Doses and Endpoints for Chlorflurenol methyl ester for Use in Human Health Risk Assessments.			
Exposure/ Scenario	**Dose Used in Risk Assessment**	**Level of Concern [LOC] for Risk Assessment and contributing factors**	**Study and Toxicological Effects**
Dermal Short-Term (1 - 30 days), intermediate-Term (1-6 months) and Long-Term (>6moths)	NOAEL = 31 mg/kg/day	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	Chronic 2-year feeding study in dogs LOAEL = 94 mg/kg/day based on decreased erythrocyte, hemoglobin and hematocrit at 4 weeks.
Inhalation Short-Term (1 - 30 days), Intermediate-Term (1-6 months) and Log-Term (>6 months)	NOAEL = 31 mg/kg/day	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	Chronic 2-year feeding study in dogs LOAEL = 94 mg/kg/day based on decreased erythrocyte, hemoglobin and hematocrit at 4 weeks.
Cancer (oral, dermal, inhalation)	**Classification: Chlorflurenol methyl ester is unlikely to be a human carcinogen**		

UF = uncertainty factor, FQPA SF = Any additional safety factor retained due to concerns unique to the FQPA, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = not applicable

4.0 Public Health and Pesticide Epidemiology Data

Incidence reports /epidemiology data are not available at this time. However, given the minimal nature of acute toxicity (Toxicity Categories III for eye and IV for other acute studies, large numbers of incidence are not expected.

5.0 Dietary Exposure/Risk Characterization

Chlorflurenol methyl ester is a nonfood use pesticide having no tolerances to reassess. Consequently, there are no residue chemistry data requirements and thus, dietary exposure or risk assessments are not applicable. Chlorflurenol methyl ester is used on pineapple after fruit harvest to stimulate production of vegetative planting material (slips). The time between pesticide treatment and the first harvest of pineapple fruit would be 1.5 to 2 years. No residues are expected in the fruit according to a HED Greyberad Committee decision in 1995 [TXR# 012504]. HED upholds this decision in this RED chapter.

5.1 Drinking Water Residue Profile

It should be noted that drinking water exposure to chlorflurenol methyl ester is

very limited. Due to the limited number of pound per year used, this water contamination is likely limited to use areas only. It follows that expanded use, would result in additional contamination.

Chronic drinking water exposure were modeled by DEEM software using surface water concentration, which showed all groups were exposed to levels below the chronic oral endpoint of 0.1 mg/kg/day. Non-nursing infants and all infants (< one year) were exposed to highest percentage of the RfD at 20% and 16 % respectively. All other groups were exposed to drinking water at 7.4% to 4.7% of the oral chronic RfD of 0.1 mg/kg/day. These levels are below EPA LOC. Selected levels for the highest exposure within a group are given in Table 7a

However, it should be noted that toddlers exposed to spray and granular treated lawns are above HED's LOC. Any additional exposure from water would exacerbate this concern.

Table 7a Selected population exposures (selected for highest surface water exposures within a group)

Population subgroup	Mg/kg/day [a]	Margin of exposure	% of the endpoint of 0.10 mg/kg/day
US population (summer season)	0.005343	5,802	5.3%
Western region	0.005699	5,439	5.7%
Hispanics	0.005646	5,490	5.6%
Non-hispanic blacks	0.004722	6,565	4.7%
Non-hispanic/non-white/non-black	0.006098	5084	6.1%
All infants (1<year)]	0.016308	1,901	16.3%
Nursing infants	0.006049	5,125	6.0%
Non-nursing infants	0.020201	1,535	20.2%
Females 20+ (not pregnant or nursing)	0.004965	6.243	5.0%
Females 13-50 years	0.004812	6,442	4.8%
Females 13+ nursing	0.006891	4,498	6.9%
Males 20+ yrs	0.004457	6,955	4.5%
Seniors 55+	0.004883	6,348	4.9%
Children 1-2 years	0.007387	4.197	7.4%
Children 3-5 years	0.006915	4,483	6.9%
Children 6-12 years	0.004770	6,499	4.8%
Youths 13-19 yrs	0.003596	8,622	3.6%

[a] For drinking water, Deem software was modeled using surface water concentration at 236 ppb.

Chronic drinking water exposures were also modeled by DEEM software using estimated ground water concentration, where only two groups were exposed to levels above the LOC. Non-nursing infants and all infants (< one year) were exposed to highest percentage of the RfD at 176% and 142% respectively. All other groups were exposed to drinking water at 31% to 60% of the oral chronic RfD of 0.1 mg/kg/day. The 176% and 142% are above OPP's LOC. Selected levels for the highest exposure within a group are given in Table 7b

Table 7b Selected population exposures (selected for highest ground water exposures within a group)

Population subgroup	Mg/kg/day [a]	% of the endpoint of 0.10 mg/kg/day

US population (summer season)	0.046414	46.2%
Western region	0.049506	49.5%
Hispanics	0.049046	49.0%
Non-hispanic blacks	0.041015	41.0%
Non-hispanic/non-white/non-black	0.052870	53.0%
All infants (1<year)]	0.141662	141.7%
Nursing infants	0.052540	52.5%
Non-nursing infants	0.175478	175.5%
Females 20+ (not pregnant or nursing)	0.043131	43.1%
Females 13-50 years	0.041801	41.8%
Females 13+ nursing	0.059862	59.9%
Males 20+ yrs	0.038717	38.7%
Seniors 55+	0.042420	42.4%
Children 1-2 years	0.064165	64.2%
Children 3-5 years	0.060069	60.1%
Children 6-12 years	0.041432	41.4%
Youths 13-19 yrs	0.031233	31.2%
For drinking water, Deem software was modeled using ground water concentration at 2050 ppb.		

Potential drinking water residues were estimated for groundwater from Tier I SCIGROW and surface water from Tier II PRZM and EXAMS models. The environmental fate information is incomplete. Due to this incomplete information, conservative default values have been substituted for missing data in order to proceed with this assessment. The OPP/EFED Florida turf scenario was selected for this assessment as a worst case based on the available usage and environmental fate information. It is likely that a more complete database for this chemical would lead to reduced estimates of chlorflurenol methyl ester concentrations in drinking water. For this assessment, it was assumed that 8 applications of chlorflurenol methyl ester were applied to turf grass at a rate of 3.0 pounds active ingredient per acre with a 28 day interval between applications and the pesticide is stable in the environment. The acute and chronic groundwater concentration of 2050 ppb is the highest estimated values. This would represent a maximum concentration in a shallow, private well in a high usage area. Surface water concentrations are for acute concentration: 386 ppb; for chronic non-cancer: 236 ppb and for ground water concentration 2050 pbb. [Table 8].

Table 8 Summary of Estimated Surface Water and Groundwater Concentrations for [Chemical].

	[Chemical]	
	Surface Water Conc., ppb [a]	**Groundwater Conc., ppb [b]**
Acute	386	2050
Chronic (non-cancer)	236	2050

[a] From the Tier II PRZM-EXAMS – Index Reservoir model. Input parameters are based on OPP/EFED Florida Turf scenario.

[b] From the SCI-GROW model assuming a maximum seasonal use rate of 3 lb a.i./A, 8 applications/year spaced at 28 day intervals; a K_{oc} of 65 L/mg and stable ½ life.

5.2 Food Residue Profile

There are no residues in food.

6.0 Residential Exposure and Risks

Chlorflurenol methyl ester is an herbicide, plant growth retardant, and plant growth regulator that is used in agricultural, commercial, and residential settings. As an herbicide and/or plant growth retardant, chlorflurenol is used for the postemergent control of annual grasses, broadleaf weeds, trees, shrubs, and vines. As a plant growth regulator, chlorflurenol is used in the production of pineapple planting material (sliplets). Chlorflurenol is registered as emulsifiable concentrate and granular formulations. The emulsifiable concentrate formulations are applied using groundboom sprayer, rights-of-way sprayer, handgun sprayer, low pressure handwand sprayer, and airblast sprayer. Granular formulations are applied using a bellygrinder, push-type spreader, and tractor-drawn spreader.

Hazard Concerns

Adverse effects were identified at durations of exposure ranging from short-term (up to 30 days) to long-term (> 6 months). The short- and intermediate-term dermal, inhalation, and incidental oral endpoints are based on a NOAEL of 31 mg/kg/day from a chronic 2-year feeding study in dogs where the LOAEL is 94 mg/kg/day. The LOAEL is based on decreased erythrocyte, hemoglobin and hematocrit at 4 weeks. Long-term exposures to chlorflurenol (i.e., greater than 6 months) are not expected for current registered uses. Additionally, no cancer endpoint was identified; therefore cancer risks are not assessed.

HED's level of concern (LOC) for chlorflurenol methyl ester occupational and residential dermal and inhalation exposures is 100 (i.e., a margin of exposure (MOE) less than 100 exceeds HED's level of concern). The dermal and inhalation margins of exposure were combined for the occupational and residential handler risk assessments because the toxicity endpoints for the dermal and inhalation routes of exposure are based on the same toxicological effects. For incidental oral exposures, HED's level of concern is 300 (i.e., a margin of exposure (MOE) less than 300 exceeds HED's level of concern). The dermal and incidental oral ingestion margins of exposure for the residential postapplication risk assessments for toddlers were also combined because the toxicity endpoints for the dermal and oral routes of exposure are based on the same toxicological effects.

6.1 Residential Handler Exposures and Non-cancer Risk Estimates

It has been determined there is a potential for exposure in residential settings during the application process for homeowners who use granular products containing chlorflurenol. There is also a potential for exposure from entering chlorflurenol-treated areas, such as lawns and golf courses. Risk assessments have been completed for both residential handler and postapplication scenarios.

In addition to homeowner uses in residential settings, chlorflurenol products are labeled for weed control at residential settings, which is applied by occupational applicators, but may result in postapplication exposures in residential settings. These potential postapplication exposures to homeowners also have been considered in this assessment.

6.1.1 Residential Handler Exposures and Risks

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task as was described under occupational handlers.

6.1.2 Handler Exposure Scenarios

Scenarios are used to define risks based on the *U.S. EPA Guidelines for Exposure Assessment* (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Assessing exposures and risks resulting from residential uses is very similar to assessing occupational exposures and risks, with the following exceptions:

- Residential handler exposure scenarios are considered to be short-term only, due to the infrequent use patterns associated with homeowner products.

- A tiered approach for personal protection using increasing levels of PPE is not used in residential handler risk assessments. Homeowner handler assessments are based on the assumption that individuals are wearing shorts, short-sleeved shirts, socks, and shoes.

- Homeowner handlers are expected to complete all tasks associated with the use of a pesticide product including mixing/loading if needed as well as the application.

- Label use-rates and use-information specific to residential products serve as the basis for the risk calculations.

- Area/volumes of spray or chemical used in the risk assessment are based on HED's guidance specific to residential use-patterns.

HED has determined that there is potential exposure to residential mixer, loader, and applicators during the usual use-patterns associated with chlorflurenol. Based on the use patterns, two major residential exposures were identified.

Mixers/Loaders/Applicators
(1) Mixing/loading/applying granular with push-type spreader (ORETF); and
(2) Mixing/loading/applying gra nular with a belly grinder (PHED).

6.1.3 Data and Assumptions for Handler Exposure Scenarios

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments. Each assumption and factor is detailed below. In addition to these factors, unit exposure values were used to calculate risk estimates. These unit exposure values were taken from the Outdoor Residential Exposure Task Force (ORETF) studies. Both PHED and ORETF studies are presented below.

Assumptions and Factors: The assumptions and factors used in the risk calculations include:

- Exposure factors used to calculate daily exposures to handlers were based on applicable data, if available. When appropriate data is unavailable, values from a scenario deemed similar might be used.

- HED always considers the maximum application rates allowed by labels in its risk assessments. If additional information such as average or typical rates is available, these values also may be used to allow risk managers to make a more informed risk management decision. Average/typical application rates were not available for residential scenarios.

- Residential risk assessments are based on estimates of what homeowners would typically treat, such as the size of a lawn or the size of a garden. The factors used for the chlorflurenol assessment were from the Health Effects Division Science Advisory Committee *Policy 12: Recommended Revisions to the Standard Operating Procedures for Residential Exposure Assessment* which was completed on February 22, 2001, and on professional judgment. The daily volumes handled and area treated used in each residential scenario are provided in Table 2 of that policy recommendation.

Residential Handler Exposure Studies: The unit exposure values that were used in this assessment were based on the Outdoor Residential Exposure Task Force studies and the Pesticide Handler Exposure Database (PHED, Version 1.1 August 1998). The ORETF data used in the residential assessment is described below.

ORETF Handler Studies -- OMA001-OMA004 (MRID 449722-01)
A report was submitted by the ORETF (Outdoor Residential Exposure Task Force) that presented data in which the application of various products used on turf by homeowners and lawncare operators (LCOs) was monitored. All of the data submitted in this report were completed in a series of studies.

OMA003: Homeowner Granular Applications with a Rotary (Push-type) Spreader (MRID 449722-01): A mixer/loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal (active ingredient DCPA, dimethyl tetrachloroterephthalate) as a surrogate compound to determine "generic" exposures of individuals applying a granular pesticide formulation to residential lawns. A total of 30 volunteers were monitored using passive dosimetry (inner and outer whole body dosimeters, hand washes, face/neck wipes, and personal inhalation monitors). Each volunteer carried, loaded, and applied two 25-lb bags of fertilizer (0.89% active ingredient) with a rotary type spreader to a lawn covering 10,000 ft^2. The target application rate was 2 lb a.i./acre (actual rate achieved was about 1.9 lbs a.i./acre). The average application time was 22 minutes, including loading the rotary push spreader and disposing of the empty bags. Each replicate handled approximately 0.45 lbs a.i. Dermal exposure was measured using inner and outer whole body dosimeters, hand washes, face/neck washes, and personal air monitoring devices with OVS tubes. The results for the rotary (push-type) spreader are summarized in Table 9 below.

Table 9: Unit Exposure Values for Homeowner Granular Applications with a Rotary (Push-type) Spreader Obtained From ORETF Study (MRID 449722-01)

Scenario Monitored	Unit Exposures			
	Dermal (mg a.i./lb handled)			Inhalation (µg a.i./lb handled)
	Short Pants, Short Sleeves	Long Pants, Short Sleeves	Long Pants, Long Sleeves	
Homeowner Granular Applications with a Push-type Spreader	0.67	0.09	0.07	0.88

[1] All unit exposure values are geometric means.

6.1.4 Residential Handler Exposure and Non-Cancer Risk Estimates

Non-cancer risks were calculated using the Margin of Exposure (MOE) as described in Section 7.1.3. Assessing exposures and risks resulting from residential uses is very similar to assessing occupational exposures and risks, except as described in Section 7.1.1. The other major difference with residential risk assessments is that the uncertainty factor which defines the level of risk concern has the additional FQPA safety factor applied. In the case of chlorflurenol, it was decided by HED that the factor for handler risk assessments is 100, which is based on the FQPA safety factor of 1X along with the 10X for inter-species extrapolation and 10X for intra-species sensitivity.

The residential exposure and risk estimates associated with the use of chlorflurenol are presented in Table 10. The risk calculations for residential chlorflurenol handlers are included in Appendix D of the June 30, 2006 Chlorflurenol Methyl Ester: Occupational and Residential Exposure Assessment for the RED.

Table 10: Residential Handler Short- and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario1	Crop or Target	Application Rate	Area Treated Daily (acres)	Baseline Unit Exposures		Baseline MOEs (Level of Concern = 100)		
				Dermal (mg/lb a.i.)	Inhalation (µg/lb a.i.)	Dermal	Inhalation	Total
Mixer/Loader/Applicator								
1) Mixing/loading/ applying granular with push-type spreader (ORETF OMA 003)	Turf	0.25 lb. a.i./acre (Label - 100% DA)	0.5 acres	0.67	0.88	26,000	2,000,000	26,000
		0.25 lb. a.i./acre (Label – 10% DA)				260,000	20,000,000	260,000
2) Mixing/loading/ applying with a belly grinder (PHED)	Turf	0.25 lb. a.i./acre (Label - 100% DA)	0.023	110	62	3,400	6,100,000	3,400
		0.25 lb ai/acre (Label – 10% DA)				34,000	61,000,000	34,000

6.1.5 Residential Handler Exposure and Risk Estimates for Cancer

No cancer endpoints of concern for chlorflurenol were identified; therefore cancer risks to residential handlers were not assessed.

6.1.6 Summary of Risk Concerns and Data Gaps for Handlers

All non-cancer risks (i.e., MOEs) to handlers associated with the scenarios are not of concern, because they exceed HED's uncertainty factor of 100.

6.1.7 Recommendations for Refining Residential Handler Risk Assessment

In order to refine this residential risk assessment, more data on actual use patterns including rates, timing, and areas treated would better characterize chlorflurenol risks. Exposure studies for many equipment types that lack data or that are not well represented in PHED (e.g., because of low replicate numbers or data quality) should also be considered based on the data gaps identified above and based on a review of the quality of the data used in this assessment.

6.2 Residential Postapplication Exposures and Assumptions

HED uses the term "postapplication" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. Chlorflurenol can be used in many areas that can be frequented by the general population including residential areas (e.g., home lawns and gardens). As a result, individuals can be exposed by entering these areas if they have been previously treated.

6.2.1 Residential Postapplication Exposure Scenarios

A wide array of individuals of varying ages can potentially be exposed to chlorflurenol when they are in areas that have been previously treated. Postapplication exposure scenarios were developed for each residential setting where chlorflurenol can be used. The scenarios likely to result in postapplication exposures are as follows:

- Dermal exposure from residue on lawns and turf (adult, youth and toddler);
- Hand-to-mouth transfer of residues on lawns (toddler);
- Ingestion of pesticide treated grass (toddler); and
- Incidental ingestion of soil from pesticide-treated residential areas (toddler).

Incidental ingestion of chlorflurenol granules from pesticide-treated residential areas was not assessed because there an acute dietary endpoint was not identified.

HED relies on a standardized approach for completing residential risk assessments that is based on current labels and guidance contained in the following four documents:

- ***Series 875, Residential and Residential Exposure Test Guidelines: Group B - Postapplication Exposure Monitoring Test Guidelines (V 5.4, Feb. 1998)*** This document provides general risk assessment guidance and criteria for analysis of residue dissipation data.

- ***Standard Operating Procedures for Residential Exposure Assessment (Dec. 1997)*** This document provides the overarching guidance for developing residential risk assessments including scenario development, algorithms, and values for inputs.

- ***Science Advisory Council For Exposure Policy 12 (Feb. 2001): Recommended Revisions To The Standard Operating Procedures (SOPs) For Residential Exposure Assessment*** This document provides additional, revised guidance for

completing residential exposure assessments.

- ***Overview of Issues Related To The Standard Operating Procedures For Residential Exposure Assessment (August 1999 Presentation To The FIFRA SAP)*** This document provides rationale for Agency changes in SOPs.

When the guidance in current labels and these documents is considered, it is clear that HED should consider children of differing ages as well as adults in its assessments. It is also clear that different age groups should be considered in different situations. The populations that were considered in the assessment include:

- Residential Adults: these individuals are members of the general population that are exposed to chemicals by engaging in activities at their residences (e.g., in their lawns or gardens) and also in areas not limited to their residence (e.g., golf courses or parks) previously treated with a pesticide. These kinds of exposures are attributable to a variety of activities and are usually addressed by HED in risk assessments by considering a representative activity as the basis for the exposure calculation.

- Residential Children: children are members of the general population that can also be exposed in their residences (e.g., on lawns and other residential turf grass areas). These kinds of exposures are attributable to a variety of activities such as playing outside. Toddlers have been selected as the sentinel (representative) population for the turf assessment. Youth-aged children (ages 10 to 12) are considered the sentinel population for a golfing assessment, because it is likely that children of this age would be playing golf. Children are addressed by HED in risk assessments by considering representative activities for each age group in an exposure calculation.

The *SOPs for Residential Exposure Assessment* defines several scenarios that apply to uses specified in current labels. These scenarios served as the basis for the residential postapplication assessment along with the modifications to them and the additional data and approaches described above. HED used this guidance to define the exposure scenarios that essentially include dermal and nondietary ingestion exposure to toddlers on treated lawns and dermal exposure to adults and youth on treated lawns. The SOPs and the associated scenarios are presented below:

- ***Dose from dermal exposure on treated turf:*** Postapplication dermal dose calculations for toddlers from playing on treated turf, for youth and adults playing golf on treated turf, and for adults mowing and exercising on treated turf

- ***Dose from hand-to-mouth activity from treated turf:*** Postapplication dose calculations for toddlers from incidental nondietary ingestion of pesticide residues on treated turf from hand-to-mouth transfer (i.e., those residues that are swallowed when toddlers get pesticide residues on their hands from touching treated turf and then put their hands in their mouth);

- ***Dose from object-to-mouth activity from treated turf:*** Postapplication dose calculations for toddlers from incidental nondietary ingestion of pesticide residues on treated turf from object-to-mouth transfer (i.e., those residues that are swallowed when toddlers put treated turf in their mouths);

- ***Dose from soil ingestion activity from treated turf:*** Postapplication dose calculations for toddlers from incidental nondietary ingestion of pesticide residues from ingesting soil in a treated turf area (i.e., those soil residues that are swallowed when toddlers get pesticide residues on their hands from touching treated soil and then put their hands in their mouth); and

The detailed residential postapplication calculations are presented in Appendix E of this document.

6.2.2 Data and Assumptions for Residential Postapplication Exposure Scenarios

Assumptions and Exposure Factors

A series of assumptions and exposure factors served as the basis for completing the residential postapplication risk assessments. The assumptions and factors used in the risk calculations are consistent with current Agency policy for completing residential exposure assessments (i.e., *SOPs for Residential Exposure Assessment*). The values used in this assessment include:

- There are many factors that are common to the occupational and residential postapplication risk assessments, such as body weights for adults, and analysis of residue dissipation data. Please refer to the assumptions and factors in Section 7.1.2 for further information concerning these common values.

- HED combines risks resulting from exposures to individual applications when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. The toxicological endpoints used in assessing risks must have the same toxicological effect in order for the risks to be combined. HED has combined risks using the aggregated risk index (ARI) for different kinds of exposures for the following scenario: toddlers on turf – dermal (high contact lawn activity) plus hand-to-mouth plus object-to-mouth plus soil ingestion.

- Exposures to adults and children on treated turf have been addressed using the latest HED standard operating procedures for this scenario including:
    - the transfer coefficients used are those presented during the 1999 Agency presentation before the FIFRA Science Advisory Panel that have been adopted in routine practice by HED;
    - 3 year old toddlers are expected to weigh 15 kilograms (representing an average weight from years one to six);
    - hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2, representing the palmar surfaces of three fingers;
    - saliva extraction efficiency is 50 percent meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed;
    - object-to-mouth exposures are based on a 25 cm^2 surface area;
    - ingestion rate of soil is 100 mg/day;
    - exposure durations for turfgrass scenarios are estimated to be 2 hours and exposure durations for home gardening (ornamental) scenarios are estimated to be 0.67 hours for adults and 0.33 hours for youth - based on

information in HED's *Exposure Factors Handbook*;
- o soil residues are contained in the top centimeter and soil density is 0.67 mL/gram; and
- o dermal, hand- and object-to-mouth, and soil ingestion are combined to represent an overall risk from exposure to turf.

- Postapplication residential risks are based on maximum application rates or values specified in the *SOPs for Residential Exposure Assessment*.

- The Jazzercize approach is the basis for the dermal transfer coefficients as described in HED's Series 875 guidelines, *SOPs for Residential Exposure Assessment*, and the 1999 FIFRA SAP Overview document.

6.2.3 Residential Postapplication Exposure and Non-cancer Risk Estimates

Non-cancer risks were calculated using the Margin of Exposure (MOE) approach, which is a ratio of the body burden to the toxicological endpoint of concern. Exposures were calculated by considering the potential sources of exposure (i.e., TTRs on lawns), then calculating dermal and nondietary ingestion exposures.

Dermal exposures and risks from lawn uses were calculated in the same manner as described above in Section 7.2.3. Along with calculating these dermal exposures, other aspects of the turf exposure scenarios were calculated such as the dose from nondietary ingestion. The algorithms used for each type of calculation are presented below which have not been previously addressed in Section 7.2.3.

Nondietary Ingestion Exposure from Treated Turf: Nondietary ingestion exposure from treated turf was calculated using the following equations. These values were then used to calculate MOEs.

Dermal Exposure from Treated Lawns (adult and toddler)

The approach used to calculate the dermal doses that are attributable to exposure from contacting treated lawns is:

$$ADD = (TTR_0 * ET * TC * DA * CF1) / BW$$

Where:

ADD	=	average daily dose (mg/kg/day);
TTR_t	=	turf transferable residue on day "0" ($\mu g/cm^2$). TTR = application rate ($\mu g/cm^2$) * fraction of a.i. retained on foliage (5% for turf activities, 20% for gardening activities) ;
ET	=	exposure time (2 hr/day);

TC = transfer coefficient (14,500 cm^2/hr for adults and 5,200 cm^2/hr for toddlers);
DA = dermal absorption factor;
CF1 = weight unit conversion factor to convert µg units to mg for the daily exposure (0.001 mg/µg); and
BW = body weight (70 kg for adults and 15 kg for toddlers).

Hand-to-mouth Transfer of Pesticide Residues on Lawns (toddler)

The approach used to calculate the nondietary ingestion exposures that are attributable to hand-to-mouth behavior on treated turf is:

$$ADD = (TTR_0 * SA * FQ * ET * SE * CF1) / BW$$

Where:
ADD = average daily dose (mg/kg/day);
TTR_t = turf transferable residue on day "0" (µg/cm^2); TTR = application rate (µg/cm^2) * fraction of a.i. retained on foliage (5%) ;
SA = surface area of the hands (20 cm^2/event);
FQ = frequency of hand-to-mouth activity (20 events/hr);
ET = exposure time (2 hr/day);
SE = extraction by saliva (50%);
CF1 = weight unit conversion factor to convert µg units in the TTR value to mg for the daily exposure (0.001 mg/µg); and
BW = body weight (15 kg).

Object-to-mouth Transfer of Pesticide Residues on Lawns (toddler)

The approach used to calculate doses that are attributable to object-to-mouth behavior on treated turf that is represented by a child mouthing on a handful of turf is:

$$ADD = (TTR_0 * IgR * CF1) / BW$$

Where:
ADD = average daily dose (mg/kg/day);
TTR_t = turf transferable residue on day "0" (µg/cm^2); TTR = application rate (µg/cm^2) * fraction of a.i. retained on foliage (20%)
IgR = ingestion rate of grass (25 cm^2/day);
CF1 = weight unit conversion factor to convert the µg of residues on the grass to mg to provide units of mg/day (1E-3 mg/µg); and
BW = body weight (15 kg).

Incidental Ingestion of Soil from Pesticide-Treated Residential Areas (toddler)

The approach used to calculate doses that are attributable to soil ingestion is:

$ADD = (SR_0 * IgR * CF1) / BW$

Where:

ADD	=	average daily dose (mg/kg/day);
SR_{0t}	=	soil residue on day "0" (0.0022 µg/g);
IgR	=	ingestion rate of soil (100 mg/day);
CF1	=	weight unit conversion factor to convert the µg of residues on the soil to grams to provide units of mg/day (1E-6 g/µg); and
BW	=	body weight (15 kg).

And

$SR_t = AR * F * CF2 * CF3 * CF4$

Where:

AR	=	application rate (lb a.i./acre);
F	=	fraction of a.i. available in uppermost cm of soil (1 fraction/cm) (100%);
CF2	=	volume to weight unit conversion factor to convert the volume units (cm^3) to weight units for the SR value (U.S. EPA, 1992) (0.67 cm^3/g soil);
CF3	=	area unit conversion factor to convert the surface are units (acres) in the application rate to cm^2 (2.47E-8 acre/cm^2); and
CF4	=	weight unit conversion factor to convert the lbs a.i. in the application rate to µg (4.54E8 µg/lb).

Non-cancer Risk Summary

Adults

Table 11 presents the postapplication MOE values calculated for adults after lawn, turf and home garden applications chlorflurenol. All postapplication non-cancer risks were below HED's level of concern, except for high contact activities on residential turf assuming the 3.0 lb a.i./A (BEAD) application rates where MOEs are 44 on day 0.

Table 11: Adult Residential Risk Estimates (Dermal) for Postapplication Exposure

Exposure Scenario	Dermal Transfer Coefficient (µg/cm^2)	Application Rate (lb a.i./acre)	MOE at Day 0 (Level of Concern = 100)
Spray			

Table 11: Adult Residential Risk Estimates (Dermal) for Postapplication Exposure			
Exposure Scenario	Dermal Transfer Coefficient ($\mu g/cm^2$)	Application Rate (lb a.i./acre)	MOE at Day 0 (Level of Concern = 100)
Residential Turf (High Contact Activities)	14,500	1.0 (Label)	130
		3.0 (BEAD)	**44**
Residential Turf (Mowing)	3,400	1.0 (Label)	570
		3.0 (BEAD)	190
Golfer	500	1.0 (Label)	1,900
		3.0 (BEAD)	650
Granular			
Residential Turf (High Contact Activities)	14,500	1.1 (Label – 100% DA)	120
		1.1 (Label – 10% DA)	1,200
		3.0 (BEAD - 100% DA)	**44**
		3.0 (BEAD - 10% DA)	440
Residential Turf (Mowing)	3,400	1.1 (Label – 100% DA)	520
		1.1 (Label – 10% DA)	5,200
		3.0 (BEAD - 100% DA)	190
		3.0 (BEAD - 10% DA)	1,900
Golfer	500	1.1 (Label – 100% DA)	1,800
		1.1 (Label – 10% DA)	18,000
		3.0 (BEAD - 100% DA)	650
		3.0 (BEAD - 10% DA)	6,500

Youths (11-12 years old)

Table 12 summarizes the risk assessment for youths [10 to 12 years old]. Short-term MOEs for chlorflurenol for these youths were >100 for all scenarios considered.

Table 12: Youth Residential Risk Estimates (Dermal) for Postapplication Exposure			
Exposure Scenario	Dermal Transfer Coefficient ($\mu g/cm^2$)	Application Rate (lb a.i./acre)	MOE at Day 0 (Level of Concern = 100)
Spray			
Residential Turf (Mowing)	3,400	1.0 (Label)	320
		3.0 (BEAD)	110
Golfer	500	1.0 (Label)	1,100
		3.0 (BEAD)	360
Granular			
Residential Turf (Mowing)	3,400	1.1 (Label- 100% DA)	290
		1.1 (Label- 10% DA)	2,900
		3.0 (BEAD - 100% DA)	110
		3.0 (BEAD - 10% DA)	1,100
Golfer	500	1.1 (Label- 100% DA)	980
		1.1 (Label- 10% DA)	9,800
		3.0 (BEAD - 100% DA)	360
		3.0 (BEAD - 10% DA)	3,600

Toddler (3 year old)

Table 13 summarizes the risk assessment for toddlers. The postapplication non-cancer risks are not of concern for the oral route (MOE's >300). For the dermal route, risks to toddlers from high contact activity on lawns exceed HED's level of concern (MOE's <100) at the 1.0/1.1 lb a.i./A (Label) and 3.0 lb a.i./A (BEAD) application rates, except when 10% dermal absorption is assumed for the granular formulations. Calculated combined risks to toddlers (i.e., dermal high contact activity plus hand to mouth activity plus object to mouth activity on treated turf plus incidental soil ingestion of pesticide residue from treated turf areas) are therefore, also of concern, except when 10 percent dermal absorption is assumed for the granular formulations.

Table 13: Toddler Residential Risk Estimates for Postapplication Exposure

Exposure Scenario	Route of Exposure	Dermal Transfer Coefficient ($\mu g/cm^2$)	Application Rate (lb a.i./acre)	MOE at Day 0 (Level of Concern = 100 for dermal and 300 for oral)
Spray				
Residential Turf (High Contact Activities)	Dermal	5,200	1.0 (Label)	**80**
			3.0 (BEAD)	**27**
Hand to Mouth Activity on Turf	Oral	NA	1.0 (Label)	2,100
			3.0 (BEAD)	690
Object to Mouth Activity on Turf		NA	1.0	8,300
			3.0 (BEAD)	2,800
Incidental Soil Ingestion		NA	1.0	620,000
			3.0 (BEAD)	210,000
Granular				
Residential Turf (High Contact Activities)	Dermal	5,200	1.1 (Label 100% DA)	**72**
			1.1 (Label 10% DA)	720
			3.0 (BEAD – 100% DA)	**27**
			3.0 (BEAD - 10% DA)	270
Hand to Mouth Activity on Turf	Oral	NA	1.1	1,900
			3.0 (BEAD)	690
Object to Mouth Activity on Turf		NA	1.1	7,500
			3.0 (BEAD)	2,800
Incidental Soil Ingestion		NA	1.1	560,000
			3.0(BEAD)	210,000

Combined Risk Assessment for Residential Scenarios

HED combines risk values resulting from separate postapplication exposure scenarios when it is likely they can occur simultaneously based on the use-pattern and the behavior associated with the exposed population. In the case of the chlorflurenol, the dermal and incidental oral ingestion toxicological endpoints have the same toxicological effect, therefore dermal and oral doses were combined.

A total aggregated risk index (ARI) was used since the target MOE values for dermal exposure (100) and incidental oral exposure (300) are different. The target ARI is 1; therefore, ARIs of less than 1 are risks of concern. The combined risk index was calculated from the aggregate risk index (ARI)-as follows.

Aggregate Risk Index (ARI) = $1/(1/RI_{\text{high contact activity}}) + (1/RI_{\text{hand-to-mouth}}) + (1/RI_{\text{object-to-mouth}}) + (1/RI_{\text{incidental soil ingestion}})$

Where:

Risk Index (RI) = MOE/Uncertainty Factor

Table 14 summarizes the combined risk assessment for toddlers. Calculated combined risks to toddlers (i.e., dermal high contact activity, hand-to-mouth activity, object-to-mouth activity on treated turf plus incidental soil ingestion of pesticide residue from treated turf areas) are of concern for applications of chlorflurenol at:

- 1.0 lb a.i./A (label) for spray applications assuming 100% dermal absorption (ARI = 0.70);
- 1.1 lb a.i./A (label and 100% dermal absorption) for granular applications (ARI = 0.63)
- 3.0 lb a.i./A (BEAD) for spray applications assuming 100% dermal absorption (ARI = 0.23); and
- 3.0 lb a.i./A (BEAD) for granular applications assuming 100% dermal absorption (ARI = 0.23.

The ARIs are greater than 1 for the 1.1 and 3.0 lb a.i./A (label and BEAD respectively) for granular applications if 10% dermal absorption is assumed. The ARI for the 1.1 lb a.i./A scenario is 3 and the ARI for the 3 lb a.i./A scenario is 1.1.

Table 14: Residential Scenarios for Short-Term Risk Estimates - Toddlers

Postapplication Exposure Scenario			Risk Index (RI)	Combined-Risk Index (ARI)
Toddler	Turf - Spray Application	Dermal – High Contact Activity	0.80	**0.70**

Table 14: Residential Scenarios for Short-Term Risk Estimates - Toddlers				
Postapplication Exposure Scenario			Risk Index (RI)	Combined-Risk Index (ARI)
	(1.0 lb a.i./acre - Label)	Hand to Mouth	6.9	
		Object to Mouth	27	
		Incidental Soil Ingestion	2100	
	Turf - Spray Application (3.0 lb a.i./acre – BEAD)	Dermal – High Contact Activity	0.27	**0.23**
		Hand to Mouth	2.3	
		Object to Mouth	9.2	
		Incidental Soil Ingestion	688	
	Turf – Granular Application (1.1 lb a.i./acre – Label - 100% DA)	Dermal – High Contact Activity	0.72	**0.63**
		Hand to Mouth	6.3	
		Object to Mouth	25	
		Incidental Soil Ingestion	1800	
	Turf – Granular Application (1.1 lb a.i./acre – Label - 10% DA)	Dermal – High Contact Activity	7.3	3
		Hand to Mouth	6.3	
		Object to Mouth	25	
		Incidental Soil Ingestion	1800	
	Turf – Granular Application (3.0 lb a.i./ acre – BEAD - 100% DA)	Dermal – High Contact Activity	0.27	**0.23**
		Hand to Mouth	2.3	
		Object to Mouth	9.2	
		Incidental Soil Ingestion	688	
	Turf – Granular Application (3.0 lb a.i./acre – BEAD - 10% DA)	Dermal – High Contact Activity	2.7	1.1
		Hand to Mouth	2.3	
		Object to Mouth	9.2	
		Incidental Soil Ingestion	688	

6.2.4 Residential Postapplication Exposure and Risk Estimates for Cancer

Residential postapplication cancer risks were not assessed for chlorflurenol because no cancer endpoints of concern were identified.

6.2.5 Summary of Residential Postapplication Risk Concerns and Data Gaps

HED considered a number of exposure scenarios for products that can be used in the residential environment representing different segments of the population including toddlers, youth-aged children, and adults. Short-term non-cancer MOEs were calculated for all scenarios. Cancer risks were not calculated, since no toxicological endpoint for cancer was selected. In residential settings, HED does not use restricted-entry intervals or other mitigation approaches to limit postapplication exposures, because they are viewed as impractical and not enforceable. As such, risk estimates on the day of application are the key concern.

For the adult populations, all postapplication non-cancer risks were below HED's level of concern, except for the 3.0 lb a.i./A (BEAD) application rate where MOEs are 44 on day 0. For the youth populations, all postapplication non-cancer risks were below HED's level of concern. For toddlers, postapplication non-cancer risks are not of concern for the oral route. For the dermal route, risks to toddlers from high contact activity on lawns exceed HED's level of concern at the 1.0/1.1 lb a.i./A (Label) and 3.0 lb a.i./A (BEAD) application rates, except when 10% dermal absorption is assumed for the granular formulations. Calculated aggregated risks to toddlers (i.e., dermal high contact activity plus hand to mouth activity plus object to mouth activity on treated turf plus incidental soil ingestion of pesticide residue from treated turf areas) are therefore, also of concern, except when 10 percent dermal absorption is assumed for the granular formulations.

6.2.6 Recommendations for Refining Residential Postapplication Risk Assessments

In order to refine this residential assessment, data on actual use patterns including rates, timing, and the kinds of tasks performed are required to better characterize chlorflurenol risks.

6.3 Residential Risk Characterization

Characterization of the residential risks included in this document must consider each of the approaches used to calculate risks as well as the information that could be forthcoming in any probabilistic assessment that is submitted for chlorflurenol methyl ester.

6.3.1 Characterization of Residential Handler Risks

The data that were used in the chlorflurenol residential handler assessment represent the best data and approaches that are currently available. The inputs for

application rate and other use/usage information (e.g., area treated and frequency of use) used by the Agency were supported by the proposed chlorflurenol labels. There are also many uncertainties in the assessment that are common with the occupational assessment as well. These factors and their impacts on the results should be considered as well in the interpretation of the results for residential handlers. Section 2.3.1 provides a summary of these issues.

In summary, with respect to residential handler risks, the Agency believes that the values presented in this assessment represent the highest quality results that could be produced given the exposure, use, and toxicology data that are available.

6.3.2 Characterization of Residential Postapplication Risks

The general population can be exposed through many different pathways that result from uses on lawns and from indoor surface treatments. To represent the wide array of possible exposures, the Agency relies on the scenarios that have been defined in the *SOPs for Residential Exposure Assessment* and accompanying documents such as the overview presented to the FIFRA Science Advisory Panel. For turf uses, the Agency considered only toddlers (3 year olds) in the assessments. Toddler MOEs were calculated for nondietary ingestion (hand-/object-to-mouth, soil ingestion and granules ingestion). MOEs from treated indoor surfaces were also evaluated for toddlers for whom exposures may occur from hand-to-mouth behavior.

The data that were used in the chlorflurenol residential postapplication assessment represent the best data and approaches that are currently available. To the extent possible, the Agency has attempted to use chlorflurenol methyl ester specific data. When chemical-specific data were unavailable, the Agency used the current approaches for residential assessment, many of which include recent upgrades to the SOPs. For example, for the toddler hand-to-mouth calculations, no TTR data were available but a 5 percent transferability factor was applied to calculate residue levels appropriate for this exposure pathway.

Finally, the Agency believes that the values presented in this assessment represent the highest quality results that could be produced based on the currently available postapplication exposure data. The Agency believes that the risks represent reasonable worse-case estimates of exposure because maximum application rates are used to define residue levels upon which the calculations are based.

7.0 OCCUPATIONAL EXPOSURE AND RISKS

7.1 Occupational Handler Exposures and Risk Estimates

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and that exposures can vary depending on the specifics of each task. Job requirements (e.g., amount of chemical to be used in an application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

HED uses exposure scenarios to describe the various types of handler exposures that may occur for a specific active ingredient. The use of scenarios as a basis for exposure assessment is very common as described in the *U.S. EPA Guidelines for Exposure Assessment* (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Information from the current labels, use and usage information, toxicology data, and exposure data were all key components in the development of the exposure scenarios. HED has developed a series of general descriptions for tasks that are associated with pesticide applications. Tasks associated with occupational pesticide handlers are categorized using one of the following terms:

- **Mixers and/or Loaders:** these individuals perform tasks in preparation for an application. For example, prior to application, mixer/loaders would mix the chemical and load it into the holding tank of the airplane or groundboom...

- **Applicators:** these individuals operate application equipment during the release of a pesticide product into the environment. These individuals can make applications using equipment such as airplanes or groundboom.

- **Mixer/Loader/Applicators and or Loader/Applicators:** these individuals are involved in the entire pesticide application process (i.e., they do all job functions related to a pesticide application event). These individuals would transfer the chemical into the application equipment and then also apply it.

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. HED classifies exposures up to 30 days as short-term and exposures greater than 30 days up to several months as intermediate-term. HED completes both short- and intermediate-term assessments for occupational scenarios in essentially all cases, because these kinds of exposures are likely and acceptable use/usage data are not available to justify deleting intermediate-term scenarios. Based on use data and label instructions, HED believes that occupational chlorflurenol exposures may occur over a single day or up to weeks at a time for many use-patterns and that intermittent exposures over several weeks also may occur. Some applicators may apply chlorflurenol over a period of weeks, because they are custom or commercial applicators who are completing a number of applications for a number of different clients. Long-term handler exposures are not expected to occur for chlorflurenol.

Other parameters are also defined from use and usage data such as application rates and application frequency. HED always completes non-cancer risk assessments using maximum application rates for each in order to ensure there are no concerns for each specific use.

Occupational handler exposure assessments are completed by HED using different levels of risk mitigation. Typically, HED uses a tiered approach. The lowest tier is designated as the baseline exposure scenario (i.e., long-sleeve shirt, long pants, shoes, socks, and no respirator). If risks are of concern at baseline attire, then increasing levels of personal protective equipment or PPE (e.g., gloves, double-layer body protection, and respirators) are evaluated. If risks remain a concern with maximum PPE, then engineering controls (e.g., enclosed cabs or cockpits, water-soluble packaging, and closed mixing/loading systems) are evaluated. This approach is used to ensure that the lowest level of risk mitigation that provides adequate protection is selected, since the addition of PPE and engineering controls involves an additional expense to the user and – in the case of PPE – also involves an additional burden to the user due to decreased comfort and dexterity and increased heat stress and respiratory stress.

7.1.1 Data and Assumptions for Handler Exposure Scenarios

7.1.1.1 Assumptions for Handler Exposure Scenarios

A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis. The assumptions and factors used in the risk calculations include:

- Occupational handler exposure estimates were based on surrogate data from: (1) the Pesticide Handlers Exposure Database (PHED) and (2) the Outdoor Residential Exposure Task Force (ORETF).

- The toxicological endpoint of concern for dermal and inhalation risks are from studies where the effects were observed in males and females, therefore, the average body weight of an adult male handler (i.e., 70 kg) is used to complete the handler dermal and inhalation non-cancer risk assessment.

- The dermal absorption for liquid concentrate formulations was assumed to be 100 percent, since no dermal absorption data are available. Certain solvents in liquid formulations can result in a high percent of dermal absorption. The dermal absorption for granular formulation was assessed assuming both 100 percent and 10 percent, since although there are no dermal absorption data available, it is rare for dermal absorption of a granular formulation to exceed 10 percent.

- Generic protection factors (PFs) were used to calculate exposures when data were not available. For example, a 50 percent protection factor was assumed for the use of a double layer body protection.

- For non-cancer assessments, HED assumes the maximum application rates allowed by the master labels in its risk assessments (see Tables 1a, 1b, 1c and 2).

- The average occupational workday is assumed to be 8 hours.

The daily areas treated were defined for each handler scenario (in appropriate units) by determining the amount that can be reasonably treated in a single day (e.g., acres, square feet, or gallons per day). When possible, the assumptions for daily areas treated are taken from the Health Effects Division Science Advisory Committee on Exposure SOP #9: Standard Values for Daily Acres Treated in Agriculture, which was completed on July 5, 2000. However, no standard values are available for numerous scenarios. Assumptions for these scenarios are based on HED estimates and could be further refined from input from affected sectors (see Tables 1a, 1b, and 1c)

7.1.1.2 Exposure Data for Handler Exposure Scenarios

HED uses *unit exposure* to assess handler exposures to pesticides. *Unit exposures* are estimates of the amount of exposure to an active ingredient a handler receives while performing various handler tasks and are expressed in terms of micrograms or milligrams of active ingredient per pound of active ingredient handled. HED has developed a series of unit exposures that are unique for each scenario typically considered in our assessments (i.e., there are different unit exposures for different types of application equipment, job functions, and levels of protection). The *unit exposure* concept has been established in the scientific literature and also through various exposure monitoring guidelines published by the U.S. EPA and international organizations such as Health Canada and OECD (Organization for Economic Cooperation and Development). Unit exposures were based on surrogate data from PHED and ORETF, which are described below.

Pesticide Handler Exposure Database (PHED) Version 1.1 (August 1998): PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts – a database of measured exposures for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates).

Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central

assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., liquids, granulars), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing).

Once the data for a given exposure scenario have been selected, the data are normalized (i.e., divided by) by the amount of pesticide handled resulting in standard unit exposures (milligrams of exposure per pound of active ingredient handled). Following normalization, the data are statistically summarized. The distribution of exposure for each body part (e.g., chest, upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposures calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. These evaluation criteria and the caveats specific to each exposure scenario are summarized in Appendix A, Table A1 of the June 30, 2006 Chlorflurenol Occupational and Residential Exposure RED. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure for many occupational scenarios that can be utilized to ensure consistency in exposure assessments. Unit exposures are used which represent different levels of personal protection as described above. Protection factors were used to calculate unit exposures for varying levels of personal protection if data were not available.

ORETF Handler Studies (MRID 449722-01): A report was submitted by the ORETF (Outdoor Residential Exposure Task Force) that presented data in which the application of various products used on turf by homeowners and lawncare operators (LCOs) was monitored. All of the data submitted in this report were completed in a series of studies. The studies relevant to the scenarios used for the chlorflurenol assessment are described below and are summarized in Appendix A, Table A1 in the June 30, 2006, Chlorflurenol Occupational and Residential Exposure Assessment for the RED .

OMA001: LCO Granular Applications with a Rotary Spreader (MRID 449722-01): A loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal (active ingredient DCPA, dimethyl tetrachloroterephthalate) as a

surrogate compound to determine "generic" exposures of lawn care operators (LCOs) applying a granular pesticide formulation to residential lawns. Surrogate chemicals were chosen by the Task Force for their representativeness based on physical chemical properties and other factors. Dacthal, which was the surrogate chemical used for the granular spreader studies, has a molecular weight of 331.97 and a vapor pressure of 1.6 x 10^{-6}, and is believed to be an appropriate surrogate for many relatively nonvolatile pesticides.

The study was designed to simulate a typical work day for a LCO applying granular pesticide formulation to home lawns. Each LCO replicate involved loading and applying approximately 3.3 lb a.i. (360 lb formulated product) over a period of about 4 hours to 15 simulated residential lawns (6480 ft^2 each) with a rotary type spreader. The average industry application rate of 2 lb a.i./acre was simulated (actual rate achieved was about 1.9 lb a.i./acre). The monitoring period included driving, placing the spreader onto and off of the truck, carrying and loading the formulation in the spreader, and the actual application. Incidental activities such as repairs, cleaning up spills, and disposing of empty bags were monitored. A total of 40 replicates (individual application events) were monitored using passive dosimetry (inner and outer whole body dosimeters, hand washes, face/neck wipes, and personal inhalation monitors with OVS tubes). The inner samples represent a single layer of clothing. Inhalation exposure was calculated using an assumed respiratory rate of 17 Lpm for light work (NAFTA, 1999), the actual sampling time for each individual, and the pump flow rate. In 20 of the replicates, the subjects wore chemical-resistant gloves while in the remaining replicates, no gloves were worn. No gloves were worn in any replicate while driving.

All results were normalized for the amount of active ingredient handled. Nearly all samples (for every body part and for inhalation) were above the level of quantitation (LOQ) for dacthal. Where results were less than the reported LOQ, ½ LOQ value was used for calculations, and no recovery corrections were applied. The overall laboratory recoveries ranged from 83 to 101% and the field recoveries ranged from 73 to 98%. The unit exposure values are presented in Table 15 below. [Note the inhalation exposure value is a median because the data were found to be neither normally nor lognormally distributed. All dermal values are geometric means as the data were lognormally distributed.]

Table 15: Unit Exposure Values for LCO Granular Applications with a Rotary Spreader Obtained From ORETF Studies (MRID 449722-01)

Type	Unit Exposure[1] (mg exp./lb a.i. handled)			
	Dermal			Inhalation
	Single Layer, No Gloves	Single Layer, Gloves	Double Layer[2], Gloves	
LCO Granular Applications with a Rotary Spreader	0.35	0.22	0.11	0.0073

[1] All dermal unit exposure values are geometric means. The inhalation value is a median. [2] Double layer value calculated using a 50% protection factor.

OMA002: LCO Spray Applications with a Low Pressure Handgun (MRID 449722-01): A mixer/loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal as a surrogate compound to determine "generic" exposures to individuals applying a pesticide to turf with a low-pressure "nozzle gun" or "handgun" sprayer. Dermal and inhalation exposures were estimated using whole-body passive dosimeters and breathing-zone air samples on OVS tubes. Inhalation exposure was calculated using an assumed respiratory rate of 17 liters per minute for light work (NAFTA, 1999), the actual sampling time for each individual, and the pump flow rate. All results were normalized for pounds active ingredient handled.

A total of 90 replicates were monitored using 17 different subjects. Four different formulations of dacthal [75% wettable powder (packaged in 4 and 24 pound bags), 75% wettable powder in water soluble bags (3 pound bag), 75% water dispersible granules (2 pound bag) and 55% liquid flowable (2.5 gallon container)] were applied by five different LCOs to actual residential lawns at each site in three different locations (Ohio, Maryland, and Georgia) for a total of fifteen replicates per formulation. An additional ten replicates at each site were monitored while they performed spray application only using the 75 percent wettable powder formulation. A target application rate of 2 pounds active ingredient was used for all replicates (actual rate achieved was about 2.2 pounds active ingredient per acre). Each replicate treated a varying number of actual client lawns to attain a representative target of 2.5 acres (1 hectare) of turf. The exposure periods averaged five hours twenty-one minutes, five hours thirty-nine minutes, and six hours twenty-four minutes, in Ohio, Maryland and Georgia, respectively. Average time spent spraying at all sites was about two hours. All mixing, loading, application, adjusting, calibrating, and spill clean up procedures were monitored, except for typical end-of-day clean-up activities, e.g. rinsing of spray tank, etc. Dermal exposure was measured using inner and outer whole body dosimeters, hand washes, face/neck washes, and personal air monitoring devices. All test subjects wore one-piece, 100 percent cotton inner dosimeters beneath 100 percent cotton long-sleeved shirt and long pants, rubber boots and nitrile gloves. Gloves are typically worn by most LCOs, and required by many pesticide labels for mixing and loading.

Overall, residues were highest on the upper and lower leg portions of the dosimeters. In general, concurrent lab spikes produced mean recoveries in the range of 78-120 percent, with the exception of OVS sorbent tube sections which produced mean recoveries as low as 65.8 percent. Adjustment for recoveries from field fortifications were performed on each dosimeter section or sample matrix for each study participant, using the mean recovery for the closest field spike level for each matrix and correcting the value to 100 percent. The unit exposure values are presented below in Table 16. [Note the data were found to be lognormally distributed. As a result, all exposure values are geometric means.]

Table 16: Unit Exposure Values Obtained for LCO Spray Applications with a Low Pressure Handgun from ORETF Handgun Studies (MRID 449722-01)				
Application Method[4]	Total Dermal Unit Exposure[1] (mg/lb a.i.)			Inhalation Unit Exposure[1,2] (µg/lb a.i.)
	Single Layer, No Gloves	Single Layer, Gloves	Double Layer, Gloves [3]	
LCO Handgun Spray Mixer/Loader/Applicator Liquid Flowable	No Data	0.45	0.245	1.8

[1] Unit exposure values reported are geometric means. [2] Air concentration (mg/m^3/lb a.i.) calculated using NAFTA '99 standard breathing rate of 17 lpm (1 m^3/hr).
[3] Exposure calculated using OPP/HED 50% protection factor (PF) for cotton coveralls on torso, arms, and legs.
[4] All commercial handlers wore long pants, long-sleeved shirt, nitrile gloves and shoes.

OMA005: Homeowner Liquid Applications to Fruit Trees and Ornamental Plants with a Hose-end Sprayer and a Low Pressure Handwand (MRID 445185-01):

Applications of Sevin Liquid® Carbaryl insecticide [RP-2 liquid (21%)] were made by volunteers to two young citrus trees and two shrubs in each replicate that was monitored in the study. The test field was located only in Florida. Twenty (20) replicates were monitored using hose-end sprayer (Ortho® DIAL or Spray® hose end sprayer), and 20 replicates were monitored using hand held pump sprayers (low pressure handwands).

Each replicate opened the end-use product, added it to the hose-end sprayer or hand held pump and then applied it to the trees and shrubs. After application to two trees and two shrubs dosimeters were collected. Inhalation exposure was monitored with personal air sampling pumps with OVS tubes attached to the shirt collar in the breathing zone. Dermal exposure was assessed by extraction of carbaryl from inner and outer 100 percent cotton dosimeters. The inner and outer dosimeters were segmented into: lower and upper arms, lower and upper legs, front and back torso. No gloves were worn therefore hand exposure was assessed with 400 ml handwash with 0.01 percent Aerosol OT-75 sodium dioctyl sulfosuccinate (OTS). One hundred percent cotton handkerchiefs wetted with 25 ml OTS were used to wipe face and neck to determine exposure.

Field fortification recoveries for passive dosimeters averaged 88.3 percent for inner and 76.2 percent for outer dosimeters. Face and neck wipe fortifications average 82.5 percent. Handwash and inhalation OVS tube field fortification averaged >90 percent. Inner and outer dosimeter and face and neck wipe residues were adjusted for field fortification results. Handwash and inhalation residues were not adjusted.

Laboratory method validation for each matrix fell within the acceptable range of 70 to 120 percent. The limit of quantitation (LOQ) was 1.0 µg/sample for all media except the inhalation monitors where the LOQ was 0.01 µg/sample. The limit of detection (LOD) was 0.5 µg/sample for all media except the inhalation monitors where the LOQ was 0.005 µg/sample.

For use in reregistration documents, the dermal exposure was calculated by adding the values from the hand rinses, face/neck wipes to the outer dosimeter lower legs and lower arms plus the inner dosimeter front and rear torso, upper legs and upper arms. This accounts for the residential handler wearing short-sleeved shirt and short pants. The results for the low pressure handwand are summarized in Table 17 below.

The distribution of the unit exposure values is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is selected from the distribution of the exposure values. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. The dermal exposure had a lognormal distribution so the geometric mean value was used to determine dermal exposure. The inhalation exposure had neither a normal or lognormal distribution so the median was used to determine inhalation exposure.

Table 17: Unit Exposure Values for Homeowner Liquid Applications to Fruit Trees and Ornamental Plants with a Low Pressure Handwand Obtained From ORETF Study (MRID 445185-01)

Scenario Monitored	Total Dermal Unit Exposure[1] (mg/lb a.i.)			Inhalation Unit Exposure[2] (µg/lb a.i.)
	Short Pants, Short Sleeves	Long Pants, Short Sleeves	Long Pants, Long Sleeves	
Homeowner Liquid Applications with a Hand Held Sprayer (Low Pressure Handwand)	56	36	30	2.6

[1] Dermal unit exposure values reported are the geometric means.
[2] Inhalation unit exposure values reported are the median values.

OMA006: Homeowner Liquid Application to Garden with a Dial type Sprayer, a Low Pressure Handwand and a Ready-to-use Bottle (MRID 444598-01): The study was designed to quantify dermal and inhalation exposure of homeowners as they mixed, loaded and applied liquid formulations of a carbaryl end-use product to home garden vegetables. A hose end sprayer and a hand held pump sprayer (low pressure handwand) were used to apply Sevin Liquid® Brand Carbaryl Insecticide. A ready-to-use sprayer was used to apply Sevin® Ready to Use Insect Spray. For each application method, twenty replicates were conducted with gloves and 20 replicates were conducted without gloves. Inhalation exposure was monitored using personal air samplers (average flow rate of 1.5 liter/minute) and dermal exposure was monitored by using inner and outer dosimeters, facial/neck wipes, and hand washes. The overall mean field fortification recovery of each matrix ranged from 77.6 ± 13.6% (outer dosimeters) to 98.4 ± 3.8%

(OVS tubes). Laboratory fortified recovery samples were analyzed with each set of samples analyzed on a particular day; however, the results of the laboratory recoveries were not provided in the Study Report. The results for the low pressure handwand are summarized in Table 18 below.

Table 18. Unit Exposure Values for Homeowner Liquid Application to Garden with a Low Pressure Handwand Obtained From ORETF Study (MRID 444598-01)							
Scenario Monitored	Total Dermal Unit Exposure[1] (mg/lb a.i.)						Inhalation Unit Exposure[1] (µg/lb a.i.)
	Short Pants, Short Sleeves		Long Pants, Short Sleeves		Long Pants, Long Sleeves		
	Gloves	No Gloves	Gloves	No Gloves	Gloves	No Gloves	
Homeowner Liquid Applications with a Low Pressure Handwand Sprayer	10.5	38	0.78	17	0.33	15	2.7

[1] Unit exposure values reported are geometric means.

7.1.2 Occupational Handler Exposure Scenarios

It has been determined that exposure to pesticide handlers is likely during the occupational use of chlorflurenol on agricultural crops, non-crop areas, and on turfgrass. The anticipated use patterns and current labeling indicate occupational exposure scenarios based on the types of equipment and techniques that can potentially be used for chlorflurenol applications. The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios.

Mixer/Loaders:
(1a) Mixing/loading liquids for airblast application (PHED);
(1b) Mixing/loading liquids for ground application (PHED);
(1c) Mixing/loading liquids to support LCO handgun applications (PHED);
(1d) Mixing/loading liquids for rights-of-way application (PHED); and
(2) Mixing/loading granules for tractor drawn spreader application (PHED).

Applicators:
(3) Applying sprays with airblast sprayer (PHED);
(4) Applying sprays with groundboom sprayer (PHED);
(5) Applying sprays with a handgun sprayer (PHED);
(6) Applying sprays with rights-of-way sprayer (PHED); and
(7) Applying granules with tractor drawn spreader (PHED).

Mixer/Loader/Applicators:
(8) Mixing/loading/applying liquids with low pressure handwand sprayer (PHED);
(9) Mixing/loading/applying liquids with low pressure handwand sprayer (ground directed) (ORETF);
(10) Mixing/loading/applying liquids with low pressure handwand sprayer (overhead directed) (ORETF);
(11) Mixing/loading/applying liquids with a handgun sprayer (LCO ORETF);
(12) Mixing/loading/applying granules with a bellygrinder (PHED); and

(13) Mixing/loading/applying granules with a push-type spreader (LCO ORETF).

7.1.3 Non-cancer Occupational Handler Exposure and Assessment

7.1.3.1 Non-cancer Occupational Handler Exposure and Risk Calculations

Daily Exposure: Daily dermal or inhalation handler exposures are estimated for each applicable handler task with the application rate, the area treated in a day, and the applicable dermal or inhalation unit exposure using the following formula:

Daily Exposure (mg a.i./day) = Unit Exposure (mg a.i./lb a.i. handled) x Application Rate (lbs a.i./area) x Daily Area Treated (area/day)

Where:

Daily Exposure	=	Amount (mg or µg a.i./day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Unit Exposure	=	Unit exposure value (mg or µg a.i./lb a.i.) derived from August 1998 PHED data or from ORETF data;
Application Rate	=	Normalized application rate based on a logical unit treatment, such as acres, square feet, or gallons. Maximum values are generally used (lb a.i./A, lb a.i./sq ft, lb a.i./gal); and
Daily Area Treated	=	Normalized application area based on a logical unit treatment such as acres (A/day), square feet (sq ft/day), gallons per day (gal/day).

Daily Dose: The daily dermal or inhalation dose is calculated by normalizing the daily exposure by body weight and adjusting, if necessary, with an appropriate dermal or inhalation absorption factor. For all dermal and inhalation exposure, an average male and female body weight of 70 kilograms was used, since the toxicological endpoint is not sex-specific. 100% absorption was used for inhalation exposures. Dermal exposure was assessed assuming 100% dermal absorption for liquid formulations and both 100% and 10% dermal absorption for granular formulations. Daily dose was calculated using the following formula:

Average Daily Dose (mg/kg/day) = Daily Exposure (mg a.i./day) x (Absorption Factor (%/100) / Body Weight (kg)

Where:

Average Daily Dose	=	Absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day);
Daily Exposure	=	Amount (mg a.i./day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Absorption Factor	=	A measure of the amount of chemical that crosses a biological boundary such as the skin or lungs (% of the total available absorbed); and
Body Weight	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Margins of Exposure: Non-cancer dermal and inhalation risks for each applicable handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint of concern to the daily dose. All MOE values were calculated separately for dermal and inhalation exposure levels using the formula below:

MOE= NOAEL or LOAEL (mg/kg/day) / Average Daily Dose (mg/kg/day)

Where:

MOE	=	Margin of Exposure, value used by HED to represent risk or how close a chemical exposure is to being a concern (unitless);
ADD	=	Average Daily Dose or the absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day); and
NOAEL or LOAEL	=	Dose level in a toxicity study, where no observed adverse effects (NOAEL) or where the lowest observed adverse effects (LOAEL) occurred in the study

Risk values are presented for each route of exposure (i.e., dermal or inhalation) in each scenario, because risk mitigation measures are specific to the route of exposure. A total MOE was also calculated because the dermal and inhalation toxicological endpoints of concern are based on the same adverse effects. The total MOE values were calculated using the formula below:

Total MOE = (1/ (1/ Dermal MOE) + (1/Inhalation MOE))

7.1.3.2 Occupational Non-cancer Risk Summary (using PHED and ORETF data)

Table 19 presents the risk assessments for short and intermediate-term dermal and inhalation exposures at baseline, with additional personal protective equipment, and with engineering controls. All of the risk calculations for occupational chlorflurenol handlers completed in this assessment are included in Appendix B of the May13, 2006 Chlorflurenol Occupational and Residential Exposure RED..

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
Mixer/Loader										
1a) Mixing/ Loading Liquids Concentrates for Airblast Applications (PHED)	Pineapple	1.0 lb a.i./A (Label & BEAD)	40 acres	**19**	2,400	3,200	45,000	**19**	2,200	3,000
1b) Mixing/ Loading Liquids Concentrates for Groundboom Applications (PHED)	Pineapple	1.0 lb a.i./A (Label & BEAD)	80 acres	**9.4**	1,200	1,600	23,000	**9.3**	1,100	1,500
	Turf: Golf Course	1.0 lb a.i./A (Label)	40 acres	**19**	2,400	3,200	45,000	**19**	2,200	3,000
		3.0 lb a.i./A (BEAD)	40 acres	**6.2**	790	1,100	15,000	**6.2**	750	990
1c) Mixing/ Loading Liquid Concentrates to Support LCO Handgun Applications (mixing/loading supports 20 LCOs) (PHED)	Lawn and Ornamental Turf (including golf course)	1.0 lb a.i./A (Label)	100 acres	**7.5**	940	1,300	18,000	**7.5**	900	1,200
		3.0 lb a.i./A (BEAD)	100 acres	**2.5**	310	430	6000	**2.5**	300	400

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
1d) Mixing/ Loading Liquid Concentrates to Support Rights of Way (PHED)	Gymnosperms	0.0025 lb a.i./gal (Label)	1,000 gal	300	38,000	51,000	720,000	300	36,000	48,000
		5 lb a.i./acre (BEAD)	80 acres	**1.9**	240	320	4,500	**1.9**	220	300
	Hardwoods, Hedges, Vines	0.01 lb a.i./gal (Label)	1,000 gal	**75**	9,400	13,000	180,000	**75**	9,000	12,000
		5 lb a.i./acre (BEAD)	80 acres	**1.9**	240	320	4,500	**1.9**	220	300
	Non-agricultural rights-of-ways/fence rows and hedge rows	3.0 lb a.i./A (Label & BEAD)	80 acres	**3.1**	390	530	7,500	**3.1**	370	500
	Turf: growing in culverts, ROW, median strip, ditches	3.0 lb a.i./A (Label & BEAD)	80 acres	**3.1**	390	530	7,500	**3.1**	370	500
	Shrubs, Shade Trees, and Vines	4.5 lb a.i./A (BEAD)	80 acres	**2.1**	260	350	5,000	**2.1**	250	330
	Hedges, Vines	0.01 lb a.i./gallon (Label)	80 acres	**75**	9,400	13,000	180,000	**75**	9,000	12,000
	High density Forestry Vegetation	4.0 lb a.i./A (BEAD)	80 acres	**2.3**	290	400	5,700	**2.3**	280	370

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
2) Mixing/ Loading Granules for Tractor Drawn Spreader Application (PHED)	Lawns and Ornamental Turf (including golf course) Lawns and Ornamental Turf (including golf course)	1.1 lb a.i./A (Label - 100% DA)	40 acres	5,900	7,100	15,000	29,000	4,900	5,700	9,700
		1.1 lb a.i./A (Label - 10% DA)	40 acres	59,000	71,000	150,000	29,000	19,000	21,000	24,000
		3.0 lb a.i./A (BEAD - 100% DA)	40 acres	2,200	2,600	5,300	11,000	1,800	2,100	3,500
		3.0 lb a.i./A (BEAD - 10% DA)	40 acres	22,000	26,000	53,000	11,000	7,100	7,600	8,900
Applying										
3) Applying Sprays via Airblast Equipment (PHED)	Pineapple	1.0 lb a.i./A (Label & BEAD)	40 acres	150	230	250	12,000	150	220	240
4) Applying Sprays via Groundboom Equipment (PHED)	Pineapple	1.0 lb a.i./A (Label & BEAD)	80 acres	1,900	1,900	2,500	37,000	1,800	1,800	2,300
	Turf: Golf Course	1.0 lb a.i./A (Label)	40 acres	3,900	3,900	4,900	73,000	3,700	3,700	4,600
		3.0 lb a.i./A (BEAD)	40 acres	1,300	1,300	1,600	24,000	1,200	1,200	1,500

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
5) Applying Sprays via Handgun Equipment (PHED)	Lawn and Ornamental Turf (including golf course)	1.0 lb a.i./A (Label)	5 acres	No Data	1,300	2,300	310,000	No Data	1,300	2,300
		3.0 lb a.i./ A (BEAD)	5 acres	No Data	430	760	100,000	No Data	420	760
6) Applying Sprays via Rights of Way Equipment (PHED)	Gymnosperms	0.0025 lb a.i./gal (Label)	1,000 gal	670	2,200	3,000	220,000	670	2,200	3,000
		5 lb a.i./A (BEAD)	80 acres	**4.2**	**14**	**19**	1,400	**4.2**	**14**	**18**
	Hardwoods	0.01 lb a.i./gal (Label)	40 gal	170	560	750	56,000	170	550	740
		5.0 lb a.i./A (BEAD)	80 acres	**4.2**	**14**	**19**	1,400	**4.2**	**14**	**18**
	Non-agricultural rights-of-ways/fence rows and hedge rows	3.0 lb a.i./A (Label & BEAD)	80 acres	**7.0**	**23**	**31**	2,300	**6.9**	**23**	**31**
	Turf: growing in culverts, ROW, median strip, ditches	3.0 lb a.i./A (Label & BEAD)	80 acres	**7.0**	**23**	**31**	2,300	**6.9**	**23**	**31**
	Shrubs, Shade Trees and Vines	4.5 lb a.i./A (BEAD)	80 acres	**4.6**	**15**	**21**	1,500	**4.6**	**15**	**21**
	Hedges and Vines	0.01 lb a.i./gallon (Label)	1000 gal	170	560	750	56,000	170	550	740

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
	High Density Forestry Management	4 lb a.i./A (BEAD)	80 acres	**5.2**	**17**	**23**	1,700	**5.2**	**17**	**23**
7) Applying granules with tractor drawn (PHED)	Lawns and Ornamental Turf (including golf course)	1.1 lb a.i./A (Label - 100% DA)	40 acres	5,000	6,800	12,000	41,000	4,400	5,900	9,100
		1.1 lb a.i./A (Label - 10% DA)	40 acres	50,000	68,000	120,000	41,000	4,400	26,000	30,000
		3.0 lb a.i./A (BEAD - 100% DA)	40 acres	1,800	2,500	4,300	15,000	1,600	2,200	3,300
		3.0 lb a.i./A (BEAD - 10% DA)	40 acres	18,000	25,000	43,000	15,000	8,300	9,400	11,000
Mixing/Loading/Applying										
8) Mixing/ Loading/ Applying Liquid Concentrates with Low Pressure Handwand (PHED)	Lawns and Ornamental Turf (including golf course)	1.0 lb a.i./A (Label)	5 acres	**4.3**	1,000	1,200	14,000	**4.3**	940	1,100
		3.0 lb a.i./A (BEAD)	5 acres	**1.4**	340	390	4,800	**1.4**	310	360
	Gymnosperms	0.0025 lb a.i./gal (Label)	40 gal	220	50,000	59,000	720,000	220	47,000	54,000
		5.0 lb a/A (BEAD)	5 acres	**0.87**	200	230	2,900	**0.87**	190	220
	Hardwoods, Hedges, Vines	0.01 lb a.i./gal	40 gal	**54**	13,000	15,000	180,000	**54**	12,000	14,000

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
		5.0 lb a/A (BEAD)	5 acres	**0.87**	200	230	2,900	**0.87**	190	220
	Non-agricultural rights-of-ways/fence rows and hedge rows	3.0 lb a.i./A (Label & BEAD)	5 acres	**1.4**	340	390	4,800	**1.4**	310	360
	Turf: growing in culverts, ROW, median strip, ditches	3.0 lb a.i./A (Label & BEAD)	5 acres	**1.4**	340	390	4,800	**1.4**	310	360
	Shrubs, Shade Trees and Vines	4.5 lb a.i./A (Label & BEAD)	5 acres	**0.96**	220	260	3,200	**0.96**	210	240
	Hedges, Vines	0.01 lb a.i./gallon (Label)	40 gal	**54**	13,000	15,000	180,000	**54**	12,000	14.000
	Trees- bark banding	0.083 lb a.i./gal (Label)	40 gal	**6.5**	1,500	1,800	22,000	**6.5**	1,400	1,600
	Ornamental Trees	2.5 lb a.i./A (BEAD)	5 acres	**1.7**	400	470	5,800	**1.7**	380	430
	High Density Forestry Vegetation	4.0 lb a.i./A (BEAD)	5 acres	**1.1**	250	290	3,600	**1.1**	240	270

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
9) Mixing/ Loading/ Applying Liquid Concentrates with Low Pressure Handwand – Ground Directed (ORETF OMA 006)	Lawns and Ornamental Turf (including golf course)	1.0 lb a.i./A (Label)	5 acres	**29**	1,300	No Data	160,000	**29**	1,300	No Data
		3.0 lb a.i./A (BEAD)	5 acres	**9.6**	440	No Data	54,000	**9.6**	430	No Data
	Non-agricultural rights-of-ways/fence rows and hedge rows	3.0 lb a.i./A (BEAD)	5 acres	**9.6**	440	No Data	54,000	**9.6**	430	No Data
	Turf: growing in culverts, ROW, median strip, ditches	3.0 lb a.i./A (BEAD)	5 acres	**9.6**	440	No Data	54,000	**9.6**	430	No Data
	Shrubs, Shade Trees, and Vines	4.5 lb a.i./A (BEAD)	5 acres	**6.4**	290	No Data	36,000	**6.4**	290	No Data
	Hedges	0.01 lb a.i./gal (Label)	40 gal	360	16,000	No Data	2,000,000	360	16,000	No Data
	Trees- bark banding	0.083 lb a.i./gal (Label)	40 gal	**44**	2,000	No Data	240,000	**44**	2,000	No Data

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
10) Mixing/ Loading/ Applying Liquid Concentrates with Low Pressure Handwand – Overhead Directed (ORETF OMA 005)	Gymnosperms	0.0025 lb a.i./gal (Label)	40 gal	720	No Data	No Data	5,700,000	720	No data	No data
		5 lb a.i./A (BEAD)	5 acres	**2.9**	No Data	No Data	33,000	**2.9**	No Data	No Data
	Hardwoods	0.01 lb a.i./gal (Label)	40 gal	180	No Data	No Data	2,100,000	180	No Data	No Data
		5.0 lb a.i./A (BEAD)	5 acres	**2.9**	No Data	No Data	33,000	**2.9**	No Data	No Data
	Vines	0.01 lb a.i./gallon (Label)	40 gal	180	No Data	No Data	2,100,000	180	No Data	No Data
	Shade Trees and Vines	4.5 lb a.i./A (BEAD)	5 acres	**3.2**	No Data	No Data	37,000	**3.2**	No Data	No Data
	Ornamental Trees	2.5 lb a.i./A (BEAD)	5 acres	**5.8**	No Data	No Data	67,000	**5.8**	No Data	No Data
	High Density Forestry Vegetation	4 lb a.i./A (BEAD)	5 acres	**3.6**	No Data	No Data	42,000	**3.6**	No Data	No Data

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
11) Mixing/ Loading/ Applying Liquid Concentrates with a Handgun Sprayer (LCO ORETF data OMA 002)	Lawn and Ornamental Turf	1.0 lb a.i./A (Label)	5 acres	No Data	960	1,800	240,000	No Data	960	1,800
		3.0 lb a.i./A (BEAD)	5 acres	No Data	320	590	80,000	No Data	320	590
	Gymnosperms	0.0025 lb a.i./gal (Label)	1,000 gal	No Data	1,900	3,500	480,000	No Data	1,900	3,500
		5.0 lb a.i./A (BEAD)	5 acres	No Data	190	350	48,000	No Data	190	350
	Hardwoods	0.01 lb a.i./gal (Label)	1,000 gal	No Data	480	890	120,000	No Data	480	880
		5.0 lb a.i./A (BEAD)	5 acres	No Data	190	350	48,000	No Data	190	350

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
11) Mixing/ Loading/ Applying Liquid Concentrates with a Handgun Sprayer (LCO ORETF data OMA 002) (cont.)	Non-agricultural rights-of-ways/fence rows and hedge rows	3.0 lb a.i./A (Label & BEAD)	5 acres	No Data	320	590	80,000	No Data	320	590
	Turf: growing in culverts, ROW, median strip, ditches	3.0 lb a.i./A (Label & BEAD)	5 acres	No Data	320	590	80,000	No Data	320	590
	Shrubs, Shade Trees, Vines	4.5 lb a.i./A (BEAD)	5 acres	No Data	210	390	54,000	No Data	210	390
	Hedges, Vines	0.01 lb a.i./gallon (Label)	5 acres	No Data	480	890	120,000	No Data	480	880
	Ornamental Trees	2.5 lb a.i./A (BEAD)	5 acres	No Data	390	710	96,000	No Data	380	700
	High density Forestry Vegetation	4.0 lb a.i./A (BEAD)	5 acres	No Data	240	440	60,000	No Data	240	440
12) Mixing/ loading/applying granules with a bellygrinder (PHED)	Lawns and Ornamental Turf (including golf course)	1.1 lb a.i./A (Label – 100% DA)	1 acre	200	210	350	32,000	200	210	340
		1.1 lb a.i./A (Label – 10% DA)	1 acre	2,000	2,100	3,500	32,000	1,900	2,000	3,100

Table 19. Occupational Handler Short-and Intermediate-term Dermal, Inhalation and Total Exposure and Risks

Exposure Scenario	Crop or Target	App Rate	Area Treated Daily	MOEs (Level of Concern = 100)						
				Dermal			Inhalation	Total		
				Baseline (unless indicated otherwise)	PPE-G, SL: Single layer w/gloves	PPE-G, DL: Double layer w/ gloves	Baseline (unless indicated otherwise)	Baseline Dermal + Baseline Inh. (unless indicated otherwise)	PPE-G, SL Dermal + Baseline Inh.	PPE-G, DL Dermal + Baseline Inh.
		3.0 lb a.i./A (BEAD – 100% DA)	5 acres	**72**	**78**	130	12,000	**72**	**77**	130
12) Mixing/ loading/applying granules with a bellygrinder (PHED) (cont.)	Lawns and Ornamental Turf (including golf course)	3.0 lb a.i./A (BEAD – 10% DA)	5 acres	720	780	1,300	12,000	680	730	1,100
13) Mixing/ loading/applying granules with a push-type spreader (LCO ORETF OMA 001)	Lawns and Ornamental Turf (including golf course)	1.1 lb a.i./A (Label – 100% DA)	5 acres	1,100	1,800	3,600	54,000	1,100	1,700	3,400
		1.1 lb a.i./A (Label – 10% DA)	5 acres	110,000	180,000	36,000	54,000	9,300	13,000	22,000
		3.0 lb a.i./A (BEAD – 100% DA)	5 acres	410	660	1,300	20,000	400	640	1,200
		3.0 lb a.i./A (BEAD – 10% DA)	5 acres	41,000	66,000	13,000	20,000	3,400	4,900	7,900

7.1.4 Cancer Occupational Handler Exposure and Risk Assessment

No cancer endpoints of concern for chlorflurenol were identified; therefore cancer risks to handlers were not assessed.

7.1.5 Summary of Risk Concerns and Data Gaps for Occupational Handlers

7.1.5.1 Summary of Risk Concerns

For dermal and inhalation exposures (short- and intermediate-term), the level of concern or target MOE is 100. The calculated dermal and inhalation risks were combined for short-term and for intermediate-term because the dermal and inhalation endpoints were based on the same toxicological effects.

For all occupational scenarios, the inhalation risks were below HED's level of concern at the baseline level.

For all occupational scenarios, the dermal risks were below HED's level of concern at some level of mitigation for all occupational scenarios except applying liquid sprays using rights-of-way equipment:

- to turf growing in culverts, rights of way, median strips, ditches, and/or under security fences at the 3 lb a.i./A rate (Label & BEAD) and 80 acres per day -- the baseline dermal MOE was 7.0 and with the highest dermal mitigation level (double layer clothing with gloves), the dermal MOE and the total MOE (dermal plus inhalation) is 31;
- to non-agricultural rights-of-ways/fence rows and hedge rows at the 3 lb a.i./A rate (Label & BEAD) and 80 acres per day -- the baseline dermal MOE was 7.0 and with the highest dermal mitigation level (double layer clothing with gloves), the dermal MOE and the total MOE (dermal plus inhalation) is 31;
- to gymnosperms at the 5 lb a.i./A rate (BEAD) and 80 acres per day -- the baseline dermal MOE was 4.2 and with the highest dermal mitigation level (double layer clothing with gloves), the dermal MOE and the total MOE (dermal plus inhalation) is 18;
- to shrubs, shade trees, and vines at the 4.5 lb a.i./A rate (BEAD) and 80 acres per day -- the baseline dermal MOE was 4.6 and with the highest dermal mitigation level (double layer clothing with gloves), the dermal MOE and the total MOE (dermal plus inhalation) is 21; and
- to high density forestry management at the 4.0 lb a.i./A rate (BEAD) and 80 acres per day -- the baseline dermal MOE was 5.2 and with the highest dermal mitigation level (double layer clothing with gloves), the dermal MOE and the total MOE (dermal plus inhalation) is 23.

For the following scenarios, the dermal and total risks were of concern at baseline level of mitigation, but were not a concern with single layer clothing plus gloves):

- mixing/loading liquid concentrates for all scenarios, except mixing/loading liquid concentrates to support rights-of-way applications to gymnosperms at the 0.0025 lb a.i./gal (label) application rate – these dermal risks were not of concern at

baseline;

- mixing/loading/applying liquid concentrates with low pressure handwand (PHED data) for all scenarios, except applications to gymnosperms at the 0.0025 lb a.i./gal (label) application rate – these dermal risks were not of concern at baseline;
- mixing/loading/applying liquid concentrates with low pressure handwand (ground directed ORETF data), for all scenarios except applications to hedges at the 0.01 lb a.i./gal (Label) application rate – these dermal risks were not of concern at baseline; and
- mixing/loading/applying liquid concentrates with low pressure handwand (upward directed ORETF data), for all scenarios except applications to hardwoods and vines at the 0.01 lb a.i./gal (Label) application rate and applications to gymnosperms at the 0.0025 lb a.i./gal (label) application rate – these dermal risks were not of concern at baseline.

For the following scenario, the dermal and total risks were of concern at baseline and single layer plus gloves levels of mitigation, but were not a concern with double layer body protection plus chemical-resistant gloves: loading/applying granular formulations with a bellygrinder (PHED data) for the 3.0 lb a.i./A (BEAD) application rate and assuming 100% dermal absorption

There are no data to assess baseline dermal risks for application via handgun equipment and mixing/loading/applying via handgun equipment. Dermal risks are below HED's level of concern for handlers of these scenarios when personal protective equipment (i.e., single layer clothing plus gloves) is considered.

7.1.5.2 Summary of Data Gaps

There are no data gaps associated with the occupational handler scenarios.

7.1.6 Recommendations for Refining Occupational Handler Risk Assessment

In order to refine this occupational risk assessment, data on actual use patterns including rates, timing, and areas treated would better characterize chlorflurenol methyl ester risks. Exposure studies for many equipment types that lack data or that are not well represented in PHED or ORETF (e.g., because of low replicate numbers or data quality) should also be considered based on the data gaps identified above and based on a review of the quality of the data used in this assessment.

7.2 Occupational Postapplication Exposures and Non-Cancer Risk Estimates

HED uses the term "postapplication" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide (also referred to as reentry exposure). HED believes that there are distinct job functions or tasks related to the kinds of activities that occur in previously treated areas. Job requirements (e.g., the kinds of jobs to cultivate a crop), the nature of the crop or target that was treated, and how the chemical residues degrade in the environment can cause exposure levels to differ over time. Each factor has been considered in this assessment.

7.2.1 Occupational Postapplication Exposure Scenarios

Currently, chlorflurenol uses are varied as it can be used on agricultural crops (i.e. pineapple) and in a variety of other outdoor occupational settings (i.e., rights-of-way, golf course turf). As a result, a wide array of individuals can potentially be exposed by working in areas that have been previously treated. HED is concerned about the kinds of exposures one could receive in the workplace.

HED uses a concept known as the *transfer coefficient* to numerically represent the postapplication exposures one would receive (generally presented as cm^2/hour). The transfer coefficient concept has been established in the scientific literature and through various exposure monitoring guidelines published by the U.S. EPA and international organizations such as Health Canada and the Organization for Economic Cooperation and Development. The establishment of transfer coefficients also forms the basis of the work of the Agricultural Reentry Task Force. A transfer coefficient is a measure of the residue transferred from a treated surface to a person who is doing a task or activity in a treated area. These values are the ratio of an exposure for a given task or activity to the amount of pesticide residue on treated surfaces available for transfer. HED has developed a series of standard transfer coefficients that are unique for variety of job tasks or activities that are used in lieu of chemical- and scenario-specific data.

To develop a postapplication assessment, HED considers the types of tasks and activities that individuals are likely to be doing in areas recently treated with a pesticide. For consistency within postapplication assessments, HED has developed a list of tasks commonly associated with specific crops or use-patterns, which are likely to result in postapplication exposures. Postapplication pesticide exposures that result from an individual's employment are considered occupational exposures. Common examples include: crop maintenance tasks (e.g., irrigating, weeding, and mowing) and crop advisor tasks (e.g., scouting).

HED considers how and when a pesticide is applied to estimate the level of transferable residues to which individuals could be exposed over time. Label directions and other use data are considered to determine application rates and application frequency. HED completes non-cancer postapplication risk assessments using maximum application rates for each scenario. When postapplication non-cancer risks are a concern

using maximum application rates, HED may also consider typical application rates or application frequency, to further evaluate the overall risks associated with the use of the pesticide. To estimate the amount of transferable residues on a treated surface, HED uses, when possible, chemical- and crop-specific studies as described in HED guidelines for exposure data collection (*Series 875, Occupational and Residential Exposure Test Guidelines: Group B - Postapplication Exposure Monitoring Test Guidelines*). For postapplication exposures, unique techniques are used to measure the amount of pesticide residue on a treated surface available for possible transfer. These techniques are distinct from those which measure total pesticide residue on a treated surface and absorbed into a treated entity. When appropriate chemical- and crop-specific transferable residue data are unavailable, HED also has developed a standard modeling approach to predict transferable residues over time (best described in HED's *SOPs for Residential Exposure Assessment*). All agricultural occupational postapplication scenarios (i.e. pineapple) were evaluated using HED's default assumptions that 20 percent of the initial application is available for transfer on day 0 (i.e., 12 hours after application) and that the residue dissipates at a rate of 10 percent per day. All commercial occupational postapplication scenarios (i.e. lawn and turf) were evaluated using HED's default assumptions that 5 percent of the initial application is available for transfer on day 0 (i.e., 12 hours after application) and that the residue dissipates at a rate of 10 percent per day.

HED also must consider the likely frequency and duration of postapplication occupational exposures to chlorflurenol. Short-term (30 days) always are considered in these assessments. Intermediate-term (greater than 30 days to several months) exposure durations are appropriate for postapplication occupational exposures scenarios where the pesticide is reapplied several times over a growing season, or the pesticide residues persist for relatively long periods of time, or the crop or use-pattern is such that occupational postapplication workers may be exposed to several different treated areas in the course of their work. For example, migrant and seasonal workers may move from farm to farm and be exposed several weeks to several months or different fields or greenhouses on an individual establishment may be treated over a period of weeks due to differing levels of infestation or staggered crop cycles. For chlorflurenol, the exposure durations for non-cancer postapplication risk assessment were short-term (30 days) and intermediate-term (greater than 30 days up to several months). However, since the dermal toxicological endpoint of concern is the same for short- and intermediate-term exposures, the short- and intermediate-term postapplication risks are numerically identical.

Inhalation exposures are thought to be negligible in outdoor postapplication scenarios, since chlorflurenol has low vapor pressure and the dilution factor outdoors is considered infinite.

HED has used the basic approach described above since the mid 1980s for calculating postapplication risks to pesticides. From that time to the present, several revisions and modifications were made to Agency policies as data, which warranted such

changes, became available. In 1995, the Agency issued a Data Call-In for postapplication agricultural data that prompted the formation of the Agricultural Reentry Task Force (ARTF). This task force has generated a number of exposure studies and associated documents that are currently under review. The work of the ARTF is not yet complete; however, sufficient data were available from the group that warranted a significant interim change in Agency policy related to the data which were already available as the efforts of the ARTF paralleled a push for tolerance reassessment stipulated by the timelines established by FQPA. As a result of the need for the revision and using the latest data, the Agency developed a revised policy on August 7, 2000 entitled *Policy 003.1 Science Advisory Council for Exposure Policy Regarding Agricultural Transfer Coefficients*. The revision to this policy entailed linking worker activities to more specific crop/agronomic groupings and making better use of the available occupational postapplication exposure data. In the new policy, transfer coefficients were selected to represent the activities associated with 18 distinct crop/agronomic groupings based on different types of vegetables, trees, berries, vine/trellis crops, turf, field crops, and bunch/bundle crops (e.g., tobacco).

Within each agronomic group, a variety of cultural practices are required to maintain the included crops. These practices are varied and typically involve light to heavy contact with immature plants as well as with more mature plants. HED selected transfer coefficient values in its revision of Policy 003 to represent this range of exposures within each agronomic group. In the policy, transfer coefficients were placed in 1 of 5 generic categories based on the exposures relative to that group. These 5 categories include: very low exposure, low exposure, medium exposure, high exposure, and very high exposure. Numerical values were not necessarily assigned to each category for each crop group. Selections depended upon the actual agronomic practices that were identified for each group (i.e., some groups had 2 assigned transfer coefficients while others had 5). The transfer coefficient values which have been used for pineapple are excerpted directly from Agency Policy 003.1 for the vegetable, stem/stalk category. The ARTF Scoping Survey does not specifically include pineapple; therefore, all exposure levels (low, medium, and high) for the vegetable, stem/stalk category were used. For lawn and turf activities, transfer coefficient values from Agricultural Reentry Task Force (ARTF) study were used.

In addition to transfer coefficients, occupational postapplication exposures to workers are estimated, in general, using transferable turf residue, dislodgeable foliar residue or soil transferable residue values. Transferable turf residues (TTRs) are the amounts of pesticide available on the turf surface that can potentially be transferred to the skin of workers who contact treated turf. Dislodgeable foliar residues (DFRs) are the amounts of pesticide available on the surface of crops (other than turf) that can potentially be transferred to the skin of workers who contact treated crop. DFRs and TTRs are measured using techniques that specifically determine the amount of residues on the surface treated leaves or other plant surfaces. In order to define the amount of *transferable residues* to which individuals can be exposed, whenever possible HED relies

on chemical- and crop-specific studies as described in HED guidelines for exposure data collection (*Series 875, Occupational and Residential Exposure Test Guidelines: Group B - Postapplication Exposure Monitoring Test Guidelines*). However, when no chemical- and crop-specific TTR or DFR studies are available, HED uses a standard modeling approach to predict transferable residues over time (best described in HED's *SOPs for Residential Exposure Assessment*).

7.2.2 Data/Assumptions for Postapplication Exposure Scenarios

A series of assumptions and exposure factors served as the basis for completing the occupational postapplication worker risk assessments. Each assumption and factor is detailed below on an individual basis. In addition to these values, transfer coefficient values were used to calculate risk estimates. The transfer coefficients for pineapple were taken from HED's revised policy entitled *Policy 003.1 Science Advisory Council for Exposure Policy Regarding Agricultural Transfer Coefficients* (August 7, 2000). The transfer coefficients for turf were taken a more recent study by the Agricultural Reentry Task Force. The assumptions and factors used in the risk calculations are presented below:

- There are many factors that are common to handler and postapplication risk assessments such as body weights, duration, and application rates. See Section 2.1.1.1 for these values. In the postapplication risk assessment, maximum application rates were considered.

- Levels of Concern: HED has established levels of concern (LOC) for occupational postapplication risks – margins of exposure of less than 100 for occupational non-cancer dermal and inhalation risks are a concern.

- Dislodgeable Foliar Residues: No chlorflurenol-specific dislodgeable foliar residue (DFR) data were available for pineapple. Therefore, this assessment uses HED's default assumption that 20 percent of the application rate is available on day 0 (i.e., 12 hours after application) and the residue dissipates at a rate of 10 percent per day.

- Transferable Turf Residues: No chlorflurenol-specific transferable turf residue (TTR) data were available. Therefore, this assessment uses HED's default assumption that 5 percent of the application rate is available on day 0 (i.e., 12 hours after application) and the residue dissipates at a rate of 10 percent per day.

- Exposures were calculated to reflect default DFR and TTR values over time coupled with surrogate transfer coefficients.

7.2.3 Occupational Postapplication Exposure and Non-cancer Risk Estimates

Occupational non-cancer risks were calculated using a Margin of Exposure (MOE), which is a ratio of the daily dose to the toxicological endpoint of concern.

Daily Exposure: Daily dermal exposures were calculated on each postapplication day after application using the following equation (see equation D2-20 from *Series 875-Occupational and Residential Test Guidelines: Group B-Postapplication Exposure*

Monitoring Test Guidelines and *Residential SOP 3.2: Postapplication Dermal Potential Doses from Pesticide Residues on Gardens*):

$DE_{(t)}$ (mg/day) = ($TR_{(t)}$ (µg/cm^2) x TC (cm^2/hr) x Hr/Day)/1000 (µg/mg)

Where:

DE(t)	=	Daily exposure or amount deposited on the surface of the skin at time (t) attributable for activity in a previously treated area, also referred to as potential dose (mg a.i./day);
TR(t)	=	Transferable residues that can either be dislodgeable foliar or turf transferable residue at time "t" (µg/cm^2);
TC	=	Transfer Coefficient (cm^2/hour); and
Hr/day	=	Exposure duration meant to represent a typical workday (hours).

Note that the ($TR_{(t)}$) input may represent levels on the day of application in the case of short-term risk calculations.

Daily Dose and Margins of Exposure: The manner in which daily postapplication dermal exposures were calculated is inherently different than with handler exposures. However, once daily exposures are calculated, the calculation of daily absorbed dose and the resulting Margin of Exposures use the same algorithms that are described above for the handler exposures (See Section 2.1.3). These calculations are completed for each day or appropriate block of time after application.

Non-cancer Risk Summary

For pineapple applications, the MOEs are greater than 100 on day 0 (REI = 12 hours) for all of the exposure levels.

For the golf course turf using the 1.0 and 1.1 lb a.i./A (Label) rates for sprays and granular applications respectively, the calculated MOE on day 0 (12 hours following application) is 71 for liquid applications and 65 for granular applications (assuming 100% dermal absorption) at the highest exposure level (hand weeding and transplanting). For these postapplication scenarios, the target MOE is not reached until the 4th day after application (MOE =110) for liquid formulations, and the target MOE is not reached until the 5th day after application (MOE = 110) for granular formulations. All other postapplication turf scenarios using the 1.0 and 1.1 lb a.i./A (Label) rates have risks below HED's level of concern on day 0 (12 hours following application).

For the golf course turf using the 3.0 lb a.i./A (BEAD) rates for sprays and granular applications, the calculated MOE on day 0 (12 hours following application):

- for liquid and granular applications (assuming 100% dermal absorption) is 24 at the

higher exposure level (hand weeding and transplanting) and the target MOE is not reached until day 14 (MOE=100);

- for liquid and granular applications (assuming 100% dermal absorption) is 47 at the lower exposure level (mowing) and the target MOE is not reached until day 8 (MOE=110);
- for granular applications (assuming 10% dermal absorption) is 240 at the higher exposure level (hand weeding and transplanting);
- for granular applications (assuming 10% dermal absorption) is 470 at the lower exposure level (mowing).

Table 20 presents a summary of occupational postapplication risks associated with use of chlorflurenol. The risk calculations for occupational chlorflurenol handlers are included in Appendix C.

Table 20. Summary of Occupational Postapplication Risks				
Crop Grouping	Application rate (lb a.i./acre)	Transfer Coefficient (μg/cm^2)	Day after Application	MOE (Level of Concern = 100)
Pineapple	1.0 (Label & BEAD)	300 (irrigation, scouting, thinning, hand weeding)	0 (12 hours)	400
		500 (irrigation, scouting)	0 (12 hours)	240
		1,000 (hand harvesting, hand pruning)	0 (12 hours)	120
Turf	1.0 – liquid (Label)	3,400 (mowing)	0 (12 hours)	140
		6,800 (hand weeding, transplanting)	4	110
	3.0 – liquid (BEAD)	3,400 (mowing)	8	110
		6,800 (hand weeding, transplanting)	14	100
	1.1 – granular (LABEL) 100% dermal absorption	3,400 (mowing)	0 (12 hours)	130
		6,800 (hand weeding, transplanting)	5	110
	1.1 – granular (LABEL) 10% dermal absorption	3,400 (mowing)	0 (12 hours)	1,300
		6,800 (hand weeding, transplanting)	0 (12 hours)	650
	3.0 – granular (BEAD) 100% dermal absorption	3,400 (mowing)	8	110
		6,800 (hand weeding, transplanting)	14	100
	3.0 – granular (BEAD) 10% dermal absorption	3,400 (mowing)	0 (12 hours)	470
		6,800 (hand weeding, transplanting)	0 (12 hours)	240

7.2.4 Occupational Postapplication Exposure and Risk Estimates for Cancer

Since no toxicological endpoint of concern was identified for cancer, cancer risks from occupational postapplication exposures were not assessed.

7.2.5 Summary of Occupational Postapplication Risk Concerns and Data Gaps

There are several occupational postapplication scenarios that have risks above HED's level of concern for non-cancer risk assessments. For hand weeding and transplanting of golf course turfgrass treated at 1.0/1.1 lb a.i./A, the target MOE is not reached until the 4th day after application (MOE =110) for liquid formulations, and the target MOE is not reached until the 5th day after application (MOE = 110) for granular formulations. For the golf course turf using the 3.0 lb a.i./A (BEAD) rates for sprays and granular applications, the calculated MOE on day 0 (12 hours following application):

- for liquid and granular applications (assuming 100% dermal absorption) is 24 at the higher exposure level (hand weeding and transplanting) and the target MOE is not reached until day 14 (MOE=100);
- for liquid and granular applications (assuming 100% dermal absorption) is 47 at the lower exposure level (mowing) and the target MOE is not reached until day 8 (MOE=110);
- for granular applications (assuming 10% dermal absorption) is 240 at the higher exposure level (hand weeding and transplanting);
- for granular applications (assuming 10% dermal absorption) is 470 at the lower exposure level (mowing).

HED has used the most up-to-date information available to complete this postapplication risk assessment for chlorflurenol. Several data gaps exist, such as a lack of chlorflurenol-specific postapplication studies. Additionally, the ARTF Scoping Survey does not include pineapple, though pineapple was assigned to the vegetable stem/stalk transfer coefficient category in Policy 003.1.

7.2.6 Recommendations for Refining Occupational Postapplication Risk Assessment

To refine this occupational risk assessment, data on actual use patterns including rates, timing, and the kinds of tasks that are required to produce agricultural commodities and other products would better characterize chlorflurenol risks. Exposure studies for many cultural practices that lack data or that are not well represented in the revised transfer coefficient policy should also be considered based on the data gaps identified above.

8.0 Data Needs and Label Requirements

8.1 Toxicology

Toxicology data requirements are acceptable and satisfied. However, another study on reproduction with a more definitive NOAEL for effects on pups and fertility will be necessary to remove the 3X uncertainty factor.

8.2 Residue Chemistry

A study on the UV/visible spectra is necessary.

8.3 Occupational and Residential Exposure

No studies are required at this time.

References:

Memorandum from Shana Recore to David G Anderson , dated June 30, 2006, Subject: Chlorflurenol: Occupational and Residential Exposure Assessment for the Reregistration Eligibility/Decision [RED].

Appendix A: Toxicology Assessment

A.1 Toxicology Data Requirements

A confirmatory study on reproduction [guideline 870.300] is necessary to remove the extra 3X uncertainty factor and establish a NOAEL for pup effects and fertility effects in adult offspring.

The requirements (40 CFR 158.340) for Non food use for CHLORFLURENOL METHYL ESTER are in Table 1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table A.1: Data Requirements for a non-food use pesticide, such as chlorflurenol methyl ester.

Test		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes
870.3150	Oral Subchronic (nonrodent)	no	no [A]
870.3200	21-Day Dermal	no	no
870.3250	90-Day Dermal	no	no
870.3465	90-Day Inhalation		
870.3700a	Developmental Toxicity (rodent)	yes	Yes [B]
870.3700b	Developmental Toxicity (nonrodent)	no	no [B]
870.3800	Reproduction	no	no [B]
870.4100a	Chronic Toxicity (rodent)	no	No [C]
870.4100b	Chronic Toxicity (nonrodent)	no	yes [C]
870.4200a	Oncogenicity (rat)	no	no [D]
870.4200b	Oncogenicity (mouse)	no	yes [D]
870.4300	Chronic/Oncogenicity	no	no
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5300	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5550	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a	Acute Delayed Neurotox. (hen) [E]	no	-
870.6100b	90-Day Neurotoxicity (hen) [E]	no	-
870.6200a	Acute Neurotox. Screening Battery (rat) [F]	no	-
870.6200b	90-Day Neuro. Screening Battery (rat) [F]	no	-
870.6300	Develop. Neuro [F]	no	-
870.7485	General Metabolism	no	no [G]
870.7600	Dermal Penetration	no	no

Test	Technical	
	Required	Satisfied
Special Studies for Ocular Effects [H] Acute Oral (rat)..... Subchronic Oral (rat) ..... Six-month Oral (dog).....		
See next page for explanation for superscripts A to H.		

Footnotes for Table A.1: [A] A formulation rather than the technical grade of chlorflurenol was studied [technical grade is required]. [B] The unacceptable developmental rabbit study and unacceptable reproduction studies submitted were not required. [C] The acceptable chronic dog study submitted was not required. [D] The acceptable carcinogenicity study in the mouse was not required. [E] Required only for organophosphate pesticides. [F] Required if the pesticide shows evidence of neurotoxicity. [G] Not required for pesticides with this use pattern.

A.2 Toxicity Profiles

Table A.2.1 Acute Toxicity Profile – Chlorflurenol methyl ester

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral [rat]	43355402	LD_{50} > 5000 mg/kg	IV
870.1200	Acute dermal [rabbit]	43355403	LD_{50} > 5000 mg/kg	IV
870.1300	Acute inhalation [rat]	45147201	LC_{50} > 5.07 mg a.i./L	IV
870.2400	Acute eye irritation [rabbit]	43355404	Mild irritation, cleared in 72 hours	III
870.2500	Acute dermal irritation [rabbit]	43355405	Practically non irritating	IV
870.2600	Skin sensitization [Guinea pig]	43361701	Not a sensitizer	Negative

Table A.2.2: Subchronic, Chronic, Developmental, Reproduction , mutagenicity and other toxicity profile of chlorflurenol methyl ester.

Guideline/ Study type/ Acceptability	MRID#/Date/ Doses	Results
870.3100 90-Day oral/SD rat Acceptable Lot# 45, 99.9%	45441001 [2001] Acceptable 0,1000,5000,10000 ppm [M: 0,74,361, 697; F: 0,87,390,750 mg/kg/day]	NOAEL = M/F 697/87 mg/kg/day LOAEL = M/F None/390 mg/kg/day based decreased body weight gain in females [Female BWt accompanied by decreased food efficiency]. Males showed a possible treatment related nominal decreased body weight gain of 11% at 697 mg/kg/day.

Table A.2.2: Subchronic, Chronic, Developmental, Reproduction , mutagenicity and other toxicity profile of chlorflurenol methyl ester.		
Guideline/ Study type/ Acceptability	MRID#/Date/ Doses	Results
870.3100 90-Day oral/Wistar rat Unacceptable	00120854 & 00120867 [1968] 0, 1000, 5000, 10000 ppm [0, 50, 250, 500 mg/kg/day]	NOAEL = 250 mg/kg/day LOAEL = 500 mg/kg/day based on body weight decrement in females. Unacceptable: lacking hematology clinical chemistry & some histology
870.3150 90-Day oral/dog Unacceptable	00120868 [1968] Unacceptable 0,300,1000,3000 ppm 0, 8.95, 29.9, 89.5 mg/kg/day	NOAEL = >89.5 mg/kg/day LOAEL = None. No treatment related decreases in hematological parameters, which showed only random fluctuation from control animals and from pre-dosing conditions in males and female up to 8 weeks. Although, some parameters at the HDT were slightly numerically less than control values, they were not consistently less or consistently numerically less than the initial values for the group. The 90-day dog was not entirely inconsistent with the 2-year dog study. Unacceptable; only 3 dogs/sex/group and dose levels were not verified.
870.3150NG 21-Day dermal toxicity/ rabbit, Proj# 1385 Lot# 759-78 Acceptable/NG	00120883 [1970] Acceptable/NG Test material CF-125 [12.5% a.i.] Doses 0, 0.5, 1.0 ml/kg/day or .0, 62.5, 125 mg a.i./kg	NOAEL = None LOAEL = 62.5 mg a.i./kg/day based on dose related local degeneration of hair follicles and epithelial thickening at the 2 dose levels used. No systemic effects reported. Since the test material was applied as a neat formulation, the dermal effects may have been due to the dispersing agent in CF-125. CF-125 is 12.5% active ingredient with 87.5% being inert ingredients of which most were known skin irritants in the context of this study. Acceptable as a non-guideline study. The toxicity of the technical grade of the pesticide could not be evaluated.
870.4100b Chronic toxicity Dog Acceptable	00082863 [1975] 0, 300, 1000, 3000 ppm or [M/F: 0/0, 8.7/8.8, 30.6/29.9, 94.0/94.4 mg/kg/day	NOAEL = 30.6/29.9 mg/kg/day for males/females. LOAEL = 94.0/94.4 mg/kg/day for male/females based on decreased erythrocytes, hemoglobin and hematocrit by week 4 in males and females, supported by hemosiderin deposits in liver and incidence of gastritis and possible decreased body weight in males and females by month 13 of the study, but not in females by study termination at 24 months. Transient alkaline phos. and elevated SGPT was seen at the HDT.
870.4100a Chronic toxicity rats Unacceptable	00082864 [1971] 0, 300, 1000, 3000 ppm or 0, 15, 50, 150 mg/kg/day	52 week interim report. Tentative NOAEL = 50 mg/kg/day LOAEL = 150 mg/kg/day based on one male with elevated SGPT and alkaline phos. Unacceptable: Inadequate number of rats were studied histologically

Table A.2.2: Subchronic, Chronic, Developmental, Reproduction , mutagenicity and other toxicity profile of chlorflurenol methyl ester.		
Guideline/ Study type/ Acceptability	MRID#/Date/ Doses	Results
		for too short a period.
870.4200b Carcinogenicity Mouse Acceptable	00082865 [1976] 0, 1000, 3000, 10000 ppm or 0, 150, 450, 1500 mg/kg/day	NOAEL = 1500 mg/kg/day LOAEL = None, no dose related carcinogenic response was noted. Acceptable
Non GDL Carcinogenicity Rats Unacceptable	0082866 [1969] subcutaneous 0, 30 mg/kg/week, and feeding about 92 mg/kg/day or about 700 mg/kg/week.	Subcutaneous dose: NOAEL = 30 mg/kg/week LOAEL= None Feeding study: NOAEL = 92 mg/kg/day LOAEL= None Unacceptable because studied for 1-year only
870.3700a Developmental toxicity/ SD rat Acceptable	4510901 [2000] Acceptable 0, 250, 750, 1000 mg/g/day	Maternal: NOAEL = 250 mg/kg/day LOAEL = 750 mg/kg/day based on statistically significant and treatment related reduced body weight gain during the treatment period, GD 6-16. Devel: NOAEL = 250 mg/kg/day LOAEL = 750 mg/kg/day based on treatment related increased incompletely ossified anterior skull bones [nasal and frontal bones about doubled that of controls]. In addition a cleft palate was seen in each of two litters and one diaphragmatic hernia at 1000 mg/kg/day and one cleft palate at 750 mg/kg/day [cleft palate is rare in rats, historical incidence not given].
870.3700b Developmental toxicity/NZW rabbit Unacceptable	00120862 [1969] Unacceptable Proj# 1624-97 0, 25, 50, 100 mg/kg/day	Maternal NOAEL = 100 mg/kg/day LOAEL = None Devel NOAEL = 100 mg/kg/day LOAEL = None, although a wide variation in skeletal variants were seen among the groups. Unacceptable due to no demonstrated toxicity and lack of individual animal data and no indication that fetal soft tissue was evaluated.
870.3800 3-Generation reproduction/Charles River rat Unacceptable	00082867 [1973] 0, 300, 1000, 3000 ppm or 0, 15, 50, 150 mg/kg/day	Parental, systemic NOAEL = 50 mg/kg/day. Systemic LOAEL = 150 mg/kg/day for nominal decreased body weight. Offspring NOAEL = 15 or 50 mg/kg/day LOAEL = 50 or150 mg/kg/day based on decreased pup weight at birth and/or litter size from the P0b, F1a and F1b generations. Decreased absolute thymus and testes weights in the F3b generation weanling pups [The only group from which organ weight were collected]. Reproduction NOAEL = Unknown. LOAEL = Unknown. Appears to be considerable variation in results generation to generation such that

Table A.2.2: Subchronic, Chronic, Developmental, Reproduction , mutagenicity and other toxicity profile of chlorflurenol methyl ester.		
Guideline/ Study type/ Acceptability	MRID#/Date/ Doses	Results
		NOAEL/LOAEL was not definitive. Reviewer could not assign a NOAEL. Decreased variable pregnancy rate in the F1a, F1b, F2a and F2b generation [only F2a shows a dose relationship], decreased absolute thymus in F3b weanlings [The only group from which organ weight were collected]. Female F0 and F2 body weight gain was lower than controls premating in the 150 mg/kg/day group. Unacceptable due to uncertainty and variability in pregnancy rates in control and all doses.
870.5100 Ames, *S typhimurium*	43562802 [1995] Acceptable	In a reverse mutation assay with *S tryphimurim* [TA1535, TA 1537, TA1538, TA98 and TA100] was exposed with and without S9 activation at 250, 500, 750, 1000 or 2500 µg/plate. Cytotoxicity was seen in all strains at 2500 µg/plate. There were no signs of a mutagenic response with or without S9.
870.5300 *In vitro* cell (CHO) Chromosomal Aberration	43562801 [1995] Acceptable	In this Chinese hamster ovary cell in vitro assay, cells were exposed to non-activated doses of 5.0-75 µg/mL and activated doses of 50-200 µg/mL. Treated cultures were scored for structural aberrations. Cytotoxicity was indicated by approximately 40% reduction in mitotic index at the highest dose in the non-activated and activated systems. There was no indication of clastogenic effects in the non-activated or activated systems.
870.5550 *In vitro* rat hepatocyte UDS	45137404 [1988] Acceptable	Chlorflurenol was studied for unscheduled DNA synthesis in rat hepatocytes at 0, 1.5, 5, 15, 50 or 150 µg/mL. Cytotoxicity was seen at 150 µg /mL indicated by decrease [^{3}H] thymidine incorporation. Since there was no evidence UDS with or without S9 activation, the study was considered negative for mutagenic evidence.
870.5300 *In vitro* mammalian cell HGPRT test	45137405 [1988] Acceptable	In two independently performed mammalian cell gene mutation assays at the HPRT locus (MRID 45137405), V79 cells cultured *in vitro* were exposed to Chlorflurenol-methyl ester in ethanol at 0, 6, 20, 40, or 60 µg/mL with and without S9 to the solubility limit. There was no evidence that Chlorflurenol-methyl ester induced mutant colonies over background in the presence or absence of S9-activation.
NG Metabolism & Pharmacokinetics Unacceptable/NG	00082868 [1972] Unacceptable/NG	Majority eliminated via the rat kidney and about 1/20 in the feces. The small amounts detected in the mammary gland suggested that the test material was not secreted in milk. Recovered test material from the feces and urine within 72 hours after administration were 64% IT-3456, 75% of IT-5733 and 83% of IT-3294. Biliary recyclization was indicated. Small amounts were detected in the mammary gland of lactating females, but not in their pups.

Table A.2.2: Subchronic, Chronic, Developmental, Reproduction , mutagenicity and other toxicity profile of chlorflurenol methyl ester.		
Guideline/ Study type/ Acceptability	MRID#/Date/ Doses	Results
		Identification of potential metabolites was not investigated. Unacceptable due to inadequate replication, distribution not quantitated, test material inadequately identified.

A.3 Executive Summaries

Summaries included are acceptable and unacceptable studies considered, but not necessarily used to assess risk.

A.3.1 Subchronic Toxicity

870.3100 90-Day Oral Toxicity – Rat [MRID# 45441001]

EXECUTIVE SUMMARY: In a 90-day dietary study (MRID 45441001), chlorflurenol methyl ester (Lot# 45, 99.9% pure) was administered to 10 Sprague Dawley rats/sex/group at dietary levels of 0, 1000, 5000 or 10000 ppm (males: 0.0, 74, 361 or 697 mg/kg/day; females: 0.0, 87, 390 or 750 mg/kg/day). Body weights, food consumption, and clinical observations were recorded. Ophthalmoscopic examinations were conducted. At study termination, rats were sacrificed and blood collected for hematology and clinical chemistry studies. Organ weights were recorded and gross and microscopic examinations were conducted.

All rats survived to terminal sacrifice. There were no clinical signs of toxicity and there were treatment related effects on hematology or clinical chemistry parameters, organ weights or necropsy findings. All treated groups of female rats had dose-related lower final body weight than control group (not significant) and dose-related lower body weight gains (reduced in Groups 2, 3 and 4 by 15, 21 and 24%, respectively) which were statistically significant in the 5000 ppm and 10000 ppm groups ($p<0.01$). The food consumption and food efficiency were also lower in all treated groups compared with the control group.

Under the conditions of this study, a NOAEL for females was established at 1000 ppm (87 mg/kg/day) and a LOAEL at 5000 ppm (390 mg/kg/day) based on dose-related decrease in body weight gain. For males the NOAEL was 10000 ppm 697 mg/kg/day and a LOAEL was not established.

This study is considered to be **ACCEPTABLE/GUIDELINE** as a 90-day study and fulfills FIRA Guideline requirements for a subchronic oral toxicity study in the rat [870.3100 (82-1a)].

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data confidentiality statements were provided.

870.3100 90-Day Oral Toxicity – Mouse

Not required and none was submitted.

870.3150 90-Day Oral Toxicity – Dog [MRID# 00120868]

Not required and unacceptable because only 3 dogs/sex/group were used and no toxicity was demonstrated

870.3200 21/28-Day Dermal Toxicity – Rat [MRID# 00120883]

EXECUTIVE SUMMARY: In a 21-day dermal toxicity study (MRID 00120883), formulated chlorflurenol methyl ester [Lot# 759-78 (12.5% a.i., batch/lot # 759-78)] was applied to the shaved skin of 5 New Zealand rabbits/sex/group at dose levels of 0, 0.5 or 1.0 ml/kg bw/day [equivalent to 0, .62.5 mg a.i./kg/day or .125 mg a.i./kg/day, assuming a density of 1.0 g/ml for CF 125] 24 hours/day for 5 days/week during a 21-day period. Equal numbers of rabbits and dose levels were evaluated with abraded and intact skin.

The only treatment related effects seen were in the treated skin. Drying and slight fissuring of the skin midway through the study was noted, which at termination resulted in epithelial thickening and varying amounts of keratonization with varying destruction of hair follicles. Although the varying degrees of destruction of hair follicles was shown in most dosed animals, the damage was observed to be less severe among the lowest dosed animals. The treated skin effects were believed to be due to the 87.5% of the CF 125 formulation that were skin reactive inerts. Only mild skin effects were noted at mid study.

No treatment related changes were noted in body weight, weight gain, hematology, clinical chemistry, organ weights, or systemic toxicity in treated animals. Histological findings were consistent with random effects in controls and treated animals.

There were no systemic effects. The LOAEL is 62.5 mg/kg/day, based on epithelial thickening, keratinization and destruction of hair follicles. A NOAEL was not seen for skin effects.

This 21-day dermal toxicity study in the (rabbit) is an **ACCEPTABLE/NON-GUIDELINE** study and does not satisfy the guideline requirement for a 21/28-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rabbit. The technical grade of the test material was not studied. It is not upgradeable because some of the recommended parameters were not studied, including some hematology, clinical chemistry and histopathology parameters, but the major parameters were studied. The study is useful in that it shows no systemic toxicity at 125 mg/kg/day with a reasonable degree of certainty.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were (not) provided. The study was conducted prior to publication of these regulatory requirements.

870.3465 90-Day Inhalation – Rat

A.3.2 Prenatal Developmental Toxicity

870.3700a Prenatal Developmental Toxicity Study – Rat

EXECUTIVE SUMMARY: In a developmental toxicity study (MRID 45190901) with chlorflurenol-methyl ester [calculated as 99.1% a.i.; batch/lot# UT 047843] was administered to 31 female, Crl:CD(SD):BR strain of Sprague Dawley rats/group by gavage at dose levels of 0, 250, 750 or 1000 mg a.i./kg bw/day from days 6 through 15 of gestation. Doses were administered in 1% carboxymethyl cellulose/water in a volume of 5 mL/kg/day. Maternal toxicity was evaluated and fetal evaluations were conducted one-half the fetuses viscerally or skeletally.

Maternal toxicity was seen as a statistically significant decrement in body weight gain gestational days 6 to 16 at 750 and 1000 mg/kg/day and at 1000 mg/kg/day gestational day 6-9. Supporting this body weight decrement was nominally decreased food efficiency at 750 and 1000 mg/kg/day.

The maternal NOAEL was 250 mg/kg/day. The maternal LOAEL is 750 mg/kg bw/day based on body weight gain decrement and nominally decreased food efficiency. Delayed ossification was seen in skull bones. The incidence of incompletely ossified nasal bones and frontal bone were increased at 750 and 1000 mg/kg/day (60.9-63.0% vs. 28.6% in control] and 55.6%-60.9% vs. 33.3% in control], respectively. Intrauterine death was borderline statistically significant [p = 0.0529] at 1000 mg/kg/day [1.7 vs. 0.3 in control]. The post-implantation loss and early resorptions, which were nominally increased at 1000 mg/kg/day supported the intrauterine death at 1000 mg/kg/day.

The developmental NOAEL is 250 mg/kg/day. The developmental LOAEL is 750 mg/kg bw/day, based on treatment related delayed ossification in skull bones [nasal and frontal] in fetuses and litters.

The developmental toxicity study in the rat is classified **ACCEPTABLE [guideline]**; and satisfies the guideline requirement for a developmental toxicity study (OPPTS 870.3700; OECD 414) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. Historical control data was submitted for fetuses, but not for litters.

870.3700b Prenatal Developmental Toxicity Study – Rabbit

Study not required and unacceptable [MRID# 00120862] due to failure to submit data on fetal soft tissue and study showed no toxicity in dams or fetuses.

EXECUTIVE SUMMARY: In a developmental toxicity Study (MRID#s 00120862, 00069980 and 00073536), IT 3456 (chlorflurenol methyl ester, 98% a.i.) was administered by gastric intubation to 13-14 New Zealand female rabbits/group at dose levels of 0, 25, 50 or 100 mg/kg/day from days 6 through 18 of gestation. The submitted study consists of a summary of the data that was previously submitted to the Agency prior to implementation of GLP standards as well as copies of the original MRIDs. There were no treatment related effects in mortality, clinical signs of toxicity, body weight, or cesarean parameters. Equivocal reductions in body weight gain were noted at the mid dose (50 mg/kg/day). **A maternal LOAEL was not observed. The maternal NOAEL under the conditions of the study is => 100 mg/kg/day.**
There were no treatment related effects in developmental parameters including mortality, body weight, abnormalities or skeletal parameters. **A developmental LOAEL was not observed**. **The developmental NOAEL under the conditions of the study is => 100 mg/kg/day.**
The study is classified **UNACCEPTABLE/GUIDELINE** (870.3500 OR 83-3b) and does not satisfy the guideline requirements for a developmental study in rabbits and a new study must be conducted. No maternal or developmental toxicity was observed. It appears that the animals could have tolerated a higher dose level, however, the dose rationale was not provided. In addition the following acceptance criteria were not met: individual fetal soft tissue and skeletal examinations were not performed; at least 12 pregnant animals/dose group were not available because 3 pregnant rabbits died during the study; and food consumption was not reported. Moreover, this study should have been properly reformatted as per EPA requirements. It therefore seems unlikely this study can be upgraded. .

A.3.3 Reproductive Toxicity

Not required for a non-food use pesticide, but may show subfertility in offspring.

870.3800 Reproduction and Fertility Effects – Rat [MRID# 0008267]

EXECUTIVE SUMMARY: In a three-generation study on reproduction [MRID# 00082867], Charles River rats [20 females/group and 10 males/group] were administered chlorflurenol methyl ester at 0, 300, 1000 or 3000 ppm [Standard table equivalent for P0 males and females: 0, 15, 50 or 150 mg a.i./kg/day] in the diet continuously for 3 generations. Twenty-one-day old pups [10/sex/group] from only the 3rd generation were subjected to necropsy; organs were weighted and microscopically examined.

Female body weight was consistently lower in the 1000 and 3000 ppm group than in controls in all generations, P0 [96% and 89% of control, respectively], F1 [93% and

87% of control, respectively] and F2 [93% and 91% of control, respectively]; none of the reductions in weight were statistically significant. Male body weight was unchanged.

Pup weight was statistically significantly decreased at 1000 and 3000 ppm in the P0, first litter [91% and 89% of control, respectively] at day 4, but not at birth and only at 3000 ppm in the second litter at birth (96% of control)and day 4 (91% of control). Again for the F2 generation at 1000 and 3000 ppm, the first litter weight was statistically significantly reduced [91% and 92% of control, respectively] at day 4, but not at birth of for the second litter at either dose. Litter size appeared to be sporadically decreased at 3000 ppm in the P0 second litter at birth and at day 4, and the F1 for both litters, but not for the F2 for both litters.

Litter size at birth was statistically significantly reduced at 3000 ppm in 3 of the 6 sets of litters produced during the study [P0 second litter, F1 first and second litter, but not in the F2 first or second litter].

Body weight of the F3, 21-day old pups was significantly reduced at 3000 ppm. Absolute and relative brain weight was statistically significantly reduced [90% of control]. Absolute gonad weight was reduced at 1000 and 3000 ppm [85.1% and 84.6% of control, respectively], but the relative weight did not differ from control. Microscopic examination showed no histopathology. The only comment about the gonads was that all animals showed immaturity as may be expected from 21-day old gonads.

There was a problematic apparent decrease in fertility at all dose levels in this 1973 study, which showed a statistically significant dose relationship only in the first mating of the F2 generation at 1000 [50%] and 3000 ppm [40%] compared with control at 90% and the 300 ppm group at 80%. The other matings showed lower fertility than control, but little to no dose response was shown [See accompanying table in the Appendix]. The P0 first and second matings showed no dose related effects on fertility, while the F1 first and second matings were lower than control and for the F2 second matings, control and high dose groups were equally low. The suggestion of subfertility in these rats may have been shown, but unproven. Another study on reproduction is needed to confirm or reject the potential effects on fertility and pups.

Out of 479 matings, 145 showed sperm negative vaginal smears of which 29 of these females produced litters. This appears to be a high number of pregnancies for which no vaginal sperm were shown. When all pregnant females showing no sperm during cohabitation were added together for the 6 total matings, a treatment related increased response was seen in the data [last four rows of the table of matings, pregnancies, and pregnancies with out demonstrated sperm during cohabitation in the Appendix]. {The method used in determining the presence of vaginal sperm was not stated and may have been inadequate or the sperm count for some rats was extremely low.} In addition, if estrous cycles were noted they were not recorded. Only the time to pregnancy was recorded. Historical control levels were not presented for vaginal sperm negative females producing litters. It is the experience of this reviewer that out of 145 sperm negative vaginal spears, no more than 2-3 of these rats would produce pregnancies and none would be expected to produce pregnancies.

The study raises unanswered questions about possible effects of chlorflurenol on fertility in rats. Histopathology on 21 day old F3 pups showed no histological effects on

testes or ovaries [the only pups studied for these effects]. No gonadal effects were noted in the 2-year chronic dog study or the 90-day study in rats. The study on reproduction should be repeated to clarify the questionable results in MRID# 00082867.

Neither the NOAEL nor the LOAEL can be determined due to the variability from generation to generation. However, litter size at birth and pup weight decrement were statistically significantly reduced at the HDT of 3000 ppm..

The study is **UNACCEPTABLE/GUIDELINE** and is not satisfactory for a study on reproduction in rats [870.3800] . The data in the study was too variable for adequate interpretation.

Table of Response of litters in the 3-generation study on reproduction [MRID# 00082867]

Generation	Parameter	Control	15 mg/kg/day	50 mg/kg/day	150 mg/kg/day
P0 1st mating	Pup wt at birth	6.3	6.1	6.0	6.0
	At day 4	11.1	10.4	10.1*	9.9*
	At day 12	29.0	27.1	25.3**	24.9**
	At day21	58.2	50.8	49.9*	47.2**
	Litter size at birth	12.0	12.2	13.1	12.0
	At day 4	12.1	11.2	12.1	11.4
	At day12	12.0	11.2	11.8	11.4
	At day 21	12.0	11.2	11.8	11.4
P0 2nd mating	Pup wt at birth	6.5	6.6	6.4	6.2*
	At day 4	11.6	11.7	11.0	10.6*
	At day 12	31.2	30.5	29.9	28.5**
	At day21	58.7	55.5	55.4	52.8
	Litter size at birth	12.4	11.8	11.91	10.7*
	At day 4	12.0	10.9	11.2	9.8**
	At day12	11.9	10.9	11.1	9.8**
	At day 21	11.9	10.9	11.1	9.7**
F1 1st mating	Pup wt at birth	6.2	6.7	6.6*	6.6
	At day 4	10.2	10.8	9.4	10.1
	At day 12	27.1	28.2	23.7	26.9
	At day21	54.7	53.2	47.1**	50.8
	Litter size at birth	13.1	11.3	11.2	8.8**
	At day 4	12.2	9.9	10.4	8.1***
	At day12	11.9	9.7	10.0	7.9***
	At day 21	11.8	9.7	10.0	7.9***
F1 2nd mating	Pup wt at birth	6.7	6.6	6.8	6.7
	At day 4	11.4	10.9	11.1	11.0
	At day 12	28.9	26.2	26.0	26.8
	At day21	55.0	48.5	50.6	49.8
	Litter size at birth	12.9	12.5	11.6	9.8*
	At day 4	12.3	12.2	12.0	9.3**
	At day12	12.1	11.9	10.7	9.2**
	At day 21	11.9	11.8	11.9	9.2*
F2 1st mating	Pup wt at birth	6.2	6.3	6.2	6.1
	At day 4	10.5	10.5	9.6*	9.7*
	At day 12	27.7	26.9	24.8*	25.6
	At day21	53.4	51.5	48.4*	49.7
	Litter size at birth	12.3	12.9	12.8	10.5
	At day 4	11.6	12.1	12.2	10.0

Table of Response of litters in the 3-generation study on reproduction [MRID# 00082867]

Generation	Parameter	Control	15 mg/kg/day	50 mg/kg/day	150 mg/kg/day
	At day12	11.4	11.9	12.0	9.8
	At day 21	11.4	11.9	12.0	9.6
F2 2nd mating	Pup wt at birth	6.2	6.6	6.4	6.0
	At day 4	10.4	10.7	10.3	10.3
	At day 12	26.0	26.2	24.6	23.9
	At day21	51.0	51.9	50.4	46.1
	Litter size at birth	12.1	13.8	12.2	11.4
	At day 4	11.0	13.0*	11.5	11.0
	At day12	10.7	12.7	11.3	11.0
	At day 21	10.5	12.2	11.2	11.0

* , **, *** = $p < 0.05$. <0.01 or 0.001

Table of matings, pregnancies and pregnancies without apparent sperm for P0, F1 and F2 generations [MRID# 00082867] Data taken from page 42 - 46.

Dose group [mg/kg/day]	Total mating with positive sperm smears [a]	Total pregnancies [with positive & negative sperm]	Not pregnant [with positive & negative sperm]	# rats without sperm positive smears			Pregnancy rate [%]
				Total	Pregnant	Not pregnant	
1st P0 Mating with 20 females/group							
0	19	20	0	1	1	0	100
300	14	13	7	6	2	4	65**
1000	19	18	2	1	1	0	90
3000	16	18	2	4	2	2	90
2nd P0 mating with 20 females/group							
0	18	18	2	2	0	2	90
300	14	15	5	6	2	4	75*
1000	20	20	0	0	0	0	100
3000	18	20	0	2	2	0	100
1st F1 mating with 20 females/group							
0	13	14	6	7	2	5	70
300	14	11	9	6	2	4	55
1000	11	12	8	9	1	8	60
3000	9	11	9	11	4	7	55
2nd F1 mating with females/group							
0	16	14	6	4	0	4	70
300	12	11	9	8	1	7	55
1000	11	10	10	9	2	7	50
3000	10	12	8	10	2	8	60
1st F2 mating with 20 females/group							
0	19	18	2	1	0	1	90
300	15	16	4	5	1	4	80
1000	9	10	10	11	1	10	50*
3000	7	8	12	13	2	11	40**
2nd F2 mating with 19 females in control and 20 females/.dose group							
0	12/19	12/19	7/19	7/19	0/19	7/19	63
300	12	11	9	8	1	7	55
1000	7	6	14	13	0	13	30
3000	9	7	13	11	0	11	35

Table of matings, pregnancies and pregnancies without apparent sperm for P0, F1 and F2 generations [MRID# 00082867] Data taken from page 42 - 46.							
Dose group [mg/kg/day]	Total mating with positive sperm smears [a]	Total pregnancies [with positive & negative sperm]	Not pregnant [with positive & negative sperm]	# rats without sperm positive smears			Pregnancy rate [%]
				Total	Pregnant	Not pregnant	
Summary results of total P0, F1 and F2 matings, including controls							
Total	324/479	325/479	154/479	155/479	29/479	126/479	68
Summary data from the first and second matings of the PO, F1 and F2 generations							
0	97/119	97/119	21/119	22/119	3/119	19/119	80.7
300	81/120	77/120	43/120	39/120	9/120	30/120	64.2
1000	77/120	76/120	44/120	43/120	5/120	38/120	63.3
3000	69/120	76/120	44/120	51/120	12/120	39/120	63.3

[a] = # females mated with positive sperm smears. * = $p > 0.05$, ** = $p > 0.01$.

A.3.4 Chronic Toxicity

870.4100a (870.4300) Chronic Toxicity – Rat [MRID# 00082864]

Unacceptable as a chronic study due to several factors, especially microscopic examination was conducted on only 3 rats/sex

870.4100b Chronic Toxicity – Dog {MRID# 00082863]

EXECUTIVE SUMMARY: In a chronic toxicity study (MRID 00082863) IT 3456 [Chlorflurenol, technical (96% a.i., batch/lot # 5/69)] was administered to 4 Beagle dogs/sex/group in the diet at dose levels of 0, 300, 1000 or 3000 ppm (for male/female equivalent to 0, 8.7/8.8, 30.6/29.9 or 94.0/94.4 mg/kg bw/day, calculated from test material consumption) for 104 weeks. One extra dog/sex/group was treated with test material for 104 weeks, after which the dogs were untreated for 8 weeks. Hematology and clinical chemistry evaluation was performed at 6 intervals during the study. Animals were subjected to gross pathology and microscopic examination.

Body weight appeared to be slightly reduced by month 13 at the highest dose tested [HDT]. Dogs showed this body weight decrement at month 13 when compared with initial body weights for males [the HDT gained 0% vs. 22.3% for control weight] and for females [the HDT gained 6.6% vs. 20.3% for control body weight]. Male body weight gain appeared to be reduced for the remainder of the study. Male body weight gain was decreased at 104 weeks [body weight gain was 0.8 kg at the HDT and 2.5 kg for controls]. At the end of the study female body weight gain was the same as control weight gain. Food consumption was unaffected in both sexes.

Erythrocytes [ERY], hemoglobin concentration [Hb] and hematocrit [Ht] values appeared to be slightly decreased at the HDT in males and females starting at week 4 [the first time period evaluated] and male dogs maintained a decrease through out the study. Some of the values in the HDT were statistically significantly reduced, but were still within the normal range for dogs. The □ERY, □Hb and □Ht values [difference between measured values and week -2 values] appeared to decrease in males and females at the

HDT starting at week 4 and male dogs maintained the decrease through out the study. This decrease is consistent with the slightly higher incidence and/or severity of siderous in the spleen, liver and Kupffer cells at the HDT. Hemosiderin in the 1000 ppm group was not considered sufficiently consistent to show that the mid dose group was affected. In addition the values for ERY, Hb and Ht from the 1000 ppm group of animals did not show consistent effects. From week 26-52 to termination, the values for ERY, Hb and Ht for treated female dogs did not appear to differ from control.

Clinical chemistry values showed no consistent treatment related effects. Organ weights were unchanged from control values.

On microscopic examination increased hemosiderin in liver and liver Kupffer cells and possibly in the spleen at the HDT seemed to confirm the hematological effects. In addition, the highest dose group showed higher incidence of gastritis and possible stomach lymphatic hyperplasia.

A single dog/sex was allowed to recover for 2 months and although the hemosiderin appeared to decrease, effects in one dog are difficult to interpret.

The NOAEL was 30.6/29.9 mg/kg/day for males/females. The LOAEL was 94.0/94.4 mg/kg/day for male/females based on decreased erythrocytes, hemoglobin and hematocrit by week 4 in males and females, supported by hemosiderin deposits in liver and increased incidence of gastritis and possible decreased body weight in males and females by month 13 of the study, but not in females by study termination at 24 months.

This study is **ACCEPTABLE/GUIDELINE** and satisfies the guideline requirement [870.4100b] for a dog chronic study. This DER takes precedence over previous conclusions.

A.3.5 Carcinogenicity

870.4200a Carcinogenicity Study – rat [MRID# 00082866]

Unacceptable due to only1-year interim report of a 2-year study was submitted. and other factors Not required.

870.4200b Carcinogenicity (feeding) – Mouse [MRID# 00082865]

SUMMARY: In a carcinogenicity study in mice [MRID 00082865], 50 NMBI-FMD-SPF mice/sex were administered IT 3456 [chlorflurenol methyl ester] in the feed at 0, 1000, 3000 or10000 ppm [equivalent to Males: 0, 136, 397 or 1538 mg/kg/day; Females: 0,158, 504 or 1905 mg/kg/day] for 18 months. Weekly body weights were determined up to week 12 and every two weeks to termination. Weekly food consumption was determined up to week 12 and every two weeks to termination. Necropsy and microscopic examination of the tissue were performed at termination.

No dose related or treatment related effects were noted in any parameter studied. Mortality, body weight, and food consumption were unchanged. Random tumors were seen after microscopic examination, but a dose or treatment relationship was absent. Neoplasms of the reticular tissue were 8.25%, 15.96, 15.63 and 14.13%, respectively in control, 1000 ppm, 3000 ppm and 10000 ppm. Since historical control data for this neoplasm ranges from 5% to 28%, control appear to be low compared with dosed groups. In addition, although over a 10 fold dose range, no dose response was seen. The highest incidence of tumors were pulmonary adenomas. Total pulmonary adenomas [benign and malignant] were 15.5%, 9.6%, 12.5% and 9.8%, respectively in control, 1000 ppm, 3000 ppm and 10000 ppm.

No dose related toxic or carcinogenic effects were noted in mice above the limit dose level of 1 g/kg/day.

The NOAEL was the highest dose tested of 1538/1905 mg/kg/day in male and female mice. A LOAEL was not seen.

The study is **ACCEPTABLE/GUIDELINE** and satisfies the requirements for a carcinogenicity study in mice [870.4200]. The study was done prior to GLPs. Organ weights were not determined and some summary table were not presented, but the study results appeared to be adequate to show that there were no carcinogenic response in mice to chlorflurenol administration.

A.3.6 Mutagenicity

See Table A.2.2 for summary of the mutagenicity studies.

A.3.7 Neurotoxicity

These studies are not required. Chlorflurenol methyl ester is neither an organic phosphate nor shows evidence of neurotoxicity.

870.6100 Delayed Neurotoxicity Study - Hen

870.6200 Acute Neurotoxicity Screening Battery

870.6200 Subchronic Neurotoxicity Screening Battery

870.6300 Developmental Neurotoxicity Study

A.3.8 Metabolism

870.7485 Metabolism – Rat

Not required, but an unacceptable study was submitted Study showed some information, but study was inadequately replicated since most of the tests were conducted in only one female rat.

EXECUTIVE SUMMARY: Kinetics and distribution of radiolabeled IT 3456, IT 3294 and IT 5733 [3 components of chlorflurenol methyl ester] were each assessed [MRID 0082868]. The kinetic were conducted in 3 experiments. Experiment 1: One female Wistar rat each was administered a single dose of 5 mg of IT 3456, IT 3294 or IT 5733/kg and the amount excreted n the urine and feces collected at 24 hours. Another set of 3 females were dosed similarly and urine and feces collected at 72 hours and whole body radio-autography conducted to located residual radiolabel. Experiment 2: One lactating female/ test material was dosed with 10 mg/kg and 3 days later radio-autography conducted to locate residual radiolabel. Experiment 3: One nursing dam with 10 pups/dam was dosed with 5 mg/kg and 3 days later radiolabel was counted in 2 pups/time period of 1, 2, 4 8 and 24 hours. Doses were administered in 0.5 mL DMSO/kg by intravenously into the caudal vein in Experiment 1 and 3 and by gavage in 0.5 ml DMSO/kg in Experiment 2.

Each of all 3 test materials were excreted almost completely within 24 hours primarily in the urine with lesser amounts in the feces; small amounts were excreted between 24 and 72 hours. Enterohepatic circulation was noted. Most of the radiolabel detected were in the lungs and kidney with small amounts of radiolabel detected in the mammary gland in Experiment 2. Pups from Experiment 3 showed no measurable radiolabeled test material.

Thus, each of all three test materials were rapidly excreted in the urine and feces, with small amounts being seen in the mammary gland and none in the milk.

The study is **UNACCEPTABLE/NG** for a metabolism study in rodents. The study results were no replicated and some of the data was not presented and/or readable and thus conclusions were not verifiable. Test materials were inadequately identified. Distribution of the radiolabel in the rats was not adequately quantified. The study may have been a range-finding study.

COMPLIANCE: These studies were conducted in 1972 prior to GLP Guideline requirements. No quality Assurance or Data Confidentiality Claim statements were provided.

A.3.9 Dermal Absorption

870.7600 Dermal Absorption – Rat

A dermal absorption was not submitted.

A.4 References

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Environmental Fate and Ecological Risk Assessment for Chlorflurenol Methyl Ester Reregistration

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I. Executive Summary

A. Nature of Chemical Stressor

Chlorflurenol methyl ester (ME) is used as an herbicide and plant growth regulator to control perennial and annual weeds and grasses. It is applied to ornamentals, hedge and fence rows, turf, shade trees, woody shrubs, and vines, and also is used to produce planting material for pineapples. It is formulated as an emulsifiable concentrate, which is applied as a spray; or as a granule, which is broadcast with a spreader. Chlorflurenol ME penetrates into herbaceous plants (via foliage and/or roots) and moves freely inside the plant (acro and basipetal transport). Growth and development of growing tips and buds of herbaceous plants are blocked or slowed down.

Chlorflurenol ME consists of three components. The major component is methyl 2-chloro-9-hydroxyfluorene-9-carboxylate (PC code 098801). The minor components are methyl 2,7-dichloro-9-hydroxyfluorene-9-carboxylate (PC code 098803) and methyl 9-hydroxyfluorene-9-carboxylate (PC code 098802). The latter (PC code 098802) is used as the starting material for the production of the major component (PC code 098801) and the former (PC code 098803) is obtained as a byproduct during the manufacture of the latter compound (PC code 098802). Since the chemical structures for these two minor components are very similar to that of the major component, it is reasonable to believe that they all have herbicidal activity. According to the registrant, these three components are inseparable and are synthesized in a relatively constant ratio. For example, the ratio among PC code 098801, PC code 098802, and PC code 098803 on the label EPA Reg. No. 69361-1 are 5.6:1.4:1 whereas the corresponding ratio on the label EPA Reg. No. 69361-6 are 5.5:1.3:1. As a result, although many environmental fate and ecological studies stated that methyl-2-chloro-9-hydroxyfluorene-9-carboxylate (the major component) was used as the test substance, EFED assumed that a mixture of all three components was used. Therefore, this ecological risk assessment is based on this assumption.

The environmental persistence of chlorflurenol ME is difficult to determine with any certainty due to the limited number of studies available, and the deficiencies within these studies. Based

on these limited data, chlorflurenol ME appears to be highly to very highly mobile in soil, and hydrolytically stable at pH 6. The study submitted by the registrant in order to fulfill the aerobic soil metabolism data requirements was determined to be unacceptable because the study was conducted outdoors. However, since this aerobic soil metabolism study could be considered supplemental as a small-scale quasi field dissipation study, its results could be interpreted qualitatively. Chlorflurenol ME appears to degrade rapidly under field conditions.

B. Potential Risks to Non-target Organisms

This is the Environmental Fate and Effects Division's (EFED) national screening-level ecological risk assessment for the proposed re-registration of chlorflurenol ME. **Table 1** summarizes the major conclusions and uncertainties of this assessment for aquatic and terrestrial receptors. The results suggest the potential for acute risk to listed terrestrial birds, reptiles, and mammals, and chronic risk to mammals. In addition, there is the potential for acute risk to non-listed terrestrial birds and reptiles from restricted use applications. Functionally, the estimated risks may translate to reduced survival and reproduction of impacted species with subsequent effects at higher levels of biological organization.

Acute and chronic risk to all aquatic invertebrates, fish, and terrestrial invertebrates, and chronic risk to birds cannot be precluded because data are not available. In addition, data are unavailable for aquatic and terrestrial plants; however, since chlorflurenol ME is used as an herbicide/plant growth regulator, risk to aquatic vascular and non-vascular plants and non-target terrestrial and semi-aquatic plants is expected.

Table 1. Summary of Environmental Risk Conclusions for Aquatic and Terrestrial Organisms and Plants exposed to Chlorflurenol ME.

Acute and Chronic Risk to Freshwater and Estuarine/marine Fish and Invertebrates	Risk could not be precluded due to lack of data.
Risk to Aquatic Vascular and Non-Vascular Plants	Risk could not be precluded due to lack of data.
Acute Risk to Birds	Definitive acute dose-based RQ values for avian receptors could not be derived because there are no definitive LD_{50} values.
Chronic Risk to Birds	Risk could not be precluded due to lack of data.
Acute Risk to Mammals	Definitive acute dose-based RQ values for mammalian receptors could not be derived because there are no definitive LD_{50} values.
Chronic Risk to Mammals	The reported RQ values are above the chronic LOC (1.0) for species that feed on short grass, tall grass, and broadleaf plants/small insects (RQ range = 0.02 to 2.90).
Terrestrial Plants	Risk could not be precluded due to lack of data.
Non-target Invertebrates	Risk could not be precluded due to lack of data.

C. Conclusions - Exposure Characterization

The registrant has submitted three studies to fulfill the environmental fate data requirements; however, these studies were considered to be either supplemental or unacceptable. As a result, the analysis could not be performed with confidence. No aquatic modelling was conducted due to lack of fate and toxicity data.

To estimate exposure of terrestrial animals, terrestrial EECs were generated using the Tier 1 model T-REX for chlorflurenol ME spray use based on maximum application rates and use patterns. Granular application was not assessed. For foliar spray applications, EECs and acute and chronic RQs were estimated for residues on various forage categories (short grass, tall grass, broadleaf plants/small insects, fruits/pods/large insects, and seeds). Chlorflurenol ME concentrations were highest on the surfaces of short grass and lowest on the surfaces of fruits, pods, and large insects.

D. Conclusions - Effects Characterization

Results of acute toxicity studies on birds suggest that chlorflurenol ME is practically nontoxic on an acute oral basis (LD_{50} >10,000 mg a.i./kg body weight) and practically nontoxic on an acute dietary basis (LC_{50} >5,000 mg a.i./kg diet). Mammalian data suggest that chlorflurenol ME is practically nontoxic (LD_{50} >5,000 mg a.i./kg body weight) on an acute oral basis.

A chronic toxicity study with rats showed that the maternal NOAEL was 250 mg/kg bw/day. The maternal LOAEL is 750 mg/kg bw/day based on body weight gain decrement and nominally decreased food efficiency. The developmental NOAEL is 250 mg/kg bw/day. The developmental LOAEL is 750 mg/kg bw/day, based on treatment-related delayed ossification in skull bones (nasal and frontal) in fetuses and litters.

No quantitative data are available to characterize risks from exposure of chlorflurenol ME to freshwater and estuarine/marine fish and invertebrates (acute and chronic risk), birds (chronic risk), and aquatic and terrestrial plants. EFED cannot preclude risk to these taxa. In addition, since chlorflurenol ME is used as an herbicide or a plant growth regulator, risk to non-target plants is expected.

E. Data Gaps and Uncertainties

The screening-level assessment for chlorflurenol ME has been conducted despite unfulfilled guideline requirements and existing environmental fate and ecological data gaps (**Tables H1** and **H2**, **Appendix H**). The following is a brief synopsis of the major environmental fate and ecological effects data gaps and uncertainties. Additional detail can be found in Section IV C, Description of Assumptions, Limitations, Uncertainties, Strengths and Data Gaps.

1. Environmental Fate

- Guideline 161-1 Hydrolysis (the submitted study (MRID 43496201) was determined to be supplemental and the hydrolysis data requirements have not been fulfilled. A new study including pH 7 is required)
- Guideline 161-2 Aqueous photolysis
- Guideline 161-3 Soil photolysis
- Guideline 162-1 Aerobic soil metabolism (the submitted study (MRID 43595403) was determined to be unacceptable. A new study using four soils is required)
- Guideline 162-2 Anaerobic soil metabolism
- Guideline 162-3 Anaerobic aquatic metabolism

- Guideline 163-1 Adsorption/desorption (the submitted study (MRID43496202) was determined to be supplemental and the adsorption/desorption data requirements have not been fulfilled. A new study including three soils is required)
- Guideline 164-1 Terrestrial field dissipation
- Guideline 165-4 Fish bioaccumulation
- Guideline 201-1 Droplet Size Spectrum (a waiver request was denied by EPA on 3/2/05)
- Guideline 202-1 Drift Field Evaluation (a waiver request was denied by EPA on 3/2/05)

2. Ecological Effects

- Guidelines 72-1, 72-2, 72-3, 72-4: Acute and chronic data for freshwater and estuarine/marine fish and invertebrates are not available; therefore risk could not be assessed.
- Guideline 71-4: There are no avian reproduction studies available; therefore risk could not be assessed.
- Guideline 123-1, 123-2: Terrestrial Plant Seedling Emergence and Vegetative Vigor studies are not available. In addition, aquatic plant growth studies are not available; therefore risk could not be assessed. Since chlorflurenol ME is used as an herbicide and growth regulator, toxicity data on non-target plants are necessary to estimate risk. Available literature suggests that chlorflurenol causes reproductive effects in terrestrial plants.
- Guideline 141-1: Honey Bee Acute Contact Toxicity; no data are available; therefore risk could not be assessed.
- Acute oral and dietary toxicity studies in birds and acute oral toxicity to mammals failed to establish definitive acute LD_{50}/LC_{50} values (i.e., the LC_{50} was expressed as "greater than" the highest dietary concentration tested); thus, acute RQ could not be calculated.
- The study testing oral toxicity to birds did not state which components were included in the test material. EFED assumes the test material contained all three components which may underestimate risk to birds on an acute oral basis if in fact the test material only contained one of the three components.
- The mammalian chronic RQs are based on a developmental study that shows evidence of delayed skull ossification and cleft palates in young rats. These endpoints are not adequate for determining risk to the survival and fecundity of a population. However, without other studies EFED used these data. Therefore, the RQs may not accurately portray chronic risk to mammals. Risk may be under- or over-estimated.
- Application interval and number of applications per year are not indicated on the label. For multiple application scenarios, the T-Rex model requires both of these parameters in order to estimate exposure to terrestrial organisms. In the absence of these numbers an application interval of 28 days and 8 applications per year (as derived by HED, Appendix **B**) were used. HED used information provided on the labels along with their best professional judgment of the crop/weed growth cycles, pest pressure timing, etc. to determine the application interval and yearly number of applications. EFED used the HED data to maintain consistency between EFED and HED. Since these numbers are considered "likely" applications per year, risk to terrestrial organisms may be underestimated.

F. Summary of Endangered Species

Table 2 summarizes the potential risk to listed species associated with the application of chlorflurenol. For all taxa except acute risk to birds and mammals and chronic risk to mammals, risk is presumed to occur due to lack of data.

Table 2. Listed species risks associated with direct or indirect effects due to applications of chlorflurenol for turf use.

Listed Taxon	Direct Effects	Indirect Effects
Terrestrial and semi-aquatic plants - monocots	Yes [a]	Yes
Terrestrial and semi-aquatic plants – dicots	Yes [a]	Yes
Insects	Yes [a]	Yes
Birds	Acute – Yes [c]; Chronic – Yes [a]	Yes
Terrestrial phase amphibians	Yes [a]	Yes
Reptiles	Acute – Yes [c]; Chronic – Yes [a]	Yes
Mammals	Acute – Yes [c]; Chronic – Yes [b]	Yes
Aquatic vascular plants	Yes [a]	Yes
Freshwater fish	Yes [a]	Yes
Aquatic phase amphibians	Yes [a]	Yes
Freshwater crustaceans	Yes [a]	Yes
Mollusks	Yes [a]	Yes
Marine/estuarine fish	Yes [a]	Yes
Marine/estuarine crustaceans	Yes [a]	Yes

[a] We cannot preclude risk due to lack of data.
[b] The reported RQ values are above the chronic LOC (1.0) for species that feed on short grass, tall grass, and broadleaf plants/small insects (RQ range = 0.02 to 2.90).
[c] RQs could potentially exceed acute listed species LOCs unless the actual LD_{50} values are established in laboratory studies to be greater than ~16,715 mg a.i./kg body weight or if the amount available in the environment was lowered below 500 ppm

II. Problem Formulation

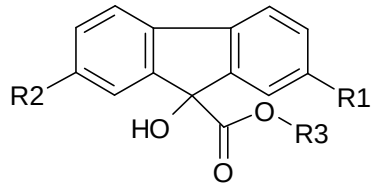
A. Stressor Source and Distribution

1. Source and Intensity

Chlorflurenol ME formulations are currently registered for use on turf, fencerows, hedgerows, rights-of-ways, forests, industrial areas, recreational areas, and pineapples as ground or aerial sprays. The rates of application range from 0.25 to 3.0 lb a.i./acre with no maximum number of applications/season and no set interval between applications specified on the label.

2. Physicochemical, Fate, and Transport Properties

Chlorflurenol ME is used as an herbicide and plant growth regulator. It consists of three components (see table below). The major component is methyl 2-chloro-9-hydroxyfluorene-9-carboxylate (PC code 098801). The minor components are methyl 2,7-dichloro-9-hydroxyfluorene-9-carboxylate (PC code 098803) and methyl 9-hydroxyfluorene-9-carboxylate (PC code 098802). The latter (PC code 098802) is used as the starting material for the production of the major component (PC code 098801) and the former (PC code 098803) is obtained as a byproduct during the manufacture of the latter compound (PC code 098802). Since the chemical structures for these two minor components are very similar to that of the major component, it is reasonable to believe that they all have herbicidal activity. According to the registrant, these three components are inseparable and are synthesized in a relatively constant ratio. For examples, the ratio among PC code 098801, PC code 098802, and PC code 098803 on the label EPA Reg. No. 69361-1 are 5.6:1.4:1 whereas the corresponding ratio on the label EPA Reg. No. 69361-6 are 5.5:1.3:1. As a result, although many environmental fate and ecological studies stated that methyl-2-chloro-9-hydroxyfluorene-9-carboxylate (the major component) was used as the test substance, EFED assumed that a mixture of all three components was used. Therefore, this ecological risk assessment is based on this assumption.

Chlorflurenol ME		
	A mixture of 65-70% methyl-2-chloro-9-hydroxyfluorene-9-carboxylate, 10-15% methyl-2,7-dichloro-9-hydroxyfluorene-9-carboxylate and 15-20% methyl-9-hydroxyfluorene-9-carboxylate.	
		
Methyl-2-chloro-9-hydroxyfluorene-9-carboxylate; R_1 = Cl; R_2 = H; R_3 = CH_3.		
Methyl-2,7-dichloro-9-hydroxyfluorene-9-carboxylate; R_1 = R_2 = Cl; R_3 = CH_3.		
Methyl-9-hydroxyfluorene-9-carboxylate; R_1 = R_2 = H; R_3 = CH_3.		

No information on the physical and chemical properties could be found for those two minor components (PC codes 098802 and 098803). Limited information was found for the major component (PC code 098801), which has very low water solubility and is moderately volatile:

Common Name:	Chlorflurenol ME
Chemical Name (IUPAC):	
(RS)-2-Chloro-9-hydroxyfluorene-9-carboxylic acid methyl ester	
Chemical Name (CAS):	
2-Chloro-9-hydroxy-9H-fluorene-9-carboxylic acid methyl ester	
CAS No.:	2536-31-4
PC Code:	098801
Molecular Formula:	C15H11ClO3
Molecular Weight:	274.7 g/mol
Vapor Pressure (temperature unknown):	2.5 x 10-5 torr
Water Solubility (temperature and pH unknown):	21.8 ppm

The environmental persistence of chlorflurenol ME is difficult to determine with any certainty due to the limited number of studies available, and the deficiencies within these studies. Based on these limited data, chlorflurenol ME appears to be highly to very highly mobile in soil, and hydrolytically stable at pH 6. The study submitted by the registrant in order to fulfill the aerobic soil metabolism data requirements was determined to be unacceptable because the study was conducted outdoors. However, since this aerobic soil metabolism study could be considered supplemental as a small-scale quasi field dissipation study, its results could be interpreted qualitatively. Chlorflurenol ME appears to degrade rapidly under field conditions. Efforts were made; however, no chemicals which have similar chemical structures as chlorflurenol ME were found.

Chlorflurenol ME degraded by hydrolysis with a half-life of 161.2 days and 0.2 days at pHs 6 and 9, respectively. The most environmentally relevant pH of 7 for aquatic systems was not tested. At study termination, 77.8% (50 days, pH 6), 55.6% (0.19 days, pH 9) and 41.7% (0.29 days, pH 9) of the applied chlorflurenol ME was undegraded. The major transformation product was 2-chloro-9-hydroxyfluorene-9-carboxylic acid; however, quantitative data and further details were not reported.

Chlorflurenol ME degraded in sandy loam soil (pH 6.0) in outdoor plots with a half-life of 1.3 days. Chlorflurenol ME was completely degraded by 26 days (study termination). One major degradation product was detected, 2-chloro-9-fluorenone at a maximum of 14.3% of the applied at 5-12 days and was not detected at 26 days.

In laboratory mobility studies, chlorflurenol ME was highly to very highly mobile in a sandy loam soil from Germany.

3. Pesticide Type, Class, and Mode of Action

Chlorflurenol ME is used as an herbicide and plant growth regulator. It consists of three components. The major component is methyl 2-chloro-9-hydroxyfluorene-9-carboxylate (II). The minor components are methyl 2,7-dichloro-9-hydroxyfluorene-9-carboxylate (III) and methyl 9-hydroxyfluorene-9-carboxylate (I). The latter (I) is used as the starting material for the

production of the major component (II) and the former (III) is obtained as a byproduct during the manufacture of the latter compound (I). This chemical readily penetrates into herbaceous plants (via foliage and/or roots). It moves freely inside the plant (acro and basipetal transport). Growth and development of growing tips and buds of herbaceous plants are blocked or slowed down as a result of chlorflurenol ME usage. EFED could not find information on the mode of action for this chemical.

4. Overview of Pesticide Usage

There are no data on the actual usage of chlorflurenol ME.

B. Receptors

1. Ecological Effects

Each assessment endpoint requires one or more measures of ecological effect, which are defined as changes in the attributes of an assessment endpoint itself or changes in a surrogate entity or attribute in response to exposure to a pesticide. Ecological measures of effect for this screening-level risk assessment are based on a suite of registrant-submitted toxicity studies performed on a limited number of organisms in broad groupings. A complete discussion of all toxicity data available for this risk assessment and the resulting measures of effect selected for each taxonomic group are included in **Appendix D**.

a. Aquatic Effects

Toxicity data sufficient for use in a risk assessment for chlorflurenol ME are **not** available for freshwater fish and invertebrates, estuarine/marine fish and invertebrates, algae, and vascular plants. No studies on chlorflurenol ME are available for acute or chronic exposure for any of these taxa. In addition, since there are very limited fate data, no aquatic exposure models were run. Therefore, risk cannot be precluded.

b. Terrestrial Effects

Registrant-submitted laboratory studies on chlorflurenol ME formulations are available for acute exposure of birds and mammals. In addition chronic studies have been submitted for mammals but not for birds. No toxicity studies on the effects of chlorflurenol ME on terrestrial plants or honeybees were submitted. Details of all registrant and open literature studies are provided in **Appendix D**. Where data are lacking, risk could not be precluded.

2. Ecosystems at Risk

Ecosystems potentially at risk are expressed in terms of the selected assessment measures of effect. The typical assessment measures of effect for screening-level pesticide ecological risk assessments are reduced survival and reproductive and growth impairment for both aquatic and terrestrial animal species. Aquatic animal species of potential concern include freshwater fish and invertebrates, estuarine/marine fish and invertebrates, and amphibians. Terrestrial animal

species of potential concern include birds, mammals, reptiles, and beneficial insects. For both aquatic and terrestrial animal species, acute and chronic exposures are considered.

C. Assessment Endpoints

This risk assessment considers the maximum application rate of chlorflurenol ME spray (granular was not assessed) on vulnerable soils as reported on the label, the likely number of applications as derived by HED (**Appendix B**), and the likely application intervals as reported by HED (**Appendix B**) to estimate exposure concentrations as a result of the use of chlorflurenol ME. This assessment is not intended to represent a site or time-specific analysis. Likewise, the most sensitive toxicity endpoints are used from surrogate test species to estimate treatment-related direct effects on acute mortality and chronic reproductive, growth and survival assessment endpoints. Surrogate aquatic organisms include freshwater and saltwater fish and invertebrates. In the absence of toxicity data on amphibians, it is assumed that aquatic-phase amphibians are approximately as sensitive as fish to potential effects of a pesticide. Surrogate terrestrial animal species include birds and mammals. The risk assessment also assumes that reptiles and terrestrial-phase amphibians are approximately as sensitive to pesticide-induced effects as birds. These tests include short-term acute, subacute, and reproduction studies and are typically arranged in a hierarchical or tiered system that progresses from basic laboratory tests to applied field studies.

For plants in terrestrial and semi-aquatic environments, the screening assessment endpoint is the perpetuation of populations of non-target species (crops and non-crop plant species). Endpoints assessed include emergence of seedlings and vegetative vigor. Although it is recognized that the endpoints of seedling emergence and vegetative vigor may not address all plant life cycle components, it is assumed that impacts at emergence and in active growth have the potential to impact individual competitive ability and reproductive success. For aquatic plants, the assessment endpoint is the maintenance and growth of standing crop or biomass.

In order to protect federally endangered and threatened (listed) species, all assessment endpoints are measured at the individual level. They also provide insight about risks at higher levels of biological organization (e.g. populations and communities). For example, pesticide effects on individual survivorship have important implications for both population rates of increase and habitat carrying capacity.

The ecological relevance of selecting the above-mentioned assessment endpoints is as follows: 1) complete exposure pathways exist for these receptors; 2) the receptors may be potentially sensitive to pesticides in affected media and in residues on plants, seeds, and insects; and 3) the receptors could potentially inhabit areas where pesticides are applied, or areas where runoff and/or spray drift may impact the sites because suitable habitat is available.

The toxicity studies are used to evaluate the potential of chlorflurenol ME to cause adverse effects, to determine whether further testing is required, and to determine the need for precautionary label statements to minimize the potential adverse effects to non-target animals and plants (40 CFR §158.202, 2002). A summary of the assessment endpoints and measures of effect selected to characterize potential ecological risks associated with exposure to chlorflurenol ME is provided in **Table 3**.

Table 3. Summary of Assessment Endpoints and Measures of Effect for Chlorflurenol ME.	
Assessment Endpoint	**Measure of Effect**
1. Abundance (i.e., survival, reproduction, and growth) of individuals and populations of birds.	1a. Bobwhite quail acute oral LD_{50} (guideline-recommended species). 1b. Bobwhite quail subacute dietary LC_{50} (guideline-recommended species). 1c. Avian chronic/reproduction: **data gap**
2. Abundance (i.e., survival, reproduction, and growth) of individuals and populations of mammals.	2a. Laboratory rat acute oral LD_{50}. 2b. Rat developmental NOAEL
3. Survival and reproduction of individuals and communities of freshwater fish and invertebrates.	3a. Rainbow trout and bluegill sunfish acute LC_{50} : **data gap** 3b. Water flea acute LC_{50}: **data gap** 3c. Freshwater fish chronic: **data gap** 3d. Freshwater invertebrate chronic: **data gap**
4. Survival and reproduction of individuals and communities of estuarine/marine fish and invertebrates.	4a. Estuarine/marine fish acute: **data gap** 4b. Estuarine/marine invertebrate acute: **data gap** 4c. Estuarine/marine fish chronic: **data gap** 4d. Estuarine/marine invertebrate chronic: **data gap**
5. Survival of terrestrial invertebrate populations (beneficial insects and earthworms).	5a. Honeybee acute contact LD_{50}: **data gap**
LD_{50} = Lethal dose to 50% of the test population. LC_{50} (EC_{50}) = Lethal (effective) concentration to 50% of the test population.	

D. Conceptual Model

1. Risk Hypotheses

Risk hypotheses are specific assumptions about potential adverse effects (i.e., changes in assessment endpoints) and may be based on theory and logic, empirical data, mathematical models, or probability models (US EPA 2004). For this assessment, the risk is stressor-initiated, where the stressor is the release of chlorflurenol ME spray to the environment. The following risk hypothesis is presumed for this screening-level assessment:

> *Non-target aquatic and terrestrial plants and animals may be exposed to chlorflurenol ME when it is applied in agricultural and/or non-agricultural settings to control unwanted plants. Based on available information regarding the persistence, mode of action, direct and indirect toxicity, chlorflurenol ME may have the potential to compromise growth, reproduction, and/or survival of non-target terrestrial and aquatic animals and plants.*

Ecological receptors that may potentially be exposed to chlorflurenol ME and its transformation products include terrestrial and semi-aquatic wildlife (i.e., mammals, birds, amphibians, and reptiles), terrestrial and semi-aquatic plants, and soil invertebrates. In addition, aquatic receptors (e.g., freshwater and estuarine/marine fish and invertebrates, and amphibians) may also be exposed as a result of potential migration of chlorflurenol ME via spray drift and/or runoff/erosion from the site of application to various watersheds and other aquatic environments. These data formed the basis for identifying potential endpoints, stressors, and ecological effects associated with uses of chlorflurenol ME.

2. Diagram

Based on the preliminary iterative process of examining fate and effects data, the conceptual model or the risk hypothesis model for spray application to non-agricultural crops and pineapples has been established, refined and included in **Figure 1**. Granular application was not assessed. In establishing the diagram for the conceptual model it was necessary to go through an iterative process to identify: (1) likely stressors/exposure pathways and (2) organisms that are most relevant and applicable to this assessment.

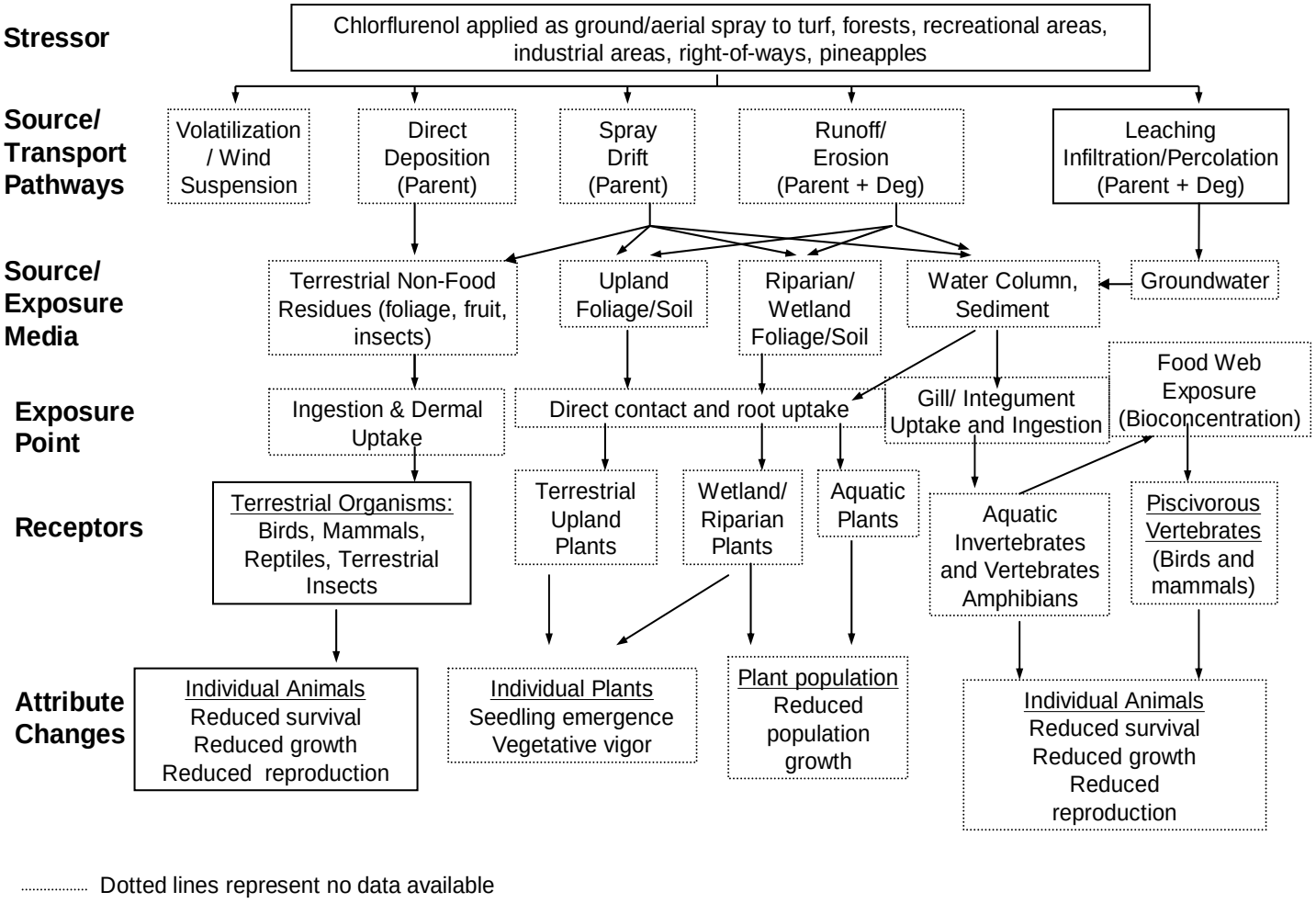


Figure 1. Ecological conceptual exposure model for chlorflurenol.

E. Analysis Plan

1. Methods for Conducting Ecological Risk Assessment and Identification of Data Gaps

The primary method used to assess risk in this screening-level assessment is the risk quotient (RQ) and follows closely methods outlined in the EPA Overview Document (US EPA, 2004). The RQ is the primary risk value for the screening-level assessment and is the result of comparing measures of exposure to measures of effect. A commonly used measure of exposure is the estimated exposure concentration (EEC) and commonly used measures of effect include toxicity values such as the LD_{50} or NOAEC. Assessment endpoints and their respective measures of effect are listed in **Table 3**. The resulting RQ is then compared to a specified level of concern (LOC), which represents a point of departure for concern; if the RQ exceeds the LOC, then risks are triggered. Although not necessarily a true estimate of risk since there is no estimated

probability of effect, in general, the higher the RQ, the more certain the potential risks. Risk presumptions, along with the corresponding RQs, equations, and LOCs are summarized in **Appendix E**.

Levels of concern (LOC) are the policy tool for interpreting risks from direct pesticide effects and have a magnitude, duration, frequency, and spatial extent. The magnitude is set by the risk presumption for each endpoint. The frequency of potential risk is once every ten years for aquatic endpoints and reasonable upper bound for terrestrial risk. The spatial extent is defined by the use area, and the areas downstream and areas potentially affected by spray drift.

Generation of robust RQs is dependent on the quality of data from both fate and toxicological studies. The adequacy of the submitted data was evaluated relative to Agency guidelines. The following identified data gaps for ecological fate and toxicity endpoints result in a degree of uncertainty in evaluating the ecological risk of chlorflurenol ME.

For fate and transport, **Table H1** (**Appendix H**) lists the status of the fate and transport data requirements for chlorflurenol ME. The adequacy of the submitted data was evaluated relative to Agency guidelines. Data gaps identified for fate and transport include

- Guideline 161-1 Hydrolysis
- Guideline 161-2 Aqueous photolysis
- Guideline 161-3 Soil photolysis
- Guideline 162-1 Aerobic soil metabolism
- Guideline 162-2 Anaerobic soil metabolism
- Guideline 162-3 Anaerobic aquatic metabolism
- Guideline 163-1 Adsorption/desorption
- Guideline 164-1 Terrestrial field dissipation
- Guideline 165-4 Fish bioaccumulation
- Guideline 201-1 Droplet Size Spectrum
- Guideline 202-1 Drift Field Evaluation

For the ecological assessment, **Table H2** (**Appendix H**) lists the status of ecological data requirements for chlorflurenol ME. Hereunder is a summary of identified data gaps and associated uncertainties:

- Guidelines 72-1, 72-2, 72-3, 72-4: Acute and chronic data for freshwater and estuarine/marine fish and invertebrates are not available; therefore risk could not be assessed.
- Guideline 71-4: Avian reproduction studies are not available; therefore risk could not be assessed.
- Guideline 123-1 (a, b), 123-2: Terrestrial plant seedling emergence and vegetative vigor studies are not available. In addition, aquatic plant growth studies are not available; therefore risk could not be assessed. Since chlorflurenol ME is used as an herbicide and growth regulator, toxicity data on non-target plants are necessary to estimate risk.
- Guideline 141-1: Data for honey bee acute contact toxicity are not available; therefore risk could not be assessed.
- Acute oral and dietary toxicity studies in birds and acute oral toxicity studies in mammals failed to establish definitive acute LD_{50}/LC_{50} values (i.e., the LD_{50}/LC_{50} were expressed

as "greater than" the highest concentration tested); thus, acute RQ could not be calculated.

- The mammalian chronic RQs are based on a developmental study that shows evidence of delayed skull ossification and cleft palates in young rats. These endpoints are not adequate for determining risk to the survival and fecundity of a population. However, without other studies EFED used these data. Therefore, the RQs may not accurately portray chronic risk to mammals. Risk may be under- or over-estimated.

2. Measures to Evaluate Risk Hypotheses and Conceptual Model

a. Measures of Exposure

Due to the absence of fate data and aquatic toxicity data, no aquatic exposure modeling was conducted for this assessment. Exposure was assumed to occur.

Measures of exposure for terrestrial mammals, birds, reptiles and amphibians incorporate maximum proposed use rates but rely less on fate properties. Terrestrial exposures were estimated using a number of methods. Acute and chronic terrestrial exposure estimates are derived directly from empirically determined observations of pesticide residues on various terrestrial food items. The Kenaga nomogram, as modified by Fletcher et al., (Hoerger and Kenaga, 1972; Fletcher et al., 1994) is used to relate pesticide application rates to residues on terrestrial food items. The surface residue concentration (ppm) is estimated by multiplying the application rate (pounds active ingredient (a.i.) per acre) by a value specific to each food item. For multiple applications of a given use, the exposure model incorporates a first-order decay rate dependent on the foliar dissipation half-life of the chemical. In the absence of data, a default foliar dissipation half-life of 35 days is used. The T-REX model was run for chlorflurenol ME turf use with the maximum proposed application rate (3.0 lb a.i./A; as stated on the label), a maximum of 8 applications (HED derived with best professional judgment, see **Appendix B**), and a 28-day application interval (HED derived with best professional judgment, see **Appendix B)** to assess risk to terrestrial organisms. EFED used the HED data to maintain consistency between EFED and HED. The conceptual approach taken to estimate residues (upper-bound and mean) on potential dietary sources for mammals and birds is presented in the model T-REX Version 1.2.3 (T-REX, 2005)(For more details see **Appendix C** and the Exposure Characterization section of this document).

b. Measures of Effect

Measures of ecological effects are obtained from a suite of registrant-submitted guideline studies conducted with a limited number of surrogate species. The test species are not intended to be representative of the most sensitive species but rather were selected based on their ability to thrive under laboratory conditions. Measures of effect are based on deleterious changes in a receptor as a result of chemical exposure. Functionally, measures of effect typically used in risk assessments include changes in survival, reproduction, or growth as determined from standard laboratory toxicity tests. The focus on these effects for quantitative risk assessments is due to their clear relationship to higher-order ecological systems such as populations, communities, and ecosystems. Monitoring data may also be used to provide supporting lines of evidence for the risk characterization. In addition, although effects other than survival, reproduction, and growth may be considered, rarely are they used quantitatively to estimate risks since, in many cases, the

relationship between these effects and higher-order processes is tenuous at best. Commonly used laboratory-derived toxicity values include estimates of acute mortality (*e.g.*, LD50, LC50, or EC50) and estimates of effects due to longer term, chronic exposures (*e.g.*, NOAEC, NOAEL). The latter can reflect changes seen in mortality, reproduction, or growth. In general, for a given assessment endpoint the lowest relevant measure of effect is used when calculating the RQ.

Since preliminary review of the available ecological effects data suggests that chlorflurenol ME is practically nontoxic to birds and mammals on an acute exposure basis, acute effects to non-listed birds and mammals are not expected. Chronic exposure studies indicate that mammals may be at chronic risk; no chronic avian toxicity data are available. No guideline data are available for aquatic species, terrestrial plants, and insects. However, there are literature studies that show reproductive effects on terrestrial plants.

A search of the open literature using EPA's Ecotoxicology database, ECOTOX, was conducted to identify studies to fill the data gap for acute and chronic exposure of chlorflurenol ME to aquatic fish and invertebrates, terrestrial invertebrates; search of the ECOTOX database did not identify studies to fill these data gaps. The ECOTOX search did identify additional chronic toxicity studies on the following: terrestrial plants (See section IV.B.2.d).

c. Measures of Ecosystem and Receptor Characteristics

The ecosystems selected for modeling, using T-REX for the Tier 1 terrestrial animal assessment, are intended to be generally representative of any aquatic or terrestrial ecosystem associated with areas where chlorflurenol ME is used. The receptors addressed by the aquatic and terrestrial risk assessments are summarized in **Table 3**. For aquatic assessments, generally fish and aquatic invertebrates in both freshwater and estuarine/marine environments are represented, when available. For terrestrial assessments, mammals are represented by three different size classes and five potential foraging categories (short grass, tall grass, broadleaf plants/small insects, fruits/pods/seeds/large insects, and seeds). For the three different size classes of small birds, four potential foraging categories are considered (short grass, tall grass, broadleaf plants/small insects, and fruits/pods/seeds/large insects). For terrestrial plants, generally both dicots and monocots are represented. Detailed information regarding the data available for these various classes of aquatic and terrestrial receptors is provided in **Appendix D**.

III. Analysis

A. Use Characterization

Chlorflurenol ME [(RS)-2-chloro-9-hydroxyfluorene-9-carboxylic acid methyl ester; CF 125, 12.5% a.i.] is an herbicide/plant growth regulator (PGR) used to control weeds and grasses for ornamentals, hedge and fence rows, turf, shade trees, woody shrubs and vines, and is specifically used to produce planting material for pineapple production. The maximum application rate is 3 lb a.i./A for ornamental lawns, turf, and non-agricultural right-of-ways, fencerows, and hedgerows; 1 lb a.i./100 gal for shade trees (due to lack of information, EFED is unable to convert it to lb ai/A), woody shrubs and vines, forest conifers and junipers, recreational areas and industrial areas (outdoors); and 1.0875 lb a.i./A for pineapples. The labels indicate that for optimum results, chlorflurenol ME can be used in conjunction with other traditional herbicides.

B. Exposure Characterization

1. Environmental Fate and Transport Characterization

Environmental Persistence

The environmental persistence of chlorflurenol ME is difficult to determine with any certainty due to the limited number of studies available, and the deficiencies within these studies. However, based on these limited data, chlorflurenol ME appears to be highly to very highly mobile in soil, and hydrolytically stable at pH 6. The study submitted by the registrant in order to fulfill the aerobic soil metabolism data requirements was determined to be unacceptable because the study was conducted outdoor. However, since this aerobic soil metabolism study could be considered supplemental as a small-scale quasi field dissipation study, its results could be interpreted qualitatively. Chlorflurenol ME appears to degrade rapidly under field conditions. The primary route of dissipation could not be determined. Photodegradation may also occur; however, no studies were submitted, so this degradation route could not be confirmed.

In buffered aqueous solutions, the half-life of chlorflurenol ME at pH 6 and pH 9 was 161.2 and 0.20 days, respectively. The phototransformation of chlorflurenol ME could not be evaluated because no studies were submitted. In the registrant-claimed aerobic soil metabolism study (which was considered by EFED as a small-scale quasi field dissipation study), chlorflurenol ME degraded with a half-life of 1.3 days in a sandy loam soil from Germany. However, these experimental plots were outdoors under uncontrolled environmental conditions, and without a phototransformation study to reference, it is uncertain to what extent degradation occurred due to microbial metabolism, and/or photodegradation. The metabolism of chlorflurenol ME under aerobic aquatic, anaerobic soil, and anaerobic aquatic conditions, and the potential for bioaccumulation could not be evaluated because no studies were submitted in these areas.

Expected Mobility

Chlorflurenol ME is highly to very highly mobile in sandy loam soil from Germany, with a K_{Foc} of 109. The field dissipation of chlorflurenol ME could not be evaluated because no studies were submitted.

Environmental Metabolites

The major transformation product of chlorflurenol ME that was quantified was 2-chloro-9-fluorenone (Compound IV; fluorenone). 2-Chloro-9-hydroxyfluorene-9-carboxylic acid (Compound II) was also identified as a major transformation product of hydrolysis, but was not quantified.

The transformation pathway of chlorflurenol ME in the environment is difficult to determine with any certainty due to the limited number of studies available, and the deficiencies within these studies.

2. Measures of Aquatic Exposure

a. Aquatic Exposure Modeling

Since there are limited fate data for chlorflurenol ME no aquatic modeling was conducted.

b. Aquatic Exposure Monitoring (Field Data)

There are no aquatic exposure monitoring data.

3. Terrestrial Exposure Assessment

Terrestrial wildlife exposure estimates are typically calculated for birds and mammals, emphasizing a dietary exposure route for uptake of pesticide active ingredients. These exposures are considered as surrogates for terrestrial-phase amphibians as well as reptiles. For exposure to terrestrial organisms, such as birds and small mammals, pesticide residues on food items are estimated, based on the assumption that organisms are exposed to a single pesticide residue in a given exposure scenario.

a. Terrestrial Animal Exposure Modeling

A primary concern with chlorflurenol ME is that birds and mammals may be exposed shortly after application through oral or dietary exposure to vegetative plant material or insects when foraging in the treated fields for nesting material or food. Therefore estimation of pesticide concentrations in wildlife food items focuses on quantifying possible dietary ingestion of residues on vegetative matter and insects. The EFED terrestrial exposure model T-REX (T-REX, Version 1.2.3, dated August 8, 2005) is used to estimate exposures and risks to avian and mammalian species. Input values for avian and mammalian toxicity as well as chemical application and foliar dissipation half-life data are required to run the model. The model provides estimates of exposure concentrations and risk quotients (RQs). Specifically, the model provides estimates of concentrations (upper-bound and mean) of chemical residues on the surface of different types of foliage and insects that may be dietary sources of exposure to avian, mammalian, reptilian, or terrestrial-phase amphibian receptors. The surface residue concentration (ppm) is estimated by multiplying the application rate (pounds active ingredient per acre) by a value specific to each food item. These values (termed the Hoerger-Kenaga estimates) along with a more detailed discussion of the methodology implemented by T-REX, are presented in **Appendix C** (T-REX Model).

For multiple applications, the EEC is determined by adding the mass on the surface immediately following the application to the mass of the chemical still present on the surfaces on the day of application (determined based on first order kinetics using the foliar dissipation half-life as the rate constant). Input values used for estimating avian and mammalian exposure risks to chlorflurenol ME are summarized in **Table 4**.

Table 4. Input parameters used in T-REX v1.2.3 to determine terrestrial EECs for the maximum chlorflurenol ME spray application scenario.

Input Variable	Parameter Value	Source
Maximum application rate	3.0 lb a.i./A	Product Label

Table 4. Input parameters used in T-REX v1.2.3 to determine terrestrial EECs for the maximum chlorflurenol ME spray application scenario.

Input Variable	Parameter Value	Source
Likely # of applications per year	8	HED [a]
Likely application interval	28 days	HED [a]
Foliar dissipation half-life	35 days	T-REX Default Value

[a] HED used information provided on the labels along with their best professional judgment of the crop/weed growth cycles, pest pressure timing, etc. to determine the application interval and yearly number of applications. EFED used the HED data to maintain consistency between EFED and HED.

Uncertainties in the terrestrial EECs are associated with a lack of data on dissipation from foliar surfaces. When data are absent, as in this case, EFED assumes a 35-day foliar dissipation half-life, based on the work of Willis and McDowell (1987). In this respect, the EECs for chlorflurenol ME may be an overestimation of actual concentrations if the half-life under field conditions is lower than the default value. Because foliar dissipation data are not available, the extent to which EECs may be overestimated or underestimated is uncertain.

In addition, EFED used a "likely" application interval and yearly application rate, since no information was provided on the label. Risks could be underestimated if the actual application rate, frequency of application, and/or number of applications are higher than the input parameters used for the exposure scenario that was modeled. For this risk assessment, the T-REX model was run for turf use with the maximum proposed application rate (3.0 lb a.i./A), 8 applications/year (derived by HED, see **Appendix B**), and a 28-day application interval (derived by HED, see **Appendix B**), to assess risk to terrestrial organisms. HED used information provided on the labels along with their best professional judgment of the crop/weed growth cycles, pest pressure timing, etc. to determine the application interval and yearly number of applications. EFED used the HED data to maintain consistency between EFED and HED.

By comparing estimated exposure concentrations to acute and chronic toxicity reference values, RQs are calculated. The EECs on food items may be compared directly with dietary toxicity data or converted to an oral dose, as is done for small mammals. For mammals, the residue concentration is converted to daily oral dose based on the fraction of body weight consumed daily as estimated through mammalian allometric relationships. The screening-level risk assessment for chlorflurenol ME uses upper-bound predicted residues as the measure of exposure. Summaries of the predicted upper-bound and mean residues of chlorflurenol ME that may be expected to occur on selected avian or mammalian food items immediately following application for the maximum use scenario are presented in **Table 5**.

For the maximum chlorflurenol ME application scenario, acute concentrations for different forage types ranged from 104.22 to 1671.50 ppm for upper-bound residues and 48.75 to 591.99 ppm for mean residues. Chlorflurenol ME concentrations were highest on the surfaces of short grass and lowest on the surfaces of fruits, pods, and large insects.

Table 5. Upper-bound and mean terrestrial EECs estimated for the chlorflurenol ME spray application scenario using Kenaga values.

Forage Type	Upper-bound Residues (ppm)	Mean Residues (ppm)
short grass	1671.50	591.99
tall grass	766.10	250.72
broadleaf plants and small insects	940.22	313.41
fruits/pods/large insects	104.22	48.75

b. Terrestrial Exposure Monitoring (Field Data)

No data were identified to provide information on terrestrial monitoring.

4. Non-Target Plant Exposure Assessment

No toxicity data were identified to provide information on terrestrial plants.

C. Ecological Effects Characterization

In screening-level ecological risk assessments, effects characterization describes the types of effects a pesticide can produce in an aquatic or terrestrial organism. This characterization is based on registrant-submitted studies that describe acute and chronic effects toxicity information for various aquatic and terrestrial animals and plants. **Appendix D** summarizes the results of the registrant-submitted toxicity studies used to characterize effects for this risk assessment. Toxicity testing reported in this section does not represent all species of birds, mammals, or aquatic organisms. Only a few surrogate species for both freshwater fish and birds are used to represent all freshwater fish (2000+) and bird (680+) species in the United States. For mammals, acute studies are usually limited to Norway rat or the house mouse. Estuarine/marine testing is usually limited to a crustacean, a mollusc, and a fish. Also, neither reptiles nor amphibians are tested. The risk assessment assumes that avian and reptilian toxicities are similar. The same assumption is used for fish and aquatic amphibians.

In general, categories of acute toxicity ranging from "practically nontoxic" to "very highly toxic" have been established for aquatic organisms (based on LC_{50} and EC_{50} values or limit of solubility), mammals (based on LD_{50} values), avian species (based on LD_{50} and LC_{50} values), and non-target insects (based on LD_{50} values for honey bees) (U.S. EPA 2001). These categories are presented in **Appendix D**.

1. Aquatic Effects: Animals and Plants

No aquatic animal or plant toxicity studies are available for chlorflurenol ME. There were several fish and aquatic invertebrate studies submitted; however they were considered unacceptable due to major deviations from guidelines. Therefore, effects cannot be determined.

2. Terrestrial Effects

The toxicity endpoints used to characterize risks of chlorflurenol ME exposure to birds and mammals are summarized in **Table 6**. Results of all studies in terrestrial organisms are summarized in **Appendix D**, Tables D1 to D3.

Table 6. Chlorflurenol ME Toxicity Reference Values for Terrestrial Organisms.

Exposure Scenario	Species	Scientific Name	Exposure Duration	Toxicity Reference Value	Effects	Reference (Classification)
Mammals						
Acute	Rat	*Rattus norvegicus*	Acute Oral	LD_{50} > 5000 mg/kg body weight	Mortality	43355402 (Acceptable)
Chronic	Rat	*Rattus norvegicus*	Days 6-15 of gestation	Maternal NOAEL = 250 mg/kg/day	body weight gain decrement and nominally decreased food efficiency	45190901 (Acceptable)
				Developmental NOAEL = 250 mg/kg/day	delayed ossification in skull bones	
Birds						
Acute (Dose-based)	Bobwhite Quail	*Colinus virginianus*	Single Oral Dose	LD_{50} >10,000 mg a.i./kg body weight	Mortality	43595401 (Acceptable)
Acute (Dietary-based)	Bobwhite Quail Mallard Duck	*Colinus virginianus* *Anas Platyrhynchos*	8 days	LC_{50} > 5,000 mg a.i./kg diet	Mortality	43623601 (Acceptable) 43623602 (Acceptable)
Chronic	Data gap					
Plants						
Acute	Data gap					
Chronic	Data gap					

a. Terrestrial Animals

Mammalian Species

Results of an acute oral exposure study in laboratory rats (MRID 43355402; Acceptable) show that the LD_{50} for chlorflurenol ME is >5,000 mg a.i./kg body weight; therefore, chlorflurenol ME is categorized as practically nontoxic to mammalian species on an acute oral basis. EFED will use the acute oral LD_{50} of >5,000 mg a.i./kg body weight to evaluate acute dose-based risk to mammalian species.

In a developmental toxicity study (MRID 45190901), chlorfurenol-methyl ester was administered to pregnant Sprague Dawley rats by gavage. The maternal NOAEL was 250 mg/kg bw/day. The maternal LOAEL is 750 mg/kg bw/day based on body weight gain decrement and nominally decreased food efficiency. The developmental NOAEL is 250 mg/kg bw/day. The developmental LOAEL is 750 mg/kg bw/day, based on treatment-related delayed ossification in skull bones [nasal and frontal] in fetuses and litters. In addition a cleft palate was seen in each of two litters

and one diaphragmatic hernia at 1000 mg/kg bw/day and one cleft palate at 750 mg/kg bw/day (cleft palate is rare in rats).

Avian Species

Results of an acute oral exposure study in bobwhite quail (MRID 43595401; Acceptable) indicate that the LD_{50} for chlorflurenol ME is >10,000 mg a.i./kg body weight; therefore, chlorflurenol ME is categorized as practically nontoxic to avian species on an acute oral basis. EFED will use the acute oral LD_{50} of >10,000 mg a.i./kg body weight to evaluate acute dose-based risk to avian species.

Results of subacute dietary studies in mallard ducks (MRID 43623602; Acceptable) and bobwhite quail (MRID 43623601; Acceptable), show that the acute dietary LC_{50} value is >5,000 mg a.i./kg diet, indicating that chlorflurenol ME is practically nontoxic on an acute dietary basis. EFED will use the LC_{50} value of >5,000 mg a.i./kg diet to assess the risk of acute dietary exposure of birds to chlorflurenol ME.

Non-target Insects

No data are available for non-target insects.

b. Terrestrial Plants

No data are available for terrestrial plants.

IV. Risk Characterization

Risk characterization is the integration of exposure and effects characterization to determine the ecological risk from the use of chlorflurenol ME and the likelihood of effects on aquatic life, wildlife, and plants based on varying pesticide-use scenarios. The risk characterization provides an estimation and a description of the risk; articulates risk assessment assumptions, limitations, and uncertainties; synthesizes an overall conclusion; and provides the risk managers with information to make regulatory decisions.

A. Risk Estimation - Integration of Exposure and Effects Data

Results of the exposure modeling and toxicity effects data are used to evaluate the likelihood of adverse ecological effects on non-target species. For the assessment of chlorflurenol ME risks, the risk quotient (RQ) method is used to compare exposure and measured toxicity values (refer to **Appendix E**). Estimated environmental concentrations (EECs) are divided by the most sensitive acute and chronic toxicity values. The RQs are then compared to the Agency's levels of concern (LOCs). These LOCs, summarized in **Appendix E**, are the Agency's interpretive policy and are used to analyze potential risk to non-target organisms and the need to consider regulatory action. These criteria are used to indicate when a pesticide's use as directed on the label has the potential to cause adverse effects on non-target organisms. Details of all RQs are provided in **Appendix F**.

1. Non-target Aquatic Animals and Plants

a. Acute and Chronic Risk to Animals

Acute and chronic risk to fish and invertebrates cannot be evaluated at this time because no toxicity data are available. Risk cannot be precluded.

b. Aquatic Plants

Risk to aquatic plants cannot be evaluated at this time because no toxicity data are available. Risk cannot be precluded.

2. Non-target Terrestrial Animals

a. Acute Risk to Birds and Mammals

Mammalian Species

Definitive acute dose-based RQ values for mammalian receptors could not be derived because all treated animals survived and gained weight in the submitted acute oral toxicity study on mammals (the oral LD_{50} was >5000 mg a.i./kg body weight). Based on these results, chlorflurenol ME TGAI is categorized as practically non-toxic to mammals on an acute oral basis.

Avian Species

Definitive acute dose- and dietary-based RQ values for avian receptors could not be derived because the acute effects data show that chlorflurenol ME is practically non-toxic to birds (LD_{50} >10,000 mg a.i./kg bodyweight and LC_{50} > 5,000 mg a.i./kg diet).

b. Chronic Risk to Birds and Mammals

Mammalian Species

T-REX was used to calculate chronic RQs for mammals using the chronic toxicity value for the rat (MRID 45190901). Dose- and dietary-based chronic RQs for mammals are summarized in Table 7 (also in Table F-4 of Appendix F). Dose-based RQs exceed the chronic risk level (LOC 1) to mammalian species for 15-g and 35-g mammals that forage on short grass, tall grass, and broadleaf plants/small insects (RQ range = 1.14 to 2.90) and for 1000-g mammals that forage on short grass (RQ = 1.33). Dietary-based RQs do not exceed chronic risk (LOC 1) to mammalian species (RQ range = 0.02 to 0.33). These RQs were calculated using upper-bound residues.

Table 7. Dose- and Dietary-based Chronic RQs for Mammals Exposed to Chlorflurenol ME Based on Upper Bound Residues as Calculated by T-REX.

Crop Use (Application Rate)	Body Weight (g)	Mammalian Risk Quotients				
		Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/Pods/Large Insects	Seeds

Table 7. Dose- and Dietary-based Chronic RQs for Mammals Exposed to Chlorflurenol ME Based on Upper Bound Residues as Calculated by T-REX.

Crop Use (Application Rate)	Body Weight (g)	Mammalian Risk Quotients				
		Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/Pods/Large Insects	Seeds
Dose-based Chronic Mammalian RQs [a]						
Turf (3.0 lb a.i./A)	15	**2.90 [c]**	**1.33 [c]**	**1.63 [c]**	0.18	0.04
	35	**2.48 [c]**	**1.14 [c]**	**1.39 [c]**	0.15	0.03
	1,000	**1.33 [c]**	0.61	0.75	0.08	0.02
Dietary-based Chronic Mammalian RQs [b]						
Turf (3.0 lb a.i./A)		0.33	0.15	0.19	0.02	NA

[a] Chronic dose-based RQ = EEC/NOAEL, where EEC values are upper bound residues expressed as equivalent dose (mg a.i./kg body weight) generated from T-REX and the toxicity value is the chronic dose-based NOAEL = 250 mg a.i./kg/day in the rat.
[b] Chronic dietary-based RQ = EEC/NOAEC, where EEC values are upper bound residues expressed as dietary concentrations (mg a.i./kg diet) generated from T-REX and the toxicity value is the chronic dietary-based NOAEC = 5000 mg a.i./kg diet in rats (converted from the rat oral dose study).
[c] RQs are above the LOC for chronic risk (LOC 1).

Avian Species

No toxicity data are available to quantitatively assess chronic risk of chlorflurenol ME exposure to birds. Risk cannot be precluded.

c. Risk to Terrestrial Invertebrates

No toxicity data are available to quantitatively assess risk of chlorflurenol ME exposure to terrestrial invertebrates. Risk cannot be precluded.

3. Non-target Terrestrial and Semi-Aquatic Plants

No toxicity data are available to quantitatively assess risk of chlorflurenol ME exposure to terrestrial plants. However, since chlorflurenol ME is used as an herbicide and as a growth regulator, risk to non-target plants may occur.

B. Risk Description - Interpretation of Direct Effects

There are no data on the usage of chlorflurenol ME; however, the registrant suggests it is used in low volumes. Therefore, even though RQs may indicate risk, exposure may be overestimated due to the low volume applied yearly across the contiguous United States. RQs, and therefore risk, may also be under- or over-estimated due to major uncertainties and gaps in the fate and toxicity data (see section IV.C). In most instances RQs could not be calculated due to data gaps.

1. Risks to Aquatic Organisms

There are no acceptable toxicity studies and little environmental fate data to evaluate potential exposure; therefore, EFED is unable to preclude risk to aquatic animals and plants.

Since chlorflurenol ME is applied as a spray to non-food crops that are ubiquitous (i.e. turf, rights of ways, fence rows), a wide variety of non-target aquatic organisms may come into contact with chlorflurenol ME and its degradates in runoff or spray drift. Based on limited fate data, chlorflurenol ME may leach through the ground quickly decreasing the amount of chlorflurenol ME available for runoff to surface water. However, this study was conducted on sandy loam soils which do not occur throughout the U.S. In addition, this does not account for chlorflurenol ME moving to aquatic systems via spray drift. This study was classified as supplemental due to guideline deviations which increases the amount of uncertainty. Once in the water, the fate cannot be determined. Therefore, if chlorflurenol ME enters water systems, non-target aquatic organisms may be at risk.

2. Risks to Terrestrial Organisms

a. Acute Risk to Birds and Mammals

Based on the submitted acute oral toxicity studies on birds and mammals, chlorflurenol ME is categorized as practically non-toxic to birds and mammals on an acute oral and/or dietary (birds only) basis (LD_{50} > 10000 mg a.i./kg body weight for birds; LC_{50} > 5000 mg a.i./kg diet for birds; LD_{50} > 5000 mg a.i./kg body weight for mammals). No effects were seen in the acute avian studies; however, the mammal study showed rats with hunched posture, lethargy and diarrhea. RQs could potentially exceed acute listed species LOCs unless the actual LD_{50} values are established in laboratory studies to be greater than ~16,715 mg a.i./kg body weight or if the amount available in the environment was lowered below 500 ppm (see **Appendix C** on how to calculate adjusted LD_{50} values, dose-based EECs, and acute dose-based RQs). Therefore, some uncertainty concerning acute oral risk to birds and mammals as a result of exposure to chlorflurenol ME does exist. In addition, the study testing oral toxicity to birds did not state which components were included in the test material. EFED assumes the test material contained all three components which may underestimate risk to birds on an acute oral basis.

b. Chronic Risk to Birds and Mammals

Relative to the use patterns identified in this assessment, exposure of chlorflurenol ME spray application is expected to result in chronic risk to listed and non-listed mammals. As shown in **Table 7**, some dose-based RQs for chronic risk to mammalian species are above the chronic risk LOC (1) for the maximum spray application scenario considered in this risk assessment (RQ range = 0.02 to 2.90). Specifically, chronic dose-based RQs exceed the LOC for mammals feeding on short grass (RQ range = 1.33 to 2.90), tall grass (RQ range = 0.61 to 1.33), and

broadleaf plants/small insects (RQ range = 0.75 to 1.63). The chronic LOC is not exceeded for mammals of any size feeding on fruits/pods/large insects (RQ range = 0.08 to 0.18) or seeds (RQ range = 0.02 to 0.04). Chronic dietary-based RQs do not exceed the chronic LOC for mammals (RQ range = 0.02 to 0.33).

To bound the estimates of risk to mammals resulting from chronic exposure to chlorflurenol ME, RQs using mean Kenaga residue values in addition to upper-bound values were calculated (See Table F-5;**Appendix F**). Using the non-conservative mean residue values, implying that higher predicted residue values are expected half the time, only the RQ for 15g mammals that feed on short grass (RQ = 1.02) exceeds the chronic LOC.

These RQs are based on a developmental study that shows evidence of delayed skull ossification and cleft palates in young rats. These endpoints are not adequate for determining risk to the survival and fecundity of a population. However, without other studies EFED used these data. Therefore, the RQs may not accurately portray chronic risk to mammals. Risk may be under- or over-estimated.

There are uncertainties associated with the RQ values derived with T-REX. In the absence of foliar dissipation half-life data, application interval, and number of yearly applications, the default half-life and "likely" interval and yearly applications were used, which may have overestimated or underestimated the risk to terrestrial species.

The dose-based approach considers the uptake and absorption kinetics of a gavage toxicity study to approximate exposure associated with uptake from a dietary matrix. Toxic response is a function of duration and intensity of exposure. For many compounds a gavage dose represents a very short-term high intensity exposure. Although the dose-based estimates may not reflect reality in that animals do not receive a gavage while feeding, it is possible that a short-duration, high-intensity exposure could occur associated with feeding on an agricultural field since many birds may gorge themselves when food items are available. While the dietary-based estimates may suggest greater "realism," they too suffer from some uncertainties. Primarily, the dietary-based approach assumes that animals in the field are consuming food at a rate similar to that of confined laboratory animals despite the fact that energy content in food items differs between the field and the laboratory as does the energy requirements of wild and captive animals.

No quantitative data are available to characterize chronic risks from application of chlorflurenol ME to birds; therefore, EFED cannot preclude chronic risk to birds.

c. Non-target Terrestrial Invertebrates

No quantitative data are available to characterize risks from application of chlorflurenol ME to terrestrial invertebrates. Since chlorflurenol ME is applied in areas where there may be pollinators and other invertebrates, EFED cannot preclude risk to terrestrial invertebrates.

d. Terrestrial Plants

No quantitative data from guideline studies are available to characterize risks from application of chlorflurenol ME to terrestrial plants. However, since chlorflurenol ME is used as an herbicide and growth regulator, risk to terrestrial plants is assumed.

Chlorflurenol ME has been shown to induce parthenocarpy in cucumbers (Robinson et al. 1971) and interrupt ovule development in muskmelons (Snyder et al. 1983). Robinson et al. (1971) stated that at lower concentrations (10 -20 ppm), parthenocarpy was induced when cucumber plants were treated in the flowering stage; however, at a higher concentration (40 ppm) parthenocarpy was induced two week prior to the flowering stage. In muskmelons, ovule development was halted when chlorflurenol was applied 10 – 12 days before anthesis (Snyder et al. 1983). Since parthenocarpic plants produce fruits with no seeds, sexual reproduction cannot occur. Nontarget plants that come in contact with chlorflurenol ME may also suffer from increased parthenocarpy, severely limiting their ability to reproduce.

3. Review of Incident Data

Incident reports submitted to EPA since approximately 1994 have been tracked by assignment of "incident numbers" in an Incident Data System (IDS), microfiched, and then entered into a second database, the Ecological Incident Information System (EIIS). An effort has also been made to enter information to EIIS on incident reports received prior to establishment of current databases. Incident reports are not received in a consistent format (e.g., states and various labs usually have their own formats), may involve multiple incidents involving multiple chemicals in one report, and may report only part of a given incident investigation (e.g., residues). While some progress has been made in recent years in getting incident reports submitted and entered, there has never been the level of resources assigned to incidents that there has been assigned to the tracking and review of laboratory toxicity studies, for example.

No incident reports involving aquatic or terrestrial exposure to chlorflurenol ME have been reported.

4. Endocrine Effects

Under the Federal Food, Drug and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act (FQPA), EPA is required to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen- and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, and the FFDCA authority to require the wildlife evaluations. As the science develops and the resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). When the appropriate screening and or testing protocols being considered under the Agency's Endocrine Disruptor Screening Program have been developed, chlorflurenol ME may be subjected to additional screening and or testing to better characterize effects related to endocrine disruption.

Results of the submitted developmental study in mammals show exposure to chlorflurenol ME produces adverse effects on reproductive parameters. Observed effects in the submitted

mammalian study include maternal body weight gain decrement and nominally decreased food efficiency, as well as treatment related delayed ossification in skull bones (nasal and frontal) in fetuses and litters. Results of this developmental study suggest that chlorflurenol ME could be a candidate for additional screening and/or testing to better characterize effects related to endocrine disruption.

Chronic exposure studies on the effects of chlorflurenol have not been conducted in aquatic organisms or birds. Therefore, EFED must consider the possibility that chlorflurenol ME may have detrimental effects on the endocrine system in these taxa.

5. Threatened and Endangered Species Concerns

a. Action Area

For listed species assessment purposes, the action area is considered to be the area affected directly or indirectly by the Federal action and not merely the immediate area involved in the action. At the initial screening-level, the risk assessment considers broadly described taxonomic groups and so conservatively assumes that listed species within those broad groups are collocated with the pesticide treatment area. This means that terrestrial plants and wildlife are assumed to be located on or adjacent to the treated site and aquatic organisms are assumed to be located in a surface water body adjacent to the treated site. The assessment also assumes that the listed species are located within an assumed area which has the relatively highest potential exposure to the pesticide, and that exposures are likely to decrease with distance from the treatment area. Section III(A) of this risk assessment presents the pesticide use sites that are used to establish initial collocation of species with treatment areas.

If the assumptions associated with the screening-level action area result in RQs that are below the listed species LOCs, a "no effect" conclusion is made with respect to listed species in that taxa, and no further refinement of the action area is necessary. Furthermore, RQs below the listed species LOCs for a given taxonomic group indicate no concern for indirect effects upon listed species that depend upon the taxonomic group covered by the RQ as a resource. However, in situations where the screening assumptions lead to RQs in excess of the listed species LOCs for a given taxonomic group, a potential for a "may affect" conclusion exists and may be associated with direct effects on listed species belonging to that taxonomic group or may extend to indirect effects upon listed species that depend upon that taxonomic group as a resource. In such cases, additional information on the biology of listed species, the locations of these species, and the locations of use sites could be considered to determine the extent to which screening assumptions regarding an action area apply to a particular listed organism. These subsequent refinement steps could consider how this information would impact the action area for a particular listed organism and may potentially include areas of exposure that are downwind and downstream of the pesticide use site.

b. Taxonomic Groups Potentially at Risk

The Level I screening assessment process for listed species uses the generic taxonomic group-based process to make inferences on direct effect concerns for listed species. The first iteration of reporting the results of the Level I screening is a listing of pesticide use sites and taxonomic groups for which RQ calculations reveal values that meet or exceed the listed species LOCs. In

the majority of cases, the screening-level risk assessment process reports RQ calculations for the following broad taxonomic groupings:

- Birds (also used as surrogate for terrestrial-phase amphibians and reptiles)
- Mammals
- Freshwater fish (also used as a surrogate for aquatic phase amphibians)
- Freshwater invertebrates
- Estuarine/marine fish
- Estuarine/marine invertebrates
- Terrestrial plants
- Algae and aquatic plants

i. Discussion of Risk Quotients

Should estimated exposure levels occur in proximity to listed resources, the available screening-level information suggests a potential concern for direct effects to listed fish (freshwater and estuarine/marine), aquatic invertebrate (freshwater and estuarine/marine), beneficial insect, avian, reptile, amphibian, and mammalian species associated with areas where chlorflurenol ME is used. More specifically, the available screening-level information indicates the following:

Fish and Aquatic Invertebrates

Risk quotients for acute and chronic effects to freshwater and estuarine/marine fish and invertebrates could not be calculated because there are no acceptable toxicity studies.

Aquatic Plants and Algae

Risk quotients for aquatic plants and algae could not be calculated because there are no acceptable toxicity studies.

Birds

Definitive acute dose- or dietary-based RQ values for avian receptors could not be derived because there are no definitive LD_{50} or LC_{50} values.

Risk quotients for chronic effects to birds could not be calculated because there are no acceptable toxicity studies.

Mammals

Definitive acute dose- or dietary-based RQ values for mammalian receptors could not be derived because there are no definitive LD_{50} or LC_{50} values.

The use of chlorflurenol ME under the maximum application rate scenarios results in dose-based RQs for mammals exceeding the chronic risk LOC (1) for exposure via short grass, tall grass, and broadleaf plants/small insects.

Terrestrial Plants

Risk quotients for terrestrial plants could not be calculated because there are no acceptable toxicity studies.

ii. Probit Dose Response Relationship

The probit slope response relationship is evaluated to calculate the chance of an individual event corresponding to the listed species acute LOCs. The analysis uses the EFED spreadsheet IECv1.1.xls, developed by Ed Odenkirchen (6/22/04). It is important to note that the IEC model output can go as low as 1×10^{-16} in estimating the event probability. This cut-off is a limit in the Excel spreadsheet environment and is not to be interpreted as an agreed upon lower bound threshold for concern for individual effects in any given listed species.

If an LD_{50} or LC_{50} has been established for a particular taxonomic group, but information is unavailable to estimate a slope from a study, a default slope assumption of 4.5 is used as per original Agency assumptions of typical slope cited in Urban and Cook (1986). In instances where an LC_{50} or LD_{50} has not been established for a particular taxonomic group, an individual effects probability is not estimated.

Freshwater and Estuarine/Marine Fish and Invertebrates

No toxicity data are available to quantitatively assess individual risk of chlorflurenol ME exposure to aquatic organisms.

Mammals and Birds

Definitive LC_{50}/LD_{50}s are not available to quantitatively assess individual risk of chlorflurenol ME exposure to terrestrial organisms.

c. Indirect Effects Analysis

The Agency acknowledges that pesticides have the potential to exert indirect effects upon the listed organisms by, for example, perturbing forage or prey availability, altering the extent of nesting habitat, and creating gaps in the food chain. In conducting a screen for indirect effects, direct effect LOCs for each taxonomic group are used to make inferences concerning the potential for indirect effects upon listed species that rely upon non-listed organisms in these taxonomic groups as resources critical to their life cycle. Species-specific concerns for chlorflurenol ME indirect effects to listed

organisms will require a determination of the coincidence of chlorflurenol ME use with locations of listed species and the biologically based resources upon which they depend.

The Agency uses the dose response relationship from the toxicity study used for calculating the RQ to estimate the probability of acute effects associated with an exposure equivalent to the EEC (see Probit Dose response Relationship above). In instances where information on the dose response is available, it serves as a guide to establish the need for and extent of additional analysis that may be performed using Services-provided "species profiles" as well as evaluations of the geographical and temporal nature of the exposure to ascertain if a "not likely to adversely affect" determination can be made. The degree to which additional analyses are performed is commensurate with the predicted probability of adverse effects from the comparison of the dose response information with the EECs. The greater the probability that exposures will produce effects on a taxa, the greater the concern for potential indirect effects for listed species dependant upon that taxa, and therefore, the more intensive the analysis on the potential listed species of concern, their locations relative to the use site, and information regarding the use scenario (e.g., timing, frequency, and geographical extent of pesticide application).

Relative to chlorflurenol ME proposed usage, EFED's screening level analysis shows that there is a concern for indirect effects to listed species that may depend upon other taxonomic group for their survival (e.g., invertebrates as a food source for listed fish, etc.). Screening-level RQs for avian species potentially exceed the acute risk LOC and RQs for mammalian species exceed the acute and chronic risk LOC. Therefore, the nature of the toxicological endpoint, Services-provided "species profiles," and further evaluation of the geographical and temporal nature of the exposure will need to be considered to determine if a rationale for a "not likely to adversely affect" determination is possible. Using our best professional judgment, EFED concludes that due to the lack of toxicity data for fish, aquatic invertebrates, aquatic plants, birds (chronic), and terrestrial plants, risk cannot be precluded and there may be a potential concern for indirect effects to the following groups of organisms in the action area:

- Terrestrial plants
- Aquatic plants
- Birds
- Mammals
- Reptiles
- Aquatic Invertebrates
- Fish
- Amphibians
- Terrestrial Insects

For listed species that may potentially be indirectly affected by the Federal action, see **Appendix G** (Locates run).

d. Critical Habitat

In the evaluation of pesticide effects on designated critical habitat, consideration is given to the physical and biological features (constituent elements) of a critical habitat identified by the U.S. Fish and Wildlife and National Marine Fisheries Services as essential to the conservation of a listed species and which may require special management considerations or protection. The evaluation of impacts for a screening-level pesticide risk assessment focuses on the biological features that are constituent elements and is accomplished using the screening-level taxonomic analysis (risk quotients, RQs) and listed species levels of concern (LOCs) that are used to evaluate direct and indirect effects to listed organisms.

The screening-level risk assessment has identified potential concerns for indirect effects on listed species for those organisms dependent upon aquatic fish and invertebrates (including benthic animals), birds, reptiles, and mammals. In light of the potential for indirect effects, the next step for EPA and the Service(s) is to identify which listed species and critical habitat are potentially implicated. Analytically, the identification of such species and critical habitat can occur in either of two ways. First, the agencies could determine whether the action area overlaps critical habitat or the occupied range of any listed species. If so, EPA would examine whether the pesticide's potential impacts on non-listed species would affect the listed species indirectly, or directly affect a constituent element of the critical habitat. Alternatively, the agencies could determine which listed species depend on biological resources, or have constituent elements that fall into the taxa that may be directly or indirectly impacted by the pesticide. Then EPA would determine whether use of the pesticide overlaps the critical habitat or the occupied range of those listed species. At present, the information reviewed by EPA does not permit use of either analytical approach to make a definitive identification of species that are potentially impacted indirectly or critical habitats that is potentially impacted directly by the use of the pesticide. EPA and the Service(s) are working together to conduct the necessary analysis.

This screening-level risk assessment for critical habitat provides a listing of potential biological features that, if they are constituent elements of one or more critical habitats, would be of potential concern. These correspond to the taxa identified above as being of potential concern for indirect effects and include the following: terrestrial plants, aquatic plants, reptiles, birds, mammals, fish and aquatic invertebrates, terrestrial insects, and amphibians. This list should serve as an initial step in problem formulation for further assessment of critical habitat impacts outlined above, should additional work be necessary.

Table 8 provides a list of the taxa that may be directly or indirectly affected.

Table 8. Listed species risks associated with direct or indirect effects due to applications of chlorflurenol for turf use.

Listed Taxon	Direct Effects	Indirect Effects

Terrestrial and semi-aquatic plants - monocots	Yes [a]	Yes
Terrestrial and semi-aquatic plants – dicots	Yes [a]	Yes
Insects	Yes [a]	Yes
Birds	Acute – Yes [c]; Chronic – Yes [a]	Yes
Terrestrial phase amphibians	Yes [a]	Yes
Reptiles	Acute – Yes [c]; Chronic – Yes [a]	Yes
Mammals	Acute – Yes [c]; Chronic – Yes [b]	Yes
Aquatic vascular plants	Yes [a]	Yes
Freshwater fish	Yes [a]	Yes
Aquatic phase amphibians	Yes [a]	Yes
Freshwater crustaceans	Yes [a]	Yes
Mollusks	Yes [a]	Yes
Marine/estuarine fish	Yes [a]	Yes
Marine/estuarine crustaceans	Yes [a]	Yes

[a] We cannot preclude risk due to lack of data.
[b] The reported RQ values are above the chronic LOC (1.0) for species that feed on short grass, tall grass, and broadleaf plants/small insects (RQ range = 0.02 to 2.90).
[c] RQs could potentially exceed acute listed species LOCs unless the actual LD_{50} values are established in laboratory studies to be greater than ~16,715 mg a.i./kg body weight or if the amount available in the environment was lowered below 500 ppm

e. Co-occurrence Analysis

The goal of the analysis for co-location is to determine whether sites of pesticide use are geographically associated with known locations of listed species. At the screening level, this analysis is accomplished using the LOCATES database. The database uses location information for listed species at the county level and compares it to agricultural census data for crop production at the same county level of resolution. The product is a listing of federally listed species that are located within counties known to produce the crop upon which the pesticide will be used. Because the Level I screening assessment considers **both direct and indirect effects** across generic taxonomic groupings, it is **not possible to exclude any taxonomic group from a LOCATES database run** for a screening risk assessment. Given the extent of potential chlorflurenol ME usage across the U.S. and the expected large number of listed species that are likely to occur in counties where chlorflurenol ME is used, a list of endangered/threatened species and crop acreage at the county level for the taxonomic groups and crops of concern is not included in this phase of the risk assessment process.

Given that the potential extent of chlorflurenol ME usage includes every state, and that all taxonomic groups are included in the initial LOCATES run for a screening-level risk assessment, **Appendix G** provides the entire list of endangered/threatened species at the state level. The registrant must provide information on the proximity of federally listed birds, fish, mammals, amphibians, crustaceans, reptiles, arachnids, insects, plants, snails, and clams to the chlorflurenol ME use sites. This requirement may be satisfied in one of three ways: 1) having membership in the FIFRA Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2); 2) citing FIFRA Endangered Species Task Force data; or 3) independently producing these data, provided the information is of sufficient quality to meet FIFRA requirements. The information will be used by the OPP Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

C. Description of Assumptions, Limitations, Uncertainties, Strengths and Data Gaps

This risk assessment relies on best available estimates of environmental fate and physicochemical properties, maximum application rate of chlorflurenol ME, maximum number of applications, and the shortest interval between applications. However, several uncertainties and model limitations are noted and should be considered in interpreting the results of this risk assessment.

1. Assumptions, Limitations, Uncertainties, Strengths and Data Gaps Related to Exposure For All Taxa

There are a number of areas of uncertainty in the aquatic and terrestrial risk assessments. There are no valid toxicity data for any aquatic species, birds (chronic only), terrestrial invertebrates, and plants. The toxicity assessment for terrestrial animals is limited by the number of species tested in the available toxicity studies. Use of toxicity data on representative species does not provide information on the potential variability in susceptibility to acute and chronic exposures.

2. Assumptions, Limitations, Uncertainties, Strengths and Data Gaps Related to Exposure For Aquatic Species

The registrant has submitted three studies to support the environmental fate data requirements; however, these studies were considered either supplemental or unacceptable (see reasons below). As a result, the uncertainty analysis could not be performed with confidence.

Guideline 161-1: The study was conducted at pHs 3, 6 and 9 rather than pHs 5, 7 and 9 as required in Subdivision N Guidelines. This study was determined to be supplemental. The hydrolysis data requirements have not been fulfilled. A new study including pH 7 is required.

Guideline 162-1: The study was conducted outdoors in the summer where the environmental conditions, soil aerobicity, microbial viability, and soil moisture were neither controlled nor reported. Subdivision N Guidelines require that the study be conducted in the dark at 25 ± 1°C. This study was determined to be unacceptable. The aerobic soil metabolism data requirements have not been fulfilled. A new study using four soils is required.

Guideline 163-1: Only one test soil type was used in the adsorption study and it could not be determined if this German soil was comparable to soils found in typical use areas in the United States. Subdivision N guidelines specify that four different soil types should be used. This study was determined to be supplemental. The adsorption/desorption data requirements have not been fulfilled. A new study including three soils is required.

3. Assumptions, Limitations, Uncertainties, Strengths and Data Gaps Related to Exposure For Terrestrial Species

The dataset available to support the terrestrial exposure assessment for chlorflurenol ME is substantially incomplete. Application interval, number of applications per year, and a foliar dissipation study, which are input variables for modeling of risks to birds and mammals (i.e., T-REX), are lacking. The terrestrial modeling for chlorflurenol ME was conducted using "likely" application intervals and yearly applications, as derived by HED. Also a default foliar dissipation half-life value of 35 days, based on the work of Willis and McDowell (1987), was used. Therefore, if these values are lower or higher terrestrial EECs may be overestimated or underestimated.

a. Location of Wildlife Species

For screening terrestrial risk assessments, a generic bird or mammal is assumed to occupy either the treated field or adjacent areas receiving the pesticide at a rate commensurate with the treatment rate on the target field. This assumption may lead to an overestimation of exposure to species that

do not occupy the treated field. The actual habitat requirements of any particular terrestrial species are not considered, and it is assumed that species occupy, exclusively and permanently, the treated area being modeled. This assumption leads to a maximum level of exposure in the risk assessment.

b. Routes of Exposure

Screening-level risk assessments for spray applications of pesticides consider dietary exposure alone, and assume that 100% of the diet is relegated to single food types foraged only from treated fields. These assumptions are likely to be conservative for many species and will tend to overestimate potential risks. The assumption of 100% diet from a treated area may be realistic for acute exposures, but long-term exposures modeled as single food types composed entirely of material from a treated field is uncertain. Other routes of exposure, not considered in this assessment, are discussed below.

Incidental Soil Ingestion Exposure

This risk assessment does not consider incidental soil ingestion. Available data suggest that up to 15% of the diet can consist of incidentally ingested soil depending on the species and feeding strategy (Beyer et al. 1994). A simple first approximation of soil concentration of pesticide from spray application shows that ingestion of soil at an incidental rate of up to 15% of the diet would not increase dietary exposure.

Inhalation Exposure

The screening risk assessment does not consider inhalation exposure. Such exposure may occur through three potential sources: (1) spray material in droplet form at the time of application (2) vapor phase pesticide volatilizing from treated surfaces, and (3) airborne particulate (soil, vegetative material, and pesticide dusts).

Available data suggest that inhalation exposure at the time of application is not an appreciable route of exposure for birds. According to research on mallards and bobwhite quail, respirable particle size in birds (particles reaching the lung) is limited to a maximum diameter of 2 to 5 microns. Theoretically, inhalation of pesticide active ingredient in the vapor phase may be another source of exposure for some pesticides under some exposure situations.

The impact from exposure to dusts contaminated with the pesticide cannot be assessed generically as partitioning issues related to application site soils and chemical properties render the exposure potential from this route highly situation-specific.

Dermal Exposure

The screening assessment does not consider dermal exposure, except as it is indirectly included in calculations of RQs based on lethal doses per unit of pesticide treated area. Dermal exposure may occur through three potential sources: (1) direct application of spray to terrestrial wildlife in the treated area or within the drift footprint, (2) incidental contact with contaminated vegetation, or (3) contact with contaminated water or soil.

The available measured data related to wildlife dermal contact with pesticides are extremely limited. The Agency is actively pursuing modeling techniques to account for dermal exposure via direct application of spray and by incidental contact with vegetation.

Drinking Water Exposure

Drinking water exposure to a pesticide active ingredient may be the result of consumption of surface water or consumption of the pesticide in dew or other water on the surfaces of treated vegetation. For pesticide active ingredients with a potential to dissolve in runoff, puddles on the treated field may contain the chemical.

c. Incidental Pesticide Releases Associated with Use

This risk assessment is based on the assumption that the entire treatment area is subject to chlorflurenol ME application at the rates specified on the label. In reality, there is the potential for uneven application of chlorflurenol ME through such plausible incidents as changes in calibration of application equipment, spillage, and localized releases at specific areas of the treated field that are associated with specifics of the type of application equipment used (e.g., increased application at turnabouts when using older ground application equipment).

d. Residue Levels Selection

As discussed earlier in the exposure section of this document, the Agency relies on the work of Hoerger and Kenaga (1972) and Fletcher et al. (1994) for setting the assumed pesticide residues in wildlife dietary items. The Agency believes that these residue assumptions reflect a realistic upper-bound residue estimate, although the degree to which this assumption reflects a specific percentile estimate is difficult to quantify. It is important to note that the field measurement efforts used to develop the Fletcher estimates of exposure involve highly varied sampling techniques. It is entirely possible that much of these data reflect residues averaged over entire above ground plants in the case of grass and forage sampling. Depending upon a specific wildlife species' foraging habits, whole aboveground plant samples may either underestimate or overestimate actual exposure.

e. Dietary Intake - The Differences Between Laboratory and Field Conditions

The acute and chronic characterization of risk rely on comparisons of wildlife dietary residues with LC_{50} or NOAEC values expressed in concentrations of pesticides in laboratory feed. These comparisons assume that ingestion of food items in the field occurs at rates commensurate with those in the laboratory. Although the screening assessment process adjusts dry-weight estimates of food intake to reflect the increased mass in fresh-

weight wildlife food intake estimates, it does not allow for gross energy and assimilative efficiency differences between wildlife food items and laboratory feed.

On gross energy content alone, direct comparison of a laboratory dietary concentration- based effects threshold to a fresh-weight pesticide residue estimate would result in an underestimation of field exposure by food consumption by a factor of 1.25 - 2.5 for most food items. Only for seeds would the direct comparison of dietary threshold to residue estimate lead to an overestimate of exposure.

Differences in assimilative efficiency between laboratory and wild diets suggest that current screening assessment methods do not account for a potentially important aspect of food requirements. Depending upon species and dietary matrix, bird assimilation of wild diet energy ranges from 23 - 80%, and mammal's assimilation ranges from 41 - 85% (U.S. Environmental Protection Agency, 1993). If it is assumed that laboratory chow is formulated to maximize assimilative efficiency (e.g., a value of 85%), a potential for underestimation of exposure may exist by assuming that consumption of food in the wild is comparable with consumption during laboratory testing. In the screening process, exposure may be underestimated because metabolic rates are not related to food consumption.

Finally, the screening procedure does not account for situations where the feeding rate may be above or below requirements to meet free living metabolic requirements. Gorging behavior is a possibility under some specific wildlife scenarios (e.g., bird migration) where the food intake rate may be greatly increased. Kirkwood (1983) has suggested that an upper-bound limit to this behavior might be the typical intake rate multiplied by a factor of 5.

In contrast, there is the potential for avoidance, operationally defined as animals responding to the presence of noxious chemicals in their food by reducing consumption of treated dietary elements. This response is seen in nature where herbivores avoid plant secondary compounds. However, reduced food intake, particularly over an extended period, could result in reduced survival or reproductive output.

4. Assumptions, Limitations, Uncertainties, Strengths and Data Gaps Related to Effects Assessment

The dataset available to support the terrestrial and aquatic effects assessment for chlorflurenol ME is incomplete. Data gaps, uncertainties, and limitations are summarized as follows:

- Guidelines 72-1, 72-2, 72-3, 72-4: Acute and chronic data for freshwater and estuarine/marine fish and invertebrates are not available; therefore, risk could not be assessed.
- Guideline 71-4: Avian reproduction studies are not available; therefore, risk could not be assessed.

- Guideline 123-1, 123-2: Terrestrial plant seedling emergence and vegetative vigor studies are not available. In addition, aquatic plant growth studies are not available; therefore risk could not be assessed. Since chlorflurenol ME is used as an herbicide and growth regulator, toxicity data on non-target plants are necessary to estimate risk.
- Guideline 141-1: Data for honey bee acute contact toxicity are not available; therefore, risk could not be assessed.
- Acute oral and dietary toxicity studies in birds and acute oral toxicity studies in mammals failed to establish definitive acute LD_{50}/LC_{50} values (i.e., the LC_{50} was expressed as "greater than" the highest dietary concentration tested); thus, acute RQ could not be calculated.
- The study testing oral toxicity to birds did not state which components were included in the test material. EFED assumes the test material contained all three components which may underestimate risk to birds on an acute oral basis if in fact the test material only contained one of the three components.
- The mammalian chronic RQs are based on a developmental study that shows evidence of delayed skull ossification and cleft palates in young rats. These endpoints are not adequate for determining risk to the survival and fecundity of a population. However, without other studies EFED used these data. Therefore, the RQs may not accurately portray chronic risk to mammals. Risk may be under- or over-estimated.
- Application interval and number of applications per year are not indicated on the label. For multiple application scenarios the T-REX model requires both of these parameters in order to estimate exposure to terrestrial organisms. In the absence of these numbers an application interval of 28 days and 8 applications per year were used as derived by HED (**Appendix B**). HED used information provided on the labels along with best professional judgment of the crop/weed growth cycles, pest pressure timing, etc. to determine the application interval and yearly number of applications. EFED used the HED data to maintain consistency between EFED and HED. Since these numbers are considered "likely" applications per year, risk to terrestrial organisms may be underestimated.

a. Age Class and Sensitivity of Effects Thresholds

It is generally recognized that test organism age may have a significant impact on the observed sensitivity to a toxicant. The screening risk assessment acute toxicity data for fish are collected on juvenile fish between 0.1 and 5 grams. Aquatic invertebrate acute testing is performed on recommended immature age classes (*e.g.*, first instar for daphnids, second instar for amphipods, stoneflies and mayflies, and third instar for midges). Similarly, acute dietary testing with birds is also performed on juveniles, with mallard being 5-10 days old and quail at 10-14 days of age.

Testing of juveniles may overestimate the toxicity of direct acting pesticides in adults. As juvenile organisms do not have fully developed metabolic systems, they may not possess the ability to transform and detoxify xenobiotics equivalent to the older/adult organism. The screening risk assessment has no current provisions for a generally applied method that accounts for this uncertainty. In so far as the available toxicity data may provide ranges of sensitivity information with respect to age class, the risk assessment uses the most sensitive life-stage information as the conservative screening endpoint.

b. Lack of Effects Data for Amphibians and Reptiles

Currently, toxicity studies on amphibians and reptiles are not required for pesticide registration. Since these data are lacking, the Agency uses fish as surrogates for aquatic phase amphibians and birds as surrogates for terrestrial phase amphibians and reptiles. These surrogates are thought to be reflective of or protective (more sensitive) of herpetofauna. Amphibians are characterized by a permeable skin. The most important route of exposure for aquatic amphibians would likely be the dermal route. Using freshwater fish may be suitable surrogates since exposure would likely be surface area dependent and the gill surface of many fish is a fairly large surface area. Also, both fish and amphibians are ectothermic so metabolic rates and demands would likely be similar. For terrestrial species, however, the difference between amphibians and birds and reptiles and birds is quite large. Terrestrial amphibians and reptiles are both ectothermic while birds are endothermic; birds have a higher basal metabolic rate required to maintain constant body temperature. The higher metabolic demands of birds may be predispose birds to higher relative exposures. However, this does not address any potential differences in toxicity. To date, there are few controlled studies on reptile species that could be used to compare to similar studies on birds. *A priori*, there is no strong reason to think that one taxon is more or less sensitive than another. Therefore, it was assumed that the use of surrogate effects data is sufficiently conservative to apply the broad of species within taxonomic groups. If other species are more or less sensitive to chlorflurenol ME than the surrogates, risks may be under- or overestimated, respectively. The Agency is not limited to a base set of surrogate toxicity information in establishing risk assessment conclusions. The Agency also considers toxicity data on non-standard test species when available. Further research is required to determine whether, in general, reptiles and terrestrial-phase amphibians are suitably represented by bird species in assessing risks for chlorflurenol ME.

c. Use of the Most Sensitive Species Tested

Although the screening risk assessment relies on a selected toxicity endpoint from the most sensitive species tested, it does not necessarily mean that the selected toxicity endpoints reflect sensitivity of the most sensitive species existing in a given environment. The relative position of the most sensitive species tested in the distribution of all possible species is a function of the overall variability among species to a particular chemical. The relationship between the sensitivity of the most sensitive tested species versus wild species (including listed species) is unknown and a source of significant uncertainty. In addition, in the case of listed species, there is uncertainty regarding the relationship of the listed species' sensitivity and the most sensitive species tested.

The use of laboratory species has historically been driven by availability and ease of maintenance. A widespread comparison of species is lacking, however, even variation within a species can be quite high. For example, in this assessment, acute studies on honey bees yielded different values.

5. Assumptions, Limitations, Uncertainties, Strengths and Data Gaps Related to the Acute and Chronic LOCs

The risk characterization section of the assessment document includes an evaluation of the potential for individual effects to listed species at an exposure level equivalent to the LOC. This evaluation is based on the median lethal dose estimate and dose/response relationship established for the effects study corresponding to each taxonomic group for which the LOCs are exceeded. The slope of the probit-dose response is used to generate a

probability of individual effects near the low end tail of the curve. Predictions based on low probability events are by nature highly uncertain. Moreover, for this assessment the dose-response curve representing a given taxon is generated from one study using one species. It is likely that the resulting dose-response relationship does not represent the response of all species within a taxon. Calculating the probability of individual effects at the lower and upper bounds of the slope is designed to address this source of uncertainty but the extent to which this captures the variability within a taxon is unknown. In some cases, a probit dose-response relationship cannot be calculated. In these instances, event probabilities are calculated based on a default slope assumption of 4.5 with upper and lower confidence intervals of 2 and 9 (Urban and Cook, 1986).

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