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Aminocyclopyrachlor

Human Health and Ecological Risk Assessment

FINAL REPORT

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
APHIS	Animal and Plant Health Inspection Service
ASAE	American Society of Agricultural Engineers
ATV	all terrain vehicle
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
CEQ	Council on Environmental Quality
ChE	cholinesterase
CI	confidence interval
cm	centimeter
DAA	days after application
DAT	days after treatment
DER	data evaluation record
d.f.	degrees of freedom
DT_{50}	degradation half-time
DuPont™	E. I. du Pont de Nemours and Company
dw	dry weight
EC_x	effective concentration causing X% inhibition of a process
EC_{25}	effective concentration causing 25% inhibition of a process
EC_{50}	effective concentration causing 50% inhibition of a process
ECOSAR	Ecological Structure-Activity Relationship Model
EHE	2-ethylhexyl ester
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ER_x	effective application rate for X% response
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FOB	Functional Observation Battery
FOIA	Freedom of Information Act
FQPA	Food Quality Protection Act
g	gram
GLP	Good Laboratory Practices
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter

lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
m	meter
M	male
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOE	margin of exposure
MOI	most exposed individual
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MW	molecular weight
NAWQA	National Ambient Water Quality Assessment
NCOD	National Drinking Water Contaminant Occurrence Database
NEPA	National Environmental Policy Act
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
NTP	National Toxicology Program
OECD	Organization for Economic Cooperation and Development (Europe)
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
Pa	Pascal
PBPK	physiologically-based kinetic
PPE	personal protective equipment
ppm	parts per million
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
SMILES	Simplified Molecular-Input Line-Entry System
TEP	typical end-use product
UF	uncertainty factor
ULV	ultra-low volume
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
VMD	volume median diameter
WCR	water contamination rate

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

To convert ...	Into ...	Multiply by ...
acres	hectares (ha)	0.4047
acres	square meters (m^2)	4,047
atmospheres	millimeters of mercury	760
centigrade	Fahrenheit	1.8 C+32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	0.556 F-17.8
feet per second (ft/sec)	miles/hour (mi/hr)	0.6818
gallons (gal)	liters (L)	3.785
gallons per acre (gal/acre)	liters per hectare (L/ha)	9.34
grams (g)	ounces, (oz)	0.03527
grams (g)	pounds, (oz)	0.002205
hectares (ha)	acres	2.471
inches (in)	centimeters (cm)	2.540
kilograms (kg)	ounces, (oz)	35.274
kilograms (kg)	pounds, (lb)	2.2046
kilograms per hectare (hg/ha)	pounds per acre (lb/acre)	0.892
kilometers (km)	miles (mi)	0.6214
liters (L)	cubic centimeters (cm^3)	1,000
liters (L)	gallons (gal)	0.2642
liters (L)	ounces, fluid (oz)	33.814
miles (mi)	kilometers (km)	1.609
miles per hour (mi/hr)	cm/sec	44.70
milligrams (mg)	ounces (oz)	0.000035
meters (m)	feet	3.281
ounces (oz)	grams (g)	28.3495
ounces per acre (oz/acre)	grams per hectare (g/ha)	70.1
ounces per acre (oz/acre)	kilograms per hectare (kg/ha)	0.0701
ounces fluid	cubic centimeters (cm^3)	29.5735
pounds (lb)	grams (g)	453.6
pounds (lb)	kilograms (kg)	0.4536
pounds per acre (lb/acre)	kilograms per hectare (kg/ha)	1.121
pounds per acre (lb/acre)	mg/square meter (mg/m^2)	112.1
pounds per acre (lb/acre)	µg/square centimeter ($\mu g/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

Note: All references to pounds and ounces refer to avoirdupois weights unless otherwise specified.

CONVERSION OF SCIENTIFIC NOTATION

Scientific Notation	Decimal Equivalent	Verbal Expression
$1 \cdot 10^{-10}$	0.0000000001	One in ten billion
$1 \cdot 10^{-9}$	0.000000001	One in one billion
$1 \cdot 10^{-8}$	0.00000001	One in one hundred million
$1 \cdot 10^{-7}$	0.0000001	One in ten million
$1 \cdot 10^{-6}$	0.000001	One in one million
$1 \cdot 10^{-5}$	0.00001	One in one hundred thousand
$1 \cdot 10^{-4}$	0.0001	One in ten thousand
$1 \cdot 10^{-3}$	0.001	One in one thousand
$1 \cdot 10^{-2}$	0.01	One in one hundred
$1 \cdot 10^{-1}$	0.1	One in ten
$1 \cdot 10^{0}$	1	One
$1 \cdot 10^{1}$	10	Ten
$1 \cdot 10^{2}$	100	One hundred
$1 \cdot 10^{3}$	1,000	One thousand
$1 \cdot 10^{4}$	10,000	Ten thousand
$1 \cdot 10^{5}$	100,000	One hundred thousand
$1 \cdot 10^{6}$	1,000,000	One million
$1 \cdot 10^{7}$	10,000,000	Ten million
$1 \cdot 10^{8}$	100,000,000	One hundred million
$1 \cdot 10^{9}$	1,000,000,000	One billion
$1 \cdot 10^{10}$	10,000,000,000	Ten billion

EXECUTIVE SUMMARY

This document provides human health and ecological risk assessments regarding the environmental consequences of using aminocyclopyrachlor in Forest Service vegetation management programs. Aminocyclopyrachlor is a new pyrimidine carboxylic acid herbicide developed by DuPont™, for which the U.S. EPA granted a conditional registration for the control of broadleaf weeds and woody vegetation. As detailed in Section 4.1.2.5 (Hazard Identification for Terrestrial Plants), the U.S. EPA/OPP suspended the sale and distribution of one formulation of aminocyclopyrachlor (i.e., Imprelis®) because of reports of damage to conifers, particularly Norway spruce and white pine.

The current risk assessment is concerned with the reports of damage to conifers following applications of Imprelis® to turf. While Imprelis® will not be used in Forest Service programs, the incidents of conifer damage following applications of Imprelis® to turf raise concerns that damage to conifers might occur in applications of other aminocyclopyrachlor formulations. The reasons for the atypically frequent and severe reports of damage to conifers following applications of Imprelis® to turf are not clear. The revised product labels for formulations of aminocyclopyrachlor that may be used in Forest Service programs contain cautionary language concerning the potential for runoff following applications of aminocyclopyrachlor. Based on the Gleams-Driver modeling conducted as part of the current Forest Service risk assessment, damage due to runoff losses could occur under conditions that that are conducive to high rates of runoff (i.e., soils saturated with water or soils such as hard clay with very low porosity and sites in which runoff would occur from a relatively large treated area to a smaller area). At sites with low rainfall and/or well-drained soils, damage to conifers or other tress and shrubs due to runoff would not be anticipated.

There is no basis for asserting that applications of aminocyclopyrachlor will lead to significant or even detectable signs of toxicity in humans, terrestrial wildlife, aquatic animals, or aquatic algae. Based on a single efficacy study in which aminocyclopyrachlor was evaluated as an aquatic herbicide, damage to sensitive species of nontarget aquatic macrophytes cannot be ruled out.

Terrestrial applications of any effective herbicide are likely to alter vegetation within the treatment area, which may lead to secondary effects on terrestrial or aquatic animals as well as nontarget plants. While these concerns are acknowledged, they are common to any effective method for vegetation management, including mechanical methods that do not involve herbicide use.

1. INTRODUCTION

1.1. Chemical Specific Information

This document provides human health and ecological risk assessments regarding the environmental consequences of using aminocyclopyrachlor in Forest Service vegetation management programs. Aminocyclopyrachlor is a new herbicide for which no previous risk assessment was conducted for the Forest Service.

In the preparation of this risk assessment, literature searches were conducted in TOXLINE and AGRICOLA. To determine the amount of information in the unpublished studies held by the U.S. EPA's Office of Pesticide Programs (U.S. EPA/OPP), the ECOTOX database maintained by the Environmental Fate and Effects Division of the U.S. EPA/OPP (http://cfpub.epa.gov/ecotox/) and the E-Docket (http://www.regulations.gov) were searched. Additional literature searches were conducted using standard reference sources on the internet (e.g., www.Greenbook.com, www.CMDS.net, on other label sources, and the PAN Pesticide Database (http://www.pesticideinfo.org/).

Most of the pertinent mammalian toxicology and ecotoxicology studies are unpublished reports submitted to the U.S. EPA as part of the registration process for aminocyclopyrachlor. No Data Evaluation Records (DERs) or other summaries of the registrant-submitted studies are currently available at the U.S. EPA's web site for cleared reviews (http://www.epa.gov/pesticides/foia/reviews.htm), which is not unusual for a new pesticide. A Freedom of Information Act (FOIA) request was submitted to the U.S. EPA/OPP for all available DERs as well as a current list of all registrant-submitted studies (HQ-FOI-00749-12 dated February 11, 2012). In response to the FOIA, a complete list of the registrant-submitted studies was received on March 8, 2012. This list is provided in Attachment 3, sorted by guideline number and the EPA Master Record Identification (MRID) number.

As discussed in Section 2, U.S. EPA/OPP registered aminocyclopyrachlor for use on non-crop areas, sod farms, turf, and residential lawns (U.S. EPA/OPP 2010k), and numerous documents related to the registration process are available in the E-Docket: www.regulations.com, Docket ID -HQ-OPP- 2009-0789). A complete list of these documents is included in Section 5. The data most relevant to the current Forest Service risk assessment are covered in the EPA human health risk assessment (U.S. EPA-OPP 2010a) and in the EPA ecological risk assessment (U.S. EPA/OPP 2010b). Another important document is the "Stop Sale, Use, or Removal Order" issued by the U.S. EPA/OPP (2011f) for Imprelis®, a formulation of the potassium salt of aminocyclopyrachlor labeled for broadleaf weed control in lawns. The withdrawal of the registration of Imprelis® relates to reports of adverse effects on trees, as discussed in Section 4.1.2.5.

E. I. du Pont de Nemours and Company (DuPont™) is the sole registrant for aminocyclopyrachlor. In the conduct of the current risk assessment, SERA contacted DuPont™ to request relevant information on aminocyclopyrachlor. The DuPont™ registration manager for aminocyclopyrachlor, Ms. Rebecca M. Ashley, kindly provided 75 U.S. EPA Data Evaluation Records (DERs), 4 summaries of studies formatted for submission to the Organization for Economic Cooperation and Development (OECD), 6 full studies, and one additional summary of

a recent subchronic bioassay on a degradate of aminocyclopyrachlor. These studies are identified in Section 5 (References) as DuPont™01 (DERs), DuPont™02 (OECD study summaries and full studies), and DuPont™03 (study summary on aminocyclopyrachlor degradate).

1.2. Workbooks and Other Attachments

As with all Forest Service risk assessments, almost no risk estimates presented in this document are given as single numbers. Usually, risk is expressed as a central estimate and a range, which is sometimes quite large. The risk assessment includes numerous calculations to encompass the many types of exposure as well as the uncertainties associated with the analyses. The relatively simple calculations are included in the body of the document; whereas, the more cumbersome calculations involving exposure scenarios are included in the EXCEL workbooks (sets of EXCEL worksheets) attached to this risk assessment. The workbooks provide the detail for the exposure and risk estimates cited in the body of the current risk assessment. The documentation for these workbooks is available in SERA (2011b).

Two EXCEL workbooks accompany the current risk assessment. Attachment 1 is the EXCEL workbook for aminocyclopyrachlor. This workbook contains the details for standard exposure scenarios used in most Forest Service risk assessments as discussed in Section 3.2 for human health and Section 4.2 for ecological effects. Attachment 2 is the EXCEL workbook for cyclopropanecarboxylic acid, an environmental degradate of aminocyclopyrachlor. As detailed in Section 3.1.15.1, the U.S. EPA/OPP (2010a) has identified cyclopropanecarboxylic acid as a degradate of concern. As discussed by U.S. EPA/OPP (2010a) and detailed further in Section 3.2.3.4.3.1.3 of the current risk assessment, exposures to cyclopropanecarboxylic acid will occur primarily as a result of the aqueous photolysis of aminocyclopyrachlor. Consequently, Attachment 2 contains only the subset of standard exposure scenarios that are associated with contaminated surface water.

The EXCEL workbooks are an integral part of the risk assessment. The worksheets contained in these workbooks are designed to isolate the numerous calculations from the risk assessment narrative. In general, all calculations of exposure scenarios and quantitative risk characterizations are derived and contained in the worksheets. In these worksheets as well as in the text of this risk assessment, the hazard quotient (HQ) is the ratio of the estimated exposure to a toxicity value, typically a no-adverse-effect level or concentration (i.e., NOAEL or NOAEC). Both the rationale for the calculations and the interpretation of the HQs are contained in this risk assessment document.

In addition to the two EXCEL workbooks, Attachment 3 to the current risk assessment contains a bibliography of studies submitted to the U.S. EPA/OPP in support of the registration of aminocyclopyrachlor. Because aminocyclopyrachlor is a new pesticide, most of the information relevant to the current risk assessment comes from studies submitted by DuPont™ to the U.S. EPA. While Data Evaluation Records, other study summaries, and some full studies relating to the toxicology and environmental fate of aminocyclopyrachlor were available for the conduct of the current risk assessment, other types of studies (e.g., product chemistry, impurities, inerts) were not available for the current risk assessment but these studies have been reviewed by the U.S. EPA/OPP. Attachment 3 is referenced in the current risk assessment to better document the studies that U.S. EPA/OPP has reviewed.

1.3. General Information

This document has four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species. Each of the two risk assessment chapters has four major sections, including an identification of the hazards, an assessment of potential exposure to this compound, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure.

This is a technical support document which addresses some specialized technical areas. Nevertheless, an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2011a). The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. The information presented in the appendices and the discussions in chapters 2, 3, and 4 of the risk assessment are intended to be detailed enough to support a review of the risk analyses.

The Forest Service will update this risk assessment at some future date, and welcomes input from the general public and other interested parties on the selection of studies included in the risk assessment. The recommendations for including additional studies, however, are helpful only if they specify why and/or how the new or not previously included information is likely to alter the conclusions reached in the risk assessments.

2. PROGRAM DESCRIPTION

2.1. Overview

Aminocyclopyrachlor is a new herbicide developed by DuPont™, which the U.S. EPA granted a conditional registration for the control of broadleaf weeds and woody vegetation. Because aminocyclopyrachlor is effective in controlling leafy spurge (*Euphorbia esula*), the Forest Service anticipates its use in vegetation management programs. Based on the distribution of leafy spurge, the Forest Service may use aminocyclopyrachlor in most areas of the United States, except the southeast. The greatest use of aminocyclopyrachlor is anticipated in northwestern states, particularly Idaho, Wyoming, Montana, and North Dakota. Aminocyclopyrachlor is labeled for numerous weeds, particularly terrestrial and riparian invasive and noxious weeds. Although the stated intention of the Forest Service is to use aminocyclopyrachlor primarily to control leafy spurge, the current risk assessment covers all target species for which the herbicide is labeled.

The active ingredients in aminocyclopyrachlor formulations include either the acid form, or the potassium salt, or the methyl ester. DuPont™ is not commercializing formulations containing the methyl ester of aminocyclopyrachlor. Based on the available EPA product labels, it seems likely that the Forest Service may use DuPont™ Method® 50SG (acid) and DuPont™ Method® 240SL (potassium salt) to control leafy spurge as well as other noxious and invasive weeds. Accordingly, these formulations are covered explicitly in the current risk assessment. In addition, the current risk assessment is designed to encompass the use of all formulations of aminocyclopyrachlor labeled for vegetation management, except those labeled solely for residential use.

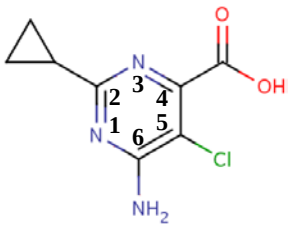
Aminocyclopyrachlor is also available in formulations which contain chlorsulfuron, metsulfuron methyl, and metsulfuron methyl plus imazapyr. These formulations, which are also labeled for the control of terrestrial and riparian invasive and noxious weeds, are noted in this program description but are not otherwise addressed in the risk assessment. Nonetheless, Forest Service risk assessments are available on chlorsulfuron, metsulfuron methyl, and imazapyr; therefore, Forest Service personnel can use WorksheetMaker to consider the effects of applying these mixtures formulations.

The maximum labeled application rate for aminocyclopyrachlor, which is 0.28 lb a.e./acre, is used in the exposure scenarios discussed in Section 3.2 (exposure assessments for human health) and Section 4.2 (exposure assessments for ecological effects). The consequences of using lower application rates are discussed in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

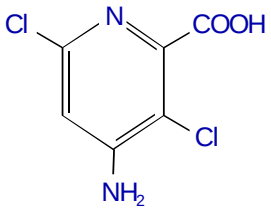
2.2. Chemical Description and Commercial Formulations

2.2.1. Aminocyclopyrachlor and Related Compounds

Aminocyclopyrachlor is the common name for 6-amino-5-chloro-2-cyclopropylpyrimidine-4-carboxylic acid:



Aminocyclopyrachlor is a pyrimidine carboxylic acid herbicide. Aminocyclopyrachlor is structurally similar to aminopyralid. One structural difference between aminopyralid and aminocyclopyrachlor are that aminopyralid has a chlorine atom in the 2-carbon position whereas aminocyclopyrachlor has a cyclopropyl-group. In addition, aminocyclopyrachlor is based on a pyrimidine ring (two nitrogen atoms in the ring structure) and aminopyralid is based on a pyridine ring (one nitrogen atom in the ring structure):



As noted in the Forest Service risk assessment on aminopyralid (SERA 2007a), aminopyralid is also similar in structure to other auxin herbicides, like clopyralid, picloram, and triclopyr.

As discussed in Section 4.1.2.5 (hazard identification for terrestrial plants), aminocyclopyrachlor is an auxin mimicking herbicide that interferes with normal plant growth (DuPont™ 2011; Roten 2011). As with many auxin-like herbicides, aminocyclopyrachlor is most effective against broadleaf weeds and woody vegetation (dicots) (Flessner et al. 2011a). Aminocyclopyrachlor is not currently used in Forest Service vegetation management programs; however, the Forest Service anticipates that its primary use of this herbicide will be to control leafy spurge, *Euphorbia esula* L, an invasive dicot introduced into the United States in the early 1800s. As discussed in Section 2.5, leafy spurge is a major pest species in North America, particularly in the northwestern United States (USDA/NAL 2011).

Aminocyclopyrachlor is a new herbicide developed by DuPont™. The EPA announced DuPont™'s initial application for the registration of aminocyclopyrachlor on January 27, 2010 (U.S. EPA/OPP 2010d) and granted a conditional registration for use on non-crop areas, sod farms, turf, and residential lawns on August 26, 2010 (U.S. EPA/OPP 2010k).

The term "*conditional registration*" indicates that the EPA required additional studies to support a full/unconditional registration and that the available information indicates that the use of the pesticide prior to the completion of additional studies is in the public interest. In assessing public benefit, the conditional registration for aminocyclopyrachlor specifically notes the benefit of using this herbicide for the control of leafy spurge:

> *In particular, aminocyclopyrachlor demonstrates very good long-term control of Leafy Spurge, considered one of the most difficult to control invasive weeds in the western United States. Leafy Spurge is listed as a noxious weed in 22 states, making control mandatory by legal statute in those areas. Very few alternative chemicals provide effective long-term control of Leafy Spurge, which reproduces aggressively, actively destroying native biodiversity and rendering pastures and rangelands unfit for cattle and horses grazing due to its unpalatability and toxicity.*
>
> U.S. EPA/OPP 2010k, p. 16

The additional studies required by EPA are discussed in the appropriate subsections of the human health risk assessment (Section 3) and ecological risk assessment (Section 4) of the current risk assessment.

The aminocyclopyrachlor formulations that might be used in Forest Service programs may contain aminocyclopyrachlor acid or the potassium salt of aminocyclopyrachlor. These different forms of aminocyclopyrachlor are illustrated in Figure 1, which also includes the major metabolites or degradates of the compound. Selected chemical and physical properties of aminocyclopyrachlor acid, potassium salt, and methyl ester are summarized in Table 1. Figure 1 also includes the methyl ester of aminocyclopyrachlor.

Aminocyclopyrachlor is readily soluble in water (i.e., 4200 mg/L at pH 7). In aqueous solutions, the hydrogen atom of the carboxylic acid group (**COOH**) may be associated (e.g., **-COOH**) or dissociated (e.g., $\mathbf{-COO^-} + \mathbf{H^+}$), depending on the pH of the solution. The dissociation constant, or pK_a, for the carboxylic acid group is approximately 4.6. Thus, at a pH of 4.6, 50% of the acid is associated and 50% is disassociated. As the acidity of the solution decreases (i.e., the pH of the solution increases), the proportion of aminocyclopyrachlor that is ionized or dissociated increases. The pH of most biological fluids ranges from approximately 5 to 9. Thus, within this range of pH, aminocyclopyrachlor has a net negative charge ($\mathbf{-COO^-}$).

The data on aminocyclopyrachlor are sufficient to support the exposure assessments typically developed in Forest Service risk assessments. The environmental half-lives as well as the K_{oc} and K_{ow} values are used quantitatively in the current risk assessment, as discussed in Section 3.2.3.4.3 (Gleams-Driver modeling). Virtually all of this information comes from registrant-submitted studies, which is not unusual for a new pesticide.

Experimental data on the metabolites and degradates of aminocyclopyrachlor are limited. The chemical structures and identifiers—i.e., chemical names and SMILES (simplified molecular-input line-entry system) notations—for the major degradates of aminocyclopyrachlor are given in Table 2. As discussed in Section 3.1.15 (Impurities and Metabolites), the current risk

assessment adopts the approach taken in U.S. EPA/OPP (2010c) in which the potential toxicity of the metabolites is estimated based on structure-activity relationships. U.S. EPA/OPP (2010c) uses ECOSAR, a computer program used to estimate toxicity values focused on potential ecological risk. The current Forest Service risk assessment uses EPI Suite (2011), a program that incorporates ECOSAR as well as other methods for estimating environmental fate properties.

2.2.2. Formulations

2.2.2.1. Aminocyclopyrachlor as Sole Active Ingredient

Representative formulations of the acid, potassium salt, and methyl ester of aminocyclopyrachlor are summarized in Table 3, which is adapted from the list of formulations in the conditional registration document for aminocyclopyrachlor (U.S. EPA/OPP 2010k). Currently, formulations that contain aminocyclopyrachlor as the sole active ingredient are not commercially available (Ashley 2012d). Formulations containing aminocyclopyrachlor with other herbicides are discussed further in Section 2.2.2.2.

As with many new pesticides, the commercial names of aminocyclopyrachlor formulations appear to be in a state of flux, and the available information on the formulations is limited. For example, The CDMS Agro-chemical database (http://www.cdms.net/LabelsMsds/LMDefault.aspx), a common source of pesticide labels, does not provide any product labels for aminocyclopyrachlor. Similarly, only a label for Imprelis® was found on the DuPont™ label website (http://www2.DuPont™.com/Production_Agriculture/en_US/label_msds_info/label.html). As discussed, Imprelis® is a formulation of aminocyclopyrachlor that will not be used in Forest Service programs. In addition, DuPont™ is not commercializing the methyl ester formulation of aminocyclopyrachlor (Ashley 2012a). The methyl ester formulation is included in Table 3 to reflect and acknowledge the discussion in U.S. EPA/OPP (2010k) but is not otherwise considered in this risk assessment.

Three of the aminocyclopyrachlor formulations identified in U.S. EPA/OPP (2010k) are labeled specifically for the control of leafy spurge and other noxious and invasive weeds: DuPont™ Method 50SG, DuPont™ Method® 240SL, and DuPont™ DPX-KJM44 80XP Herbicide. Since DuPont™ is not commercializing formulations containing the methyl ester of aminocyclopyrachlor, only DuPont™ Method® 50SG and DuPont™ Method® 240SL are the focus of the current risk assessment.

Table 4 summarizes additional information on the aminocyclopyrachlor formulations labeled specifically for leafy spurge. DuPont™ Method® 50SG is a 50% a.e. soluble granular formulation of aminocyclopyrachlor acid and DuPont™ Method® 240SL is a 21% a.e. soluble liquid formulation of the potassium salt of aminocyclopyrachlor. As discussed in Section 2.4, these formulations are mixed with water and adjuvants prior to application.

Other aminocyclopyrachlor formulations are likely to become available; therefore the list of formulations in Table 4 is not intended to be an exclusive list of formulations to be used in Forest Service programs. The Forest Service may elect to use any formulation of aminocyclopyrachlor registered for forestry applications. If other formulations are used in Forest Service programs

subsequent to the completion of the current risk assessment, steps should be taken to ensure that those formulations are comparable in toxicity to the formulations listed in Table 4.

Pesticide formulations contain ingredients other than the active ingredients, formerly referred to as *inerts*, and the identity of the other ingredients is typically classified as proprietary or Confidential Business Information (CBI). Material Safety Data Sheets (MSDS) sometimes specify inerts used in pesticide formulations. U.S. EPA/OPPTS (2003a, p. 5-2) encourages but does not require expanded inert statements on product labels which specifically identify the inert ingredients in the product. To date, MSDS were obtained for DuPont™ Method® 50SG and DuPont™ Method® 240SL. As summarized in Table 4, the labels and MSDSs do not provide expanded inert statements. An MSDS for DuPont™ DPX-KJM44 80XP was not located. Although U.S. EPA/OPP is currently considering a rule that would require a fuller disclosure of inert ingredients (http://www.epa.gov/opprd001/inerts/inertdisclosure.html), the rule has not been implemented.

As discussed further in Section 3.1.14 (Adjuvants and Other Ingredients), the only approach to assessing the potential toxicological significance of inerts involves comparing the toxicity studies conducted on the formulations with toxicity studies conducted on the active ingredients. For aminocyclopyrachlor, the information available to permit such comparisons is limited.

Aminocyclopyrachlor is somewhat unusual in that the registration for one formulation, Imprelis®, is effectively suspended. Like DuPont™ Method® 240SL, Imprelis® is a 25% a.i. liquid formulation of the potassium salt of aminocyclopyrachlor. Unlike DuPont™ Method® 240SL, however, Imprelis® is not labeled for the control of leafy spurge. The primary labeled use for Imprelis® is the control of broadleaf weeds on turf. As discussed in Section 4.1.2.5 (Hazard Identification for Terrestrial Plants), the U.S. EPA/OPP suspended the sale and distribution of Imprelis® because of reports of damage to conifers, particularly Norway spruce and white pine.

The initial product labels for Imprelis® and all other formulations of aminocyclopyrachlor indicate that the herbicide may cause damage to trees if applied improperly. The reason for the unanticipated damage to trees following normal applications of Imprelis® is currently under investigation (U.S. EPA/OPP 2011c), and there is pending litigation relating to tree damage associated with the use of Imprelis® on turf (e.g., McAuley 2012).

DuPont™ has recently revised the product labels for formulations containing aminocyclopyrachlor to add additional cautionary language concerning the toxicity of aminocyclopyrachlor to trees and the potential for aminocyclopyrachlor to runoff from the treated area in amounts that may damage nontarget vegetation. Example of a revised product labels for DuPont™ Method® 50SG (DuPont™ 2012a) and DuPont™ Method® 240SL (DuPont™ 2012b) have been provided by DuPont™. The specific cautionary language on the product label for DuPont™ Method® 240SL is given below.

> *During periods of intense rainfall, applications made to roadsides or other non-crop areas, to soils saturated with water, or soils through which rainfall will not readily penetrate may result in runoff and movement of*

METHOD® 240SL. Do not apply METHOD® 240SL when these conditions exist.

…

This product is classified as having high potential for reaching surface water via runoff for several months after application.

Product Label for Method® 240SL (DuPont™ 2012b)

The same language, except for a change in the product name, is included on the product label for DuPont™ Method® 50SG (DuPont™ 2012a). A general discussion of the potential for aminocyclopyrachlor runoff to damage vegetation is given in Section 4.4.2.5.2 and a more specific consideration of the potential impact and trees is given in Section 4.4.2.5.5.

2.2.2.2. Aminocyclopyrachlor with Other Herbicides

Although the formulations of aminocyclopyrachlor are still under development, the Forest Service has identified three formulations of aminocyclopyrachlor as well as other active ingredients that may be used in Forest Service programs: Perspective® (a mixture of aminocyclopyrachlor and chlorsulfuron), Streamline® (a mixture of aminocyclopyrachlor and metsulfuron methyl), and Viewpoint® (a mixture of aminocyclopyrachlor, imazapyr, and metsulfuron methyl). Chlorsulfuron, metsulfuron methyl, and imazapyr appear to be the only herbicides currently available with aminocyclopyrachlor in commercial formulations (Roten 2011). A summary of the composition and potential uses of these formulations is given in Table 5. Based on preliminary field trials in California, the Forest Service may have particular interest in Perspective®, which reportedly evidences good control of yellow starthistle, knapweeds, field bindweed, and marestail/Canadian horseweed (Bakke 2012).

The current Forest Service risk assessment does not explicitly consider risks associated with either formulations consisting of multiple active ingredients or tank mixtures. Nonetheless, Forest Service risk assessments are available on chlorsulfuron (SERA 2004a), metsulfuron methyl (SERA 2004a), and imazapyr (SERA 2011d). Consequently, Forest Service personnel have the option of considering the mixture formulations of aminocyclopyrachlor using the utility in WorksheetMaker for combining workbooks (SERA 2011b, Section 3.4.3).

2.3. Application Methods

As summarized in Table 4, various methods may be used to apply aminocyclopyrachlor formulations, including ground or aerial broadcast, directed foliar (including spot treatments), and various cut surface treatments, specified as cut stubble or cut stump on the product labels. Aminocyclopyrachlor has not been used in Forest Service programs; therefore, the current risk assessment covers all labeled application methods.

Ground broadcast (boom spray) application is used primarily in rights-of-way management. Spray equipment mounted on tractors or trucks is used to apply the herbicide on either side of the roadway. Usually, about 8 acres are treated in a 45-minute period (approximately 11 acres/hour). Some special truck mounted spray systems may be used to treat up to 12 acres in a 35-minute period with approximately 300 gallons of herbicide mixture (approximately 21 acres/hour and 510 gallons/hour) (USDA 1989b, p 2-9 to 2-10).

All formulations of aminocyclopyrachlor labeled for leafy spurge are registered for aerial applications, either fixed wing or helicopter. The formulation is applied under pressure through specially designed spray nozzles and booms. The nozzles are designed to minimize turbulence and maintain a large droplet size, both of which contribute to a reduction in spray drift. In aerial applications, approximately 40-100 acres may be treated per hour.

In selective foliar applications, the herbicide sprayer or container is carried by backpack or all terrain vehicle (ATV), and the herbicide is applied to selected target vegetation. Application crews may treat up to shoulder high brush, which means that chemical contact with the arms, hands, or face is a credible risk. To reduce the likelihood of significant exposure, application crews are directed not to walk through treated vegetation and not to spray above shoulder height. Usually, a worker treats approximately 0.5 acre/hour with a plausible range of 0.25-1.0 acre/hour.

Formulations of aminocyclopyrachlor are labeled for basal bark and cut surface treatments. Basal bark, as the name implies, involves spraying the bottom portion of a plant stem with the herbicide. Cut surface treatments involve creating an open surface on the tree by either cutting the tree or woody vegetation down [cut stump treatment] or cutting non-woody vegetation with a mower [cut stubble]. The herbicide is then applied using a backpack sprayer [cut stump] or broadcast application [cut stubble].

2.4. Mixing and Application Rates

As summarized in Table 4, the labeled application rates for the control of leafy spurge range from about 0.12 to 0.28 lb a.e./acre. The upper bound of this range, 0.28 lb a.e./acre, is also the maximum cumulative rate that can be applied in 1 year. All of the workbooks that accompany this risk assessment are based on the application rate of 0.28 lb a.e./acre. The impact of using lower application rates is discussed in the risk characterization (Section 3.4 for the human health risk assessment and Section 4.4 for the ecological risk assessment).

In addition to application rates, application volumes, meaning the number of gallons of pesticide solution applied per acre, have an impact on the estimates of potential risk. The extent to which a formulation of aminocyclopyrachlor is diluted prior to application primarily influences dermal and direct spray scenarios, both of which depend on ‘field dilution’ (i.e., the concentration of pesticide in the applied spray). In all cases, risk increases as the concentration of aminocyclopyrachlor in the field solution increases. As summarized in Table 4, the recommended application volumes for aminocyclopyrachlor formulations range from 10 to 400 gallons/acre. This range of application volumes is used in the EXCEL workbook that accompanies the current risk assessment (Attachment 1). The central estimate of the application volume is taken as 20 gallons/acre, which is an application volume that may be used with any of the application methods considered in the current risk assessment. As detailed in Worksheet A01 of Attachment 1, these dilution volumes and an application rate of 0.28 lb a.e./acre result in field solutions that contain concentrations of aminocyclopyrachlor of 1.7 (0.084 to 3.4) mg a.e./mL.

As indicated in Table 4, the product labels for aminocyclopyrachlor recommend the use of nonionic surfactants for broadcast foliar applications at a concentration of at least 0.25% v/v or the use of a methylated seed oil or vegetable oil at a concentration of 1.0% v/v. How the use of

surfactants affects the current risk assessment is discussed in Section 3.1.14.2 with respect to the human health risk assessment and Section 4.1.3.5 with respect to the ecological risk assessment.

The selection of application rates and dilution volumes in this risk assessment is intended to reflect conservative but plausible estimates of potential exposures. In the assessment of specific program activities, the Forest Service will use program-specific application rates and application volumes.

2.5. Use Statistics

As illustrated in Figure 2, the USDA Forest Service tracks and reports pesticide use by geographical areas referred to as "*Regions*". The Forest Service classification scheme divides the United States into nine regions designated from Region 1 (Northern) to Region 10 (Alaska). [Note: There is no *Region 7* in the Forest Service system.]

Most Forest Service risk assessments characterize regional herbicide or pesticide use relative to the use in agricultural applications. Information on Forest Service use is typically taken from Forest Service pesticide use reports (http://www.fs.fed.us/foresthealth/pesticide/reports.shtml), and information on agricultural use is typically taken from use statistics compiled by the U.S. Geologic Survey (http://water.usgs.gov/nawqa/pnsp/usage/maps/) and/or detailed pesticide use statistics compiled by the state of California (http://www.calepa.ca.gov/). Because aminocyclopyrachlor is a new herbicide, these types of use statistics are not available.

The Forest Service, however, indicated that the primary intended use of aminocyclopyrachlor is for the control of leafy spurge. As illustrated in Figure 3, leafy spurge is distributed widely in both the United States and Canada. Within the United States, leafy spurge is found in all of the contiguous states except for Texas and south-eastern states. Thus, it seems likely that aminocyclopyrachlor could be applied throughout most Forest Service regions except for Region 8 in which only Virginia has reported infestations of leafy spurge. Figure 3, however, is somewhat misleading in that infestations in many states are scattered and limited to one or only a few counties. A major exception to this pattern occurs in Region 1 (Northern), Region 2 (Rocky Mountain), and Region 4 (Intermountain). In these regions, many states (e.g., Idaho, Wyoming, Montana, and North Dakota) report infestations of leafy spurge in all or most counties. Albeit speculative, it seems likely that the greatest use of aminocyclopyrachlor will occur in the states with the greatest prevalence of leafy spurge. Nonetheless, aminocyclopyrachlor might be applied intensely in localized areas of states like Missouri, where leafy spurge is limited to only a single county, as part of eradication efforts.

As discussed in Section 2.2.2.2, formulations of aminocyclopyrachlor with or without other herbicides may also be used in Forest Service programs for the control of numerous species of noxious and invasive weeds. The major geographical areas where these mixtures might be used, though undefined, will probably include any of the Forest Service regions.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

The only consistent signs of toxicity associated with aminocyclopyrachlor involve decreased body weight, decreased weight gain, decreased food consumption, and decreased food conversion efficiency. Decreased body weight or weight gain accompanied by a decrease in food consumption can be secondary to other toxic effects (i.e., severely poisoned animals will often decrease their food consumption, which in turn leads to decreases in body weight and/or body weight gain). This pattern does not appear to be the case with aminocyclopyrachlor. Aminocyclopyrachlor does not cause other signs of toxicity which might be associated with decreased food consumption. Decreased food conversion efficiency may be but is not necessarily associated with changes in endocrine function; however, the mechanism by which aminocyclopyrachlor causes decreased food conversion efficiency has not been identified. The available subchronic and chronic toxicity studies do not report histopathological changes in endocrine tissues.

Based on standard acute oral toxicity studies, the LD_{50} of aminocyclopyrachlor cannot be determined—i.e., doses of up to 5000 mg/kg bw do not cause mortality or signs of toxicity in rats. The dose of 5000 mg/kg bw is a *limit dose*, a term used to designate the highest dose typically used in acute oral toxicity studies of pesticides. No remarkable signs of toxicity are reported in standard toxicity studies involving dermal, ocular, or inhalation exposure. Inhalation studies are available only on technical grade aminocyclopyrachlor. For all other routes of exposure, studies are available on technical grade aminocyclopyrachlor as well as DuPont™ Method® 240SL and DuPont™ Method® 50SG formulations, both of which may be used in future Forest Service programs. Technical grade aminocyclopyrachlor and DuPont™ Method® 50SG cause a somewhat greater degree of eye irritation, compared with DuPont™ Method® 240SL. The relatively modest differences may be due to the fact that technical grade aminocyclopyrachlor and DuPont™ Method® 50SG were tested as a powder; whereas, the DuPont™ Method® 240SL formulation is and was tested as a liquid. It is not uncommon for powders to cause modest levels of eye irritation due to general particulate exposure rather than specific toxicity.

The only reservation with the largely benign hazard identification for aminocyclopyrachlor involves the nature of the available data. Virtually all of the available information on the toxicity of aminocyclopyrachlor and aminocyclopyrachlor formulations to mammals comes from standard studies submitted to the U.S. EPA/OPP in support of the registration of aminocyclopyrachlor, and these studies are considered proprietary. Nonetheless, as discussed in Section 1, DuPont™ (the sole registrant for aminocyclopyrachlor) provided copies of some full studies as well as OECD study summaries along with several U.S. EPA/OPP reviews (i.e., Data Evaluation Records). While these studies appear to be appropriately designed and conducted and were, with few exceptions, accepted by the U.S. EPA/OPP, the available information on aminocyclopyrachlor is much less diverse than the information available on some other herbicides (e.g., glyphosate and triclopyr) for which the open literature is rich and varied.

3.1.2. Mechanism of Action

Aminocyclopyrachlor is a new herbicide, and studies concerning its mechanism of action in mammals are not published in the open literature. As discussed in Section 4.1.2.5, aminocyclopyrachlor is a pyrimidine carboxylic acid herbicide that acts by mimicking the activity of plant auxins and thereby interfering with the normal growth of plants. While this general mechanism of action in plants is well understood, any specific mechanism of action for aminocyclopyrachlor in humans or experimental animals is unclear.

No signs of toxicity associated with exposures to aminocyclopyrachlor are noted in acute toxicity studies (Section 3.1.4), and few signs of toxicity are noted in longer-term studies (Section 3.1.5) or reproduction and developmental studies (Section 3.1.9). At very high doses, oral exposures to aminocyclopyrachlor are associated with decreased body weight gain in one subchronic study in rats (Anand 2008a,b) and decreased body weight gains in pups and adults in a developmental study in rats (Lewis 2008a). As discussed in Section 3.3, U.S. EPA/OPP (2010a) bases the short-term and chronic RfDs for aminocyclopyrachlor on weight, weight gain, food consumption, and food efficiency. These are the only signs of toxicity for aminocyclopyrachlor, and the specific mechanism of action, if any, associated with these effects has not been identified.

Like many herbicides, aminocyclopyrachlor is a weak acid. As indicated in Table 2, the pK_a for this herbicide is about 4.6. At physiological pH, aminocyclopyrachlor will be predominantly in the anionic form ($–COO^-$). Both the liver and the kidney have efficient mechanisms for excreting weak acids by active transport (e.g., Goldstein and Schnellmann 1996; Moslen 1996). As discussed in Section 3.1.3, aminocyclopyrachlor is excreted predominantly in the urine and feces but does not appear to be concentrated or to cause adverse effects in either the kidney or liver (Himmelstein 2010).

U.S. EPA/OPP (2010a) identifies cyclopropanecarboxylic acid as a metabolite of concern. Cyclopropanecarboxylic acid is an environmental metabolite formed primarily through the aqueous photolysis of aminocyclopyrachlor (Lowrie 2008). As discussed in Section 3.1.15.1, cyclopropanecarboxylic acid causes fatty changes in the liver. This has been demonstrated in studies in rats with cyclopropanecarboxylic acid (Carpenter 2012) as well as in studies with rabbits using panadiplon, a drug that is metabolized to cyclopropanecarboxylic acid (Ulrich et al. 1994, 2001). Fatty changes in the liver have not been noted in studies with aminocyclopyrachlor. Based on this admittedly limited data, the mechanisms of action of aminocyclopyrachlor and cyclopropanecarboxylic acid do not appear to be similar.

3.1.3. Pharmacokinetics and Metabolism

Pharmacokinetics concerns the behavior of chemicals in the body, including their absorption, distribution, alteration (metabolism), and elimination as well as the rates at which these processes occur. This section of the risk assessment addresses the pharmacokinetic processes involved in aminocyclopyrachlor exposure, including a general discussion about metabolism (Section 3.1.3.1), with a focus on the kinetics of absorption (Section 3.1.3.2) and excretion (Section 3.1.3.3). Absorption kinetics, particularly the kinetics of dermal absorption, is important to this risk assessment because many of the exposure scenarios (Section 3.2) involve

dermal exposure. Rates of excretion are generally used in Forest Service risk assessments to evaluate the likely body burdens associated with repeated exposure.

An additional consideration is the behavior of aminocyclopyrachlor in the environment and the extent to which its environmental metabolism must be considered quantitatively in the risk assessment. The environmental metabolites of aminocyclopyrachlor are discussed in Section 3.1.15.1.

3.1.3.1. General Considerations

Two studies are available on the pharmacokinetics of aminocyclopyrachlor in rats (Himmelstein 2008, 2010); additional observations on the potential metabolism of aminocyclopyrachlor in rats are available from the subchronic study by Anand (2008a,b).

In the Himmelstein (2008) study, aminocyclopyrachlor (with C^{14}-labeled in the C-2 position of the pyramidine ring) was administered by gavage at doses of 25 or 500 mg/kg bw. Aminocyclopyrachlor was rapidly absorbed with peak plasma and red blood cell concentrations occurring at 20 minutes to 1 hour after dosing. Based on areas under the blood concentration curves, no dose-dependent differences in pharmacokinetics were noted. Similarly, no dose-dependent or sex differences were noted in elimination with half-lives of about 5.6 to 5.7 hours. At 24 hours post-dosing, cumulative radioactivity was recovered about equally in the urine (35.8-53.71 %) and feces (31.4-48.0%). No metabolites were identified, and all excreted radioactivity appeared to consist of the parent compound.

The Himmelstein (2010) study involved single as well as multiple doses of aminocyclopyrachlor. As with the Himmelstein (2008) study, the aminocyclopyrachlor was C^{14}-labeled in the C-2 position of the pyramidine ring. The single dose component of this study also involved doses of 25 and 500 mg/kg bw. The multiple dose study involved 14 consecutive daily doses of 25 mg/kg bw/day. The single dose studies are essentially identical to the results from Himmelstein (2008). Following doses, aminocyclopyrachlor was rapidly absorbed and distributed to all tissues. Aminocyclopyrachlor was rapidly excreted with about equal amounts of aminocyclopyrachlor recovered in the urine (40% to 56.5%) and feces (39.5% to 54.8%). While no marked dose-dependent kinetics were noted, the proportion of aminocyclopyrachlor in the feces was slightly greater at the 500 mg/kg dose than at the 25 mg/kg dose. Himmelstein (2010) suggests that this pattern may be associated with decreased absorption at the higher dose. No substantial differences in kinetics were noted following multiple doses, except that excretion in the feces (55.3% and 57.3%) was somewhat greater than excretion in the urine (38.8% and 36.6%). Excretion of radioactivity was rapid with only about 0.03% recovered in the carcass. In both male and female rats, most of the administered dose was recovered in the contents of the gastrointestinal tracts (i.e., about 96% in males and 97% in females).

While the metabolism studies by Himmelstein (2008, 2010) suggest that aminocyclopyrachlor is not extensively metabolized in rats, the 90-day feeding study in rats by Anand (2008a,b) detected low plasma concentrations of IN-LXT69. The presence of IN-LXT69 (i.e., 5-chloro-2-cyclopropyl-pyrimidin-4-ylamine) suggests that decarboxylation is at least a minor pathway for the metabolism of aminocyclopyrachlor in mammals (Figure 1).

3.1.3.2. Dermal Absorption

Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared with an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies in animals. Thus, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which aminocyclopyrachlor is likely to be absorbed from the surface of the skin.

Two types of dermal exposure scenarios are considered: immersion and accidental spills. As detailed in SERA (2011a), the calculation of absorbed dose for dermal exposure scenarios involving immersion or prolonged contact with chemical solutions uses Fick's first law and requires an estimate of the skin permeability coefficient, K_p, expressed in cm/hour. For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the surface of the skin, dermal absorption rates (proportion of the deposited dose that is absorbed per unit time) rather than dermal permeability rates are used in the exposure assessment.

Studies regarding the dermal absorption kinetics of aminocyclopyrachlor were not identified in the available literature. As noted in the EPA human health risk assessment for aminocyclopyrachlor (U.S. EPA/OPP 2010a), aminocyclopyrachlor dermal absorption studies were not submitted to the EPA. In the absence of experimental studies, U.S. EPA/OPP (2010a) assumes 100% dermal absorption. This assumption is clearly, and perhaps grossly conservative. As discussed in Section 3.1.3.1, the oral absorption of aminocyclopyrachlor appears to be incomplete, and there is no basis for asserting that aminocyclopyrachlor will be completely absorbed following dermal exposure.

In the absence of experimental data, Forest Service risk assessments use quantitative structure activity relationships, described in SERA (2011a), to estimate dermal absorption rates. For estimating the dermal permeability coefficient (K_p), the EPA developed an algorithm based on the K_{ow} and molecular weight (U.S. EPA/ORD 1992, 2007). Using the molecular weight of 213.62 and the K_{ow} at pH 7 of 0.0033 (Table 1), the estimated dermal permeability coefficient for aminocyclopyrachlor is about 0.0000016 (0.00000043 to 0.0000061) cm/hour. Details of these calculations are given in Worksheet B03a of Attachment 1. These estimates of the K_p are used in all exposure assessments based on the assumption of zero-order dermal absorption kinetics. Note that the values for K_p given in Worksheet B03a are not rounded; whereas, the values for K_p used in all exposure assessments (i.e., those entered in worksheet B01) are rounded to two significant places.

As discussed in SERA (2011a, Section 3.1.3.2.1, Eq. 1), a similar algorithm, also based on molecular weight and K_{ow}, was developed for estimating first-order dermal absorption rates. Applying the above values for the molecular weight and K_{ow} of aminocyclopyrachlor, the estimated first-order dermal absorption rate coefficient for aminocyclopyrachlor is estimated at 0.00052 $hour^{-1}$ with a 95% confidence interval of 0.00011 to 0.0025 $hour^{-1}$. The calculations for these estimates are detailed in Worksheet B03b in Attachment 1. As with the estimates of the K_p, the values given in Worksheet B03b are not rounded; whereas, the values given in Worksheet B01 and used in all exposure assessments involving first-order dermal absorption are rounded to two significant figures.

For some compounds, acute dermal and oral LD_{50} values can be used to assess the plausibility of the estimated dermal absorption rates relative to oral absorption rates. This approach is not possible for aminocyclopyrachlor due to its low toxicity which resulted in a lack of definitive LD_{50} values in the acute oral toxicity studies (Section 3.1.4) and acute dermal toxicity studies (Section 3.1.12).

The use of quantitative structure activity relationships, unsupported by experimental data, to estimate the dermal absorption of aminocyclopyrachlor adds uncertainty to the scenarios associated with dermal exposures. This type of uncertainty is common to any risk assessment for which studies on dermal absorption kinetics are unavailable. As discussed in Section 3.4 (risk characterization), all of the HQs for aminocyclopyrachlor associated with dermal exposure scenarios are far below the level of concern (HQ=1).

3.1.3.3. Excretion

Although excretion rates are not used directly in either the dose-response assessment or risk characterization, excretion half-lives can be used to infer the effect of longer-term exposures on body burden, based on the *plateau principle* (e.g., Goldstein et al. 1974, p. 320 ff). Under the assumption of first-order elimination, the first-order elimination rate coefficient (***k***) is inversely related to the half-life (t_{50}) [$\boldsymbol{k} = \ln(2) \div \boldsymbol{t_{50}}$]. If a chemical with a first-order elimination rate coefficient of ***k*** is administered at a fixed time interval (***t****) between doses, the body burden after the $\boldsymbol{N^{th}}$ dose ($\boldsymbol{X_{N\ Dose}}$) relative to the body burden immediately following the first dose ($\boldsymbol{X_{1\ Dose}}$) is:

$$\frac{X_{N\,Dose}}{X_{1Dose}} = \frac{(1-\left(e^{-kt*}\right)^{N})}{1-e^{-kt*}} \qquad \text{(Eq. 1)}$$

As the number of doses (***N***) increases, the numerator in Equation 2 approaches a value of 1. Over an infinite period of time, the plateau or steady-state body burden ($\boldsymbol{X_{Inf}}$) can be calculated as:

$$\frac{X_{Inf}}{X_1} = \frac{1}{1-e^{-kt*}} \qquad \text{(Eq. 2)}$$

As discussed in Section 3.1.3.1, aminocyclopyrachlor is eliminated rapidly from the body with a half-life of about 5.6 to 5.7 hours, corresponding to an excretion rate of about 0.12 $hour^{-1}$ [$\ln(2) \div 6$ hours ≈ 0.1155 $hour^{-1}$]. An excretion rate of 0.12 $hour^{-1}$ corresponds to a rate of 2.88 day^{-1}. Substituting this value into the above equation for the plateau principle, the estimated plateau in the body burden after daily doses over a prolonged period of time would be about 1.1 [$1 \div (1 - e^{-2.88}) \approx 1.05947$]. In other words, daily doses of aminocyclopyrachlor should not lead to any substantial accumulation in humans over prolonged periods of exposure. This assessment is consistent with the lack of bioaccumulation of aminocyclopyrachlor in the multi-dose kinetic study in rats by Himmelstein (2010). In addition and as discussed further in Section 3.1.5, the lack of bioaccumulation is also consistent with the lack of toxic effects observed in longer-term toxicity studies in mammals.

3.1.4. Acute Oral Toxicity

Basic acute toxicity values include time-specific LD_{50} or LC_{50} values (i.e., doses or concentrations of a toxicant that result in or are estimated to result in 50% mortality of the test species during a specified exposure or observation period). These values can be viewed as an index of acute lethal potency. LD_{50} studies involve different levels of oral exposure which result in mortality rates that bracket 50% of the treated animals. These data are then used to estimate an oral LD_{50}. In the registration process, however, the U.S. EPA will accept *limit tests* in which the compound is tested at only a single high dose, typically 2000 mg/kg bw or 5000 mg/kg bw. If the compound does not cause mortality rates of 50% or more, the requirement for a full study to determine the LD_{50} value may be waived. In these instances, LD_{50} values are expressed as greater than the limit dose—e.g., >2000 mg/kg bw or >5000 mg/kg bw. Consistent with the terminology used in U.S. EPA/OPP risk assessments, LD_{50} values expressed as greater than a particular value are referred to as *non-definitive* LD_{50} values, and LD_{50} values expressed as a specific value (with or without confidence intervals) are referred to as *definitive* LD_{50} values.

As summarized in Appendix 1, Table A1-1, three acute gavage limit assays are available: one on technical grade aminocyclopyrachlor (Carpenter 2007c), one on DuPont™ Method® SL (Carpenter 2008b), and one on DuPont™ Method® 50SG (Moore 2008a). All studies were conducted at a limit dose of 5000 mg/kg bw. For the study on technical grade aminocyclopyrachlor (Carpenter 2007c), this corresponds to a dose of 5000 mg a.e./kg bw. For the studies on DuPont™ Method® SL (Carpenter 2008b) and DuPont™ Method® 50SG (Moore 2008a), the doses corresponded to 1120 mg a.e./kg bw and 2490 mg a.e./kg bw, respectively. The only adverse effect observed was diarrhea in one of three rats dosed with DuPont™ Method® 240SL at 2490 mg a.e./kg bw. Diarrhea is not an atypical observation following acute gavage dosing, and this observation may have been incidental rather than a sign of aminocyclopyrachlor toxicity. All three acute gavage toxicity studies are classified as acceptable by the U.S. EPA. Based on these studies, U.S. EPA/OPP (2010b, p. 41; 2010k, p. 16) classifies aminocyclopyrachlor as *practically non-toxic* to mammals.

In addition to these standard acute oral toxicity studies in rats, other single-dose studies in mammals include an acute neurotoxicity study in rats (Barnett 2009a) as well as a bone marrow assay in mice (Krsmanovic and Huston 2007). These studies also report no signs of toxicity in mice or rats at doses of up to 2000 mg a.e./kg bw. The Barnett (2009a) study is discussed in Section 3.1.6, and the Krsmanovic and Huston (2007) study is discussed in Section 3.1.10.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

As discussed in SERA (2011a, Section 3.1.5), *subchronic* and c*hronic* are somewhat general terms that refer to studies involving repeated dosing. Some studies are designed to detect toxic endpoints, like reproductive and neurological effects. Except for some comments in this subsection on general signs of toxicity, these more specialized studies are discussed in subsequent subsections of this hazard identification. The focus of this subsection is toxicity studies designed to detect more general signs of systemic toxicity and to quantify no-observable-adverse-effect levels (NOAELs) for the identified endpoints as well as levels associated with adverse effects—i.e., lowest-observed-adverse-effect-levels (LOAELS).

The U.S. EPA typically requires subchronic and chronic feeding studies in mice, rats, and dogs to support registration of pesticides intended for uses on food crops. Since the initial registrations of DuPont™ Method® 50SG (acid) and DuPont™ Method® 240SL (potassium salt) were for non-food uses, chronic studies were not required and were not available at the time of registration. U.S. EPA/OPP (2010a), reviewed and accepted standard 90-day feeding studies in mice (Anand 2008c,d), rats (Anand 2008a,b), and dogs (Luckett 2008a; Luckett and Mawn 2008) as well as 28-day immunotoxicity feeding studies in mice (Hoban 2008c) and rats (Hoban 2008b). Chronic studies on aminocyclopyrachlor have been completed in dogs (Han 2010), mice (Huh 2010), and rats (Moon 2010). These studies have been submitted to the U.S. EPA/OPP; however, EPA evaluations of the chronic studies are not currently available.

The subchronic feeding studies on aminocyclopyrachlor are summarized in Appendix 1, Table A1-2. No adverse effects were noted at dietary concentrations of up to 30,000 ppm in dogs (Han 2010) and 7000 ppm in mice (Anand 2008c,d; Hoban 2008c; Huh 2010). Rats appear to be more sensitive than mice or dogs. In the subchronic (96-97 days) feeding study in mice, the dietary NOAEL in rats was 6000 ppm with a LOAEL of 18,000 ppm, based on decreased body weights, body weight gains, food consumption, and food efficiency in both sexes (Anand 2008a,b). A decrease in food conversion efficiency was also noted at 18,000 ppm in the chronic (2-year) feeding study in rats (Moon 2010). In the 28-day feeding study (Hoban 2008b), the body weight gains of rats in the 18,000 ppm dose group were lower than those in the control group by a factor of about 9.9%. This difference, however, was not statistically significant. As discussed further in Section 3.1.9.1, decreases in food consumption and body weight were noted also in a developmental study in rabbits (Fleeman 2008).

None of the summaries of the subchronic and chronic toxicity of aminocyclopyrachlor in mammals note adverse effects on blood or lymphoid tissue. As discussed in Section 1.7, adverse effects on these tissues may be indicative of a potential for an impact on immune function.

3.1.6. Effects on Nervous System

A neurotoxicant is a chemical that disrupts the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. As defined, neurotoxicants, which act directly on the nervous system (direct neurotoxicants), are different from those agents (indirect neurotoxicants), which may cause neurological effects secondary to other forms of toxicity. Practically any chemical will cause signs of neurotoxicity in severely poisoned animals, and, therefore, can be classified as an indirect neurotoxicant. The U.S. EPA/OPPTS (1998b) defines general protocols for assessing neurotoxicity. The protocols include a functional observation battery (FOB) of several endpoints for general behavior, motor activity, and neuropathology.

Aminocyclopyrachlor has been assayed for neurotoxicity in acute studies (Appendix 1, Table A1-1), subacute and chronic studies (Appendix 1, Table 2), and developmental studies (Appendix 1, Table 3) with no indication of either direct or indirect neurotoxicity. In an acute neurotoxicity study, including a functional observation battery, no signs of toxicity were noted in rats at doses up to a limit dose 2000 mg/kg bw (Barnett 2009a). Similarly, no signs of neurotoxicity were noted in a subchronic feeding study in mice at dietary concentrations of up to 7000 ppm (Anand 2008c,d), a subchronic feeding study in rats at a dietary concentration of up 18,000 ppm (Anand 2008a,b), or a subchronic feeding studies in dogs at dietary concentrations

of up to 15,000 ppm (Luckett 2008a; Luckett and Mawn 2008). The multigenerational reproduction study in rats conducted by Lewis (2008a) includes observations for abnormal behavior in both parental rats and offspring; however, no adverse effects were noted at dietary concentrations of up to 17,000 ppm (corresponding to doses of 1285 mg/kg bw/day in males and 1454 mg/kg bw/day in females). A lack of neurotoxicity is noted also in a single generation reproduction study in rats at dietary concentrations of up to 17,000 ppm for the methyl ester of aminocyclopyrachlor (MRID 47560018 as summarized in U.S. EPA/OPP 2010a, Table A.2.4, p. 47). All of these studies were reviewed and accepted by the U.S. EPA/OPP (2010a).

Based on the studies discussed above, the EPA concludes that: … *no evidence of acute or subchronic neurotoxicity in OPPTS guideline studies in adult animals and no evidence of increased susceptibility of offspring* (U.S. EPA/OPP 2010a, p. 19). Based on the lack of apparent neurotoxicity, the EPA recommended waivers for neurotoxicity studies in hens and developmental neurotoxicity studies in rats (U.S. EPA/OPP 2010a, pp. 46-47).

As discussed in Section 3.1.5, although chronic studies have been completed since the conditional registration of aminocyclopyrachlor—i.e., dogs (Han 2010), mice (Huh 2010), and rats (Moon 2010)—reviews of these studies by the U.S. EPA/OPP are not currently available. Based on the available OECD summaries of these studies, no signs of neurotoxicity were noted.

3.1.7. Effects on Immune System

There are various methods for assessing the effects of chemical exposure on immune responses, including assays of antibody-antigen reactions, changes in the activity of specific types of lymphoid cells, and assessments of changes in the susceptibility of exposed animals to resist infection from pathogens or proliferation of tumor cells. As with neurotoxicity, the EPA has a standard screening test for immunotoxicity (U.S. EPA/OPP 1998c). This assay involves exposing animals to the test substance at different dietary concentrations for a period of 28 days and injecting the test animals with sheep red blood cells on Day 21. Immune suppression is assayed as decreases in serum immunoglobin M antibody response relative to the control group.

As summarized in Appendix 1 (Table A1-2), 28-day immunotoxicity studies were conducted in rats at dietary concentrations of up to 18,000 ppm (Hoban 2008b) and mice at dietary concentrations of up to 7000 ppm (Hoban 2008c). Both studies involve doses equivalent to more than 1000 mg/kg bw/day, and neither study notes any suppression of immune response. Based on the data summaries in the EPA DERs for these studies, average immune responses (i.e., IgM antibody titers) in exposed groups were somewhat higher than in the control groups; however, the differences were neither statistically significant from the controls nor dose related. Based on these studies, U.S. EPA/OPP (2010a) notes that there is no evidence that aminocyclopyrachlor causes adverse effects on the immune system.

In addition to these specific assays for immunotoxicity, typical subchronic or chronic animal bioassays conduct morphological assessments of the major lymphoid tissues, including bone marrow, major lymph nodes, spleen and thymus (organ weights are sometimes measured as well), and blood leukocyte counts. These assessments can detect signs of inflammation or injury indicative of a direct toxic effect of the chemical on the lymphoid tissue. Changes in morphology/cellularity of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected. As discussed in Section 3.1.5, however,

adverse effects in blood or other lymphoid tissues are not reported in the available summaries of subchronic and chronic toxicity studies on aminocyclopyrachlor.

3.1.8. Effects on Endocrine System

The direct effects of pesticides on endocrine function are most often assessed in mechanistic studies of estrogen, androgen, corticosteroid, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). The EPA developed a battery of screening assays for endocrine disruption (U.S. EPA/OCSPP (2011b). Neither the open literature nor the registrant-submitted studies include specific assays of aminocyclopyrachlor for endocrine disruption. The EPA human health risk assessment for aminocyclopyrachlor (U.S. EPA/OPP 2010b) does not specifically address the potential for adverse effects on endocrine function.

In terms of functional effects that have important public health implications, effects on endocrine function could be expressed as diminished or abnormal reproductive performance. This issue is addressed specifically in the following section (Section 3.1.9), and there is no indication that aminocyclopyrachlor causes adverse reproductive effects.

The available subchronic and chronic toxicity studies do not report histopathological changes in endocrine tissues (Section 3.1.5). As discussed in Section 3.1.5, the only adverse effects associated with dietary exposures to aminocyclopyrachlor involve decreased body weights, body weight gains, food consumption, and food efficiency in rats (Anand 2008a,b; Moon 2010). As discussed further in Section 3.1.9, decreased body weights, decreased food consumption, and decreased food conversion efficiency are also reported in a reproduction study in rats (Lewis 2008a). Decreases in body weight and/or body weight gain accompanied by decreased food consumption are commonly observed in experimental animals and may be secondary to other toxic effects. Such changes do not suggest an impact on endocrine function. Decreases in food conversion efficiency, however, are less common and could be consistent with hormonal effects. Nonetheless, none of the animal studies reports abnormal thyroid histology or changes in other endocrine tissue.

While the impact of aminocyclopyrachlor on food conversion efficiency cannot be clearly associated with an effect on endocrine function, an impact on endocrine activity cannot be ruled out. As discussed further in Section 3.3, effects on body weight and food conversion efficiency are considered quantitatively in the current risk assessment as the basis for the dose-response assessment.

3.1.9. Reproductive and Developmental Effects

3.1.9.1. Developmental Studies

Developmental studies are used to assess whether a compound has the potential to cause birth defects—also referred to as teratogenic effects—as well as other effects during development or immediately after birth. These studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required for pesticide registration. Specific protocols for developmental studies are established by U.S. EPA/OPPTS and are available at http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized.

As detailed in Appendix 1 (Table A1-3), standard developmental studies with technical grade aminocyclopyrachlor are available in rats (Lewis 2008b) and rabbits (Fleeman 2008). Both studies involve gavage administration at doses of up to 1000 mg/kg bw/day during gestation. No adverse effects were noted in rats and no developmental effects were noted in rabbits.

In the rabbit assay, the death of one dam on Day 13 of gestation was attributed to treatment. Signs of toxicity in this dam included increased respiration 1 hour after dosing on Day 7 as well as rales (abnormal sounds from the lung), decreased defecation, decreased food consumption, and decreased body weight on Days 9 through 13. The DER for the rabbit study by Fleeman (2008) does not report lung pathology. Two other females exhibited weight loss from Day 7, and these females aborted, one on Day 20 and the other on Day 26. All of these effects were attributed to aminocyclopyrachlor. One additional female in the 1000 mg/kg bw dose group died; however, this death was attributed to gavage error. One female in the 100 mg/kg bw dose group died, and the cause of death was not identified. While several malformations in pups were noted in both controls and exposed groups, the incidence of malformations was not dose related, and no malformations were attributed to treatment.

The EPA review of these studies (U.S. EPA/OPP 2010a, p. 18) concludes that they provide no evidence that aminocyclopyrachlor causes developmental toxicity.

3.1.9.2. Reproduction Studies

Reproduction studies involve exposing one or more generations of the test animal to a chemical compound. Generally, the experimental method involves dosing the parental (P or F_0) generation (i.e., the male and female animals used at the start of the study) to the test substance prior to mating, during mating, after mating, and through weaning of the offspring (F_1). In a 2-generation reproduction study, this procedure is repeated with male and female offspring from the F_1 generation to produce another set of offspring (F_2). These studies include standard observations of the animals for gross signs of toxicity. Additional observations often include the length of the estrous cycle, assays on sperm and other reproductive tissue, and number, viability, and growth of offspring. The EPA requires only one acceptable multi-generation reproduction study.

As summarized in Appendix 1 (Table A1-3), a single 2-generation reproduction study in rats (Lewis 2008a) was submitted to and accepted by the EPA (U.S. EPA/OPP 2010a, p. 56). This study involved dietary exposures of rats to aminocyclopyrachlor at concentrations of 0, 500, 1500, 5000, or 17,000 ppm (mg a.e/kg diet). As with other subchronic studies (Section 3.1.5), the only adverse effect attributable to aminocyclopyrachlor was a dose-related decrease in body weight gain and food conversion efficiency in the high dose group. Some statistically significant effects were noted in the 1500 ppm and 5000 ppm dose groups, including decreased food conversion efficiency and increased adrenal weights without signs of histopathology . Because of the transient nature of these effects and the lack of a strong dose-response relationship, the U.S. EPA/OPP considers these effects to be incidental and classifies the NOAEL as 5000 ppm for both the offspring and parental generation. Changes in sex ratio were also noted in the 1500 ppm dose group, which was regarded as incidental to exposure, due to the lack of a dose-response relationship. For reproductive effects, the EPA classifies the high dose group (17,000

ppm) as a NOAEL—i.e., this study demonstrates no reproductive effects from exposure to aminocyclopyrachlor.

3.1.10. Carcinogenicity and Mutagenicity

As reviewed in U.S. EPA/OPP (2010a, pp. 57-60), aminocyclopyrachlor was tested in several standard assays for mutagenicity, including reverse mutation assays in *Salmonella*, *in vitro* assays for mutagenic activity in Chinese hamster ovary cell cultures, and *in vitro* chromosomal aberrations in lymphocyte cell cultures. All of these assays failed to demonstrate either mutagenic activity or chromosomal damage. As summarized in Appendix 1 (Table A1-1), an *in vivo* assay in mice failed to demonstrate any effect on the formation of micronuclei in bone marrow red blood cells following single oral doses of aminocyclopyrachlor at up to 2000 mg/kg bw (Krsmanovic and Huston 2007). The U.S. EPA/OPP typically requires an *in vivo* study of chromosomal damage in bone marrow; however, this assay was waived because of the lack of evidence of mutagenic activity in the other assays (U.S. EPA/OPP 2010a, p. 59).

As discussed in Section 3.1.5, chronic studies were not available to the EPA at the time that the conditional registration was granted (U.S. EPA/OPP 2010k). Based solely on the lack of mutagenic activity, the EPA classifies aminocyclopyrachlor as *Not likely to be Carcinogenic to Humans*. As discussed in Section 3.1.5, DuPont™ has completed life-time studies in both rats (Moon 2010) and mice (Huh 2010). According to summaries of these studies, there was no evidence of carcinogenicity in either study. EPA evaluations of these studies by the U.S. EPA/OPP (i.e., DERs) were not available at the time this Forest Service risk assessment was prepared.

3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes)

The U.S. EPA/OPP requires standard studies with pesticide formulations for skin and eye irritation as well as skin sensitization (U.S. EPA/OCSPP 2011a). For all three endpoints, the U.S. EPA/OPP classifies the responses according to a ranking system ranging from Category I (most severe response) to Category IV (least severe response). The available studies on these endpoints are summarized in Appendix 1: Table A1-6 for skin irritation, Table A1-7 for skin sensitization, and Table A1-8 for eye irritation.

3.1.11.1. Skin Irritation

Standard skin irritation studies were conducted on technical grade aminocyclopyrachlor (Carpenter 2007a), DuPont™ Method® 240SL (Carpenter 2008f), and DuPont™ Method® 50SG (Moore 2008h). As summarized in Table 3, the Forest Service anticipates that both of Method® formulations will be used in Forest Service programs. Based on the lack of skin irritation in the study with technical grade aminocyclopyrachlor (Carpenter 2007a), the EPA classifies aminocyclopyrachlor as Category IV, non-irritating to the skin (U.S. EPA/OPP 2010a, Table A.2.1, p. 44). No dermal irritation was noted in the skin irritation study with DuPont™ Method® 240SL (Carpenter 2008f). Based on the DER for the study by Carpenter (2008f), DuPont™ Method® 240SL is also classified as Category IV for skin irritation. In the study on DuPont™ Method® 50SG (Moore 2008h), mild and transient erythema was observed. As with DuPont™ Method® 240SL, however, the DER for this study also indicates that the EPA classifies DuPont™ Method® 240SL as Category IV.

As discussed in Section 3.1.12, minor skin irritation is noted in standard acute dermal toxicity studies on technical grade aminocyclopyrachlor (Carpenter 2007b) and DuPont™ Method® 240SL (Carpenter 2008e). The same effect is noted also by Merkel (2008) in a subchronic dermal toxicity study on technical grade aminocyclopyrachlor. This observation is not consistent with the skin irritation studies discussed above. For the study on technical grade aminocyclopyrachlor, Carpenter (2007b) suggests that the skin irritation could be due to gauze pads adhering to the skin at the time the skin was washed.

3.1.11.2. Skin Sensitization

Standard test procedures for skin sensitization have traditionally involved assays in guinea pigs. More recently, however, the U.S. EPA/OPP has also approved the use of a Local Lymph Node Assay (LLNA) in mice (U.S. EPA/OPPTS 2003b). All skin sensitization studies on aminocyclopyrachlor involve assays in mice. Skin sensitization studies are available on technical grade aminocyclopyrachlor (Carpenter 2007e), DuPont™ Method® 240SL (Carpenter 2008c), and DuPont™ Method® 50SG (Carpenter 2008a). None of the skin sensitization assays in mice resulted in a positive response and aminocyclopyrachlor is classified by U.S. EPA/OPP (2010a, Table A.2.1, p. 43) as Category IV (i.e., non-sensitizing).

3.1.11.3. Ocular Effects

Standard eye irritation studies in rabbits were conducted with technical grade aminocyclopyrachlor (Carpenter 2007d), DuPont™ Method® 240 SL (Carpenter 2008d), and DuPont™ Method® 50SG (Moore 2008g). Details of these studies are provided in Appendix 1 (Table A1-8). All three studies involved groups of three rabbits. One eye of each rabbit was treated with the test material and the other eye served as a control. Both technical grade aminocyclopyrachlor and DuPont™ Method® 50SG caused mild eye irritation and are classified by the U.S. EPA/OPP as Category III—slightly irritating. DuPont™ Method® 240 SL did not cause any ocular irritation and is classified as Category IV—non-irritating. Based on the DERs for these studies, it appears that both aminocyclopyrachlor (Carpenter 2007d) and DuPont™ Method® 50SG (Moore 2008g) were applied as finely ground solids; whereas, DuPont™ Method® 240 SL (Carpenter 2008d) was applied as a liquid. It is not uncommon for installations of any granular material into the eye to cause mild eye irritation. Albeit speculative, the irritant nature of granular material to the eye may account for the differences between technical grade aminocyclopyrachlor and DuPont™ Method® 50SG relative to DuPont™ Method® 240 SL.

3.1.12. Systemic Toxic Effects from Dermal Exposure

3.1.12.1. Acute Dermal Toxicity

As detailed in Appendix 1 (Table A1-4), acute dermal toxicity studies were conducted with groups of five male and five female rats exposed to technical grade aminocyclopyrachlor (Carpenter 2007b), DuPont™ Method® 240SL (Carpenter 2008e), or DuPont™ Method® 50SG (Moore 2008f). No signs of systemic toxicity were observed at the limit dose of 5000 mg/kg bw. U.S. EPA/OPP classifies each of the test agents as Category IV for systemic toxicity.

Signs of minor skin irritation are noted in the studies on technical grade aminocyclopyrachlor (Carpenter 2007b) and DuPont™ Method® 240SL (Carpenter 2008e). As discussed above, this observation is not consistent with the skin irritation studies discussed in Section 3.1.11.1. For

the study on technical grade aminocyclopyrachlor, Carpenter (2007b) suggests that the skin irritation could be due to gauze pads adhering to the skin at the time of washing.

3.1.12.2. Subchronic Dermal Toxicity

One subchronic dermal toxicity study was conducted in rats (Merkel 2008). As detailed in Appendix 1 (Table A1-4), this study involved dermal doses of 150, 400, or 1000 mg a.e./kg bw/day 6 hours/day for 28 days. No mortality or signs of toxicity were observed in any rats.

In the high dose group, a statistically significant increase in absolute adrenal weight (15% relative to control) in female rats may reflect systemic toxicity; however, the DER does not provide details regarding adrenal weights and body weights and does not specify whether the relative adrenal weights were significantly different from controls.

In the 150 mg/kg bw/day dose group, significant decreases were noted in ovarian weights (i.e., 20% based on absolute weight, 19% relative to body weight, and 22% relative to brain weight). A 10% decrease in kidney weight, relative to brain weight, was also noted in female but not male rats in this dose group. These changes were not associated with changes in histopathology and were not observed at higher doses.

The effects discussed above are not considered to be treatment related, and the U.S. EPA/OPP (2010a) classifies the 1000 mg/kg bw/day dose group as a NOAEL. In addition, the U.S. EPA/OPP (2010a, p. 33) does not assess dermal exposures: *Quantification of dermal exposures was not performed because no toxicity was observed in a subchronic dermal toxicity study at the limit dose (1000 mg/kg)*. As discussed further in Section 3.2 (Exposure Assessment), the current Forest Service risk assessment quantitatively considers several dermal exposure scenarios. Consistent with the EPA position, none of the dermal exposure scenarios considered in this risk assessment approaches a level of concern (Section 3.4).

Given the lack of toxicity in the 28-day dermal toxicity study, the EPA waived the requirements for a 90-day dermal toxicity study (U.S. EPA/OPP 2010k, p. 8, Section 1.2.2.4).

3.1.13. Inhalation Exposure

As summarized in Appendix 1 (Table A1-5), standard acute inhalation studies are available on technical grade aminocyclopyrachlor (Anand 2007a) as well as Method 240 SL (the potassium salt formulation) (Wineberg 2008a). Both studies involve nose-only exposures for 4 hours followed by a 14-day observation period. No mortality, signs of systemic toxicity, changes in organ weights were observed. In the study by Wineberg (2008a), gross pathology noted pale kidneys in one female and a dark red area on the thymus of another female. Based on the study by Anand (2007a), the U.S. EPA/OPP (2010a, Table A.2.1, p. 44) classifies technical grade aminocyclopyrachlor as Category IV for inhalation toxicity. Similarly, the DER for the study by Wineberg (2008a) classifies Method 240 SL as Category IV for inhalation toxicity. Category IV is the lowest (i.e., least toxic) category used by U.S. EPA/OPP in the classification of responses from acute toxicity studies.

Based on the projected use pattern, the EPA judged that inhalation exposures would be insubstantial and waived the requirement for a 90-day inhalation toxicity study (U.S. EPA/OPP 2010a, p. 52).

3.1.14. Adjuvants and Other Ingredients

3.1.14.1. Other Ingredients (Inerts)

U.S. EPA is responsible for regulating both the active ingredients (a.i.) in pesticide formulations as well as other chemicals added to the formulation. As implemented, these regulations affect only pesticide labeling and testing requirements. The term *inert* was used to designate compounds that are not classified as active ingredient on the product label. While the term *inert* is codified in FIFRA, some inerts can be toxic, and the U.S. EPA now uses the term *Other Ingredients* rather than *inerts* (http://www.epa.gov/opprd001/inerts/). For brevity, the following discussion uses the term *inert*, recognizing that *inerts* may be biologically active and potentially hazardous components.

As discussed in Section 2.2.2.1, the MSDS for DuPont™ Method® 50 SG and DuPont™ Method® 240SL do not identify inerts in the formulations, and hazardous inerts are not specified on the product labels. As discussed previously, essentially parallel toxicity studies are available for technical grade aminocyclopyrachlor, DuPont™ Method® 50 SG, and DuPont™ Method® 240SL for acute oral toxicity (Section 3.1.4), skin irritation (Section 3.1.11.1), skin sensitization (Section 3.1.11.2), eye irritation (Section 3.1.11.3), and dermal toxicity (Section 3.1.12). These studies do not indicate that the biological activity of the aminocyclopyrachlor formulations is substantially different from technical grade aminocyclopyrachlor. This lack of differences in biological activity suggests that the inerts in DuPont™ Method® 50 SG and DuPont™ Method® 240SL do not contribute substantially to the toxicity of the formulations. This comparison is limited in that the parallel studies cover only acute effects, which is common with most pesticides and their formulations.

3.1.14.2. Adjuvants

As summarized in Table 4, adjuvants, including nonionic surfactants, methylated seed oils, or vegetable oil concentrates are recommended for applications of aminocyclopyrachlor. These adjuvants are commonly used with herbicides.

Product labels recommend the use of nonionic surfactants at a concentration of 0.25% v/v or the use of methylated seed oil or vegetable oil at a concentration of 1% (v/v). For some herbicides, like glyphosate, available studies suggest that at least some nonionic surfactants may be much more toxic than the herbicide itself to both humans and nontarget species (e.g., SERA 2011b). Adjuvants enhance the efficacy of aminocyclopyrachlor by increasing its absorption in plants (Bukun et al. 2009; Bukun et al. 2010). There is no information regarding the impact of adjuvants in combination with aminocyclopyrachlor or aminocyclopyrachlor formulations on humans or other mammals.

Although methylated seed oils and vegetable oil concentrates are somewhat vague terms, there is no basis for asserting that these adjuvants are likely to enhance the toxicity of aminocyclopyrachlor to humans. Several seed and vegetable oils are approved food additives (Clydesdale 1997); moreover, many vegetable and fruit oils are classified as *minimal risk inerts* (U.S. EPA/OPPTS 2009). Nonionic surfactants comprise a large and complex group of materials (e.g., Kosswig 1994). In the absence of mammalian studies regarding the potential toxicity of aminocyclopyrachlor in combination with various nonionic surfactants, it is not possible to generalize about potential hazards to human health. As discussed further in the ecological risk

assessment, some nonionic surfactants are much more toxic than aminocyclopyrachlor to aquatic species (Section 4.1.3.5).

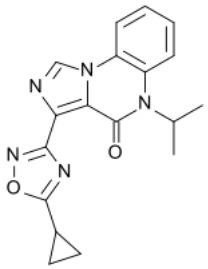
3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

The *in vivo* mammalian metabolism of aminocyclopyrachlor is not extensive (Section 3.1.3). The current section concerns the environmental metabolism of aminocyclopyrachlor. It is necessary to consider the environmental metabolism of a pesticide quantitatively, if the metabolites are more toxic and/or more persistent than the parent compound.

The chemical structures of aminocyclopyrachlor and its known degradates are illustrated in Figure 1. There is little information about the toxicity of aminocyclopyrachlor degradates. U.S. EPA/OPP (2010a, p. 26 ff) identifies cyclopropanecarboxylic acid as a degradate of potential concern. As discussed further in Section 3.2.3.4.1.2, cyclopropanecarboxylic acid is formed from the aqueous photolysis of aminocyclopyrachlor.

The EPA hazard assessment (U.S. EPA/OPP 2010a) is not based on a toxicity study on cyclopropanecarboxylic acid. As detailed in Appendix 1 (Table A1-2), the assessment is based on a 14-day gavage toxicity study on panadiplon by Ulrich et al. (1994). Panadiplon is the common name for (3-[5-cyclopropyl-I ,2,4-oxadiazol-3yl]-5-[I -methylethyl]-imidazo (1,5-a)-quinoxalin-4[5H]-one):



Panadiplon is an anti-anxiety drug. As part of a series of toxicology studies conducted on this drug, Ulrich et al. (1995) observed signs of liver damage in rabbits following gavage doses of 20 mg/kg bw/day for 14 days. Details of this study are given in Appendix 1 (Table A1-9). Signs of liver damage included liver necrosis and steatosis (fatty degeneration) as well as increases in serum transaminase and triglyceride levels, all of which are effects typical of carboxylic acids that may induce Reye's syndrome. These hepatotoxic effects were not observed at a dose of 10 mg/kg bw/day. The development of liver damage following exposure to panadiplon was attributed to the metabolism of panadiplon to cyclopropanecarboxylic acid (Ulrich et al. 1995, 2001).

As detailed further in Section 3.3.3, the EPA considered the association between liver toxicity and exposure to cyclopropanecarboxylic acid in the study by Ulrich et al. (1995) sufficiently strong to derive both acute and chronic RfDs for cyclopropanecarboxylic acid based on these data (U.S. EPA/OPP 2010a). On the basis of molecular weight—cyclopropanecarboxylic acid (86.09 g/mole) and panadiplon (337.35 g/mole)—the EPA converted the LOAEL for panadiplon of 10 mg/kg bw/day to an equivalent LOAEL for cyclopropanecarboxylic acid of 2.55 mg/kg

bw/day [10 mg/kg bw/day x 86.09 g/mole ÷ 337.35 g/mole ≈ 2.5519 mg/kg bw/day] (U.S. EPA/OPP (2010a).

The conditional registration for aminocyclopyrachlor requires the repeated-dose study on cyclopropanecarboxylic acid to support any new uses for this herbicide (U.S. EPA/OPP 2010a, p. 18). The requirement does not specify a minimum duration for the study or the test species but indicates that a sensitive species should be used. DuPont™ has completed a 90-day subchronic toxicity study on cyclopropanecarboxylic acid (Carpenter 2012), which was submitted to the U.S. EPA/OPP on May 15, 2012 (Ashley 2012b). For the current Forest Service risk assessment, DuPont™ provided a summary of Carpenter (2012).

As detailed in Appendix 1 (Table A1-9), Carpenter (2012) dosed groups of 10 rats/sex/day with cyclopropanecarboxylic acid at 0, 2, 10, 30, or 60 mg/kg bw for periods of 92 to 94 days. As in the study by Ulrich et al. (1995), fatty changes in the liver were noted. These effects occurred at 60 mg/kg bw/day in male and female rats and at 30 mg/kg bw/day in female but not male rats. The histological changes in the liver are associated with increases in liver weight. Other effects noted at 30 and 60 mg/kg bw/day include increases in kidney weight (with no changes in kidney histology). At 60 mg/kg bw/day, histological changes were evident in the thymus and pancreas. No effects were observed in male or female rats at 2 or 10 mg/kg bw/day.

A major difference between the studies by Ulrich et al. (1995) and Carpenter (2012) is the estimated doses at which adverse effects attributed to cyclopropanecarboxylic acid occurred. As discussed above, the LOAEL (as cyclopropanecarboxylic acid equivalents) from Ulrich et al. (1995) is about 2.55 mg/kg bw/day and the LOAEL from Carpenter (2012) is 30 mg/kg bw/day with a corresponding NOAEL of 10 mg/kg bw/day. The other major and obvious difference between these studies involves the agent that was tested—i.e., panadiplon in the study by Ulrich et al. (1995) and cyclopropanecarboxylic acid in the study by Carpenter (2012). As illustrated above, panadiplon is a complex heterocyclic compound. While cyclopropanecarboxylic acid is a metabolite of panadiplon and appears to contribute to the effects of panadiplon on the liver, the greater toxicity of panadiplon, expressed as cyclopropanecarboxylic acid equivalents, could be associated with other metabolites of panadiplon and/or changes in the disposition of the cyclopropanecarboxylic acid metabolite.

An interpretation of the differences between these two studies is further complicated by differences in the test species—i.e., rabbits in the study by Ulrich et al. (1995) and rats in the study by Carpenter (2012). While rabbit bioassays of aminocyclopyrachlor are available for eye irritation (Carpenter 2007d; Moore 2008g) and skin irritation (Carpenter 2007a,f; Moore 2008g), no bioassays of aminocyclopyrachlor for systemic toxicity to rabbits are available. Consequently, the lower LOAEL from the Ulrich et al. (1995) study, relative to the Carpenter (2012) study, could be due to innate differences in the test species.

3.1.15.2. Impurities

There is no information in the published literature concerning the manufacturing impurities in aminocyclopyrachlor. Nonetheless, virtually no chemical synthesis yields a totally pure product. Technical grade aminocyclopyrachlor, like other technical grade products, contains some impurities. These impurities were disclosed to U.S. EPA in 45 separate submissions, as specified in the consolidated EPA bibliography (Attachment 3) under the headings *830.1670: Discussion*

of formation of impurities. Because specific information concerning impurities may provide insight into the manufacturing process used to synthesize aminocyclopyrachlor, it is considered proprietary, is protected under FIFRA (Section 10), and was not available for the preparation of the current Forest Service risk assessment.

To some extent, concern for impurities in technical grade aminocyclopyrachlor is reduced because the existing toxicity studies were conducted with the technical grade product or formulated products. Thus, toxic impurities present in the technical grade product are likely to be encompassed by the available toxicity studies.

3.1.16. Toxicological Interactions

No information is available on the interactions of aminocyclopyrachlor with other compounds. As discussed above, there is remarkably little information suggesting that aminocyclopyrachlor will be substantially toxic to mammals. Consequently, there is no basis for inferring toxicological interactions of aminocyclopyrachlor with other agents. Nonetheless, aminocyclopyrachlor is a weak acid. In terms of mechanism of action, it is likely that aminocyclopyrachlor would influence and be influenced by other weak acids excreted by the kidney or liver. These influences, however, would be significant only at relatively high doses that saturate the active transport processes involved in excretion (e.g., Schnermann and Sayegh 1998).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

The exposure assessments used in the current risk assessment are given in the accompanying EXCEL workbooks: Attachment 1 for aminocyclopyrachlor and Attachment 2 for cyclopropanecarboxylic acid. As discussed in Section 3.1.15.1, the U.S. EPA/OPP (2010a) has identified cyclopropanecarboxylic acid as an environmental degradate of concern. Cyclopropanecarboxylic acid is formed primarily by the aqueous photolysis of aminocyclopyrachlor. Consequently, the exposure scenarios used for cyclopropanecarboxylic acid involve only those scenarios associated with contaminated surface water, which is consistent with the exposure assessments developed by the EPA (U.S. EPA/OPP 2010a).

The EXCEL workbooks contain a set of worksheets that detail each exposure scenario discussed in this risk assessment as well as summary worksheets for both workers applying aminocyclopyrachlor (Worksheet E01 in Attachment 1) and members of the general public (Worksheet E02 in Attachments 1 and 2). Documentation for these worksheets is presented in SERA (2011b). All exposure assessments for both terrestrial and aquatic applications are based on the maximum labeled application rate of 0.28 lb a.e./acre. The impact of using lower application rates is discussed in the risk characterization (Section 3.4).

For terrestrial applications, worker exposures are modeled for backpack spray, broadcast ground spray, and aerial spray. In non-accidental scenarios involving the normal application of aminocyclopyrachlor, central estimates of exposure for workers are approximately 0.0037 mg/kg/day for backpack applications, 0.0063 mg/kg/day for ground broadcast applications, and 0.0041 mg/kg bw/day for aerial spray. Upper ranges of exposures are approximately 0.022 mg/kg/day for backpack and aerial applications and 0.042 mg/kg/day for ground broadcast applications. All of the accidental exposure scenarios for workers involve dermal exposures. The dose estimates for the accidental exposure scenarios are lower than those estimated for the general exposure of workers. This detail reflects the limited dermal absorption rates for aminocyclopyrachlor (Section 3.1.3.2) and the relatively brief periods of exposure (i.e., 1 minute and 1 hour) used for the accidental exposure scenarios.

For members of the general public, acute non-accidental exposure levels to aminocyclopyrachlor range from about $6x10^{-11}$ mg/kg/day (the lower bound of exposure for swimming in contaminated water for 1 hour) to about 0.38 mg/kg bw (the upper bound associated with the consumption of contaminated vegetation). Acute non-accidental exposures to cyclopropanecarboxylic acid range from $1.3x10^{-10}$ mg/kg/day (the lower bound of exposure for swimming in contaminated water for 1 hour) to 0.00022 mg/kg bw (the upper bound for the consumption of contaminated water). Of the accidental exposure scenarios, the greatest exposure levels are associated with the consumption of contaminated water by a small child—an upper bound of about 0.29 mg/kg bw for aminocyclopyrachlor and 0.0053 mg/kg bw for cyclopropanecarboxylic acid.

As discussed in Section 3.2.3.4 and summarized in Table 9, aminocyclopyrachlor is relatively persistent. Consequently, the longer-term exposure levels are not substantially less than the acute exposure levels. The highest estimated doses are associated with the consumption of

contaminated vegetation—i.e., 0.033 (0.0023 to 0.028) mg/kg bw/day. Aminocyclopyrachlor is not expected to bioaccumulate, and the lowest exposure levels are associated with the consumption of contaminated fish by non-subsistence populations—i.e., about 7.6×10^{-6} (1.1×10^{-7} to 4.4×10^{-5}) mg/kg bw/day. Estimated exposures to cyclopropanecarboxylic acid are essentially negligible with a maximum estimated dose of 6.7×10^{-6} mg/kg bw/day, the upper bound dose for the consumption of contaminated water.

3.2.2. Workers

Two types of exposure assessments are considered for workers: general exposure and accidental/incidental exposure. The term *general exposure* is used to designate exposures involving absorbed dose estimates based on handling a specified amount of chemical during specific types of applications. The accidental/incidental exposure scenarios involve specific events that may occur during any type of application. All exposure assessments (i.e., those for workers as well as members of the general public and ecological receptors) are based on the maximum application rate of 0.28 lb a.e./acre. For most exposure scenarios, exposure and consequent risk will scale linearly with the application rate. The consequences of using lower application rates are considered in the risk characterization (Section 3.4).

3.2.2.1. General Exposures

As described in SERA (2011a), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. Based on analyses of several different pesticides using a variety of application methods, default exposure rates are estimated for three different types of applications: directed foliar (backpack), boom spray (hydraulic ground spray), and aerial. These exposure rates are summarized in Table 6 of the current Forest Service risk assessment. The ranges of estimated occupational exposure rates vary substantially among individuals and groups, (i.e., by a factor of 50 for backpack applicators and a factor of 100 for mechanical ground and aerial applications).

In addition to the application rate and absorbed dose rate, the other factor affecting worker exposure is the number of acres per day that a worker will treat. Table 6 includes the estimated number of acres per day that a worker might treat. These values are based on treatment rates used in several Forest Service Environmental Impact Statements (USDA/Forest Service 1989a,b,c).

Attachment 1, the EXCEL workbook for terrestrial applications, is modified to include three worksheets for general exposures, including backpack applications (Worksheet C01a), ground broadcast applications (Worksheet C01b), and aerial applications (Worksheet C01c). As noted in Section 2.3, other application methods may be used for aminocyclopyrachlor, including various cut surface treatments. As summarized in these worksheets, the central estimates of exposure for workers are approximately 0.0037 mg/kg/day for backpack applications, 0.0063 mg/kg/day for ground broadcast applications, and 0.0041 mg/kg bw/day for aerial spray.

The worker exposure levels estimated in the current Forest Service risk assessment are higher than the occupational exposure estimates developed by the EPA (U.S. EPA/OPP 2010f) using the Pesticide Handlers Exposure Database (PHED). The major reason for this difference is that the EPA estimates include inhalation exposures but not dermal exposures: *Quantification of dermal exposures is not required because no toxicity was observed in a dermal study conducted*

at the limit dose (U.S. EPA/OPP 2010f, p. 5). As discussed in SERA (2011a) and documented further in Keigwin (1998), the worker exposure rates from PHED associated with dermal exposures are much higher than the rates associated with inhalation exposures. The methods used in Forest Service risk assessments involve biomonitoring studies in which dermal exposures predominate. While the methods used in the current Forest Service risk assessment are substantially different from those used in U.S. EPA/OPP (2010f), the risk characterization for workers developed in the current Forest Service risk assessment is consistent with the EPA assessment (U.S. EPA/OPP 2010f), in that none of the HQs for workers exceeds the level of concern (Section 3.4.2).

As discussed in Section 2.3, aminocyclopyrachlor is also labeled for basal bark and cut surface treatments. Standard exposure rates for these application methods have not been developed for Forest Service risk assessments. In addition, the U.S. EPA has not developed worker exposure assessments for these application methods for the conditional registration of aminocyclopyrachlor (U.S. EPA/OPP (2010f). The most prudent approach to evaluating Forest Service programs that use these application methods is to calculate the amount of aminocyclopyrachlor that a worker would apply in a single day and use the exposure rates for backpack applications given in Table 6.

For some pesticides, either the product label or standard Forest Service practice will require the use of personal protective equipment (PPE). When handling concentrated formulations, the product labels for most formulations require the use of chemically resistant gloves. Otherwise, no special PPE is required. This level of PPE is typical in many pesticide applications, including those in the worker exposure studies that are the basis for the worker exposure rates provided in Table 6. Consequently, the worksheets for worker exposures (i.e., C01 series) use a clothing protection factor of 0 (i.e., no protection). As documented in Section 3.4.2 (Risk Characterization for Workers), all of the HQs for general worker exposure are substantially below the level of concern, and the lack of a requirement for extraordinary PPE does not have an impact on the risk characterization for workers.

Typical occupational exposures involve multiple routes of exposure, including oral, dermal, and inhalation. The exposure rates used in the current Forest Service risk assessment are all based on estimates of absorbed doses during field applications. Thus, the general exposure assessments for workers encompass all routes of exposure.

3.2.2.2. Accidental Exposures

The skin surface and eyes of workers are most likely to be affected by accidental spills or splashes of pesticide solutions. Quantitative exposure scenarios for eye exposures are not developed in this or other Forest Service risk assessments. As discussed in Section 3.1.11.3 (Ocular Effects), some formulations of aminocyclopyrachlor may cause slight eye irritation. Quantitative exposure and dose-response assessments for eye irritation are not developed. The potential for eye irritation is considered qualitatively in the risk characterization (Section 3.4.2).

Generally, dermal exposure is the predominant route of exposure for pesticide applicators (Ecobichon 1998; van Hemmen 1992), and accidental dermal exposures are considered quantitatively in all Forest Service risk assessments. The two types of dermal exposures modeled in the risk assessments include direct contact with a pesticide solution and accidental

spills of the pesticide onto the surface of the skin. In addition, two exposure scenarios are developed for each of the two types of dermal exposure, and the estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Both sets of exposure scenarios are summarized in Worksheet E01 of the EXCEL workbook for aminocyclopyrachlor that accompanies this risk assessment (i.e., Attachment 1). Additionally, Worksheet E01 references other worksheets in which the calculations of each exposure assessment are detailed.

Exposure scenarios involving direct contact with solutions of aminocyclopyrachlor are characterized either by immersion of the hands in a field solution for 1 hour or wearing pesticide contaminated gloves for 1 hour. The assumption that the hands or any other part of a worker's body will be immersed in a chemical solution for a prolonged period of time may seem unreasonable; however, it is possible that the gloves or other articles of clothing worn by a worker may become contaminated with a pesticide. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in the solution. In both cases, the chemical concentration in contact with the skin and the resulting dermal absorption rate are essentially constant.

For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. For these types of exposures, the rate of absorption is estimated based on a zero-order dermal absorption rate (K_p). Details regarding the derivation of the K_p value for aminocyclopyrachlor are provided in Section 3.1.3.2.

The amount of the pesticide absorbed per unit time depends directly on the concentration of the chemical in solution. For terrestrial applications, the current risk assessment uses an application volume of 20 gallons/acre with a range of 10 to 500 gallons per acre, which encompasses the potential range of applications to be used in ground and aerial applications (Section 2.4). At the maximum application rate of 0.28 lb a.e./acre, the estimated concentrations in a field solution are 1.7 mg/mL with a range of 0.084 to 3.4 mg/mL (Worksheet A01 in Attachment 1).

The details of the accidental dermal exposure scenarios for workers consist of spilling a chemical solution on to the lower legs as well as spilling a chemical solution on to the hands, at least some of which adheres to the skin. The absorbed dose is then calculated as the product of the amount of chemical on the skin surface (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the chemical concentration in the liquid), the first-order absorption rate, and the duration of exposure. As with the zero-order dermal absorption rate, the first-order absorption rate (k_a) is derived in Section 3.1.3.2.

Numerous exposure scenarios could be developed for direct contact or accidental spills by varying the amount or concentration of the chemical in contact with the skin surface, the surface area of the affected skin, and the duration of exposure. As discussed further in the risk characterization (Section 3.4.2), however, the accidental scenarios lead to exposure levels far below the level of concern. What is more, reasonable variations in these exposure scenarios would not affect the assessment of potential risks to workers.

3.2.3. General Public

3.2.3.1. General Considerations

3.2.3.1.1. Likelihood and Magnitude of Exposure

Members of the general public access national forests and could be exposed to aminocyclopyrachlor in Forest Service applications. Because of the conservative exposure assumptions used in the current risk assessment, neither the probability of exposure nor the number of individuals who might be exposed has a substantial impact on the risk characterization presented in Section 3.4. As noted in Section 1 (Introduction) and detailed in SERA (2011a, Section 1.2.2.2), the exposure assessments developed in this risk assessment are based on *Extreme Values* rather than a single value. Extreme value exposure assessments, as the name implies, bracket the most plausible estimate of exposure (referred to statistically as the central or maximum likelihood estimate) with lower and upper bounds of credible exposure levels.

This Extreme Value approach is essentially an elaboration on the concept of the *Most Exposed Individual* (MEI), sometimes referred to as the *Maximum Exposed Individual*. As this name implies, exposure assessments that use the MEI approach attempt to characterize the extreme but still plausible upper limit on exposure. This common approach to exposure assessment is used by U. S. EPA, other government agencies, and the International Commission on Radiological Protection (e.g., ATSDR 2002; ICRP 2005; Payne-Sturges et al. 2004). In the current risk assessment, all upper bounds on exposure are intended to encompass exposures to the MEI.

In addition to this upper bound MEI value, the Extreme Value approach used in this risk assessment provides a central estimate of exposure as well as a lower bound on exposure. Although not germane to assessing the upper bound risk, the point of using the central estimate, and especially the lower bound estimate, is not to lessen concern. To the contrary, the central and lower estimates of exposure are used to assess the prospect of mitigation—e.g., protective measures to limit exposure. If lower bound exposure estimates exceed a level of concern (which is not the case in the current risk assessment), there is strong indication that the pesticide cannot be used in a manner that will lead to acceptable risk.

In addition to concern for the most exposed individual, there is concern for individuals who may be more sensitive than most members of the general population to aminocyclopyrachlor exposure. This concern is considered in the dose-response assessment (Section 3.3) which bases exposures on the most sensitive endpoint in the most sensitive species and uses an uncertainty factor for sensitive individuals. Atypical sensitivities—i.e., special conditions that might increase an individual's sensitivity to a particular agent—are also considered separately in the risk characterization (Section 3.4.4).

3.2.3.1.2. Summary of Assessments

The exposure scenarios developed for the general public are summarized in Worksheet E03 of the EXCEL workbook for aminocyclopyrachlor that accompanies this risk assessment (Attachment 1). As with the worker exposure scenarios, details about the assumptions and calculations used in these assessments are given in the detailed calculation worksheets in the EXCEL workbook (Worksheets D01–D11).

A standard set of exposure assessments used in all Forest Service risk assessments for foliar applications are considered for aminocyclopyrachlor. As summarized in Worksheet E03, the kinds of exposure scenarios developed for the general public include acute accidental, acute non-accidental, and longer-term or chronic exposures. The acute accidental exposure scenarios assume that an individual is exposed to the compound of concern either during or shortly after its application. The nature of the accidental exposures is intentionally extreme. The acute non-accidental exposures involve dermal contact with contaminated vegetation as well as the consumption of contaminated fruit, vegetation, water, or fish. The longer-term or chronic exposure scenarios parallel the acute exposure scenarios for the consumption of contaminated fruit, water, or fish. All of the non-accidental exposure scenarios are based on levels of exposure to be expected in the routine uses of aminocyclopyrachlor at the maximum application rate of 0.28 lb a.e./acre. The upper bounds of the exposure estimates for the non-accidental scenarios involve conservative assumptions intended to reflect exposure for the MEI (*Most Exposed Individual*). The impact of lower application rates on the risk characterization is discussed in Section 3.4.

3.2.3.2. Direct Spray

Direct sprays involving ground applications are modeled in a manner similar to accidental spills for workers (Section 3.2.2.2). In other words, it is assumed that the individual is sprayed with a solution containing the compound and that an amount of the compound remains on the skin and is absorbed by first-order kinetics. Two direct spray scenarios are given, one for a young child (D01a) and the other for a young woman (D01b).

For the young child, it is assumed that a naked child is sprayed directly during a ground broadcast application and that the child is completely covered (that is, 100% of the surface area of the body is exposed). This scenario is intentionally extreme. As discussed in Section 3.2.3.1.1, the upper limits of this exposure scenario are intended to represent the *Extreme Value* upper limits of exposure for the *Most Exposed Individual* (MEI).

The exposure scenario involving the young woman (Worksheet D01b) is somewhat less extreme and more credible. In this scenario, it is assumed that the lower legs and feet of a woman are accidentally sprayed with a pesticide. The choice of a young woman rather than an adult male in this scenario is common to many of the exposure assessments and relates to concerns for both the most exposed individual as well as the most sensitive individual. As detailed in Section 3.1.9.1, aminocyclopyrachlor does not appear to cause developmental effects in mammals; nonetheless, high doses of aminocyclopyrachlor are associated with decreased body weights in the offspring of rats in a reproduction study (Lewis 2008a). Consequently, the exposure of a young woman of reproductive age is used to better assess the potential for adverse effects in the population at risk of effects associated with exposures during pregnancy—i.e., the most exposed and the most sensitive individual. For this exposure scenario, assumptions are made regarding the surface area of the skin and the body weight of the individual, as detailed in Worksheet A03. The rationale for using specific values in these and other exposure scenarios as well as the sources of the specific values is provided in SERA (2011a,b).

3.2.3.3. Dermal Exposure from Contaminated Vegetation

In this exposure scenario, it is assumed that the herbicide is sprayed at a given application rate and that a young woman comes in contact with sprayed vegetation or other contaminated surfaces at some period after the spray operation (D02). For these exposure scenarios, some estimates of dislodgeable residue (a measure of the amount of the chemical that could be freed from the vegetation) and the rate of transfer of the chemical from the contaminated vegetation to the surface of the skin must be available.

No data are available on dermal transfer rates for aminocyclopyrachlor, which is not a severe limitation in this risk assessment. As detailed in Durkin et al. (1995), dermal transfer rates are reasonably consistent for numerous pesticides, and the methods and rates derived in Durkin et al. (1995) are used as defined in Worksheet D02. Similarly, no data are available on dislodgeable residues for aminocyclopyrachlor, which proves to be a somewhat greater source of uncertainty. For this exposure scenario, a default dislodgeable residue rate of 0.1 of the nominal application rate is used.

The exposure scenario assumes a contact period of 1 hour and further assumes that the chemical is not effectively removed by washing for 24 hours. Other approximations used in this exposure scenario include estimates of body weight, skin surface area, and first-order dermal absorption rates, as discussed in the previous section.

3.2.3.4. Contaminated Water

3.2.3.4.1. Accidental Spill

3.2.3.4.1.1. Aminocyclopyrachlor

The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill of a field solution into a small pond. The calculation of the concentration of aminocyclopyrachlor in water following the spill is given in Worksheet B04b, and the estimate of the dose to a small child is given in Worksheet D05. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation is considered. Since this exposure scenario is based on assumptions that are somewhat arbitrary and highly variable, the scenario may overestimate exposure. The actual chemical concentrations in the water will vary according to the amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs, relative to the time of the spill. In addition, the amount of contaminated water that might be consumed is uncertain. All Forest Service risk assessments assume that the accidental spill occurs in a small pond with a surface area of about one-quarter of an acre (1000 m^2) and a depth of 1 meter. Thus, the volume of the pond is 1000 m^3 or 1,000,000 liters.

A spill volume of 100 gallons with a range of 20 to 200 gallons is used to reflect plausible spill events. These spill volumes are used in all Forest Service risk assessments involving terrestrial applications. The concentrations of aminocyclopyrachlor in the field solution are also varied to reflect the plausible range of concentrations in field solutions—i.e., the material that might be spilled—using the same values as in the accidental exposure scenarios for workers (Section 3.2.2.2). Based on these assumptions, the estimated concentration of aminocyclopyrachlor in a small pond ranges from about 0.006 to about 2.6 mg/L, with a central estimate of about 0.6 mg/L (Attachment 1, Worksheet B04b).

3.2.3.4.1.2. Cyclopropanecarboxylic acid

As discussed in Section 3.1.15.1, the U.S. EPA/OPP (2010a, p. 26) identifies cyclopropanecarboxylic acid (IN-V0977) as a degradate of concern. As detailed further in Section 3.3 (Dose-Response Assessment), the acute and chronic RfDs for cyclopropanecarboxylic acid are substantially lower than the acute and chronic RfDs for aminocyclopyrachlor. Consequently, peak exposures to cyclopropanecarboxylic acid following an accidental spill of aminocyclopyrachlor must be considered. This subsection discusses a method for estimating the concentration of cyclopropanecarboxylic acid in water following an accidental spill of aminocyclopyrachlor. Details of these calculations are given in Worksheet B04b of Attachment 2, the EXCEL workbook for cyclopropanecarboxylic acid.

For formation of metabolites (**C → X → Z**), two first-order differential equations involve the rate of formation of the metabolite (***k_1***) and rate of degradation (***k_2***) of the metabolite and the kinetics of this process are well characterized (e.g., Goldstein et al. 1974). In the general case (i.e., $k_1 \neq k_2$), the concentration of the metabolite at time ***t*** will be:

$$X_t = \frac{k_1 C_0}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right) \qquad \textbf{Equation 1}$$

The peak level of the metabolite (X_{Max}) relative to the starting concentration of the parent compound (C_0) is:

$$\frac{X_{Max}}{C_0} = \left[\frac{k_1}{k_2}\right]^{k_2/(k_2-k_1)} \qquad \textbf{Equation 2}$$

The time to maximum concentration of the metabolite (t_{Max}) is given by:

$$t_{Max} = \frac{1}{k_1 - k_2}\ln\left(\frac{k_1}{k_2}\right) \qquad \textbf{Equation 3}$$

As discussed by U.S. EPA/OPP (2010b, 2010g), photolysis is the major degradation pathway in the formation of cyclopropanecarboxylic acid from aminocyclopyrachlor. Based on the aqueous photolysis study by Lowrie (2008), the photolysis half-life of aminocyclopyrachlor is 1.3 days in natural water (pH 5.66 to 7.78) and 7.3 days in pH 4 buffer.

The Lowrie (2008) study is a standard assay for direct photolysis in water (U.S. EPA/OPPTS 1998a) that involves continuous irradiation by a xenon arc lamp emitting light with a spectral distribution similar to that of natural sunlight for up to 15 days. As discussed further in Section 3.2.3.4.4, the U.S. EPA/OPP does not use experimental photolysis rates directly as inputs into environmental fate models (e.g., FIRST 2001; GENEEC 2001), because the experimental exposure conditions (i.e., continuous irradiation in a small experimental vessel) will not mimic

exposure conditions in which the impact of sunlight is attenuated by water depth, turbidity, and shade. As a general procedure, the EPA divides the experimental rate constant by a factor of 124.

In modeling the fate of aminocyclopyrachlor in surface water, the EPA uses a photolysis half-life for aminocyclopyrachlor of 7.8 days (U.S. EPA/OPP 2010g, p. 4). The reference for the 7.8 day half-life is given as MRID 47560211, which is the Lowrie (2008) aqueous photolysis study. It is not clear whether the 7.8 day half-life, rather than the 7.3 half-life at pH 4 reported by Lowrie (2008), represents a reanalysis of the Lowrie (2008) data or is simply a typographical error.

In any event, the EPA appears to use the longer half-life at pH 4 because it will lead to greater concentrations of aminocyclopyrachlor, compared with the shorter half-life of 1.3 days associated with natural water. For modeling the formation of cyclopropanecarboxylic acid, however, using the shorter photolysis half-life of 1.3 days is a more conservative approach (i.e., the formation of the metabolite is more rapid). Moreover, using the half-life of 1.3 days for natural water at a neutral pH is more relevant to estimating concentrations in natural water.

A half-life of 1.3 days corresponds to a rate constant (k_1 in the above equations) of about 0.53 day^{-1} [$k= \ln(2) \div t_{50} = \ln(2) \div 1.3 \text{ days} \approx 0.53319 \text{ day}^{-1}$]. In modeling the formation of cyclopropanecarboxylic acid, the use of the 0.53 day^{-1} rate constant is highly conservative. In the Lowrie (2008) study, the proportion of radioactivity associated with cyclopropanecarboxylic acid in natural water was 0.146 after 360 hours (15 days). Using the rate constant of 0.53 day^{-1}, the proportion of cyclopropanecarboxylic acid that would be expected at 15 days is about 0.9996 [$1-e^{-0.53 \text{ per day x 15 days}}$]. The reason for this discrepancy involves the pathway for the formation of cyclopropanecarboxylic acid. Aminocyclopyrachlor does not degrade directly to cyclopropanecarboxylic acid but follows a series of pathways involving the formation of several other metabolites—IN-LXT69, IN-QFH57, IN-YY905, and IN-Q3007 (cyclopropanecarboxylic acid)—as illustrated in Figure 1. Adjusted for the attenuation of light with the factor of 124, the effective k_1 for the formation of cyclopropanecarboxylic acid from aminocyclopyrachlor is about 0.0043 day^{-1} [$0.53319 \text{ day}^{-1} \div 124 \approx 0.0042999 \text{ day}^{-1}$].

As discussed in U.S. EPA/OPP (2010b,g), very little information is available on the environmental fate of cyclopropanecarboxylic acid. In conducting the drinking water assessment for cyclopropanecarboxylic acid (U.S. EPA/OPP 2010g), the EPA used quantitative structure-activity relationships to estimate the K_{ow} for aminocyclopyrachlor. In the current Forest Service risk assessment, EPI Suite (U.S. EPA/OPPTS 2011a) was used to estimate physical properties and environmental fate parameters for cyclopropanecarboxylic acid. EPI Suite is a computer program developed by U.S. EPA for estimating several environmental fate properties for environmental contaminants. As summarized in Table 10, the half-life for cyclopropanecarboxylic acid in water is estimated to be 8.7 days, corresponding to a rate coefficient of about 0.08 day^{-1} [$\ln(2) \div 8.7 \text{ days} \approx 0.07967 \text{ days}^{-1}$].

Based on the 0.53 day^{-1} for the formation of cyclopropanecarboxylic acid from aminocyclopyrachlor (k_1) and the degradation rate of 0.08 day^{-1} for cyclopropanecarboxylic acid,

the time to the maximum concentration of cyclopropanecarboxylic acid following a spill of aminocyclopyrachlor will be about 39 days.

In calculating the maximum concentration of cyclopropanecarboxylic acid in units of mg/L, two factors must be considered: the kinetics given in Equation 2 above and the difference in the molecular weight of aminocyclopyrachlor (213.62 g/mole) and cyclopropanecarboxylic acid (86.09 g/mole). Based on Equation 2, the peak concentration of cyclopropanecarboxylic acid relative to the initial concentration of aminocyclopyrachlor is about 0.0455. Equation 2, however, does not consider differences in the molecular weight of the parent compound and metabolite. The molecular weight of cyclopropanecarboxylic acid relative to aminocyclopyrachlor is about 0.403 [86.09 g/mole ÷ 213.62 g/mole ≈ 0.403005]. Thus, correcting for differences in molecular weight, the maximum concentration of cyclopropanecarboxylic acid in water, relative to the initial concentration of aminocyclopyrachlor, is about 0.018 [0.0455 x 0.403005 ≈ 0.0183367].

As discussed in Section 3.2.3.4.1.1, the concentration of aminocyclopyrachlor following an accidental spill is about 0.6 (0.006 to 2.6) mg/L (Attachment 1, Worksheet B04b). Based on the kinetics of the formation and degradation of cyclopropanecarboxylic acid, the expected peak concentration of cyclopropanecarboxylic acid following an accidental spill is about 0.012 (0.00012 to 0.047) mg/L (Attachment 2, Worksheet B04b).

3.2.3.4.2. Accidental Direct Spray/drift for a Pond or Stream

3.2.3.4.2.1. Aminocyclopyrachlor

The exposure scenarios involving drift are less severe but more plausible than the accidental spill scenario described above. U.S. EPA typically uses a 2-meter-deep pond to develop exposure assessments (SERA 2007b). If such a pond is directly sprayed with aminocyclopyrachlor at the maximum application rate of 0.28 lb a.e./acre, the peak concentration in the pond would be about 0.0314 mg/L (Attachment 1, Worksheet D10a). This concentration is a factor of about 80 below the upper bound of the peak concentration of 2.57 mg/L after the accidental spill (Section 3.2.3.4.1, Attachment 1, Worksheets D05) [2.57 mg/L ÷ 0.0314 mg/L ≈ 81.847].

Worksheet D10a in Attachment 1 also models concentrations at distances of 25-900 feet down wind based on standard values adapted from AgDrift and assuming aerial application (SERA 2011b). Based on these estimates, aminocyclopyrachlor concentrations in a small pond contaminated by drift would range from about 0.000001 (backpack application at 900 feet downwind) to 0.007 mg/L (aerial application at 25 feet downwind) at the maximum application rate of 0.28 lb/acre.

Similar calculations can be made for scenarios involving a stream contaminated either by direct spray or drift. For this scenario, the resulting water concentrations depend on the surface area of the stream and the rate of water flow in the stream. The stream modeled in Gleams-Driver simulations (Section 3.2.3.4.3) is about 6 feet wide (1.82 meters), and it is assumed that the pesticide is applied along a 1038-foot (316.38 meters) length of the stream with a flow rate of 710,000 L/day. Using these values, the concentration in stream water after a direct spray is estimated at about 0.026 mg/L. Much lower concentrations, ranging from about 0.000008 to 0.006 mg/L are estimated based on drift at distances of 25-900 feet (Attachment 1, Worksheet D10b).

3.2.3.4.2.2. Cyclopropanecarboxylic acid

Attachment 2 details concentrations of cyclopropanecarboxylic acid due to drift of aminocyclopyrachlor into a small pond (Worksheet B04c) and a small stream (Worksheet B04d). The methods used to calculate the concentration of cyclopropanecarboxylic acid are based on the kinetics for the formation and degradation of cyclopropanecarboxylic acid, as detailed in Section 3.2.3.4.1.2 (i.e., the peak concentration of cyclopropanecarboxylic acid is taken as a factor of about 0.018 of the peak concentration of aminocyclopyrachlor). Details of the calculation of the 0.018 factor are discussed in Section 3.2.3.4.1.2 and detailed in Attachment 2, Worksheet B04b.

3.2.3.4.3. GLEAMS Modeling

3.2.3.4.3.1. Inputs to GLEAMS-Driver

3.2.3.4.3.1.1. General Considerations

The Forest Service developed a program, Gleams-Driver, to estimate expected peak and longer-term pesticide concentrations in surface water. Gleams-Driver serves as a preprocessor and postprocessor for GLEAMS (Knisel and Davis 2000). GLEAMS is a field scale model developed by the USDA/ARS and has been used for many years in Forest Service and other USDA risk assessments (SERA 2007b).

Gleams-Driver offers the option of conducting general exposure assessments using site-specific weather files from Cligen, a climate generator program developed and maintained by the USDA Agricultural Research Service (http://horizon.nserl.purdue.edu/Cligen). Gleams-Driver is used in the current risk assessment to model aminocyclopyrachlor concentrations in a small stream and a small pond.

As discussed in Section 3.1.15.1, the U.S. EPA/OPP (2010a) identifies cyclopropanecarboxylic acid (IN-V0977) as a metabolite of potential concern. As discussed in Section 3.2.3.4.4, the EPA drinking water assessment (U.S. EPA/OPP 2010a) includes a separate exposure assessment for cyclopropanecarboxylic acid in ambient water. Since GLEAMS can accommodate modeling metabolites, Gleams-Driver simulations are conducted for the generation and degradation of cyclopropanecarboxylic acid in surface water.

Table 7 summarizes the nine generic sites selected for modeling. As discussed in SERA (2007b), these locations are standard sites for the application of Gleams-Driver in Forest Service risk assessments and are intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool). For each site, Gleams-Driver was used to simulate 100 applications at a unit application rate of 1 lb/acre, and each of the simulations was followed for a period of about 1½ years after application.

The generic site parameters used in the Gleams-Driver runs are summarized in Table 8, and additional details are available in the documentation for Gleams-Driver (SERA 2007b). For each site modeled, simulations were conducted using clay (high runoff, low leaching potential), loam (moderate runoff and leaching potential), and sand (low runoff, high leaching potential) soil textures. All Gleams-Driver simulations are conducted at an application rate of 1 lb a.e./acre.

As discussed in general in SERA (2011a. Section 3.2.3.4.6) and detailed further for aminocyclopyrachlor in Section 3.2.3.4.6.1 below, the resulting water contamination rates (WCRs) are adjusted for the application rate 0.28 lb a.e./acre – i.e., the maximum application rate for aminocyclopyrachlor. This approach is taken because GLEAMS outputs pesticide loss in fixed text values rather than binary values. The application rate of 1 lb a.e./acre is used as a convention to minimize the loss numeric precision.

Since aminocyclopyrachlor will be applied to weeds such as leafy spurge rather than to trees, the site and surface conditions used in the Gleams-Driver are set to a field (GLEAMS FOREST Code 0) rather than to a conifer, hardwood, or mixed forest. The crop cover parameters are set to weeds, GLEAMS ICROP code 78. Associated with the crop cover parameter in GLEAMS is the crop height. For the simulations conducted in this risk assessment, a height of 36 inches is used based on the approximate maximum height of leafy spurge (e.g., Conservation Commission of Missouri 2012).

3.2.3.4.3.1.2. Aminocyclopyrachlor

Table 9 summarizes the chemical-specific values used in Gleams-Driver simulations. For the most part, the chemical properties used in the Gleams-Driver simulations are identical or similar to the EPA parameters used in U.S. EPA/OPP (2010g, Table 2) in the surface water modeling for aminocyclopyrachlor. The EPA modeling efforts are discussed in Section 3.2.3.4.4. In the current risk assessment, most of the model input values are based on the environmental fate studies submitted to the EPA by registrants as well as standard values for GLEAMS modeling recommended by Knisel and Davis (2000). The notes to Table 9 indicate the sources of the chemical-specific values used in the GLEAMS modeling effort.

Three of the chemical specific parameters used in Gleams-Driver modeling (i.e., soil half-lives, soil K_{oc} and sediment K_d) are based on distributions rather than single values. This approach differs from the modeling approach taken in U.S. EPA/OPP (2010d), which uses only point estimates.

The central estimate of the soil half-life is taken as 373 days based on MRID 475602-21, an aerobic soil metabolism study using the methyl ester of aminocyclopyrachlor. This value is identical to the soil half-life used in U.S. EPA/OPP (2010b, p. 33) and is the upper 90th percentile value of the soil half-lives from MRID 475602-14 and MRID 475602-21. The rationale for using a study on the ester is not clear. The ester is rapidly hydrolyzed to aminocyclopyrachlor. The upper and lower bounds of the soil half-lives are taken from MRID 475602-21, a soil metabolism study using aminocyclopyrachlor acid. The average soil half-life from MRID 475602-21 is about 224 days. While the use of the average half-life of 224 days as a central estimate could be justified, Forest Service risk assessments typically use values that are at least as conservative as those used by the U.S. EPA.

The K_{oc} and K_d values are taken from Manjunatha 2008b (MRID 475602-19). The central estimate of the K_{oc} is taken as 12 mL/g, identical to the value used in U.S. EPA/OPP (2010d). The range of K_{oc} values, 0.03 to 0.98, is taken from the observed range of K_{oc} values from Manjunatha (2008b). The central estimate and range of K_d values is also taken from Manjunatha (2008b) with all values rounded to significant figures—i.e., 0.27 (0.03 to 0.98). The only other

noteworthy component of the K_d and K_{oc} inputs for Gleams-Driver involves the open literature publication of Oliveira et al. (2011) which reports K_{oc} values for aminocyclopyrachlor ranging from 9 to 57 and corresponding K_d values ranging from 0.06 to 1.17 for various Brazilian soils. These K_{oc} and K_d values are not remarkably different from those reported in the registrant study by Manjunatha 2008b (MRID 475602-19, and the incorporation of the data from Oliveira et al. (2011) would not have a substantial impact on the estimates of concentrations of aminocyclopyrachlor in surface water. The study by Manjunatha 2008b (MRID 475602-19) is used as the sole basis of the estimated K_{oc} and K_d values to maintain consistency with the U.S. EPA/OPP.

GLEAMS requires estimates of foliar half-life and foliar washoff fraction. These inputs are not used by EPA models. No data on the foliar half-life for aminocyclopyrachlor were identified. Based on an analysis for 41 pesticides, Juraske et al. (2008) proposes a simple approximation for estimating either dislodgeable foliar residues or total residues based on soil half-lives: plant surface half-lives can be estimated as the soil half-life divided by 4, and the half-life of total residues can be estimated as the soil half-life divided by 16. Although these relationships are not intuitive, a summary of the soil and vegetation half-lives for a far greater number of pesticides (Knisel and Davis 2000) suggests that soil half-lives are usually much greater than foliar half-lives. For the Gleams-Driver simulations, the central estimate of the foliar half-life is taken as 93 days based on the central estimate of the soil life (373 days) divided by 4 and rounded to the nearest digit [373 days ÷ 4 = 93.25 days].

Data for foliar washoff of aminocyclopyrachlor are not available. A value of 0.9 is used based on other pesticides in Knisel and Davis (2000) with comparable water solubility, including Carbon disulfide [2300 mg/L]; Naled [2000 mg/L]; Dinoseb salts [2200 mg/L]; Tebuthiuron [2500 mg/L]. Lower values are plausible; however, the use of 0.9 is conservative in that it will increase pesticide concentrations in water.

The only substantial divergence from input values used in U.S. EPA/OPP (2010g) involves aqueous photolysis. Aqueous photolysis is extremely important to the risk assessment of aminocyclopyrachlor, because the toxic metabolite of concern, cyclopropanecarboxylic acid, is formed primarily from the aqueous photolysis of aminocyclopyrachlor. The soil photolysis of aminocyclopyrachlor is relatively slow and is not a significant source of cyclopropanecarboxylic acid (U.S. EPA/OPP 2010g). As discussed further in Section 3.2.3.4.4, U.S. EPA/OPP (2010g, Table 2) uses a photolysis half-life of 7.8 days from a study using a pH4 buffer solution (MRID 475602-11). Following a standard method used in both EPA's farm pond model (GENEEC 2001) and index reservoir model (FIRST 2001), the half-life is multiplied by 124 to account for the attenuation of light in natural water relative to clear water in an experimental system. Thus, the functional photolysis half-life used by U.S. EPA is 967.2 days (U.S. EPA/OPP 2010g, Appendix 1, p. 8).

As summarized in Table 1, MRID 475602-11 also reports a half-life for the aqueous photolysis of aminocyclopyrachlor in natural water (pH 6.2) of 1.2 days. A pH of 6.2 would be representative of many surface waters, and it is not clear why U.S. EPA/OPP (2010g) uses the substantially longer half-life of 7.8 days from a pH 4 buffer. The shorter half-life of 1.2 days at pH 6.2 is more typical of natural waters and will lead to greater concentrations of

cyclopropanecarboxylic acid in surface water. Consequently, the current Forest Service risk assessment uses the shorter half-life of 1.2 days (pH 6.2). Consistent with EPA, this half-life of 1.2 days is multiplied by a factor of 124 to account for the attenuation of light, and the half-time in water for aminocyclopyrachlor is estimated at 150 days [1.2 days x 124 = 148.8 days rounded to 2 significant places].

The U.S. EPA/OPP (2010g) uses a water solubility of 2810 mg/L for aminocyclopyrachlor. As summarized in Table 1 of the current risk assessment, this value is taken from MRID 475598-16 based on the use of highly purified water (i.e., Milli-Q water). As also noted in Table 1, this MRID reports a somewhat higher water solubility of 4200 mg/L at pH 7. Following the same reasoning used above for the photolysis half-life, the water solubility of 4200 mg/L at pH 7 could be viewed as a more reasonable estimate for the functional water solubility of aminocyclopyrachlor. The lower water solubility in highly purified water probably is an artifact of the decrease in the pH of the water with the addition of aminocyclopyrachlor. As noted in Table 9, however, the water solubility of 2810 mg/L is maintained for consistency with EPA. Water solubility has little impact on the results from GLEAMS, unless the water solubility is very low.

3.2.3.4.3.1.3. Cyclopropanecarboxylic acid

No experimental data were located on the environmental fate properties of cyclopropanecarboxylic acid. In the exposure assessment for the concentrations of cyclopropanecarboxylic acid, U.S. EPA/OPP (2010g) does not model the formation and degradation of cyclopropanecarboxylic acid directly. Instead, the EPA assumes that the maximum concentration of cyclopropanecarboxylic acid in water would be a factor of 0.146 of the concentration of aminocyclopyrachlor. As summarized in Table 1 of the current risk assessment, this assumption is based on MRID 475602-11 (the aqueous photolysis study on aminocyclopyrachlor acid) in which the maximum residue of cyclopropanecarboxylic acid was 14.6% of the maximum concentration of aminocyclopyrachlor. While not explicitly stated in the available summaries of MRID 475602-11, the percentage appears to be given as a molar percent. This interpretation is based on the manner in which U.S. EPA/OPP (2010g) estimates the corresponding concentration (mg/L) of cyclopropanecarboxylic acid. As detailed in U.S. EPA/OPP (2010g, p. 2), the EPA multiplies the maximum concentration of aminocyclopyrachlor (in mg/L) by 0.146 multiplied by the ratio of the molecular weight of the metabolite to the parent compound—i.e., ($86.09 \div 213.62 \approx 0.40$). This approach is sensible only if the 14.6% value is a molar percentage. The results of the EPA modeling are discussed further in Section 3.2.3.4.4. The EPA uses this method for estimating the maximum concentration of cyclopropanecarboxylic acid in water, because insufficient experimental values are available on the fate properties of cyclopropanecarboxylic acid.

Experimental environmental fate values for cyclopropanecarboxylic acid are not available; accordingly, the current Forest Service Risk assessment uses EPI Suite (U.S. EPA/OPPTS 2011a) as an exploratory alternative to the method used in U.S. EPA/OPP (2010g) to estimate fate properties for cyclopropanecarboxylic acid based on quantitative structure-activity relationships (QSAR). EPI Suite (Estimation Program Interface (EPI) Suite, Version 4.1) is a QSAR program developed by the U.S. EPA to estimate several key environmental fate properties based on a chemical's structure. The estimates from EPI Suite for cyclopropanecarboxylic acid

as well as other metabolites of aminocyclopyrachlor are summarized in Table 10, and the input values for cyclopropanecarboxylic acid used in the GLEAMS modeling are summarized in Table 11.

Foliar half-times, which are needed for GLEAMS modeling, are not available from EPI-Suite. As with aminocyclopyrachlor (Section 3.2.3.4.3.1.2), the method of Juraske et al. (2008) was used to estimate foliar half-life from soil half-life.

The modeling of cyclopropanecarboxylic acid does not quantitatively consider residues of cyclopropanecarboxylic acid on contaminated vegetation. Aminocyclopyrachlor may come into contact with water on the surface of plants from dew, precipitation after spraying, and the presence of diluting water during application. This could increase the formation of cyclopropanecarboxylic acid. While the duration for potential photolysis on plant surfaces may be relatively short, there will also be fewer or different attenuation factors involved. While this potential pathway is acknowledged, quantitative approximations of this pathway cannot be developed in the absence of any monitoring data.

3.2.3.4.3.2.Results from GLEAMS-Driver

3.2.3.4.3.2.1. Aminocyclopyrachlor

Table 12 summarizes the results for the Gleams-Driver runs, estimates of concentrations in ponds and streams from direct spray or spray drift (Section 3.2.3.4.2), as well as modeling conducted by the U.S. EPA/OPP (Section 3.2.3.4.4). Details of the results for the Gleams-Driver runs are provided in Appendix 8. Note that all results from the Gleams-Driver runs are expressed as the median value with approximate 95% empirical limits. In other words, the two extreme lower and upper values from the 100 simulations at each site are dropped, and the lowest and highest remaining values are used for the lower and upper bound estimates reported in Table 12 and Appendix 8.

Note that all concentrations given in Table 12 are associated with a unit application rate of 1 lb a.e./acre. These concentrations are referred to as Water Contamination Rates, and Forest Service risk assessments discuss the results of Gleams-Driver modeling following a unit application rate of 1 lb/acre. As discussed in Section 2, the maximum application rate for aminocyclopyrachlor is 0.28 lb a.e./acre. The adjustment of Water Contamination Rates to concentrations of aminocyclopyrachlor in surface water is discussed in Section 3.2.3.4.6 (Concentrations in Water Used for Risk Assessment). Also note that modeled concentrations of aminocyclopyrachlor in surface water are given to 3 significant digits. Given the uncertainties associated with the use of any environmental fate model, there is no expectation that model accuracy is significant to 3 significant digits. The use of 3 significant digits is simply a convention used in Forest Service risk assessments. As also discussed in Section 3.2.3.4.6, the water concentrations used in the current risk assessment are rounded to one significant digit.

The median concentrations estimated by Gleams-Driver for a small pond (137 µg/L) and a small stream (81.7 µg/L) are comparable to concentrations estimated from the direct spray of a small pond (112 µg/L) and small stream (91 µg/L), and the peak concentrations modeled by Gleams-Driver for a small pond (720 µg/L) and small stream (700 µg/L) are substantially greater than the corresponding concentrations associated with direct spray. This pattern is not unusual. The

concentrations associated with direct spray are limited by the application rate and depth of the surface water. The concentrations in surface water estimated by Gleams-Driver are based on the treatment of a 10-acre field with subsequent pesticide loss to a relatively small pond and stream (Table 8).

The lower bound estimates from Gleams-Driver are problematic. Even in locations with low to moderate rainfall, many individual simulations (i.e., sets of 100 Gleams-Driver runs at a specific location with a specific soil texture) lead to lower bound estimates and sometimes central estimates of concentrations in surface water that are zero or nearly so. Again, this pattern is common in Gleams-Driver simulations and reflects years with low to moderate rainfall. For example, Appendix 8, Table A10-5 summarizes the results for estimates of aminocyclopyrachlor in a small stream. For dry locations, some of the central as well as the lower and upper bound estimates of aminocyclopyrachlor in surface water are zero. In other words, over the course of the 100 simulations conducted for each location and soil type, at least 3 years are sufficiently dry to yield empirical estimates of zero for the concentration of the pesticide in the stream. Finally, it is worth noting that GLEAMS outputs pesticide losses in text rather than a binary format. While scientific notation is sometimes used, zero values are typically given in fixed decimal notation out to six places—i.e., “0.000000”. As discussed further in Section 3.2.3.4.6, this feature leads to some instability and apparently erratic estimates of lower bound concentrations which must be addressed in the selection of lower bound non-zero estimates of chemical concentrations in surface water from Gleams-Driver simulations.

3.2.3.4.3.2.2. Cyclopropanecarboxylic acid

Table 13 summarizes the results for the Gleams-Driver simulations for cyclopropanecarboxylic acid. As with the corresponding table for aminocyclopyrachlor (Table 12), Table 13 also summarizes estimates of concentrations of cyclopropanecarboxylic acid in ponds and streams from direct spray or spray drift (Section 3.2.3.4.2) and modeling for cyclopropanecarboxylic acid conducted by the U.S. EPA/OPP (Section 3.2.3.4.4). Details of the Gleams-Driver results for cyclopropanecarboxylic acid are provided in Appendix 9. Also as with the results for aminocyclopyrachlor, the estimated concentrations are expressed as the median value with approximate 95% empirical limits. All of the Gleams-Driver estimates for concentrations of cyclopropanecarboxylic acid are based on an application rate of 1 lb aminocyclopyrachlor/acre.

As with the modeled concentrations of aminocyclopyrachlor (Section 3.2.3.4.3.2.1), the peak concentrations of cyclopropanecarboxylic acid are similar for both ponds and streams—i.e., 0.57 (0.0017 to 4.9) µg/L in ponds and 0.76 (0.00265 to 6.7) µg/L in streams. Also as with aminocyclopyrachlor, longer-term concentrations of cyclopropanecarboxylic acid are greater in ponds—0.085 (0.000225 to 0.7) µg/L—than in streams—i.e., 0.0248 (0.000065 to 0.2).

The estimated concentrations of cyclopropanecarboxylic acid are substantially less than those for aminocyclopyrachlor. Based on central estimates of exposure, the ratio of the modeled concentrations of aminocyclopyrachlor are greater than the corresponding concentrations of cyclopropanecarboxylic acid by factors of about 100 to 740. As discussed further in Section 3.2.3.4.4.2, the EPA modeling of cyclopropanecarboxylic acid (U.S. EPA/OPP 2010g) estimates much higher concentrations of cyclopropanecarboxylic acid than those estimated with Gleams-Driver. These differences are due primarily to the use of photolysis data on the degradation of

aminocyclopyrachlor to cyclopropanecarboxylic acid and differences in the assumptions concerning the persistence of cyclopropanecarboxylic acid.

3.2.3.4.4. Other Modeling Efforts

3.2.3.4.4.1. Aminocyclopyrachlor

Other efforts to model aminocyclopyrachlor concentrations in surface water are summarized in Table 12, which also summarizes the surface water modeling conducted for the current risk assessment (Section 3.2.3.4.3). To estimate concentrations of a pesticide in ambient water, the U.S. EPA typically uses Tier 1 screening models (e.g., GENEEC, FIRST, and SCIGROW) or PRZM/EXAMS, a more refined Tier 2 modeling system. The U.S. EPA/OPP typically models pesticide concentrations in water at the maximum labeled rate. All of the concentrations given in Table 12 are expressed as Water Contamination Rates (WCRs)—i.e., the modeled concentration divided by the application rate. This adjustment results in values expressed as µg/L per lb/acre, which are directly comparable to the concentrations estimated with Gleams-Driver.

In the human health risk assessment for aminocyclopyrachlor (U.S. EPA/OPP 2010a), the U.S. EPA used FIRST to estimate peak concentrations in surface water of about 90.3 µg a.e./L and annual average concentrations of 56.1 µg a.e./L in an index reservoir. SCIGROW, a Tier 1 model for estimating concentrations in groundwater, was used to estimate peak and longer-term concentrations of 124 µg a.e./L. In the ecological risk assessment for aminocyclopyrachlor (U.S. EPA/OPP 2010b), the EPA used GENEEC to estimate a peak concentration of 59.4 µg/L and a longer-term concentration of 58.2 µg/L in a standard farm pond. All of the peak concentrations are similar to the central estimates of peak concentrations from Gleams-Driver (i.e., about 82 to 140 µg/L). The longer-term concentrations from both FIRST and GENEEC are quite similar to the central estimate for a pond from Gleams-Driver (i.e., 62.9 µg/L).

The upper bound concentrations from Gleams-Driver (i.e., about 700 µg a.e./L for peak exposures and 350 µg a.e./L for longer-term concentrations in a pond) are higher than the corresponding concentrations from either FIRST or SCIGROW. This discrepancy is typical of many comparisons of Gleams-Driver to Tier 1 models. Because Gleams-Driver is applied to numerous site/soil combinations and because 100 simulations are conducted for each site/soil combination, the upper bound values from Gleams-Driver often exceed the concentrations obtained from conservative Tier 1 models used by U.S. EPA/OPP.

3.2.3.4.4.2. Cyclopropanecarboxylic acid

The drinking water assessment for aminocyclopyrachlor (U.S. EPA/OPP 2010g) also estimates concentrations of cyclopropanecarboxylic acid in surface water. Using FIRST, the index reservoir model, U.S. EPA/OPP (2010g) estimates peak concentrations of 89.1 µg/L and longer-term concentrations of 63.8 µg/L. The FIRST model cannot be used directly to estimate concentrations of metabolites. Consequently, the U.S. EPA/OPP adopted a somewhat unusual approach in applying FIRST.

The aqueous photolysis study by Lowrie (2008), discussed in Section 3.2.3.4.1.2, notes that 14.6% of radioactivity of ^{14}C-aminocyclopyrachlor (labeled in the 2-pyrimidine carbon) was recovered from sterile natural water as cyclopropanecarboxylic acid following 360 hours (15

days) of irradiation. No aminocyclopyrachlor was detected in irradiated water after 144 hours (6 days) (Lowrie 2008, Table 6, p. 42). The EPA adjusted these data by the molecular weights of aminocyclopyrachlor (213.62 g/mole) and cyclopropanecarboxylic acid (86.09 g/mole) and estimated that an application rate of 0.284 lb aminocyclopyrachlor/acre would be equivalent to an application rate of about 0.017 lb cyclopropanecarboxylic acid/acre [0.284 lb/acre x 0.146 x 86.09/213.62 ≈ 0.0167102 lb/acre]. Based on the input file for FIRST (U.S. EPA/OPP 2010g, p. 10), the only inputs for cyclopropanecarboxylic acid were a K_{oc} of 2.735 and a water solubility of 149,540 mg/L, both of which were estimates from quantitative structure-activity relationships (U.S. EPA/OPP 2010g, p. 5-6). No inputs were used for field degradation, hydrolysis, or photolysis. Based on these assumptions, the concentrations in surface water estimated by FIRST were 1.515 µg/L (peak) and 1.084 µg/L (annual average). In Table 13 of the current risk assessment, the peak concentration is expressed as a water contamination rate of 89.1 µg/L per lb/acre [1.515 µg/L ÷ 0.017 lb/acre ≈ 89.1176 µg/L per lb/acre], and the longer-term concentration of 1.084 µg/L is expressed as a water contamination rate of 63.8 µg/L per lb/acre [1.084 µg/L ÷ 0.017 lb/acre ≈ 63.7647 µg/L per lb/acre].

3.2.3.4.5. Monitoring Data

Monitoring data are not available on aminocyclopyrachlor or cyclopropanecarboxylic acid concentrations in surface water following aminocyclopyrachlor applications. The lack of monitoring data, particularly for cyclopropanecarboxylic acid following applications of aminocyclopyrachlor, is a substantial limitation in the current risk assessment. As discussed in Section 3.2.3.4.4.2 and summarized in Table 13, different approaches may be taken to estimating concentrations of cyclopropanecarboxylic acid in surface water, and these different approaches lead to substantially different estimates of cyclopropanecarboxylic acid concentrations. In the absence of monitoring data, the relative merits of the differing approaches cannot be assessed directly.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

3.2.3.4.6.1. Aminocyclopyrachlor

Table 14 summarizes the surface water concentrations of aminocyclopyrachlor used in the current risk assessment. The concentrations are specified as water contamination rates (WCRs)—i.e., the concentrations in water expected at a normalized application rate of 1 lb a.e./acre, converted to units of ppm or mg/L per lb a.e./acre. In Table 12, units of exposure are expressed as ppb or µg/L, as a matter of convenience. In Table 14, however, ppb is converted to ppm because ppm and mg/L are the units of measure used in the EXCEL workbook for contaminated water exposure scenarios in both the human health and ecological risk assessments. The water contamination rates are entered in Worksheet B04Rt in Attachment 1 (the EXCEL workbook for aminocyclopyrachlor). The values in Worksheet B04Rt are linked to the appropriate scenario-specific worksheets in the EXCEL workbooks.

As noted in 3.2.3.4.5, no monitoring data are available on aminocyclopyrachlor surface water concentrations. While the Gleams-Driver estimates are reasonably consistent with U.S. EPA/OPP modeling (Section 3.2.3.4.4), the lack of monitoring data adds uncertainty to this risk assessment.

As summarized in Table 12, the peak concentrations for aminocyclopyrachlor are taken as 0.1 **(**0.002 to 0.7**)** mg a.e./L. The central estimates of peak concentrations of aminocyclopyrachlor

modeled using Gleams-Driver for a small pond (137 µg/L) and small stream (81.7 µg/L) are similar, and this range of concentrations brackets the concentration of 90.3 µg/L from the U.S. EPA/OPP (2010g) application of the FIRST model. For the current risk assessment, the average of the range from the Gleams-Driver (i.e., 109. 35 µg/L) is rounded to one significant digit, and 0.1 mg/L per lb/acre is used as the central estimate of the water contamination rate. The upper bound of 0.7 mg/L is simply a unit conversion of the upper bound concentration of 720 µg/L from the Gleams-Driver pond simulations rounded to one significant place. Similarly, the lower bound of 0.002 mg a.e./L is based on the lower bounds for the pond (2.04 µg/L) and stream (2.42 µg/L) rounded to one significant place.

As also summarized in Table 14, the longer-term concentrations for aminocyclopyrachlor are taken as 0.06 (0.0009 to 0.35) mg a.e./L. The central estimate and upper bound are the central estimate of 62.9 µg/L and the upper bound of 350 ppb for a small pond based on the Gleams-Driver modeling (Table 12) converted to units of mg/L. The central estimate is rounded to one significant place, and the upper bound is rounded to two significant places. The lower bound of 0.0009 mg/L is identical to the lower bound for longer-term concentrations of aminocyclopyrachlor in the pond (i.e., 0.9 µg/L).

3.2.3.4.6.2. Cyclopropanecarboxylic acid

The Water Contamination Rates for cyclopropanecarboxylic acid are also summarized in Table 14. As with aminocyclopyrachlor, the lack of monitoring data on cyclopropanecarboxylic acid concentrations in surface water associated with aminocyclopyrachlor applications is a limitation in the current risk assessment. The limitation is more severe with cyclopropanecarboxylic acid, because, unlike the case with aminocyclopyrachlor, the modeling estimates from Gleams-Driver are not concordant with the estimates from the U.S. EPA/OPP (2010g).

As summarized in Table 13, the cyclopropanecarboxylic acid concentrations estimated by the U.S. EPA using FIRST are substantially higher than the estimates from Gleams-Driver. The major factor contributing to the discrepancies between FIRST and the Gleams-Driver modeling appears to involve the assumption that cyclopropanecarboxylic acid will not degrade. The study by Lowrie (2008) clearly supports the EPA assumption that cyclopropanecarboxylic acid is stable to photolysis and hydrolysis in that the concentration of cyclopropanecarboxylic acid in sterile natural water continued to increase over the 360-hour exposure period. The assumption that cyclopropanecarboxylic acid is stable to biological degradation in surface water is certainly conservative but is not consistent with estimates of biological degradation from EPI Suite, the EPA program for estimating environmental fate parameters. Based on BIOWIN v4.10, a component of EPI Suite, cyclopropanecarboxylic acid is estimated to biodegrade rapidly with a half-life of 4.1 days. Based on the Level II Fugacity Model in EPI Suite, the estimated half-life of cyclopropanecarboxylic acid in surface water is 208 hours (8.666 days). As summarized in Table 11, an aqueous half-life of 8.7 days was used in the Gleams-Driver modeling.

Another factor in interpreting the application of FIRST by U.S. EPA/OPP (2010g) in modeling cyclopropanecarboxylic acid involves consistency with the FIRST modeling of aminocyclopyrachlor. As summarized in Table 12, the FIRST modeling by U.S. EPA/OPP (2010g) estimates a peak concentration of 90.3 µg/L for aminocyclopyrachlor. Under the

assumption that 14.6% of aminocyclopyrachlor would degrade to cyclopropanecarboxylic acid, a peak concentration for cyclopropanecarboxylic acid based on the peak concentration of aminocyclopyrachlor would be about 5.3 µg/L [90.3 µg/L x 0.146 x 86.09/213.62 ≈ 5.313 µg/L]. This alternate approach to applying FIRST to estimate cyclopropanecarboxylic acid concentrations is consistent with Gleams-Driver. As indicated in Table 13, the upper bound peak concentrations of cyclopropanecarboxylic acid estimated by Gleams-Driver are in the range from about 4.9 to 6.7 µg/L. The geometric mean of this range is 5.7 µg/L, which is virtually identical to the estimate of 5.3 µg/L based on the peak concentration of aminocyclopyrachlor estimated by the U.S. EPA/OPP (2010g).

While the Gleams-Driver modeling is dependent on quantitative structure-activity relationships (QSAR) from EPI Suite, the same limitations apply to the FIRST modeling by U.S. EPA/OPP (2010g). The only substantial difference is that the Gleams-Driver modeling considers a greater number of QSAR estimates, specifically the estimate associated with the biodegradation of cyclopropanecarboxylic acid in surface water.

Based on the above considerations, the modeling with FIRST conducted by U.S. EPA/OPP (2010g) is viewed as a highly conservative screening estimate; whereas, the Gleams-Driver modeling is viewed as a reasonable refinement to estimating more plausible surface water concentrations of cyclopropanecarboxylic acid. Consequently, the estimated concentrations of cyclopropanecarboxylic acid used in the current Forest Service risk assessment are based on estimates from Gleams-Driver.

As summarized in Table 14, the peak estimates of cyclopropanecarboxylic acid in surface water following an application of aminocyclopyrachlor at 1 lb/acre are 0.0007 (0.000002 to 0.007) mg/L. This central estimate is based on the average of the central estimates for the pond (0.57 µg/L) and stream (0.76 µg/L) rounded to one significant place. The lower bound is also based on the average of the lower bounds for the pond (0.0017 µg/L) and stream (0.00265 µg/L) rounded to one significant place. The upper bound is based on the upper bound for a small stream (6.7 µg/L) rounded to one significant place. The upper bound is not based on an average of the pond and stream in order to estimate the plausible worst-case concentrations for the most exposed individual, as discussed in Section 3.2.3.1.1.

The longer-term concentrations for cyclopropanecarboxylic acid given in Table 14 are also based on the Gleams-Driver modeling, as summarized in Table 13, using the same approach used for the peak concentrations.

3.2.3.5. Oral Exposure from Contaminated Fish

Many chemicals may be concentrated or partitioned from water into the tissues of aquatic animals or plants. This process is referred to as bioconcentration. Generally, bioconcentration is measured as the ratio of the concentration in the organism to the concentration in the water. For example, if the concentration in the organism is 5 mg/kg and the concentration in the water is 1 mg/L, the bioconcentration factor (BCF) is 5 L/kg [5 mg/kg ÷ 1 mg/L]. As with most absorption processes, bioconcentration depends initially on the duration of exposure but eventually reaches steady state. Details regarding the relationship of the bioconcentration factor to standard pharmacokinetic principles are provided in Calabrese and Baldwin (1993).

Because exposures following applications of aminocyclopyrachlor may include both aminocyclopyrachlor and cyclopropanecarboxylic acid, these exposure scenarios are included both in Attachment 1 (the EXCEL workbook for aminocyclopyrachlor) and Attachment 2 (the EXCEL workbook for cyclopropanecarboxylic acid). In each attachment, three sets of exposure scenarios are presented: one set for acute exposures following an accidental spill (Worksheets D08a and D08b), one set for acute exposures based on expected peak concentrations of aminocyclopyrachlor in water (Worksheets D09c and D09d), and another set for chronic exposures based on estimates of longer-term concentrations in water (Worksheets D09a and D09b). The two worksheets for each set of scenarios are included to account for different consumption rates of caught fish among the general population and subsistence populations. Details of these exposure scenarios are provided in Section 3.2.3.5 of SERA (2011a).

The provisional registration document for aminocyclopyrachlor (U.S. EPA/OPP 2010k) as well as the supporting human health (U.S. EPA/OPP 2010a) and ecological (U.S. EPA/OPP 2010b) risk assessments note that aminocyclopyrachlor appears to have a low potential for bioaccumulation but do not specifically note that the requirement for a bioconcentration study in fish has been waived. Nonetheless, no bioaccumulation studies in fish have been identified in the list of registrant-submitted studies (Attachment 3). Consequently, the bioconcentration factors used for aminocyclopyrachlor (3.162, as summarized in Table 1) and cyclopropanecarboxylic acid (1.259, as summarized in Table 10) are based on estimates from EPI Suite (U.S. EPA/OPPTS 2011a).

The scenarios associated with the consumption of contaminated fish are based on the same water concentrations of aminocyclopyrachlor and cyclopropanecarboxylic acid used for the accidental spill scenario (Section 3.2.3.4.1.) and the surface water exposure estimates (Section 3.2.3.4.6).

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

Some geographical sites maintained by the Forest Service or Forest Service cooperators include surface water in which members of the general public might swim. To assess the potential risks associated with swimming in contaminated water, an exposure assessment is developed for a young woman swimming in surface water for 1 hour. Details of the exposure assessment are given in Worksheet D11 of Attachment 1 (aminocyclopyrachlor) and Attachment 2 (cyclopropanecarboxylic acid).

For aminocyclopyrachlor, the dermal permeability rates (K_p) used in this scenario are discussed in Section 3.1.3.2. As with aminocyclopyrachlor, the K_p for cyclopropanecarboxylic acid is based on the algorithm developed by the EPA (U.S. EPA/ORD 1992, 2007) using a molecular weight of 86.09 and a K_{ow} of 4.27 (Table 10). Details of the calculations of the K_p for cyclopropanecarboxylic acid are given in Worksheet B03a of Attachment 2.

Conceptually and computationally, this exposure scenario is virtually identical to the contaminated gloves scenario used for workers (Section 3.2.2.2)—i.e., a portion of the body is immersed in an aqueous solution of the compound at a fixed concentration for a fixed period of time. As in the corresponding worker exposure scenario, the 1-hour period of exposure is somewhat arbitrary given that longer periods of exposure are plausible. Nonetheless, the 1-hour period is intended as a unit exposure estimate. In other words, the exposure and consequently

the risk will increase linearly with the duration of exposure, as indicated in Worksheet D11. Thus, a 2-hour exposure would lead to an HQ that is twice as high as that associated with an exposure period of 1 hour. In cases in which this or other similar exposures approach a level of concern, further consideration is given to the duration of exposure in the risk characterization (Section 3.4). For aminocyclopyrachlor and cyclopropanecarboxylic acid, however, the HQs for this scenario are far below the level of concern.

As with the exposure scenarios for the consumption of contaminated fish, the scenarios for exposures associated with swimming in contaminated water are based on the peak water concentrations of both aminocyclopyrachlor and cyclopropanecarboxylic acid used to estimate acute exposure to drinking water (Section 3.2.3.4.6).

3.2.3.6. Oral Exposure from Contaminated Vegetation

Although none of the Forest Service applications of aminocyclopyrachlor will involve crop treatment, Forest Service risk assessments typically include standard exposure scenarios for the acute and longer-term consumption of contaminated vegetation. Two sets of exposure scenarios are provided: one for the consumption of contaminated fruit and the other for the consumption of contaminated vegetation. These scenarios, detailed in Worksheets D03a and D03b for acute exposure and Worksheets D04a and D04b for chronic exposure, apply only to terrestrial aminocyclopyrachlor (Attachment 1). As discussed in Section 3.2.3.4.1.2 as well as in the exposure assessment by U.S. EPA/OPP (2010a), cyclopropanecarboxylic acid is formed primarily by the aqueous photolysis of aminocyclopyrachlor. Consistent with the exposure assessments in U.S. EPA/OPP (2010a), dietary exposure assessments are not developed for cyclopropanecarboxylic acid.

The pesticide on contaminated fruit and vegetation is estimated using the empirical relationships between application rate and concentration on different types of vegetation (Fletcher et al. 1994). The rates provided by Fletcher et al. (1994) are based on a reanalysis of data originally compiled by Hoerger and Kenaga (1972) and represent estimates of pesticide concentration in different types of vegetation (mg chemical/kg vegetation) after a normalized application rate of 1 lb/acre. Although the EPA human health risk assessments do not consider this exposure scenario, the residue rates recommended by Fletcher et al. (1994) are used by U.S. EPA/OPP in their ecological risk assessment of aminocyclopyrachlor (U.S. EPA/OPP 2010b, p. 35).

The residue rates recommended by Fletcher et al. (1994) are given in Table 15 of the current risk assessment. Fletcher et al. (1994) and Hoerger and Kenaga (1972) provide only central and upper bound estimates of residue rates. Accordingly, the lower bound estimates in Table 10 are made under the assumption that the ratio of the central estimate to the upper bound estimate is identical to the ratio of the lower bound estimate to the central estimate (i.e., the variability is log-symmetrical).

For longer-term exposures, the time-weighted average exposure is estimated using the initial pesticide concentration and its half-life on vegetation (Worksheet D04a and D04b). These worksheets accommodate a central estimate and the lower and upper bounds on the half-life.

The half-life of aminocyclopyrachlor residues on vegetation is not reported in the available literature, including the published literature or the studies submitted to the EPA in support of

registration. Based on an analysis for 41 pesticides, Juraske et al. (2008) proposes a simple approximation for estimating either dislodgeable foliar residues or total residues based on soil half-lives—i.e., plant surface half-lives can be estimated as the soil half-life divided by 4, and the half-life of total residues can be estimated as the soil half-life divided by 16. Although these relationships are not intuitive, a summary of the soil and vegetation half-lives for a far greater number of pesticides (Knisel and Davis 2000) suggests that soil half-lives are usually much greater than foliar half-lives.

As summarized in Table 9, a soil half-life of 373 days is used for Gleams-Driver modeling, based on a registrant submitted study, MRID 475602-14 as reviewed by U.S. EPA/OPP (2010g, Table 2). Rather than estimating total residue half-lives as one-sixteenth of the soil half-lives, as recommended by Juraske et al. (2008), the current risk assessment takes a more conservative approach and divides the soil half-life by 4. Thus, the half-lives for total residues on contaminated vegetation or fruit are taken as 93 days [373 days $\div 4 \approx 93.25$ days].

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

The dose-response assessment considers both aminocyclopyrachlor and cyclopropanecarboxylic acid. As discussed in Section 3.1.15.1, U.S. EPA/OPP (2010a) identifies cyclopropanecarboxylic acid as a degradate of concern, and this compound is considered quantitatively in the current risk assessment.

An overview of the dose-response assessments for aminocyclopyrachlor is given in Table 16, and an overview for the dose-response assessment for cyclopropanecarboxylic acid is given in Table 17. For aminocyclopyrachlor, the current Forest Service risk assessment uses an acute RfD of 3.5 mg/kg bw/day and a chronic RfD of 0.35 mg/kg bw/day. For cyclopropanecarboxylic acid, the acute RfD is taken as 0.0026 mg/kg bw and the chronic RfD is taken as 0.00087 mg/kg bw/day. These RfDs are currently used by and derived by the EPA (U.S. EPA/OPP 2010a). The standard practice used in Forest Service risk assessments is to defer to U.S. EPA in the selection and derivation of RfDs.

Aminocyclopyrachlor is a new herbicide under conditional registration, and the RfDs for aminocyclopyrachlor and cyclopropanecarboxylic acid may be revised by the U.S. EPA in the near future. New registrant studies for both aminocyclopyrachlor and cyclopropanecarboxylic acid were submitted to the U.S. EPA/OPP, and these studies may lead to changes in the RfDs for aminocyclopyrachlor and cyclopropanecarboxylic acid. The description of the new studies and their likely impact on the RfDs are discussed in Section 3.3.2 for aminocyclopyrachlor and Section 3.3.3 for cyclopropanecarboxylic acid. If the EPA changes the RfDs for either or both compounds, the revised RfDs will be adopted in the current risk assessment. If the EPA revises the RfDs subsequent to the completion of this Forest Service risk assessment, the Forest Service may elect to use the newer RfDs in any application of this risk assessment to Forest Service projects or programs.

3.3.2. Aminocyclopyrachlor

3.3.2.1. Acute RfD

The U.S. EPA/OPP will sometimes derive acute RfDs for pesticides. Typically, acute RfDs are based on developmental studies, under the assumption that the endpoint observed in the developmental study could be associated with a single dose of the pesticide. For aminocyclopyrachlor, however, the EPA did not derive an acute RfD because no acute end-point of concern was identified (U.S. EPA/OPP 2010a, p. 30). As discussed in Section 3.1.9.1, weight loss is the only effect attributable to aminocyclopyrachlor in developmental studies. Weight loss is generally associated with several days of exposure and not typically used by the U.S. EPA/OPP to derive an acute RfD.

The U.S. EPA/OPP (2010a, Table 3.3.10.1, p. 22) does, however, derive an RfD for *Incidental Oral Short-Term* exposures. This RfD is intended to apply to exposure periods of 1 to 30 days. This short-term RfD is based on the 13-week feeding study in rats by Anand (2008a,b) in which decreases in body weight, weight gain, food consumption, and food conversion efficiency were observed at a dietary concentration of 18,000 ppm in both males and females. These effects were not observed at a dietary concentration of 6000 ppm. The rat NOAEL of 6000 ppm is

supported by subchronic NOAELs in mice (7000 ppm, Anand 2008c,d) and dogs (15,000, Luckett 2008a; Luckett and Mawn 2008).

Based on measured food consumption and body weights, the dietary concentration of 6000 ppm (Anand 2008a,b) corresponds to doses of about 349.4 mg/kg bw/day in male rats and 448 mg/kg bw/day in female rats (Appendix 1 Table A1-2). In deriving the short-term RfD, U.S. EPA/OPP (2010a) uses a NOAEL dose of 350 mg/kg bw/day. The NOAEL is divided by an uncertainty factor of 100 (i.e., a factor of 10 to account for sensitive individuals multiplied by the factor of 10 to account for inter-species extrapolation). Thus, the short-term RfD is taken as 3.5 mg/kg bw/day. This RfD is used in the current risk assessment to characterize the consequences of accidental and other acute exposures to aminocyclopyrachlor.

3.3.2.2. Chronic RfD

The U.S. EPA has not derived an agency-wide chronic RfD for aminocyclopyrachlor —i.e., there is no RfD for aminocyclopyrachlor listed on the U.S. EPA Integrated Risk Information System (http://www.epa.gov/IRIS/). Other than the chronic RfD from U.S. EPA/OPP (2010a) discussed below, no exposure criteria (e.g., ADIs, TLVs, etc) were identified for aminocyclopyrachlor.

As discussed in Section 3.1.5, chronic studies were completed in dogs (Han 2010), mice (Huh 2010), and rats (Moon 2010); however, these studies were not available at the time that the conditional registration for aminocyclopyrachlor (U.S. EPA/OPP 2010k) was approved. In the absence of chronic studies, U.S. EPA/OPP (2010a, Section 3.3.2, p. 19) uses the subchronic rat NOAEL of 350 mg/kg bw/day from Anand (2008c,d). Rather than applying an uncertainty factor of 100 as was done with the short-term RfD, U.S. EPA/OPP (2010a) uses an uncertainty factor of 1000, with the additional factor of 10 accounting for extrapolation of a subchronic to chronic study. Thus, the EPA derived a chronic RfD is 0.35 mg/kg bw/day (U.S. EPA/OPP 2010a).

As summarized in Appendix 1 (Table A1-2), the 2-year feeding study in rats results in a NOAEL of 6000 ppm with a LOAEL (based on a decrease in food conversion efficiency and body weight parameters) of 18,000 ppm. These dietary NOAEL and LOAEL values are identical to the corresponding subchronic value in rats from the study by Anand (2008a,b). Based on measured food consumption and body weights, the corresponding chronic doses are somewhat lower than subchronic doses. The chronic NOAEL of 6000 ppm corresponds to an average dose of about 270 mg/kg bw/day in male rats and 309 mg/kg bw/day in female rats. The chronic LOAEL of 18,000 ppm corresponds to an average dose of about 892 mg/kg bw/day in male rats and 957 mg/kg bw/day in female rats. Like the subchronic NOAEL in rats, the chronic NOAEL in rats is supported by dietary NOAELs of 30,000 ppm in mice (Han 2010) and 7000 ppm in dogs (Huh 2010).

If the U.S. EPA/OPP reviews and accepts the newly submitted chronic studies, it is likely the chronic RfD for aminocyclopyrachlor will be revised to about 3 mg/kg bw/day (i.e., the rat NOAEL of 270 mg/kg bw divided by an uncertainty factor of 100 and rounded to one significant digit).

For the current Forest Service risk assessment, the current chronic RfD of 0.35 mg/kg bw/day is used for risk characterization, in keeping with the practice in Forest Service risk assessments of

deferring to RfDs derived by the U.S. EPA unless there is a compelling reason to do otherwise (SERA 2011a). In the case of the chronic RfD for aminocyclopyrachlor, the summaries of the chronic studies given in Appendix 1 (Table A1-2) are based on OECD study summaries rather than the full studies. In addition, without their review and acceptance by U.S. EPA/OPP, the newly submitted chronic studies would not be used to derive a new RfD for aminocyclopyrachlor unless the data suggested that the current EPA RfD is not sufficiently protective, which is not the case.

While the current Forest Service risk assessment does not derive a new and higher chronic RfD for aminocyclopyrachlor, the chronic studies are discussed further in Section 3.4 (Risk Characterization) in terms of more fully characterizing risks from chronic exposures to aminocyclopyrachlor.

3.3.3. Cyclopropanecarboxylic acid

3.3.3.1. Acute RfD

The acute RfD for cyclopropanecarboxylic acid is somewhat atypical in that the RfD is based on a gavage study of panadiplon in rabbits (Ulrich et al. 1995). As discussed in Section 3.1.15.1, the EPA converted the LOAEL of 10 mg panadiplon/kg bw/day to a LOAEL of 2.55 mg cyclopropanecarboxylic acid/kg bw/day based solely on differences in the molecular weights of the two compounds (U.S. EPA/OPP 2010a). In deriving the acute RfD for cyclopropanecarboxylic acid, the EPA used an uncertainty factor of 1000 (i.e., a multiple of 10 for sensitive subgroups, 10 for animal-to-human extrapolation, and 10 for extrapolating from the LOAEL to a NOAEL) and rounded the acute RfD to two significant places (i.e., 0.0026 mg/kg bw/day.

As discussed previously in Section 3.1.15.1, DuPont™ recently completed a 90-day gavage study with cyclopropanecarboxylic acid in rats in which no effects were noted at doses of 2 and 10 mg/kg bw/day (Carpenter 2012). Liver effects comparable to those observed in rabbits (Ulrich et al. 1995) were observed at 30 and 60 mg/kg bw/day. As yet, an EPA review of the Carpenter (2012) study is not available. Although the EPA would not use the Carpenter (2012) study directly to modify the acute (single-dose) RfD, the study may be useful for developing a short-term (1 to 30 day exposure) RfD, similar to the approach taken for aminocyclopyrachlor (3.3.2.1). Taking this approach, the EPA would probably use an uncertainty factor of 100 (i.e., a multiple of 10 for species extrapolation and a factor of 10 for sensitive subgroups), and the modified acute/incidental RfD would be 0.1 mg/kg bw.

Following standard practice in Forest Service risk assessments, the current acute RfD of 0.0026 mg/kg bw/day from U.S. EPA/OPP (2010a) is used to characterize risks associated with acute exposure scenarios.

3.3.3.2. Chronic RfD

The chronic RfD for cyclopropanecarboxylic acid derived by U.S. EPA/OPP is 0.00087 mg/kg bw/day (U.S. EPA/OPP 2010a). Like the acute RfD, the chronic RfD is based on the gavage study of panadiplon in rabbits (Ulrich et al. 1995). As discussed in Section 3.3.3.1, the cyclopropanecarboxylic acid equivalent LOAEL of 2.55 mg/kg bw/day is divided by a factor of

3000 (i.e., a multiple of the three factors described for the acute RfD and an additional factor of 3 for extrapolating from a *subchronic* to a chronic value).

This chronic RfD is highly atypical. The Ulrich et al. (1995) study involves an exposure period of only 10 days. U.S. EPA/OPPTS (2000) recognizes 28-day studies as a screening assay for standard 90-day subchronic studies. Although 10-day periods of exposure are sometimes used in acute dietary toxicity studies in mammals, a duration of 10 days is not generally viewed as a standard exposure duration for a subchronic study. This atypical exposure duration raises concern that the use of the Ulrich et al. (1995) study may not be sufficiently protective.

Conversely and as discussed in Section 3.3.3.1, DuPont™ recently completed a gavage 90-day study in rats in which no effects were observed at doses of 2 and 10 mg/kg bw/day (Carpenter 2012). U.S. EPA/OPP might, if the study is judged acceptable, consider using the NOAEL of 10 mg/kg bw/day to derive an alternate chronic RfD. Following standard practice, the EPA would probably use an uncertainty factor of 1000 (i.e., a multiple of 10 for sensitive subgroups, 10 for animal-to-human extrapolation, and 10 for extrapolating from subchronic to chronic exposure), and the revised RfD would be 0.01 mg/kg bw/day. As discussed in Section 3.1.15.1, the only substantial reservation with this approach is whether rats or rabbits are considered the most sensitive species.

As with the acute RfD , the current Forest Service risk assessment uses chronic RfD of 0.00087 mg/kg bw/day derived by U.S. EPA/OPP (2010a) to characterize risks associated with chronic exposures to cyclopropanecarboxylic acid. Uncertainties regarding the possibility that the U.S. EPA/OPP might revise the chronic RfD for cyclopropanecarboxylic acid are discussed further in the risk characterization (Section 3.4).

3.4. RISK CHARACTERIZATION

3.4.1. Overview

An overview of risks to workers is given in Table 18. Similar overviews for risks to members of the general public are given in Table 19 for aminocyclopyrachlor and Table 20 for cyclopropanecarboxylic acid. In these tables, risk is characterized as the hazard quotient (HQ), the estimated level of exposure divided by an acute or chronic RfD depending on the exposure scenario. The level of concern is defined as an HQ of 1.

For workers, no exposure scenarios, acute or chronic, exceed the RfD at the upper bound of the estimated dose associated with the highest application rate of 0.28 lb a.e./acre. The HQs for directed ground spray, broadcast ground spray, and aerial applications are below the level of concern by factors of 10 to about 17. Similarly, no HQs for aminocyclopyrachlor exceed the level of concern for members of the general public. The highest HQ is 0.8, the upper bound of the HQ for the consumption of broadleaf vegetation. This exposure scenario is standard in all Forest Service risk assessments; moreover, this scenario typically leads to the highest HQs. For an effective herbicide like aminocyclopyrachlor, this exposure scenario may be viewed as implausible in that treated or contaminated vegetation would show signs of damage following the application of the herbicide, which should reduce if not eliminate the possibility of long-term consumption of the treated vegetation. Exposures associated with the consumption of contaminated water are far more likely, and the upper bound HQs for these exposure scenarios are below the level of concern by factors of about 100 (HQ of 0.01 for the longer-term consumption of contaminated water) to 10,000 (HQ of 0.0001 for the longer-term consumption of contaminated fish).

Cyclopropanecarboxylic acid is considered quantitatively because this degradate of aminocyclopyrachlor is considered a degradate of concern by the U.S. EPA/OPP. The upper bounds of the HQs for the non-accidental exposure scenarios are below the level of concern by factors of about 11 (HQ of 0.09 for the acute consumption of water by a young child) to 25,000 (HQ of 0.00004 for the longer-term consumption of contaminated fish by non-subsistence populations). The only HQ that exceeds the level of concern is the upper bound HQ of 2 for the consumption of contaminated water by a child, following an accidental spill. The peak concentration of cyclopropanecarboxylic acid in water, however, would not occur until about 40 days after the spill. Therefore, in the event of an accidental spill of aminocyclopyrachlor, there would be adequate time to take remedial actions, thus, limiting the likelihood that water contaminated with cyclopropanecarboxylic acid would be consumed.

The risk characterization given in this risk assessment is qualitatively similar to that given by the U.S. EPA: no risks to workers or members of the general public are anticipated. The current risk assessment derives higher HQs, relative to comparable measures of risk in the U.S. EPA human health risk assessment, because it uses different methods to assess worker exposure. Furthermore, the current risk assessment uses a number of extreme exposure scenarios for members of the general public that are not used by the U.S. EPA.

3.4.2. Workers

The quantitative risk characterization for workers is summarized in Table 18. The HQs given in this table are taken from Worksheets E02 in Attachment 1 (EXCEL workbook for

aminocyclopyrachlor). As with all similar risk characterization tables discussed in this risk assessment, the HQs are based on the maximum labeled application rate of 0.28 lb a.e./acre. The HQs for accidental exposures are based on the short/intermediate RfD of 3.5 mg/kg bw/day and the HQs for general exposures are based on the chronic RfD of 0.35 mg/kg bw/day, as summarized in Table 16.

The risk characterization for workers is simple and unambiguous: there is no basis for asserting that workers are likely to be at risk in applications of aminocyclopyrachlor. The highest HQ for general exposures—i.e., exposure levels anticipated in the normal use of aminocyclopyrachlor — is 0.1, the upper bound of the HQ for workers involved in ground broadcast applications of aminocyclopyrachlor.

Risks are explicitly characterized only for workers involved in ground or aerial broadcast applications or direct applications to water. As discussed in Section 2.3, various other application methods, including various forms of cut surface treatments may be used in some Forest Service programs. Exposure assessments for workers involved in these types of treatments are not developed, because adequate worker exposure studies are not available. As summarized in Table 6, the highest documented worker exposure rates are associated with directed foliar applications. In Forest Service programs considering cut surface treatments, it may be reasonable to approximate worker exposures using the rates for directed foliar applications with the amount of aminocyclopyrachlor to be handled.

As discussed in Section 3.1.11.3, some aminocyclopyrachlor formulations may cause eye irritation. From a practical perspective, eye irritation is likely to be the only overt effect as a consequence of mishandling aminocyclopyrachlor; furthermore, this effect is most likely to result from handling granular formulations prior to application. Eye irritation can be minimized or avoided by prudent industrial hygiene practices, including the use of goggles while handling granular formulations of aminocyclopyrachlor.

Aminocyclopyrachlor is not classified as a skin irritant. While some dermal toxicity studies note minor skin irritation (Section 3.1.12), studies designed specifically to assess the potential for dermal irritation are interpreted in U.S. EPA/OPP (2010a) as indicating that aminocyclopyrachlor is not a skin irritant. Nonetheless, prudent worker practices should be used when handling any pesticide, to ensure that skin contact is minimized.

The risk characterization for workers derived in the current Forest Service risk assessment is qualitatively similar to the EPA occupational risk assessment (U.S. EPA/OPP 2010f), in that the level of concern is not exceeded for any group of workers. The Margins of Exposure (MOEs) derived by the EPA range from 190,000 to 38 million. The MOEs would correspond to HQs that are much lower than those derived for workers in the current Forest Service risk assessment. As discussed in Section 3.2.2.1, the differences between the EPA derived MOEs and the HQs derived in the current risk assessment are due primarily to the EPA's decision to include only inhalation and not dermal routes of exposure in the occupational exposure assessment for aminocyclopyrachlor.

3.4.3. General Public

3.4.3.1. Aminocyclopyrachlor

The quantitative risk characterization for exposures of the general public to aminocyclopyrachlor is summarized in Table 19. This table is taken from Worksheets E04 in Attachment 1. As with the quantitative risk characterization for workers, the HQs for accidental and acute exposures are based on the short/intermediate RfD of 3.5 mg/kg bw/day, and the HQs for longer-term exposures are based on the chronic RfD of 0.35 mg/kg bw/day. As discussed in Section 3.3.2.2, additional studies were submitted to the U.S. EPA/OPP which could result in an upward adjustment of the chronic RfD. While such an adjustment would lower the chronic HQs, this action would have no substantial impact on the qualitative risk characterization, because none of the chronic HQs based on the current chronic RfD exceed the level of concern.

As with workers, there is no basis for asserting that members of the general public are likely to be at risk due to applications of aminocyclopyrachlor. The highest HQs are associated with the consumption of contaminated broadleaf vegetation. The upper bound HQ for acute exposures is 0.1, and the upper bound for chronic exposures is 0.8. These exposure scenarios are extremely conservative in that the consumption of contaminated vegetation is assumed to occur shortly after the direct spray of the vegetation at the maximum application rate of 0.28 lb a.e./acre. The chronic exposure scenarios for the consumption of contaminated vegetation may be viewed as grossly and perhaps overly conservative in that vegetation sprayed with aminocyclopyrachlor at the maximum application rate would probably show signs of damage following treatment, and it does not seem likely that an individual would consume damaged vegetation over a prolonged period of time. This exposure scenario is used consistently in Forest Service risk assessments simply as an upper bound screen for potential risks. For aminocyclopyrachlor, no risks are apparent.

Each of the HQs summarized in Table 19 involves a single exposure scenario. In some cases, individuals could be exposed by more than one route. In such cases, risks can be approximated simply by adding the HQs for different exposure scenarios. For aminocyclopyrachlor, consideration of multiple exposure scenarios has little impact on the risk assessment. For example, based on the upper bounds of HQs for being directly sprayed on the lower legs (HQ=0.0009), staying in contact with contaminated vegetation for 1 hour (HQ=0.0004), eating contaminated fruit (HQ=0.01) and contaminated broadleaf vegetation (HQ=0.1), drinking contaminated surface water (HQ=0.006), and consuming contaminated fish at rates characteristic of subsistence populations (HQ=0.002) lead to a combined HQ of 0.1193 [0.0009 + 0.0004 + 0.01 + 0.1 + 0.006 + 0.002]. In other words, for aminocyclopyrachlor, the predominant route of exposure will involve the consumption of contaminated vegetation. This pattern is apparent in most pesticide risk assessments involving foliar applications.

3.4.3.2. Cyclopropanecarboxylic acid

The quantitative risk characterization for exposures of the general public to cyclopropanecarboxylic acid following an application of aminocyclopyrachlor at the maximum application rate of 0.28 lb a.e./acre is summarized in Table 20. This table is taken from Worksheets E04 in Attachment 2. As discussed in Section 3.2.1, the assessment of cyclopropanecarboxylic acid includes only the subset of exposure scenarios associated with

contaminated water, because cyclopropanecarboxylic acid is formed primarily by the aqueous photolysis of aminocyclopyrachlor.

The HQs for accidental and acute exposures are based on the acute RfD of 0.0026 mg/kg bw, and the HQs for longer-term exposures are based on the chronic RfD of 0.00087 mg/kg bw/day. The acute and chronic RfDs for cyclopropanecarboxylic acid are unusual in that they are based on a 2-week toxicity study in rabbits dosed with panadiplon, a drug that is metabolized to cyclopropanecarboxylic acid. As discussed in Section 3.3.3, a standard subchronic toxicity study of cyclopropanecarboxylic acid has been submitted to the U.S. EPA/OPP. If the U.S. EPA/OPP accepts this study and uses it as the basis for RfDs on cyclopropanecarboxylic acid, it is likely that the acute RfD would increase to 0.1 mg/kg bw (an increase of a factor of about 38) and the chronic RfD would increase to 0.01 mg/kg bw/day (an increase of a factor of about 11).

Changes in the RfDs for cyclopropanecarboxylic acid would have an impact on the qualitative risk characterization only for the accidental spill scenario. As summarized in Table 20, the upper bound HQ for this scenario is 2, and this is the only scenario in which the HQ exceeds the level of concern (HQ>1). If the acute RfD were increased to 0.1 mg/kg bw, the upper bound HQ for this scenario would be 0.05, below the level of concern by a factor of 20.

Based on the current RfDs, all of the non-accidental exposure scenarios are below the level of concern. The highest acute HQ is 0.09, the upper bound of the HQ associated with the consumption of contaminated water by a small child. This HQ is below the level of concern by a factor of more than 10. The highest chronic HQ is 0.008, the upper bound HQ for the consumption of contaminated water by an adult male. This HQ is below the level of concern by a factor of 125.

While the upper bound HQ of 2 for the accidental spill scenario modestly exceeds the level of concern based on the current acute RfD for cyclopropanecarboxylic acid, the time-course of risk is noteworthy. As discussed in Section 3.2.3.4.1.2, the peak concentration of cyclopropanecarboxylic acid in water following an accidental spill of aminocyclopyrachlor would not occur for about 40 days. Therefore, in the event of an accidental spill of aminocyclopyrachlor, there would be adequate time to take remedial actions, thus, limiting the likelihood that water contaminated with cyclopropanecarboxylic acid would be consumed.

3.4.4. Sensitive Subgroups

There is no information to suggest that specific groups or individuals may be especially sensitive to the systemic effects of aminocyclopyrachlor. As noted in Section 3.1, it is not clear that aminocyclopyrachlor has any remarkable systemic toxic effects. The most common effects in experimental mammals involve decreases in body weight, body weight gain, and food conversion efficiency in rats. These effects have not been noted in other mammals and appear to be associated with levels of exposure that are substantially higher than any likely human exposures. Thus, it would seem highly speculative and unjustified to suggest that individuals with metabolic disorders might be more susceptible than other individuals to aminocyclopyrachlor.

Notwithstanding the above, aminocyclopyrachlor is a weak acid. As noted in Section 3.1.2 and 3.1.16, it seems reasonable to suggest that aminocyclopyrachlor would influence and be

influenced by other weak acids excreted by the kidney; however, this effect would occur only at high doses at which the ability of the kidney to excrete weak acids might be saturated or nearly so. Given the low HQs for aminocyclopyrachlor, there appears to be no basis for asserting that this or other adverse effects in a specific subgroup are plausible.

3.4.5. Connected Actions

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions (40 CFR 1508.25) as actions which occur in close association with the action of concern; in this case, pesticide use. Actions are considered to be connected if they: (i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously, and (iii) Are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this risk assessment, "connected actions" include actions or the use of other chemicals which are necessary and occur in close association with the use of aminocyclopyrachlor.

As detailed in Section 3.1.15.1 (Metabolites), applications of aminocyclopyrachlor will lead to the formation of cyclopropanecarboxylic acid in water via aqueous photolysis. The impact of this metabolite is considered quantitatively in the current risk assessment (Section 3.4.3.2).

As discussed in detail in Section 3.1.14 (Adjuvants and Other Ingredients), aminocyclopyrachlor formulations may contain other ingredients (i.e., *inerts*). The identity of the inerts used in aminocyclopyrachlor formulations was disclosed to the U.S. EPA/OPP; however, this information is not available for the conduct of the current risk assessment. Nonetheless, as discussed in Section 3.1.14.1, a comparison of the acute toxicity studies on technical grade aminocyclopyrachlor and aminocyclopyrachlor formulations does not suggest that the inerts in aminocyclopyrachlor formulations contribute to their toxicity. Given the low HQs associated with both accidental and non-accidental exposure scenarios (Section 3.4.3.1) and the generally conservative assumptions on which these HQs are based, there does not appear to be a plausible basis for suggesting that inerts will have an impact on the risk characterization for potential human health effects.

Adjuvants are a much more difficult issue to address, and it is beyond the scope of the current risk assessment to address all possible adjuvants that might be used, in the absence of specific information on the joint action of aminocyclopyrachlor with the adjuvants. This is a general issue in many Forest Service risk assessments. Nonetheless, as discussed in Section 3.1.14.2, the adjuvants specifically recommended on the formulation labels for aminocyclopyrachlor consist of compounds that are also used as food additives or compounds classified by the U.S. EPA as *minimal risk inerts*.

3.4.6. Cumulative Effects

Cumulative effects may involve either repeated exposures to an individual agent or simultaneous exposures to the agent of concern (in this case aminocyclopyrachlor) and other agents that may cause the same effect or effects by the same or a similar mode of action.

In terms of repeated exposures, the current risk assessment does specifically consider the effect of repeated and longer-term exposures to aminocyclopyrachlor for both workers and members of

the general public (Section 3.2). Consequently, the risk characterizations presented in this risk assessment for longer-term exposures specifically address and encompass the potential impact of the cumulative effects of aminocyclopyrachlor. As discussed in Sections 3.4.2 and 3.4.3, there is no basis for asserting that longer-term or repeated exposures to aminocyclopyrachlor at doses corresponding to the RfD will lead to cumulative adverse effects.

The U.S. EPA/OPP often addresses cumulative risks associated with exposures to other compounds that have similar modes of action. In the current EPA documents on aminocyclopyrachlor, however, cumulative risk is not specifically addressed (U.S. EPA/OPP 2010a,f,k). As noted in Section 3.1.2 and discussed further in Section 4.1.2.5, the mechanism of the herbicidal effects of aminocyclopyrachlor is well characterized; however, the specific mechanism of action in mammals (if any) is unclear. Consequently, risks associated with exposures to other compounds with similar mechanisms of action in mammals cannot be elaborated.

The use of aminocyclopyrachlor will involve exposures to cyclopropanecarboxylic acid. The potential for cumulative effects from combined exposures to these two agents, however, does not seem substantial. As noted in Section 3.4.3.2 (risk characterization for cyclopropanecarboxylic acid) and detailed further in Section 3.2.3.4.1.2 (accidental spill of cyclopropanecarboxylic acid), there will be a lag period of about 40 days between peak contamination of surface water with aminocyclopyrachlor and the peak formation of cyclopropanecarboxylic acid. Given the low toxicity of aminocyclopyrachlor and cyclopropanecarboxylic acid, the available data do not suggest that cumulative effects associated with co-exposure to aminocyclopyrachlor and cyclopropanecarboxylic acid are a substantial concern.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Exposure to aminocyclopyrachlor is generally not associated with identifiable hazards in animals. U.S. EPA/OPP (2010b) classifies aminocyclopyrachlor as *Practically Non-toxic* or only *Slightly Toxic* to mammals, birds, fish, and aquatic invertebrates. This classification is clearly justified by the available data. As with most ecological risk assessments of herbicides, the largely benign assessment of the hazards or lack of hazards to groups of nontarget species is tempered by the fact that toxicity data are available on only a few species, relative to the numerous species which may be exposed to aminocyclopyrachlor. In addition, the specific lack of data regarding toxicity to terrestrial-phase or aquatic-phase amphibians and the general lack of toxicity data in the open literature further constrain the hazard identification for aminocyclopyrachlor. All of the data on the potential toxicity of aminocyclopyrachlor to animals is from a limited number of registrant-submitted studies required by the U.S. EPA/OPP for pesticide registration. The general lack of toxicity data is common for new pesticides.

Aminocyclopyrachlor is an effective auxin-mimicking herbicide and is hazardous to terrestrial and, to a lesser extent, aquatic plants. Dicots (i.e., broadleaf plants) are substantially more sensitive than monocots (e.g., grasses), as is generally true for auxin-mimicking herbicides. Aminocyclopyrachlor is somewhat unusual in that incident reports from the application of Imprelis®, a specific formulation of aminocyclopyrachlor, indicate that it may be atypically toxic to some species of conifers, particularly Norway spruce (*Picea abies*) and white pine (*Pinus strobus*). The reported incidents of damage to conifers are sufficiently frequent and severe that the U.S. EPA/OPP withdrew the registration of the Imprelis® formulation, but has not released a review of the incidence of conifer damage. The available plant bioassays on the phytotoxicity of aminocyclopyrachlor are limited to standard test species of monocots and dicots. Conifers are neither dicots nor monocots; however, the available data on the toxicity of aminocyclopyrachlor to monocots and dicots together with an efficacy study involving pine suggest that the residual soil toxicity of aminocyclopyrachlor has the potential to damage conifers.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

4.1.2.1.1. Aminocyclopyrachlor

As summarized in the human health risk assessment (Section 3.1), several standard toxicity studies in experimental mammals were conducted and submitted to the EPA as part of the registration process for aminocyclopyrachlor. All of these studies, which are used in the human health risk assessment to identify the potential toxic hazards associated with exposures to aminocyclopyrachlor, can also be used to identify potential toxic effects in wildlife mammalian species.

Field studies to assess the impact of aminocyclopyrachlor applications on mammalian wildlife communities have not been conducted. Given that aminocyclopyrachlor is a new pesticide, the lack of field data is not unexpected.

In standard experimental toxicity studies, aminocyclopyrachlor has low acute oral toxicity. A common measure of acute oral toxicity is the LD_{50}, the estimate of the dose that may be lethal to 50% of the exposed animals. As summarized in Appendix 1 (Table A1-1), the acute oral LD_{50} values for aminocyclopyrachlor are greater than 5000 mg/kg (Carpenter 2008b,c; Moore 2008a). Moreover, no mortality or signs of toxicity were observed in any rats after exposure to aminocyclopyrachlor.

The most common effects noted in toxicity studies on aminocyclopyrachlor involve decreases in body weight, body weight gain, and food conversion efficiency. Decreases in body weight and/or body weight gain in rats are frequently noted in subchronic, chronic, developmental, and reproduction studies conducted on aminocyclopyrachlor (Anand 2008a,b; Lewis 2008a; Moon 2010). Effects on body weight are noted only sporadically in mice (Anand 2008c,d;) and rabbits (Fleeman 2008), but not at all in dogs (Luckett 2008a; Luckett and Mawn 2008; Han 2010). Changes in food conversion efficiency are noted only in rats (Anand 2008a,b; Hoban 2008b; Lewis 2008a). As discussed in the human health risk assessment, the specific mechanism associated with a decrease in food conversion efficiency has not been identified (Section 3.2), although an impact on endocrine activity cannot be ruled out (Section 3.1.8).

Dogs have an impaired ability to excrete some weak acid herbicides such as 2,4-D (Piper et al. 1973) and triclopyr (Timchalk and Nolan 1997). Because aminocyclopyrachlor is a weak acid, dogs and other canid species might be expected to be more sensitive than rodents to aminocyclopyrachlor. Based on the available subchronic and chronic toxicity studies, this does not appear to be the case for aminocyclopyrachlor. To the contrary, as discussed further in the dose-response assessment for mammalian wildlife (Section 4.3.2.1.1), dogs appear to be less sensitive than rats.

4.1.2.1.2. Cyclopropanecarboxylic acid

As discussed in Section 3.1.1.5.1, the human health risk assessment on aminocyclopyrachlor conducted by U.S. EPA/OPP identifies cyclopropanecarboxylic acid as a metabolite of concern and quantifies potential risks from exposure to this degradate (U.S. EPA/OPP 2010a). In the ecological risk assessment on aminocyclopyrachlor, U.S. EPA/OPP also identifies cyclopropanecarboxylic acid as a degradate of potential concern; however, the concern for this and other degradates is addressed only semi-quantitatively: … *by comparing the concentrations expected in the environment to thresholds, IN-V0977 would have to be more than two orders of magnitude more toxic* [than the] *parent compound to cause LOC exceedances* (U.S. EPA/OPP 2010b, p. 55).

The current Forest Service risk assessment addresses the potential risks of cyclopropanecarboxylic acid to mammalian wildlife in a manner similar to that used in the human health risk assessment. As detailed further in Section 4.2.2, exposures to mammalian wildlife are assessed only for contaminated water and are based on the same estimated concentrations of cyclopropanecarboxylic acid used in the human health risk assessment. Similarly, the dose-response assessment for mammalian wildlife is based on the same study used

in the human health risk assessment (Table 17). While this approach is somewhat more elaborate than that used in the EPA ecological risk assessment, U.S. EPA/OPP (2010b), the results are consistent with those of the Agency (Section 4.4.2).

4.1.2.2. Birds

Avian toxicity studies conducted with aminocyclopyrachlor are summarized in Appendix 2. The registrant submitted a relatively standard set of avian toxicity studies required for pesticide registration to the U.S. EPA: one acute gavage study on technical grade aminocyclopyrachlor in bobwhite quail (Gallagher and Beavers 2007), acute dietary studies in bobwhite quail (Hubbard et al. 2007b) and mallard ducks (Hubbard et al. 2007a), and reproduction studies in bobwhite quail (Temple et al. 2008b) and mallard ducks (Temple et al. 2008a). All of these toxicity studies are reviewed by the U.S. EPA in the ecological risk assessment for the conditional registration of aminocyclopyrachlor (U.S. EPA/OPP 2010b).

4.1.2.2.1. Gavage Administration

As summarized in Appendix 2 (Table A2-1), no mortality, sublethal effects, or changes in body weights or food consumption were noted in bobwhite quail following single-dose gavage administration of technical grade aminocyclopyrachlor at doses of 0 (vehicle control), 269, 448, 747, 1245, or 2075 mg a.e./kg bw (Gallagher and Beavers 2007). Based on the lack of any effects at the highest dose tested, the EPA classifies technical grade aminocyclopyrachlor as *Practically Non-Toxic* to quail (U.S. EPA/OPP 2010b, p. 41).

4.1.2.2.2. Acute Dietary Exposure

Acute dietary studies were conducted in both bobwhite quail (Hubbard et al. 2007b) and mallard ducks (Hubbard et al. 2007a). As summarized in Appendix 2 (Table A2-2), both studies assayed technical grade aminocyclopyrachlor at dietary concentrations ranging from 562 to 5620 ppm for 8 days followed by a 3-day observation period. No effects were observed in either study on mortality, signs of toxicity, food consumption or body weight parameters. Accordingly, the EPA classifies technical grade aminocyclopyrachlor as *Practically Non-Toxic* to quail and mallards (U.S. EPA/OPP 2010b, p. 42).

4.1.2.2.3. Reproduction Studies

One-generation dietary reproduction studies were conducted in bobwhite quail (Temple et al. 2008b) and mallard ducks (Temple et al. 2008a). Both assays used technical grade aminocyclopyrachlor at dietary concentrations 0, 160, 400, or 1000 ppm with a 22 week exposure period that included 11 weeks pre-egg laying and 11 weeks during egg laying. No dose-related effects were observed on any reproductive parameters. As with the acute dietary studies, no effects were observed on mortality, signs of toxicity, food consumption or body weight parameters.

A limitation in the use of the reproduction studies (Temple et al. 2008a,b) in the current Forest Service risk assessment is that the EPA classified both studies as *Invalid* (U.S. EPA/OPP 2010b). In general, Forest Service risk assessments do not use toxicity studies classified as invalid by the U.S. EPA to quantify exposure. The primary rationale stated in the DERs for classifying the Temple et al. (2008a,b) studies *invalid* is that the pen sizes were too small. The EPA guidelines for conducting reproduction studies in birds note that the space requirements for bobwhites and mallards are not well defined; however, the *recommended* space requirements are at least

5000 cm^2 for bobwhite and 10,000 cm^2 for mallards (U.S. EPA/OPPTS 1996, p. 10). In the Temple et al. (2008a,b) studies, the birds were housed as mated pairs in pens with surface areas of 1275 cm^2 (25 cm x 51 cm) or 637.5 cm^2/bird for quail and 6750 cm^2 (75 cm x 90 cm) or 3375 cm^2/bird for mallards.

The DERs for the avian reproduction studies in mallards and quail (Temple et al. 2008a,b) suggest that three incidental mortalities in mallards and seven incidental mortalities in quail may have been associated with small cage sizes. Furthermore, the DER for the mallard study indicates that 16 hens in control and treatment groups produced atypically low numbers of eggs (less than 10 per hen) and that peritonitis was observed in yolks of eggs produced by these hens. DuPont™ has submitted supplements to the reproduction studies on mallards (Beavers 2010a) and quail (Beavers 2010b) arguing that these studies should be classified as acceptable.

As discussed further in Section 4.3.2.2.2 (dose-response assessment for birds), Forest Service risk assessments will not typically use studies classified as invalid by the U.S. EPA/OPP. These studies, however, constitute the only information available on the longer-term toxicity of aminocyclopyrachlor to birds. In addition and as discussed further in the risk characterization for bird (Section 4.4.2.2), the use of these studies do lead to modest exceedances in the level of concern (HQ>1). Consequently, these studies are used, albeit with reservations, in the dose-response assessment for birds (Section 4.3.2.2.2).

4.1.2.3. Reptiles and Amphibians (Terrestrial-Phase)

There is no information regarding the toxicity of aminocyclopyrachlor to reptiles or terrestrial-phase amphibians in the open literature or in studies submitted to the EPA (U.S. EPA/OPP 2010b, 2010k). The open literature does not include information on the toxicity of aminocyclopyrachlor to reptiles or terrestrial-phase amphibians.

Risks to terrestrial-phase amphibians are addressed in the EPA ecological risk assessment prepared by the Environmental Fate and Effects Division (EFED) (U.S. EPA/OPP 2010b) in support of the conditional registration for aminocyclopyrachlor (U.S. EPA/OPP 2010k). In this ecological risk assessment as well as many similar ecological risk assessments prepared by U.S. EPA/OPP, birds are used as surrogates for terrestrial phase amphibians and reptiles (U.S. EPA/OPP 2010b, p. 35) in the absence of data on these groups of organisms.

The concern about using birds as surrogates for amphibians relates to the permeability of amphibian skin to pesticides and other chemicals. While no data are available on the permeability of amphibian skin to aminocyclopyrachlor, Quaranta et al. (2009) indicate that the skin of the frog *Rana esculenta* is much more permeable than pig skin to several pesticides and that these differences in permeability are consistent with differences in the structure and function of amphibian skin relative to mammalian skin.

4.1.2.4. Terrestrial Invertebrates

4.1.2.4.1. Honey Bees

The honey bee is the standard test organism for assessing the potential effects of pesticides on terrestrial insects. For pesticides applied directly to vegetation, the U.S. EPA typically requires at least one acute contact toxicity study in honey bees with the technical grade pesticide.

As detailed in Appendix 3 (Table A3-1), a combined study involving both oral and contact exposures of the honey bee to technical grade aminocyclopyrachlor were conducted by Warmers (2007a). The oral and contact studies involved nominal doses of from 6.25 to 100 µg a.e./bee to groups of 50 bees. Mortality was not observed in either study, and no signs of toxicity were observed in the contact assay. In the oral study, effects observed at 24 hours included one *apathetic* bee (presumably referring to a bee with atypical response to prodding) at a nominal dose of 25 µg/bee and incoordination in eight bees at a nominal dose of 100 µg/bee. These sublethal effects were not observed at 48 hours, and U.S. EPA/OPP (2010b) classifies the nominal dose of 100 µg/bee as an NOAEC for both the contact and oral studies. As summarized in Appendix 3 (Table A3-1) the *p*-value for the atypical response to prodding is not significant (p=0.5); whereas, the *p*-value for incoordination (0/50 vs 8/50) is highly significant. The effect of transient incoordination is discussed further in the dose-response assessment (Section 4.3.2.4.1).

Due to the lack of mortality, U.S. EPA/OPP (2010b) reports the LD_{50} values for the honey bee are >100 µg/bee. The DER for the (Warmers 2007a) study does not report the body weight of the bees, but it indicates that the bees were young adult workers. Typical body weights for worker bees range from 81 to 151 mg (Winston 1987, p. 54). Taking 116 mg as an average body weight, a dose of 100 µg/bee corresponds to about 860 mg/kg bw [0.1 mg ÷ 0.000116 kg ≈ 862.07 mg/kg bw]. This dose is comparable to the NOAELs reported in experimental mammals (Appendix 1) and birds (Appendix 2). This similarity suggests that the toxicity of aminocyclopyrachlor may be similar for terrestrial vertebrates and invertebrates. On the other hand, numerous, diverse terrestrial invertebrates exist in any environment, and usually the only available toxicity data on terrestrial insects, are honey bee assays. Thus, the ability to identify potential hazards in other species of terrestrial insects is constrained by the lack of more specific data.

4.1.2.4.2. Earthworm

Toxicity tests on the earthworm are not required by the U.S. EPA/OPP but are used in Europe to assess the consequences of exposure of fossorial invertebrates to pesticides (i.e., OECD requirements). Although there are no toxicity studies of technical grade aminocyclopyrachlor in earthworms, there is an earthworm study conducted with aminocyclopyrachlor methyl ester that follows OECD guidelines. The study is described in U.S. EPA/OPP (2010b, p. 44) and is considered in the current risk assessment. As discussed in Section 2.2.2.1, DuPont™ developed a formulation of aminocyclopyrachlor methyl ester but is not commercializing this product.

As summarized in Appendix 3 (Table A3-2), earthworms (*Eisenia fetida*) were exposed to soil containing the methyl ester of aminocyclopyrachlor at concentrations of 123, 203, 334, 551, or 909 mg a.e./kg-dw soil for 14 days (MRID 475602-08). Based on decreases in body weight, the NOAEC was 203 mg a.e./kg dry weight soil. No additional details of this study are available. As discussed further in Section 4.2.3.3, the NOAEC for weight loss is substantially higher than anticipated concentrations of aminocyclopyrachlor in soil.

4.1.2.5. Terrestrial Plants (Macrophytes)

4.1.2.5.1. Standard Studies

The testing requirements for the effects of herbicides on terrestrial plants are relatively rigorous, since terrestrial vegetation is the usual target of herbicides. The required tests typically include bioassays for vegetative vigor (i.e., foliar application to mimic post-emergence applications) and bioassays for seedling emergence (i.e., soil application to mimic pre-emergence applications). As summarized in Appendix 4, studies submitted to the EPA in support of the conditional registration of aminocyclopyrachlor (U.S. EPA/OPP 2010k) include only bioassays of the methyl ester of aminocyclopyrachlor. These studies are summarized in the EPA ecological risk assessment of aminocyclopyrachlor (U.S. EPA/OPP 2010b). After EPA approved the conditional registration for aminocyclopyrachlor, DuPont™ completed a seedling emergence assay (Porch and Kendall 2010a) and vegetative vigor assay (Porch and Kendall 2010b) for aminocyclopyrachlor 50SG (equivalent to DuPont™ Method® 50SG). DuPont™ provided full copies of these studies to SERA during the development of the current Forest Service risk assessment.

As discussed in Section 2, the methyl ester formulation is not being commercialized. Nonetheless, the data on the methyl ester formulation are discussed below, because the studies on the methyl ester are the only phytotoxicity studies discussed in EPA's ecological risk assessment (U.S. EPA/OPP 2010b).

Standard toxicity studies typically report NOAECs and EC_{25} values. As discussed in Section 4.3.2.5, the dose-response assessment focuses on NOAECs, rather than EC_{25} values. In some cases in which NOAECs are not determined, the U.S. EPA/OPP reports EC_{05} values (i.e., responses associated with a 5% effect level). As discussed in U.S. EPA/OPP (2010b), little confidence is placed in EC_{05} values, because these estimates involve extrapolation beyond the treatment concentrations.

Another noteworthy distinction between EC_{05} and EC_{25} values, compared with NOAEC values, is that the former are based on non-linear curve-fitting while NOAECs are based on non-parametric assays for differences between groups. As discussed further in the dose-response assessment (Section 4.2.3.5), the use of these different statistical methods sometimes leads to NOAEC values that exceed the EC_{25} values. For comparisons of potency, the discussion in the hazard identification focuses on the more stable EC_{25} values.

4.1.2.5.1.1. Vegetative Vigor

The vegetative vigor assays are summarized in Appendix 4, Table A4-1. As with most auxin herbicides, dicots are much more sensitive than monocots to aminocyclopyrachlor. As indicated below, the range of sensitivities between the most sensitive monocot and most sensitive dicot is a factor of more than 2300 [0.052 lb a.e./acre ÷ 0.000022 lb a.e./acre ≈ 2364] for the 50SG formulation.

In both the assays on the methyl ester (MRID 47560133) and the 50SG formulation (Porch and Kendall 2010b), the most sensitive species of dicot is the common bean (*Phaseolus vulgaris*), also known as the kidney bean, and the least sensitive species of dicot is the cucumber. Based on the EC_{25} values for the common bean, the 50SG formulation is modestly more potent than the

methyl ester by a factor of about 3 [0.000075 lb a.e./acre for the methyl ester ÷ 0.000022 lb a.e./acre for the 50SG formulation ≈ 3.409]. Based on the EC_{25} values for the cucumber (most tolerant species), the 50SG formulation and the methyl ester are about equally potent [0.00098 lb a.e./acre for the methyl ester ÷ 0.0012 lb a.e./acre for the 50SG formulation ≈ 0.8167].

Monocots are much less sensitive than dicots. Based on EC_{25} values in monocots, the most sensitive species is onion for the methyl ester (EC_{25} = 0.0058 lb a.e./acre) and corn for the 50SG formulation (EC_{25} = 0.052 lb a.e./acre). Unlike the case with dicots, the ester formulation appears to be substantially more toxic than the 50SG formulation to monocots [0.052 lb a.e./acre ÷ 0.0058 lb a.e./acre ≈ 8.9655]. For both the ester and 50SG formulations, ryegrass is the most tolerant species, and the EC_{25} values for both formulations are identical (i.e., >0.36 lb a.e./acre).

4.1.2.5.1.2. Seedling Emergence

The seedling emergence assays are summarized in Appendix 4, Table A4-2. As in the vegetative vigor studies, dicots are more sensitive than monocots in the seedling emergence assays. The magnitude of the difference between monocots and dicots in the seedling emergence assays (i.e., 0.019 lb a.e./acre ÷ 0.00022 lb a.e./acre ≈ 86.36) is much less than the magnitude of the difference in the vegetation vigor assays (i.e., about a factor of more than 2000, as detailed in Section 4.1.2.5.1.1).

No substantial differences between the methyl ester (MRID 47560133) and the 50SG formulation (Porch and Kendall 2010a) are apparent in the seedling emergence assays for either dicots or monocots. For dicots, the most sensitive species is soybean for the 50SG formulation (EC_{25} = 0.00022 lb a.e./acre) and the most sensitive species is the common bean for the methyl ester (EC_{25} = 0.00077 lb a.e./acre). Based on these EC_{25} values, the 50SG formulation is more potent than the methyl ester by a factor of 3.5 [0.00077 lb a.e./acre ÷ 0.00022 lb a.e./acre ≈ 3.5]. The most tolerant species of dicot for both forms of aminocyclopyrachlor is the cucumber, and the EC_{25} values are virtually identical (i.e., 0.037 lb a.e./acre for the 50SG formulation and 0.032 lb a.e./acre for the methyl ester).

For monocots, the most sensitive species (onions) and most tolerant species (oats) are identical for the methyl ester and 50SG formulations. As with dicots, the 50SG formulation (EC_{25} = 0.019 lb a.e./acre) is more toxic than the methyl ester formulation (EC_{25} = 0.048 lb a.e./acre) to the most sensitive species. This difference, however, is modest [0.048 lb a.e./acre ÷ 0.019 lb a.e./acre ≈ 2.53]. In terms of the most tolerant species (oats), the EC_{25} values are indefinite for both formulations (i.e., >0.36 lb a.e./acre for the 50SG formulation and >0.355 lb a.e./formulation for the methyl ester).

4.1.2.5.2. Open Literature

Aminocyclopyrachlor is an auxin mimicking herbicide that interferes with normal plant growth (DuPont™ 2011; Roten 2011). Like many auxin-like herbicides, aminocyclopyrachlor is most effective against broadleaf weeds and woody vegetation (dicots) and affects actively growing tissue rather than mature tissue (Flessner 2010; Flessner et al. 2011a; Kelley and Riechers 2007; Lewis 2012). As discussed in Section 4.1.2.5.1.1, the standard registrant bioassays indicate that to monocots, the methyl ester of aminocyclopyrachlor is much more toxic than aminocyclopyrachlor acid.

Although aminocyclopyrachlor is a new herbicide, numerous efficacy studies are available in the open literature. Many of the efficacy studies, however, are currently available only in abstract or summary form—e.g., the 2011 proceeding of the Western Society of Weed Science (WSWS 2011) as well as research progress reports from the same organization (WSWS 2012). Along with these compendia, several other efficacy studies are available on both the acid and ester of aminocyclopyrachlor (Bell et al. 2011a; Eken and Lym No Date; Hart et al. 2009a,b; Hart et al. 2010; Lewis 2012; Montgomery et al. 2009; Roten 2011; Rudenko 2009; University of Kentucky 2009; Yeiser et al. No Date). Forest Service risk assessments do not summarize efficacy studies in detail except to the extent that the studies contain relevant information regarding effects on nontarget vegetation. For example, Roten (2011) evaluated the efficacy of the methyl ester for cut surface treatment as well as aminocyclopyrachlor acid for conifer site preparation. As discussed further in Section 4.1.2.5.3, the evaluation of aminocyclopyrachlor acid for conifer site preparation is particularly relevant to the current risk assessment because it relates directly to the potential of aminocyclopyrachlor to damage pine.

While the methyl ester of aminocyclopyrachlor is not being commercialized (Section 2), contrasts between the acid and ester of aminocyclopyrachlor are addressed in this section to highlight the differences between the two forms of this herbicide. Consistent with the greater potency to monocots of the methyl ester, relative to aminocyclopyrachlor acid, in standard bioassays (Section 4.1.2.5.1), studies on the methyl ester of aminocyclopyrachlor (Flessner et al. 2011a,b; Rudenko 2009; Vassios et al. 2009) report visual damage to grasses following application rates as low as 0.01 kg a.e./ha (i.e., about 0.009 lb a.e./acre). This effect level is somewhat higher than the NOAEC for the most sensitive monocot in the standard registrant vegetative vigor assay for the methyl ester (i.e., an NOAEC of 0.0028 lb a.e./acre from MRID 47560133 as summarized in Appendix 4, Table A4-1).

There are no reports in the available literature indicating that aminocyclopyrachlor acid formulations damage grass. In a brief abstract, Umeda (2011) notes that Imprelis® applications of 0.075 to 0.15 lb a.i./acre (≈0.063 to 0.13 lb a.e./acre) can damage bermudagrass but not perennial ryegrass. As discussed in Section 2.2.2.1, the registration for Imprelis®, a formulation containing the potassium salt of aminocyclopyrachlor, was withdrawn and will not be used in Forest Service programs.

Lewis (2012) conducted a series of bioassays to assess the impact of using grass clippings from turf (mature tall fescue) treated with aminocyclopyrachlor acid at an application rate of 79 g a.e./ha (≈0.07 lb a.e./acre) as mulch. The use of turf clippings previously treated with aminocyclopyrachlor (or most other auxin-mimicking herbicides) as compost or mulch can damage sensitive nontarget vegetation—i.e., white clover in the study by Lewis (2012). Lewis (2012), however, does not report direct damage to the turf itself following the application of aminocyclopyrachlor.

Other reports on the effect of aminocyclopyrachlor on grasses variously report either no marked effects (Douglass et al. 2011; Straw and Lym 2011; Wallace and Prather 2012a,b) or signs of toxicity to at least some species of grasses (Conklin and Lym 2011;Hergert et al. 2011; Setter et al. 2011). These reports, however, consist primarily of abstracts and do not specify the form of aminocyclopyrachlor (i.e., acid or ester). Some of these reports indicate that

aminocyclopyrachlor treatments had an impact on grasses; however, the nature of the effects is not clearly stated (e.g., Greet et al. 2011).

The methyl ester of aminocyclopyrachlor is more volatile than the acid (Roten 2011); accordingly, applications of the methyl ester may lead to phytotoxicity in untreated vegetation due to volatilization (Strachan et al. 2010). There are no such reports of secondary damage attributed to aminocyclopyrachlor acid.

The methyl ester of aminocyclopyrachlor is absorbed more rapidly than the acid, at least in Canada thistle (*Cirsium arvense*); whereas, translocation of aminocyclopyrachlor appears to occur as the acid (Bukun et al. 2009, 2010). Following absorption, the methyl ester is rapidly metabolized with the free acid; however, further metabolism of the free acid in plants has not been observed in monocots or dicots (Bell et al. 2011; Bukun et al. 2010; Lewis 2012) or in pine (Roten 2011). Bell et al. (2011) note that early translocation in rush skeletonweed (*Chondrilla juncea*), resulted in preferential distribution to root tissue; yet, failed to note a correlation between absorption and sensitivity for prickly lettuce (*Lactuca serriola*, higher sensitivity but lesser absorption) and rush skeletonweed (*Chondrilla juncea*, lesser sensitivity but greater absorption).

Although typically used in foliar applications, aminocyclopyrachlor does have residual soil activity (Turner 2008). For some weeds, like Canada thistle (*Cirsium arvense*), soil applications are more effective than foliar applications (Bindenmayer et al. 2011). In a series of bioassays designed to assess the effects of simulated drift of aminocyclopyrachlor to tobacco, there appear to be no substantial differences between damage from foliar (post-transplant applications) and soil (pre-transplant) applications with or without soil incorporation (Lewis 2012, Table 2, p. 129). At the lowest dose assayed (0.31 g a.e./ha or about 0.00028 lb a.e./acre), only slight visual damage, with no substantial effect on plant height or fresh weight, was apparent. Application rates of up to 31.4 g a.e./ha (≈0.028 lb a.e./acre) resulted in visual damage to tobacco as well as reductions in plant height and fresh weight. By comparison to standard bioassays of dicots following foliar application (Appendix 4, Table A4-1), tobacco appears to be relatively tolerant to aminocyclopyrachlor.

In studies on loblolly pine (*Pinus taeda*) in soil treated with aminocyclopyrachlor acid, Roten (2011) notes an absorption rate of about 0.01 $hour^{-1}$ in roots over an initial 48-hour period. In studies conducted with the methyl ester of aminocyclopyrachlor, very low soil concentrations (i.e., 2 to about 6 µg/kg dw soil) caused overt signs of phytotoxicity in several dicots (Strachan et al. 2011). As noted by Strachan et al. (2011), the methyl ester is metabolized to aminocyclopyrachlor acid in soil very rapidly (i.e., within about 1 day). While somewhat speculative, soil concentrations of aminocyclopyrachlor acid that could damage sensitive species of dicots may be similar to the very low concentrations of aminocyclopyrachlor methyl ester that are phytotoxic.

4.1.2.5.3. Incident Reports

As discussed in Section 2.2.2.1, EPA withdrew the registration of Imprelis®, a 25% a.i. liquid formulation of the potassium salt of aminocyclopyrachlor, following reports of damage to conifers, particularly Norway spruce and white pine (U.S. EPA/OPP 2011c). There are few published details concerning incidence of damage to pine (ENewsPF 2011; McAuley 2012; Ruhl

et al. 2011). Although pine damage after herbicide applications is not uncommon (e.g., Bentley et al. 1971; Feucht 1988; Hibbs 1978), the incidence and severity of pine damage after applications of Imprelis® to turf appears to be unusually severe.

Imprelis® will not be used in Forest Service programs; however other formulations of aminocyclopyrachlor will be used. There is uncertainty in assessing the relevance of incidents associated with applications of Imprelis® to applications of aminocyclopyrachlor that may be used by the Forest Service. As discussed in Section 2.2.2.1, Imprelis® and other aminocyclopyrachlor formulations contain ingredients other than aminocyclopyrachlor (i.e., inerts). The identity of the inerts in aminocyclopyrachlor formulations was disclosed to the U.S. EPA/OPP; however, that information is considered proprietary (Confidential Business Information). Accordingly, the identity of the inerts in aminocyclopyrachlor was not available for the conduct of the current Forest Service risk assessment.

In the absence of information on the inerts in Imprelis® and other relevant aminocyclopyrachlor formulations, the reports of tree damage following applications of Imprelis® are considered relevant to other aminocyclopyrachlor formulations. In other words, damage to conifers is considered an endpoint of particular concern in the current Forest Service risk assessment.

The toxicity of aminocyclopyrachlor to trees has not been investigated extensively. Foliar applications of aminocyclopyrachlor acid are well-absorbed (≈8 to 10%) in quaking aspen (*Populus tremuloides*) and black cherry (*Prunus serotina*) (Bell et al. 2011b). Efficacy studies on the control of saltcedar (*Tamarix ramosissima*) and Russian olive (*Elaeagnus angustifolia*) indicate that younger trees appear to be more sensitive than more mature trees (Brock 2011). This report is consistent with the general observation discussed in Section 4.1.2.5.2 that aminocyclopyrachlor has more impact on actively growing tissue than mature tissue.

The only reasonably detailed account of the impact of aminocyclopyrachlor on pine is from a Master's thesis on the use of aminocyclopyrachlor acid in site preparation for loblolly pine (*Pinus taeda*) in North Carolina (Roten 2011). In this study, an aminocyclopyrachlor acid formulation (specified only as DPX-MAT28) was applied at rates of 64 to 256 g a.e./ ha (≈0.057 to 0.23 lb a.e./acre). After periods of 3 to 5 months, pine seedlings were planted in trials conducted in 2008 and 2009. In the 2008 application (Roten 2011, Table 3.1, p. 44), no significant dose-response relationship was apparent for pine injury, pine survival, or pine height. The only effect that appeared to be clearly treatment-related was an increase in the number of dead pine leaders, which increased by about 70% (0.7 vs 1.2 dead leaders per treatment across all plots) at an application rate of 64 g a.e./ha. The increase, however, was not statistically significant with respect to controls. At the next highest application rate, 128 g a.e./ha, the number of dead leaders increased by 100% (0.7 vs 1.4 dead leaders per treatment across all plots); this increase was statistically significant ($p<0.05$).

Roten (2011) also notes that:

> *…injury in the 2009 run was substantially less* [and] *there was an average loss of survival by 10% (data not shown). Further research is needed to quantify longer term aminocyclopyrachlor effects on loblolly regeneration*

and evaluate the effect of environmental conditions on loblolly pine response.

Roten 2011, p. 38.

The reason for the atypical frequency and severity of damage to conifers is not well characterized. Imprelis® is labeled for application only by certified pesticide applicators. While misapplications cannot be ruled out as a causative factor in some of the reported incidents of Imprelis® damage to conifers, it is probably not the primary factor in conifer damage. A more reasonable suggestion is that conifer damage occurs from root uptake of the herbicide from treated soil. Such exposure could occur from direct treatment of turf slightly beyond the drip line of the conifer or from herbicide runoff into soil that lies within the extent of the root system of the conifers (Purdue Extension 2011; Reicher 2011). As detailed in Section 2.2.2.1, concern for runoff is expressed on the revised product labels for DuPont™ Method® 50SG (DuPont™ 2012a) and DuPont™ Method® 240SL (DuPont™ 2012b).

Most of the information involving incidents involving tree damage following applications of aminocyclopyrachlor concerns pine. DuPont (2012c) has released a technical note indicating that some deciduous trees and shrubs have *…demonstrated sensitivity to low levels of aminocyclopyrachlor*. A listing of the apparently sensitive species from the DuPont (2012c) release is given in Table 26. No details of the incidents involving deciduous trees and shrubs have been encountered.

4.1.2.6. Terrestrial Microorganisms

The toxicity of aminocyclopyrachlor or metabolites of aminocyclopyrachlor to terrestrial microorganisms is not addressed in the available literature. The EPA does not require toxicity studies on terrestrial microorganisms for pesticide registration in the United States; accordingly the EPA ecological risk assessment on aminocyclopyrachlor (U.S. EPA/OPP 2010b) does not cover effects on terrestrial microorganisms.

Given concerns with the potential of at least some formulations of aminocyclopyrachlor to damage pines, the lack of information on the toxicity of aminocyclopyrachlor to soil bacteria represents a data gap. Nonetheless, while ectomycorrhizae may be adversely affected by some herbicides, including auxin herbicides (e.g., Busse et al. 2004; Estok et al. 1989), the effects typically occur at high concentrations. Pine damage due to herbicide effects on ectomycorrhizae were not identified in the literature.

4.1.3. Aquatic Organisms

Like the EPA human health risk assessment (U.S. EPA/OPP 2010a), the EPA ecological risk assessment (U.S. EPA/OPP 2010b) addresses the issue of aminocyclopyrachlor degradates. In the absence of experimental data on the toxicity of aminocyclopyrachlor degradates to aquatic species, the EPA uses ECOSAR (ECOlogical Structure-Activity Relationship Model), which is a computer program for implementing structure-activity relationships to estimate the toxicity of environmental contaminants to aquatic organisms (U.S. EPA/OPP 2010b). Based on the ECOSAR analysis, the EPA ecological risk assessment for aminocyclopyrachlor offers the following conclusion:

> *The major transformation products of aminocyclopyrachlor of concern at this time are IN-LXT69, IN-V0977* [cyclopropanecarboxylic acid] *and IN-YY905. However, these degradates are not expected to occur at environmentally relevant concentrations relative to effects thresholds.*
>
> U.S. EPA/OPP (2010b, p. 7)

As discussed in Section 3.4.3.2, the EPA's qualitative risk characterization for degradates is identical to the more quantitative risk characterization for the potential impact of cyclopropanecarboxylic acid on human health. In the absence of toxicity data on the effect of aminocyclopyrachlor degradates to aquatic species, the current Forest Service risk assessment defers to the EPA ecological risk assessment (U.S. EPA/OPP 2010b) (i.e., the degradates are not considered further in the hazard identification for aquatic organisms).

4.1.3.1. Fish

Standard toxicity bioassays to assess the effects of aminocyclopyrachlor on fish are summarized in Appendix 5: acute studies in Table A5-1 and the chronic study in Table A5-2. Acute toxicity studies were conducted in two species of freshwater fish, including rainbow trout (Palmer et al. 2007a) and bluegill sunfish (Gallagher et al. 2007a), and in one saltwater species, sheepshead minnow (Gallagher et al. 2008a). In addition to the acute toxicity studies, one early life cycle (egg-to-fry) study is available on rainbow trout (Gallagher et al. 2008c). These are all standard toxicity studies typically required by the U.S. EPA/OPP for pesticide registration. These studies have been reviewed by U.S. EPA/OPP, and DERs of these studies were available for the conduct of the current Forest Service risk assessment. All of the studies are classified as *Acceptable* by the U.S. EPA/OPP.

All of these bioassays involve technical grade aminocyclopyrachlor. No toxicity studies in fish are available on the formulations of aminocyclopyrachlor. The U.S. EPA/OPP typically requires fish or aquatic toxicity studies on formulations only when the available data suggest that formulation testing is necessary.

All of the acute LC_{50} values in fish are non-definitive (i.e., as discussed in Section 3.1.4, non-definitive toxicity values are expressed as greater than (>), indicating that mortality was insufficient to calculate an LC_{50}). Furthermore, none of the acute toxicity studies indicate adverse effects. Thus, the highest concentrations tested in these studies, 120 to 129 mg a.e./L, are classified by the U.S. EPA/OPP as NOAECs. Based on these studies, the U.S. EPA/OPP classifies aminocyclopyrachlor as *Practically Non-toxic* to fish.

Like the acute studies, the 90-day early life stage study in trout does not report any signs of toxicity, including the lack of effects on reproductive parameters, at 11 mg a.e./L, the highest concentration tested. Thus, the U.S. EPA/OPP classifies 11 mg a.e./L as a NOAEC, and the LOAEL is undefined.

4.1.3.2. Amphibians (Aquatic-Phase)

As is the case for reptiles and terrestrial-phase amphibians (Section 4.1.2.3), there is no information regarding the toxicity of aminocyclopyrachlor to aquatic-phase amphibians. In view of this lack of data, the EPA follows a standard approach: … *Freshwater fish (rainbow trout and*

bluegill sunfish), also [are] *used as a surrogate for aquatic phase amphibians* (U.S. EPA/OPP 2010b, p. 14).

4.1.3.3. Aquatic Invertebrates

4.1.3.3.1. Acute Studies

As with fish, acute and chronic toxicity bioassays required by the U.S. EPA/OPP are available in standard test organisms. As detailed in Appendix 6 (Table A6-1), acute toxicity studies are available in one species of freshwater invertebrate, *Daphnia magna* (Gallagher et al. 2007b) and two species of saltwater invertebrates, the oyster *Crassostrea virginica* (Gallagher et al. 2007d) and a mysid shrimp, *Americamysis bahia* (Gallagher et al. 2008b). Also as with fish, all these acute toxicity studies involve technical grade aminocyclopyrachlor acid and are classified as *Acceptable* by the U.S. EPA (U.S. EPA/OPP 2010b). No toxicity data are available on the formulations of aminocyclopyrachlor. As discussed in Section 4.1.3.1, the U.S. EPA/OPP does not typically require that toxicity tests in aquatic animals be conducted with pesticide formulations.

Unlike the case with fish, the LC_{50} for the standard freshwater invertebrate, *Daphnia magna*, is definitive (i.e., an LC_{50} of 39.7 mg a.e./L with a corresponding NOAEL of 3.7 mg a.e./L). In both of the salt water invertebrates, the LC_{50} values could not be calculated because the maximum tested concentrations of about 120 mg a.e./L did not result in mortality or signs of toxicity. Based on these data, the U.S. EPA/OPP (2010b) classifies aminocyclopyrachlor as *Slightly Toxic* to freshwater invertebrates and *Practically Non-toxic* to salt water invertebrates. While these data suggest that salt water species may be more tolerant than freshwater species to aminocyclopyrachlor, the data supporting this supposition are limited to only a single species of freshwater invertebrates and two species of marine invertebrates.

4.1.3.3.2. Chronic Studies

Two standard reproduction studies are available in *Daphnia magna*: an early study by Gallagher et al. (2008e) and a more recent study by Minderhout et al. (2011). As summarized in Appendix 6 (Table A6-2), the EPA DER for the Gallagher et al. (2008e) study indicates that it is classified as *Supplemental* rather than *Acceptable* by U.S. EPA/OPP due to the high rates of parental mortality (30 to 40%) noted at the lower test concentrations (0.37 and 1.5 mg a.e./L), whereas, only 10% parental mortality was noted at the two higher test concentrations (3.0 and 6.0 mg a.e./L) over the 21-day course of the study. The low-dose mortality and control mortality were not different, based on the Fisher's Exact Test, and no dose-response relationship is apparent. No effects were noted on reproductive parameters at any concentrations. Based on these observations, the study authors suggest that the highest dose tested, 6 mg a.e./L, should be classified as a NOAEC. The U.S. EPA/OPP did not concur with this assessment, based on the low-dose parental mortality. Consequently, the U.S. EPA/OPP classifies the lowest dose tested, 0.37 mg a.e./L as a LOAEC. Regardless, the EPA indicates that the pattern of mortality raises concerns about the health of the test organisms, which is the basis for classifying the study as *Supplemental*.

In response to the EPA review of the Gallagher et al. (2008e) study, DuPont™ conducted a second reproduction study in Daphnia magna (Minderhout et al. 2011). A review of this study by the U.S. EPA/OPP is not available; however, DuPont™ provided a full copy of the study to

SERA. Over the range of measured concentrations (0.61 to 9.9 mg a.e./L), no effects were noted on parental mortality or reproductive parameters. At the highest concentration, the only effect noted was a slight (≈5.5%) but statistically significant ($p \leq 0.05$) decrease in adult mean body length. A decrease (≈12%) in mean dry weight was also observed at 9.9 mg a.e/L; however, this decrease was not statistically significant. Based on the effect on mean body length, the study authors suggest that 4.9 mg a.e./L should be classified as a NOAEC with a corresponding LOAEC of 9.9 mg a.e./L.

The use of these studies in the current Forest Service risk assessment is discussed further in Section 4.3.3.3 (dose-response assessment for aquatic invertebrates).

4.1.3.4. Aquatic Plants

4.1.3.4.1. Algae

Four standard registrant-submitted studies are available on the toxicity of technical grade aminocyclopyrachlor acid to algae (Appendix 7, Table A7-1). All of the studies are classified as *Acceptable* by U.S. EPA/OPP (2010b, p. 40-41), even though the study on freshwater green algae, *Pseudokirchneriella subcapitata*, was conducted for only 72 hours (Porch et al. 2008c). This duration of exposure is compliant with European (OECD) guidelines; however, the U.S. EPA/OPP requires an exposure period of 96 hours. As noted in the DER for the Porch et al. (2008c) study, the EPA classifies the study as Acceptable but restricts its use to Tier 1 (i.e., screening level) analysis. This limitation has no impact on the current Forest Service risk assessment. As discussed further in Section 4.3.3.4 (dose-response assessment for aquatic plants), the NOAECs from Porch et al. (2008c) are intermediate between the most sensitive and least sensitive species of aquatic algae; thus, Porch et al. (2008c) is not used quantitatively in the current risk assessment.

The most sensitive species of algae is *Anabaena flos-aquae*, a species of freshwater blue-green algae with an EC_{50} of 7.4 mg a.e./L and a NOAEC of 1.11 mg a.e./L (Porch et al. 2008a). The least sensitive species of freshwater algae is *Pseudokirchneriella subcapitata*, a green algae, with an EC_{50} of >120 mg a.e./L for all endpoints and a NOAEC of 59.1 mg a.e./L for the inhibition of growth rate. Data are available on only one marine species, *Skeletonema costatum*, which is a marine diatom. At the highest concentration tested, 120 mg a.e./L, no statistically significant effects were noted on cell density, biomass, or growth (Porch et al. 2008b). As with aquatic invertebrates (Section 4.1.3.3.1), the available data, which are limited to three species of freshwater algae and one species of marine algae, suggest that marine algae may be less sensitive than freshwater algae to aminocyclopyrachlor.

4.1.3.4.2. Aquatic Macrophytes

As summarized in Appendix 7, Table A7-2, a standard registrant-submitted toxicity study is available on aquatic macrophytes—i.e., *Lemna gibba*, a species of duckweed (Porch et al. 2008e). As with the studies on algae, the study on duckweed was conducted using technical grade aminocyclopyrachlor acid. Aminocyclopyrachlor had no effect on biomass at the highest tested concentration (122 mg a.e./L). Effects on other endpoints (i.e., frond number, frond number yield, growth rate based on frond number) were not substantial, and EC_{50} values for these endpoints could not be calculated. Nonetheless, statistically significant decreases in these other endpoints were apparent; thus, the NOAEC for these endpoints is 3.75 mg a.e./L. This

NOAEC is only modestly higher than the NOAEC of 1.11 mg a.e./L for the most sensitive species of algae (Section 4.1.3.4.1).

Aminocyclopyrachlor is not registered for aquatic applications. Israel (2011), however, evaluated the potential efficacy of both aminocyclopyrachlor acid and aminocyclopyrachlor methyl ester on several pest species of aquatic plants. Aminocyclopyrachlor is readily absorbed by several species of aquatic plants and is concentrated in the leaves to a greater extent than in stem tissue. In controlled greenhouse bioassays, water surface applications of aminocyclopyrachlor acid were effective in the control of alligator weed, creeping water primrose, parrotfeather, and water hyacinth with approximate EC_{50} values of about 1 to 35 g/ha (≈0.0009 to 0.03 lb a.e./acre), based on visual damage (Israel 2011, Figure 2.3, p. 58). Israel (2011) does not specify the depth of the vessels used in these studies. Consequently, the surface application rates cannot be converted to nominal concentrations of aminocyclopyrachlor in water. In field trials, application rates of greater than 0.07 to 0.35 kg/ha (≈0.06 to 0.31 lb a.e./acre) aminocyclopyrachlor were effective in the control of alligator weed (Israel 2011, Table 3.1, p. 80).

Lewis (2012) notes that turf clippings from areas treated with aminocyclopyrachlor at an application rate of 84 g a.e./ha (≈0.07 lb a.e./acre) may contain sufficient residual concentrations of the herbicide to damage aquatic plants including alligator weed (*Alternanthera philoxeroides*) and parrot feather (*Myriophyllum aquaticum*). Lewis (2012), however, does not report the concentrations of aminocyclopyrachlor in water associated with damage to the aquatic macrophytes.

4.1.3.5. Surfactants

As noted in Section 3.1.14.2, nonionic surfactants, methylated seed oils, or vegetable oil concentrates are recommended as adjuvants in applications of aminocyclopyrachlor formulations.

As discussed above, aminocyclopyrachlor is relatively nontoxic to aquatic animals. At least some of the recommended nonionic surfactants may be more toxic than aminocyclopyrachlor to some aquatic animals. For example, the review by McLaren/Hart (1995) compiles LC_{50} values for fish and EC_{50} values for aquatic invertebrates in assays of several nonionic surfactants used with other herbicides. The acute LC_{50} values of these surfactants range from about 1 to >1000 mg/L.

Based on the label instructions for some aminocyclopyrachlor formulations, the minimum recommended concentration of non-ionic surfactants is 0.25% v/v and the upper bound concentration for any adjuvant is 1% v/v. Assuming a surfactant density of 1 g/mL for illustration, 0.25% w/v corresponds to a concentration of 2500 mg/L and 1% corresponds to 10,000 mg/L. Given the low toxicity of aminocyclopyrachlor to both fish and aquatic invertebrates—i.e., the lowest defined LC_{50} value of 39.7 mg a.e./L (*Daphnia magna*, Gallagher et al. 2007b) to several indefinite LC_{50} and EC_{50} values greater than 100 mg a.e./L—the use of a relatively toxic nonionic surfactant in an application of aminocyclopyrachlor may be viewed as posing a greater risk to aquatic animals than would be anticipated from exposure to aminocyclopyrachlor alone.

Notwithstanding the above discussion, there is no basis for asserting that the risks posed by the surfactants would be substantial. Aminocyclopyrachlor will not be applied directly to water, and it seems reasonable to expect that many surfactants (which are essentially soaps) would degrade in soil prior to reaching water. Even if the surfactants were as persistent as aminocyclopyrachlor, the corresponding concentrations of the surfactants in surface water would be very low. For example, the expected peak concentration of aminocyclopyrachlor in water at the maximum application rate is about 0.2 mg a.e./L [0.7 mg/L per lb/acre (Table 14) x 0.28 lb/acre = 0.196]. At the maximum recommended adjuvant concentration of 1%, the corresponding concentration of the adjuvant would be about 0.002 mg/L [0.2 mg a.e./L x 0.01]. This number is below the lower range of the LC_{50} values for the more toxic surfactants (≈1 mg/L) by a factor of 500.

As discussed in the EPA ecological risk assessment on aminocyclopyrachlor (U.S. EPA/OPP 2010b), the standard criteria used by U.S. EPA/OPP as a level of concern for endangered species of 0.05—i.e., the ratio of the anticipated concentration in water to the acute LC_{50} should be no greater than 0.05. Thus, using a very toxic surfactant with an acute LC_{50} of 1 mg/L in aquatic applications of aminocyclopyrachlor would result in a ratio of 0.002 [0.002 mg/L ÷ 1 mg/L]. This is below the EPA criterion of 0.05 by a factor of 25 [0.05 ÷ 0.002]. Thus, there is no basis for asserting that the use of surfactants with aminocyclopyrachlor applications is likely to pose an acute hazard to aquatic species. The use of a relatively nontoxic surfactant (e.g., an LC_{50} of 1000 mg/L) would result in a correspondingly lower ratio (i.e., 0.002 mg/L ÷ 1000 mg/L = 0.000002), below the EPA level of concern for endangered species [0.05] by a factor of 25,000 [0.05 ÷ 0.000002].

The above discussion applies only to potential acute risks. A useful compendium on the longer-term toxicity of nonionic surfactants to aquatic organisms has not been identified; thus, the potential for longer-term risks cannot be assessed.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

A standard set of exposure assessments for terrestrial and aquatic organisms is provided in Attachment 1 (the EXCEL workbook for aminocyclopyrachlor) for applications made at the maximum labeled rate of 0.28 lb a.e./acre. As in the human health risk assessment, three general types of exposure scenarios are considered: accidental, acute non-accidental, and longer-term.

Exposure assessments for mammals are detailed in Worksheet G01a for mammals and in Worksheet G01b for birds. Figures 4 and 5 illustrate the exposure assessments for mammals and birds, respectively. For both mammals and birds, the highest exposure scenarios are associated with the consumption of contaminated vegetation. This is a common pattern for foliar applications of any pesticide. The highest exposures are associated with the consumption of contaminated short grass by a small mammal or bird. For acute exposure scenarios, the estimated doses are 193 mg/kg bw for a small mammal and 478 mg/kg bw for a small bird. For longer-term exposure scenarios, the estimated doses are 141 mg/kg bw for a small mammal and 341 mg/kg bw for a small bird. For both acute and chronic exposures, consumption of contaminated water leads to dose estimates far below those associated with consumption of contaminated vegetation.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion, and the use of contaminated irrigation water. The highest exposures for terrestrial plants are associated with direct spray and spray drift. Nonetheless, as discussed in the risk characterization, runoff and sediment losses are also significant sources of potential exposure for terrestrial plants in sites that may favor runoff, particularly sites with predominantly clay soils.

Exposures of aquatic plants and animals to aminocyclopyrachlor are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water. As discussed in the human health risk assessment (Section 3.1.15.1) and the hazard identification for mammalian wildlife (Section 4.1.2.1.2), cyclopropanecarboxylic acid is a degradate of concern. Because significant exposures to cyclopropanecarboxylic acid are anticipated to occur via aqueous photolysis, exposure assessments are limited to the scenarios associated with the consumption of contaminated water. These exposure scenarios are detailed in Attachment 2 (the EXCEL workbook for cyclopropanecarboxylic acid).

4.2.2. Mammals and Birds

Table 21 provides an overview of the mammalian and avian receptors considered in the current risk assessment. Because of the relationship of body weight to surface area as well as to the consumption of food and water, small animals will generally receive a higher dose, in terms of mg/kg body weight, relative to large animals, for a given type of exposure. The exposure assessment for mammals considers five nontarget mammals of varying sizes: small (20 g) and medium (400 g) sized omnivores, a 5 kg canid, a 70 kg herbivore, and a 70 kg carnivore. Four standard avian receptors are considered: a 10 g passerine, a 640 g predatory bird, a 2.4 kg piscivorous bird, and a 4 kg herbivorous bird. Because of presumed differences in diet, (i.e., the consumption of food items), all of the mammalian and avian receptors are not considered in all

of the exposure scenarios (e.g., the 640 g predatory bird is not used in the exposure assessments for contaminated vegetation). Toxicity data are not available on terrestrial-phase amphibians (Section 4.1.2.3); accordingly, exposure assessments for these terrestrial vertebrates are not developed.

4.2.2.1. Direct Spray

The unintentional direct spray of wildlife during broadcast applications of a pesticide is a credible exposure scenario, similar to the accidental exposure scenarios for the general public discussed in Section 3.2.3.2. In a scenario involving exposure to direct spray, the amount of pesticide absorbed depends on the application rate, the surface area of the organism, and the rate of absorption.

For this risk assessment, two direct spray or broadcast exposure assessments are conducted for terrestrial applications. The first spray scenario (Worksheet F01a) concerns the direct spray of half of the body surface of a 20 g mammal during pesticide application. This exposure assessment assumes first-order dermal absorption using the first-order dermal absorption rate coefficient discussed in Section 3.1.3.2. The second exposure assessment (Worksheet F01b) assumes complete absorption over day 1 of exposure. This assessment is included in an effort to encompass increased exposures due to grooming.

Exposure assessments for the direct spray of a large mammal are not developed. As discussed further in Section 4.4.2.1, the direct spray scenarios lead to HQs far below the level of concern, and an elaboration for body size would have no impact on the risk assessment.

4.2.2.2. Dermal Contact with Contaminated Vegetation

As discussed in the human health risk assessment (Section 3.2.3.3), the only approach for estimating the potential significance of dermal contact with contaminated vegetation is to assume a relationship between the application rate, dislodgeable foliar residue, and transfer rates from the contaminated vegetation to the skin. Unlike the human health risk assessment for which estimates of transfer rates are available, there are no transfer rates available for wildlife species. Wildlife species are more likely than humans to spend long periods of time in contact with contaminated vegetation. It is reasonable to assume that for prolonged exposures, equilibrium may be reached between pesticide levels on the skin, rates of dermal absorption, and pesticide levels on contaminated vegetation. Since data regarding the kinetics of this process are not available, a quantitative assessment for this exposure scenario cannot be made in the ecological risk assessment.

For aminocyclopyrachlor, as well as most other herbicides and insecticides applied in broadcast applications, the failure to quantify exposures associated with dermal contact adds relatively little uncertainty to the risk assessment, because the dominant route of exposure will be the consumption of contaminated vegetation, which is addressed in the following subsection.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

In foliar applications, the consumption of contaminated vegetation is an obvious concern. Exposure assessments for the consumption of contaminated vegetation are developed for all mammals and birds listed in Table 21, except for the large carnivorous mammal and the predatory bird.

The initial concentrations of aminocyclopyrachlor on contaminated food items are based on the U.S. EPA/OPP (2001) adaptation of the residue rates from Fletcher et al. (1997), as summarized in Table 13. The methods of estimating the peak and time-weighted average concentrations of aminocyclopyrachlor are identical to those used in the human health risk assessment (Section 3.2.3.7). As summarized in Table 13, fruit and short grass are the food items which comprise the commodities with the lowest pesticide residue rates (fruit) and the highest pesticide residue rates (short grass). Tall grass and broadleaf forage plants are estimated to have intermediate residue rates. For each of these four types of vegetation, both acute and longer-term exposure scenarios are developed, as detailed in Attachment 1, Worksheet G01a for mammals and Worksheet G01b for birds.

For both the acute and chronic exposure scenarios, the assumption is made that 100% of the diet is contaminated. This may not be a realistic assumption for some acute exposures and will probably be a rare event in chronic exposures—i.e., animals may move in and out of the treated areas. While estimates of the proportion of the diet contaminated could be incorporated into the exposure assessment, the estimates would be an essentially arbitrary set of adjustments. The proportion of the contaminated diet is linearly related to the resulting HQs, and its impact is discussed further in the risk characterization (Section 4.4.2.1).

The estimated food consumption rates by various species of mammals and birds are based on field metabolic rates (kcal/day), which, in turn, are based on the adaptation of estimates from Nagy (1987) by the U.S. EPA/ORD (1993). These allometric relationships account for much of the variability in food consumption among mammals and birds. There is, however, residual variability, which is remarkably constant among different groups of organisms (Table 3 in Nagy 1987). As discussed by Nagy (2005), the estimates from the allometric relationships may differ from actual field metabolic rates by about ±70%. Consequently, in all worksheets involving the use of the allometric equations for field metabolic rates, the lower bound is taken as 30% of the estimate and the upper bound is taken as 170% of the estimate.

The estimates of field metabolic rates are used to calculate food consumption based on the caloric value (kcal/day dry weight) of the food items considered in this risk assessment and estimates of the water content of the various foods. Estimates of caloric content are summarized in Table 22. Most of the specific values in Table 27 are taken from Nagy (1987) and U.S. EPA/ORD (1993).

Along with the exposure scenarios for the consumption of contaminated vegetation, similar sets of exposure scenarios are provided for the consumption of small mammals by either a predatory mammal (Worksheet F10a) or a predatory bird (Worksheet F10b) and the consumption of contaminated insects by a small mammal, a larger (400 g) mammal, and a small bird (Worksheets F09a-c). The residue rates for insects are taken from the U.S. EPA/OPP (2001) adaptation of the residue rates in Fletcher et al. (1997), as summarized in Table 15.

4.2.2.4. Ingestion of Contaminated Water

4.2.2.4.1. Aminocyclopyrachlor

The methods for estimating aminocyclopyrachlor concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4.6.1). The only major differences in the exposure estimates concern animal weight and water consumption. Like food consumption rates, water consumption rates, which are well characterized in terrestrial vertebrates, are based on allometric relationships in mammals and birds, as summarized in Table 21. From these estimates, exposure scenarios involving the consumption of contaminated water are developed for mammals and birds for accidental spills (Worksheets F02a-f), expected peak concentrations (Worksheets F08a-f), and expected longer-term concentrations (Worksheets F16a-f) of Attachment 1, the EXCEL workbook for aminocyclopyrachlor.

Like food consumption, water consumption in birds and mammals varies substantially with diet, season, and many other factors; however, quantitative estimates regarding the variability of water consumption by birds and mammals is not well documented in the available literature and is not considered in the exposure assessments. Nevertheless, as summarized in Table 14, the upper and lower bound estimates of aminocyclopyrachlor concentrations in surface water vary substantially (i.e., by a factor of 350 for acute exposures and a factor of about 400 for chronic exposures). Given this degree of variability in surface water concentrations of aminocyclopyrachlor, it is unlikely that a quantitative consideration of the variability in water consumption rates of birds and mammals would have a substantial impact on the risk characterization. In addition and as discussed further in Section 4.4.2.1 (risk characterization for mammals) and Section 4.4.2.2 (risk characterization for birds), exposures associated with the consumption of contaminated surface water are far below the level of concern (HQ=1). Consequently, even extreme variations on the consumption of contaminated water by mammals and birds would have no impact on the risk characterization for mammals and birds.

4.2.2.4.2. Cyclopropanecarboxylic acid

As in the human health risk assessment (Section 3.2.3.4.1.2), mammalian exposure to cyclopropanecarboxylic acid is considered quantitatively. Furthermore, as with aminocyclopyrachlor, the estimated surface water concentrations of cyclopropanecarboxylic acid are identical to those used in the human health risk assessment (Table 14).

Details of the exposure scenarios are given in Attachment 2 (the EXCEL workbook for cyclopropanecarboxylic acid following applications of aminocyclopyrachlor). The exposure scenarios parallel those for aminocyclopyrachlor: accidental spills (Worksheets F02a-d), expected peak concentrations (Worksheets F08a-d), and expected longer-term concentrations (Worksheets F16a-d). Since data on the toxicity of cyclopropanecarboxylic acid to birds are not available, exposure scenarios for birds are not developed, and the potential risks to birds are discussed qualitatively in Section 4.4.2.2.

4.2.2.5. Consumption of Contaminated Fish

4.2.2.5.1. Aminocyclopyrachlor

In addition to the consumption of contaminated vegetation, insects, and other terrestrial prey (Section 4.2.2.3), the consumption of contaminated fish by piscivorous species is a potentially

significant route of exposure to aminocyclopyrachlor. Details of the exposure scenarios involving the consumption of contaminated fish by mammals and birds are given in Attachment 1 (the EXCEL workbook for aminocyclopyrachlor). Exposure scenarios are developed for the consumption of contaminated fish after an accidental spill (Worksheets F03a-c), expected peak exposures (Worksheets F011a-c), and estimated longer-term concentrations (Worksheets F17a-c). These exposure scenarios are applied to 5 and 70 kg carnivorous mammals as well as a 2.4 kg piscivorous bird. The 70 kg carnivorous mammal is typical of a black bear (which does not actively hunt fish) but could be representative of a small or immature brown bear (*Ursus arctos*), which is an endangered species that actively feeds on fish (Reid 2006). As summarized in Table 21, the 5 kg mammal is representative of a fox, and the 2.4 kg bird is representative of a heron.

Aminocyclopyrachlor exposure levels associated with the consumption of contaminated fish depend on the concentration of aminocyclopyrachlor in water and the bioconcentration factor for aminocyclopyrachlor in fish. The concentrations of aminocyclopyrachlor in water are identical to those discussed in Section 4.2.2.4. As discussed in Section 3.2.3.5, aminocyclopyrachlor does not bioconcentrate substantially in fish, and the bioconcentration factor is taken as 3.162, based on quantitative structure-activity estimates from EPI-Suite (2011). There is no expectation that the four significant digits from EPI-Suite (2011) are meaningful. Consequently, the bioconcentration factor used in Attachment 1 is rounded to 3.

4.2.2.5.2. Cyclopropanecarboxylic acid

As with the consumption of contaminated surface water (Section 4.2.2.4), exposures to cyclopropanecarboxylic acid as a metabolite of aminocyclopyrachlor are considered quantitatively. As discussed in Section 4.2.2.4.2, only mammalian receptors are considered, because toxicity data on birds are not available. The exposure scenarios for mammals parallel the exposure scenarios for the consumption of fish contaminated with aminocyclopyrachlor. These exposure scenarios are detailed in Attachment 2 (the EXCEL workbook for cyclopropanecarboxylic acid): an accidental spill (Worksheets F03a-b), expected peak exposures (Worksheets F011a-b), and estimated longer-term concentrations (Worksheets F17a-b). No experimental bioconcentration factor for cyclopropanecarboxylic acid has been identified. Consequently, as with aminocyclopyrachlor, the estimated bioconcentration factor of 1.259 is taken from EPI-Suite (2011). As with aminocyclopyrachlor, this estimate is rounded to one significant place in Attachment 2 (i.e., a BCF of 1 is used).

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

Estimated levels of exposure associated with broadcast terrestrial applications of aminocyclopyrachlor are detailed in Worksheet G09 of Attachment 1 (EXCEL workbook for aminocyclopyrachlor). This is a custom worksheet which includes aerial, ground broadcast (high boom and low boom), and backpack applications.

Honeybees are used as a surrogate for other terrestrial insects, and honeybee exposure levels associated with broadcast applications are modeled as a simple physical process based on the application rate and surface area of the bee. The surface area of the honeybee (1.42 cm^2) is based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

The amount of a pesticide deposited on a bee during or shortly after application depends on how close the bee is to the application site as well as foliar interception of the spray prior to deposition on the bee. The estimated proportions of the nominal application rate at various distances downwind given in G09 are based on Tier 1 estimates from AgDRIFT (Teske et al. 2002) for distances of 0 (direct spray) to 900 feet downwind of the treated site. Further details of the use of AgDRIFT are discussed in Section 4.2.4.2 (Off-Site Drift) with respect to nontarget vegetation.

In addition to drift, foliar interception of a pesticide may occur. The impact of foliar interception varies according to the nature of the canopy above the bee. For example, in studies investigating the deposition rate of diflubenzuron in various forest canopies, Wimmer et al. (1993) report that deposition in the lower canopy, relative to the upper canopy, generally ranged from about 10% (90% foliar interception in the upper canopy) to 90% (10% foliar inception by the upper canopy). In Worksheet G09, foliar interception rates of 0% (no interception), 50%, and 90% are used.

During broadcast applications of a pesticide, it is likely that terrestrial invertebrates other than bees will be subject to direct spray. As discussed in further detail in Section 4.3.2.3 (dose-response assessment for terrestrial invertebrates), the available toxicity data on terrestrial invertebrates do not support the derivation of separate toxicity values for different groups of terrestrial insects. As in the recent EPA ecological risk assessment of aminocyclopyrachlor (U.S. EPA/OPP 2010b, p. 43), the honeybee is used as a representative species for other terrestrial insects.

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

Like terrestrial mammals and birds, terrestrial invertebrates may be exposed to aminocyclopyrachlor through the consumption of contaminated vegetation or contaminated prey. For broadcast foliar applications, estimates of residues on contaminated vegetation or prey are based on estimated residue rates (i.e., mg/kg residues per lb applied) from Fletcher et al. (1994), as summarized in Table 15.

An estimate of food consumption is necessary to calculate a dose level for a foraging herbivorous insect. Insect food consumption varies greatly, depending on the caloric requirements in a given life stage or activity of the insect and the caloric value of the food to be consumed. The derivation of consumption values for specific species, life stages, activities, and food items is beyond the scope of the current analysis. Nevertheless, general food consumption values, based on estimated food consumption per unit body weight, are readily available.

Reichle et al. (1973) studied the food consumption patterns of insect herbivores in a forest canopy and estimated that insect herbivores may consume vegetation at a rate of about 0.6 of their body weight per day (Reichle et al. 1973, pp. 1082 to 1083). Higher values (i.e., 1.28-2.22 in terms of fresh weight) are provided by Waldbauer (1968) for the consumption of various types of vegetation by the tobacco hornworm (Waldbauer 1968, Table II, p. 247). The current risk assessment uses food consumption factors of 1.3 (0.6 to 2.2) kg food /kg bw. The lower bound of 0.6 is taken from Reichle et al. (1973), and the central estimate and upper bound are taken from the range of values provided by Waldbauer (1968).

A summary of the estimated exposures in terrestrial herbivorous insects is given in Worksheet G08a, and details of the calculations for these scenarios are provided in Worksheets G07a, G07b, G07c, and G07d of Attachment 1, the EXCEL workbook for aminocyclopyrachlor. These exposure levels pertain to the four food items included in the standard residue rates provided by Fletcher et al. (1994) as detailed in Table 15.

4.2.3.3. Contaminated Soil

Forest Service risk assessments do not typically include estimates of soil exposures, because toxicity values for soil invertebrates are not typically available. As discussed in Section 4.1.2.4.2, however, one earthworm bioassay is available on aminocyclopyrachlor (MRID 475602-08). GLEAMS provides estimates of the concentration of pesticides in soil. As summarized in Appendix 8, Table A8-2, the estimated peak concentrations of aminocyclopyrachlor in the top 12 inches of soil are 0.249 (0.194 - 0.42) mg a.e./kg dw soil at a unit application rate of 1 lb a.e./acre (i.e., the application rate used in the Gleams-Driver modeling). At the maximum labeled application rate of 0.28 lb a.e./acre, the estimated peak concentrations of aminocyclopyrachlor would be about 0.057 (0.045 to 0.097) mg a.e./kg dw soil. As discussed in Section 4.4.2.4, these concentrations are far below a level of concern for effects on earthworms.

4.2.4. Terrestrial Plants

Generally, the primary hazard to nontarget terrestrial plants associated with the application of most herbicides is unintended direct deposition or spray drift. In addition, herbicides may be transported off-site by percolation or runoff or by wind erosion of soil. As noted in Section 4.1.2.5 (Hazard Identification for Terrestrial Plants) and discussed further in Section 4.3.2.5 (Dose-Response Assessment for Terrestrial Plants), the toxicity data on aminocyclopyrachlor are sufficient to interpret risks associated with these exposure scenarios. Consequently, exposure assessments are developed for each of these exposure scenarios, as detailed in the following subsections. These exposure assessments are detailed in Worksheet G04 (runoff), Worksheet G05 (direct spray and drift), Worksheet G06a (contaminated irrigation water), and Worksheet G06b (wind erosion) for directed or broadcast foliar applications (Attachment 1).

4.2.4.1. Direct Spray

Unintended direct spray will result in an exposure level equivalent to the application rate. For many types of herbicide applications, it is plausible that some nontarget plants immediately adjacent to the application site could be sprayed directly. This type of scenario is modeled in the worksheets that assess off-site drift (see Section 4.2.4.2 below).

4.2.4.2. Off-Site Drift

Because off-site drift is more or less a physical process that depends primarily on droplet size and meteorological conditions rather than specific properties of the compound being sprayed, estimates of off-site drift can be modeled using AgDRIFT. These estimates are summarized in Worksheets G05a and G05b of the EXCEL workbook for aminocyclopyrachlor (Attachment 1). This custom worksheet includes estimates of drift for aerial, ground broadcast, and backpack applications. The drift estimates used in the current risk assessment are based on AgDRIFT (Teske et al. 2002) using Tier 1 analyses for aerial and ground broadcast applications. The term *Tier 1* is used to designate relatively generic and simple assessments which can be viewed as plausible upper limits of drift.

In Worksheet G05a, aerial drift estimates are based on Tier 1 using ASAE Fine to Medium drop size distributions. Tier 1 estimates of drift for ground broadcast applications are modeled using both low boom and high boom options in AgDRIFT. For both types of applications, the values are based on Very Fine to Fine drop size distributions and the 90th percentile values from AgDRIFT. The use of small droplet sizes in Worksheet G05a is intended to generate extremely conservative estimates of drift that would not be anticipated in typically Forest Service applications.

In Worksheet G05b, aerial drift estimates are based on Tier 1 using ASAE Course to Very Course drop size distributions (VMD≈440 µm) and the ground broadcast applications are based on ASAE fine to Medium Coarse drop size distributions (VMD≈340 µm). The product labels for DuPont™ Method® 50SG (acid) and DuPont™ Method® 240SL (potassium salt) specifically note that coarse droplet sizes (VMD >350 µm) should be used in aerial or ground applications. Thus, the drift values given in Worksheet G05b are likely to reflect estimates of drift that would be more typical of Forest Service applications rather than the extremely conservative estimates of drift given in Worksheet G05a.

Drift associated with backpack applications (directed foliar applications) are likely to be much less than drift from ground broadcast applications. Few studies, however, are available for quantitatively assessing drift after backpack applications. For the current risk assessment, estimates of drift from backpack applications are based on an AgDRIFT Tier 1 run of a low boom ground application using Fine to Medium/Coarse drop size distributions (rather than very fine to fine) as well as 50th percentile estimates of drift (rather than the 90th percentile used for ground broadcast applications).

The values for drift used in the current risk assessment should be regarded as little more than generic estimates similar to the water concentrations modeled using GLEAMS (Section 3.2.3.4.3). Actual drift will vary according to a number of conditions—e.g., the topography, soils, weather, drop size distribution, carrier, and the pesticide formulation.

4.2.4.3. Runoff and Soil Mobility

Terrestrial plant exposures associated with runoff and sediment losses from the treated site to an adjacent untreated site are summarized in Worksheet G04 of the EXCEL workbook for terrestrial applications of aminocyclopyrachlor (Attachment 1).

Any pesticide can be transported from the soil at the application site by runoff, sediment loss, or percolation. Runoff, sediment loss, and percolation are considered in estimating contamination of ambient water. Only runoff and sediment loss are considered in assessing off-site soil contamination. This approach is reasonable because off-site runoff and sediment transport will contaminate the off-site soil surface and could have an impact on non-target plants. Percolation, on the other hand, represents the amount of herbicide transported below the root zone, which may affect water quality but should not affect off-site vegetation. GLEAMS modeling provides estimates of pesticide loss in runoff. As with the estimates of aminocyclopyrachlor in surface water, runoff estimates are modeled for clay, loam, and sand at nine sites that represent different temperatures and rainfall patterns as specified in Table 7.

The exposure scenario for runoff assumes that the pesticide is lost from the treated field and spread uniformly over an adjacent untreated field of the same size. This assumption is admittedly arbitrary. Much more severe exposures could occur if all of the runoff losses were distributed into a much smaller area. Conversely, lower exposures would occur if runoff losses were distributed from the treated field to a much larger area.

For aminocyclopyrachlor, the results of the standard GLEAMS modeling of runoff and sediment losses are summarized in Appendix 8, Table A8-1. Note that amount of runoff will vary substantially with different types of climates—i.e., temperature and rainfall—as well as soils, with no runoff or sediment loss anticipated in predominantly sandy soils. The input parameters used to estimate runoff are identical to those used in the Gleams-Driver modeling for concentrations of aminocyclopyrachlor in surface water as discussed in Section 3.2.3.4 and summarized in Table 8 (site characteristics) and Table 9 (chemical-specific input parameters).

The runoff for aminocyclopyrachlor as a proportion of the application rate is taken as 0.05 (0.0005 to 0.9). The central estimate and upper bound is taken directly from the Gleams-Driver modeling—i.e., the median and empirical upper 95% bound, as detailed in Appendix 8 (Table A8-1)—rounding all values to one significant place. The lower bound is effectively zero—i.e., for sandy soils regardless of temperature and rainfall rates. The lower bound value of 0.0005 is simply the central estimate of 0.05 divided by 100. Much lower loss rates are plausible—i.e., in areas with predominantly sandy soils, as discussed further in the risk characterization (Section 4.4.2.5.2).

4.2.4.4. Contaminated Irrigation Water

Forest Service risk assessments include this standard scenario for the use of contaminated water for irrigation. Nonetheless and as discussed further in Section 4.4.2.5, the conditional registration document for aminocyclopyrachlor notes that water which may contain aminocyclopyrachlor residues should not be used for irrigation:

> *Do not contaminate water intended for irrigation. To avoid injury to crops and other desirable plants, do not treat or allow spray drift or runoff to fall onto banks or bottoms of irrigation ditches, either dry or containing water, or other channels that carry water that may be used for irrigation purposes. Do not apply to snow covered or frozen ground.*
>
> U.S. EPA/OPP (2010k, p. 22)

This is standard language that is used in the registration of most herbicides. Consequently, this standard exposure scenario, which is included in all herbicide risk assessments conducted for the Forest Service, should not be relevant if aminocyclopyrachlor is used properly. Nonetheless, this exposure assessment is included both for consistency with other herbicide risk assessments as well as to allow for the assessment of the consequences of disregarding the labeled use restrictions.

The exposure levels associated with this scenario depend on the pesticide concentration in the ambient water used for irrigation and the amount of irrigation water used. Concentrations in ambient water are based on the peak concentrations modeled in the human health risk assessment, as discussed in Section 3.2.3.4.6.

The amount of irrigation used will depend on the climate, soil type, topography, and plant species under cultivation. Thus, the selection of an irrigation rate is somewhat arbitrary. In the absence of any general approach for determining and expressing the variability of irrigation rates, the application of 1 inch of irrigation water with a range of 0.25 to 2 inches is used in this risk assessment. Details of the calculations used to estimate the functional application rates based on irrigation using contaminated surface water are provided in Worksheet G06a of the EXCEL workbook for aminocyclopyrachlor (Attachment 1).

4.2.4.5. Wind Erosion

Wind erosion can be a major transport mechanism for soil (e.g., Winegardner 1996), and wind erosion is also associated with the environmental transport of herbicides (Buser 1990). Wind erosion leading to off-site movement of pesticides is likely to be highly site-specific. The amount of aminocyclopyrachlor that might be transported by wind erosion depends on several factors, including application rate, depth of incorporation into the soil, persistence in the soil, wind speed, and topographical and surface conditions of the soil. Under desirable conditions—e.g., relatively deep (10 cm) soil incorporation, low wind speed, and surface conditions which inhibit wind erosion—it is unlikely that a substantial amount of aminocyclopyrachlor would be transported by wind.

For this risk assessment, the potential effects of wind erosion are estimated in Worksheet G06b. In this worksheet, it is assumed that aminocyclopyrachlor is incorporated into the top 1 cm of soil, which is identical to the depth of incorporation used in GLEAMS modeling (Table 9). Average soil losses are estimated to range from 1 to 10 tons/ha/year with a typical value of 5 tons/ha/year. These estimates are based on the results of agricultural field studies which found that wind erosion may account for annual soil losses ranging from 2 to 6.5 metric tons/ha (Allen and Fryrear 1977).

As noted in Worksheet G06b, offsite losses are estimated to reach as much as 0.014% of the application rate. Larney et al. (1999), however, report that wind erosion of other herbicides could be associated with losses up to 1.5% of the nominal application rate following soil incorporation or 4.5% following surface application. This difference appears to be due to the much higher soil losses noted by Larney et al. (1999)—i.e., up to 56.6 metric tons/ha from a fallow field. The losses reflected in Worksheet G06b may be somewhat more realistic for forest or rangeland applications, because herbicide applications are rarely made to fallow areas. In any event, the higher offsite losses reported by Larney et al. (1999) are comparable to exposures associated with offsite drift at distances of about 50 feet from the application site following low boom (0.017) and high boom (0.05) ground broadcast applications (Worksheet G05). All of the estimates for wind erosion and offsite drift are likely to vary dramatically according to site conditions and weather conditions.

4.2.5. Aquatic Organisms

The concentrations of aminocyclopyrachlor in surface water used to estimate exposures for aquatic species are identical to those used in the human health risk assessment, as discussed in Section 3.2.3.4.6.1 and summarized in the upper portion of Table 14.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

Table 24 summarizes the toxicity values for aminocyclopyrachlor used in the ecological risk assessment. The derivation of each of these values is discussed in the following subsections. The available toxicity data support separate dose-response assessments in eight classes of organisms: terrestrial mammals, birds, terrestrial invertebrates, terrestrial plants, fish, aquatic invertebrates, aquatic algae, and aquatic macrophytes. Different units of exposure are used for different groups of organisms, depending on the nature of exposure and the way in which the toxicity data are expressed. To maintain consistency with the exposure assessment, which is necessary for the development of Hazard Quotients (HQs) in the risk characterization, all toxicity values given in Table 24 are expressed as acid equivalents (a.e.).

For aminocyclopyrachlor, as for most herbicides, the toxicity studies on terrestrial plants are reasonably complete and adequate for deriving toxicity values for sensitive and tolerant species. One unusual aspect of the dose-response assessment for terrestrial plants, however, is that the EPA ecological risk assessment (U.S. EPA/OPP 2010b) considers only toxicity data on the methyl ester, because toxicity studies using aminocyclopyrachlor acid were not available at the time that the conditional registration for aminocyclopyrachlor was granted. Since the conditional registration, toxicity studies on aminocyclopyrachlor acid have been conducted (Porch and Kendall 2010a,b). These studies have not yet been reviewed by the U.S. EPA/OPP; however, full copies of these studies were available for the conduct of the current Forest Service risk assessment. Despite the reservations about using studies that have not been reviewed and accepted by the U.S. EPA/OPP, there are substantial differences between the potency of aminocyclopyrachlor acid and the methyl ester. Because the methyl ester is not being commercialized, the current risk assessment uses the available toxicity data on aminocyclopyrachlor acid.

As in the dose-response assessment for human health effects, the dose-response assessments for terrestrial and aquatic animals are limited, primarily because aminocyclopyrachlor is relatively nontoxic to animals, and also because the open literature on aminocyclopyrachlor is limited, and the number of animal species tested is so few. Consequently, sensitive and tolerant species are not defined for either terrestrial animals or for most groups of aquatic animals.

No toxicity data are available on reptiles, terrestrial-phase amphibians, or aquatic-phase amphibians. Consequently, no dose-response assessments for amphibians or reptiles are developed. The lack of toxicity data on amphibians is typical for a new pesticide, because toxicity tests on amphibians are not required for pesticide registration. Toxicity data for reptiles are seldom available for any herbicide.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals

4.3.2.1.1. Aminocyclopyrachlor

In characterizing risk to mammalian wildlife, Forest Service risk assessments generally consider the NOAELs on which the acute and chronic RfDs used in the human health risk assessment are

based. As summarized in Table 16, the U.S. EPA/OPP (2010a) has not derived an acute RfD for aminocyclopyrachlor. The incidental short-term RfD as well as the chronic RfD are both based on the estimated dose of 350 mg a.e./kg bw/day in rats at the dietary concentration of 6000 ppm from the subchronic feeding study by Anand (2008a,b). The EPA ecological risk assessment (U.S. EPA/OPP 2010b) uses a somewhat higher chronic toxicity value—i.e., the estimated dose of 363 mg a.e./kg bw/day from the 5000 ppm exposure group in the 2-generation reproduction study in rats by Lewis (2008a). As detailed in Appendix 1, both of these studies report comparable LOAELs based on decreased body weights—i.e., about 1000 mg a.e./kg bw/day in the study by Anand (2008a,b) and 1300 mg a.e./kg bw in the study by Lewis (2008a).

The differences in the estimated NOAELs and LOAELs in the studies by Anand (2008a,b) and Lewis (2008a) are inconsequential. The current Forest Service risk assessment uses the somewhat lower NOAEL of 350 mg a.e./kg bw/day from Anand (2008a,b). This approach is consistent with the general approach used in Forest Service risk assessments of basing the NOAEL for mammalian wildlife on the same study used to derive the RfD. As with the approach taken in the human health risk assessment, the NOAEL of 350 mg/kg a.e./day is used to characterize risks associated with both acute and longer-term exposures.

As discussed in Section 3.3.2.1, the EPA may modify the RfDs for aminocyclopyrachlor, based on chronic studies in mice, rats, and dogs submitted to the U.S. EPA/OPP since the release of the conditional registration for aminocyclopyrachlor (U.S. EPA/OPP 2010k). It is likely that the most substantial changes to the RfD would involve the selection of the uncertainty factor for extrapolating from subchronic to chronic exposures. This change would not affect the toxicity value for mammalian wildlife. As summarized in Appendix 1, Table A1-2, the lowest NOAEL from the chronic studies is 279 mg/kg/day—i.e., male rats in the chronic feeding study by Moon (2010). If this study were to be used to derive an RfD, the chronic NOAEL for mammalian wildlife would be reduced from 350 to 280 mg/kg bw/day. As discussed further in Section 4.4.2.1 (risk characterization for mammalian wildlife), this change would have no impact on the qualitative interpretation of potential risks to mammals.

As noted in Section 4.1.2.1.1, dogs and presumably other canids do not excrete weak acids as well as other groups of mammals do. Consequently, concerns could be expressed that some canid species (e.g., foxes, wolves, coyotes) might be at greater risk from exposures to a weak acid such as aminocyclopyrachlor. For aminocyclopyrachlor, however, both subchronic studies reviewed and accepted by the U.S. EPA/OPP as well as chronic studies submitted to the U.S. EPA/OPP indicate that dogs appear to be comparable to or somewhat less sensitive than rats. For example, taking 350 mg/kg bw/day as the subchronic NOAEL in rats, the corresponding subchronic NOAEL in dogs is 388 mg a.e./kg bw/day (Luckett 2008a; Luckett and Mawn 2008). Similarly, the chronic NOAEL in rats is 279 mg a.e./kg bw/day (Moon 2010) and the chronic NOAEL in dogs is about 1000 mg a.e./kg bw/day (Han 2010). Because of the similarities in the subchronic NOAELs for rats and dogs, the current Forest Service risk assessment does not derive a separate NOAEL for canids (i.e., the NOAEL of 350 mg a.e./kg bw/day is used for all species of mammalian wildlife).

4.3.2.1.2. Cyclopropanecarboxylic acid

Similar to the approach taken with aminocyclopyrachlor, the NOAELs that form the basis of the acute and chronic RfDs in the human health risk assessment are used in the dose-response

assessment for mammalian wildlife. As summarized in Table 17 and discussed in Section 3.3.3, the RfDs for cyclopropanecarboxylic acid are atypical in that they are based on a toxicity study of panadiplon, which is metabolized to cyclopropanecarboxylic acid. The RfDs are also unusual, in that the study from which they are derived (Ulrich et al. 1994) involves an exposure period of only 14 days and the study does not define a NOAEL.

The LOAEL of 2.55 mg/kg bw/day is divided by a factor of 10 to estimate an acute mammalian NOAEL of 0.255 mg/kg bw/day. Following the convention used in the dose-response assessment for ecological receptors, the NOAEL is rounded to two significant places (i.e., 0.26 mg/kg bw).

The chronic NOAEL is taken as 0.026 mg/kg bw/day (i.e., the estimated acute NOAEL divided by 10 for extrapolating from an acute repeated-dose study to a longer-term exposure). While this approach is unusual, it should be noted that U.S. EPA/OPP (2010a) uses an uncertainty factor of 3 rather than 10. As discussed in Section 3.3.3.2 and detailed in U.S. EPA/OPP (2010a), the EPA appears to regard the 10-day exposure period as subchronic rather than acute. The approach used in the current Forest Service risk assessment is somewhat more conservative, which seems reasonable, because a 10-day period of exposure is not typically viewed as subchronic.

As with the RfD for aminocyclopyrachlor, the RfD for cyclopropanecarboxylic acid is likely to be modified upward by the U.S. EPA/OPP. In the case of cyclopropanecarboxylic acid, however, it is likely that the modification of the RfD would substantially modify the toxicity value used for mammalian wildlife. As discussed in Section 3.3.3.2, a 90-day gavage study (Carpenter 2012) has been completed by DuPont™ and submitted to the U.S. EPA/OPP. Based on a study summary of Carpenter (2012), no adverse effects were observed in rats at doses of 2 and 10 mg/kg bw/day. If this study is accepted by the U.S. EPA/OPP, the longer-term NOAEL used in the current Forest Service risk assessment would probably be taken as 1 mg/kg bw/day (i.e., the subchronic NOAEL divided by a factor of 10 for extrapolating from a subchronic to a chronic duration) which would be a factor of about 40 [1 mg/kg bw/day ÷ 0.026 mg/kg bw/day ≈ 38.46] higher than the NOAEL currently used in the current Forest Service risk assessment.

While a factor of 40 is substantial, the upward adjustment of the chronic NOAEL would have no impact on the qualitative characterization of risk. As discussed further in Section 4.4.2.1.2, the HQs for mammals exposed to cyclopropanecarboxylic acid via the consumption of contaminated water or contaminated fish are substantially below the level of concern (HQ=1).

4.3.2.2. Birds

4.3.2.2.1. Acute Exposures

The dose-response assessment for acute exposures of birds is relatively simple. As discussed in Section 4.1.2.2 and detailed in Appendix 2, aminocyclopyrachlor is classified by the U.S. EPA/OPP as practically non-toxic to birds, based on gavage administration to quail (Gallagher and Beavers 2007) or 5-day dietary exposures to both quail (Hubbard et al. 2007b) and mallard ducks (Hubbard et al. 2007a). In these studies, no adverse effects were noted at the highest doses tested (i.e., 2075 mg a.e./kg bw for the gavage study in quail and 2423 mg a.e./kg bw for the

dietary study in mallards). For the acute dose-response assessment in birds, the gavage NOAEL of 2075 mg a.e./kg bw is used to assess the potential risks of acute exposures in birds.

4.3.2.2.2. Longer-term Exposures

The dose-response assessment for characterizing risks associated with chronic exposure scenarios is more problematic than the acute dose-response assessment. As discussed in Section 4.1.2.2.3, U.S. EPA/OPP (2010b) classifies both reproduction studies in birds as *Invalid* because the cage sizes used in the studies were smaller than the cage sizes required in the EPA guidelines for avian toxicity studies. Forest Service risk assessments typically do not use studies classified as invalid. Nonetheless, an exploratory application of these studies indicates a modest exceedance in the level of concern (HQ>1) using a 100.9 mg/kg bw/day for quail (Temple et al. 2008b). As discussed further in Section 4.4.2.2 (risk characterization for birds), the significance of these modest increases is questionable, because neither study identifies a clear LOAEL.

In the absence of an *Acceptable* or *Supplemental* study in birds, the NOAEL of 100.9 mg/kg bw/day for quail from the reproductive study by Temple et al. (2008b) is used to characterize risks associated with longer-term exposures in birds, only because this NOAEL does not exclude the possibility of adverse effects (i.e., the use of the NOAEL may be viewed as highly conservative).

4.3.2.3. Reptiles and Amphibians (Terrestrial Phase)

Since toxicity data are not available for terrestrial-phase reptiles or amphibians (Section 4.1.2.3), no dose-response assessment can be derived for this group of organisms.

4.3.2.4. Terrestrial Invertebrates

4.3.2.4.1. Oral Toxicity Value

Forest Service risk assessments attempt to characterize risks to terrestrial invertebrates from the consumption of contaminated vegetation following broadcast applications (Section 4.2.3.2). The results of oral toxicity studies in honeybees are typically used to assess risks associated with this scenario. The only information available on the oral toxicity of aminocyclopyrachlor to honeybees is the feeding study by Warmers (2007a). U.S. EPA/OPP (2010b, p. 44) classifies the NOAEL for this study as a nominal dose of 100 µg/bee (the highest nominal dose tested), based on mortality. As discussed in Section 4.1.2.4.1, however, Warmers (2007a) observed incoordination in 8/50 bees at the oral dose of 100 µg/bee, and this incidence is statistically significant (p=0.0002885) from the control response (0/50) based on the Fisher Exact test. Consequently, the current Forest Service risk assessment uses the next lower measured dose of 53.58 µg/bee and the average body weight of 116 mg to estimate an oral NOAEL for sublethal effects of about 460 mg a.e./kg bw [0.05386 mg ÷ 0.000116 kg ≈ 464.31 mg/kg bw]. The 100 µg/bee dose may be viewed as a LOAEL for sublethal effects, which corresponds to about 860 mg a.e./kg bw [0.1 mg ÷ 0.000116 kg ≈ 862.069 mg/kg bw].

The low acute NOAEL for bees is consistent with the toxicity data on mammals (acute NOAEL of 350 mg a.e./kg bw) and birds (2075 mg a.e./kg bw), as discussed above. No quantitative consideration can be given to other potential subchronic or non-lethal effects, and no oral toxicity data are available on other invertebrate species.

4.3.2.4.2. Contact Toxicity Value (for Direct Spray)

The only information available on the contact toxicity of aminocyclopyrachlor also comes from Warmers (2007a). Unlike the oral toxicity study discussed in the previous section, Warmers (2007a) reports no mortality or signs of sublethal toxicity at doses of up to 100 µg/bee. As discussed in Section 4.1.2.4.1., the dose of 100 µg/bee corresponds to a dose of about 860 mg a.e./kg bw. This NOAEL is used to assess the consequences of direct spray or spray drift to a terrestrial invertebrate.

4.3.2.4.3. Contact Toxicity Value (for Soil Exposures)

As discussed in Section 4.1.2.4.2, no information is available on the toxicity of aminocyclopyrachlor acid to soil invertebrates, which precludes the development of a formal dose-response assessment for aminocyclopyrachlor acid. Nonetheless, a registrant-submitted study on aminocyclopyrachlor methyl ester (MRID 475602-08) indicates that no adverse effects were observed in earthworms (*Eisenia fetida*) after 14 days of exposure to soil concentrations of up to 203 mg a.e./kg dry weight soil. As detailed in U.S. EPA/OPP (2010b, pp. 12), the methyl ester of aminocyclopyrachlor rapidly degrades to aminocyclopyrachlor in soil. Thus, the earthworm study with the methyl ester probably involved exposures primarily to aminocyclopyrachlor. Consequently, the application of the NOAEL of 203 mg a.e./kg dry weight soil to anticipated soil exposures is discussed semi-quantitatively in Section 4.4.2.4.

4.3.2.5. Terrestrial Plants (Macrophytes)

As with most herbicides, there are adequate data for developing toxicity values for both sensitive and tolerant plant species involving soil exposures (i.e., herbicide runoff to an untreated field) and foliar exposures (direct spray, wind erosion, or drift). The available studies are discussed in Section 4.1.2.5 and summarized in Appendix 4. Studies on seedling emergence are used to assess risks associated with exposures to residues of aminocyclopyrachlor in soil. Studies on vegetative vigor are used to assess risks associated with the deposition of aminocyclopyrachlor onto plants as a result of direct spray or spray drift.

Table 23 provides an overview of the NOAECs from the available standard phytotoxicity studies on aminocyclopyrachlor. Details of these data are discussed in the following subsections. NOAECs rather than EC_{25} values are used in the dose-response assessment because the Forest Service prefers to base risk characterizations on NOAECs rather than on effect levels like an EC_{25}. The available studies include vegetative vigor and seedling emergence assays on the methyl ester of aminocyclopyrachlor as well as studies on a 50SG formulation of aminocyclopyrachlor acid. The studies on the ester are summarized in U.S. EPA/OPP (2010b), the ecological risk assessment on aminocyclopyrachlor. The studies on the acid formulation (Porch and Kendall 2010a,b) have been submitted to the U.S. EPA/OPP; however, EPA evaluations of these studies are not yet available. For the conduct of the current Forest Service risk assessment, DuPont™ provided full copies of these studies.

The dose-response assessment for terrestrial plants is somewhat complicated by concerns for adverse effects in conifers. As discussed in Section 4.1.2.5.3, atypically frequent and severe damage to pine is associated with applications of Imprelis®, a 25% a.i. liquid formulation of the potassium salt of aminocyclopyrachlor. As discussed in Section 4.1.2.5.3, the potential for other formulations of aminocyclopyrachlor to damage conifers is an endpoint of concern, because

there are not sufficient data to suggest that Imprelis® is substantially different from other formulations of aminocyclopyrachlor.

4.3.2.5.1. Vegetative Vigor

As summarized in Table 23 and discussed in Section 4.1.2.5.1, dicots are much more sensitive than monocots to aminocyclopyrachlor and aminocyclopyrachlor ester. This pattern in plant sensitivity is common among many auxin-mimicking herbicides (e.g., Kelley and Riechers 2007). Based on NOAECs for tolerant species, differences in the potency of aminocyclopyrachlor acid and ester are insubstantial—i.e., NOAECs of 0.36 (acid) and 0.335 (ester) lb a.e./acre for tolerant monocots and NOAECs of 0.00078 (acid) and 0.00035 (ester) lb a.e./acre for tolerant dicots. Based on NOAECs for sensitive species, however, aminocyclopyrachlor ester is substantially more toxic than the acid. For monocots, the difference is about a factor of about 8 [0.022 lb a.e./acre (acid) ÷ 0.0028 lb a.e./acre (ester) ≈ 7.857 acid/ester]. For dicots, the difference is about a factor of 56 [0.000044 lb a.e./acre (acid) ÷ 0.00000078 lb a.e./acre (ester) ≈ 56.4103 acid/ester]. The comparison for dicots, however, is not direct, because the NOAEC for the ester is based on an EC_{05} value rather than an experimental NOAEC. As noted in U.S. EPA/OPP (2010b), a NOAEC was not identified in the dicot study; thus, the EC_{05} is used to approximate a NOAEC. Confidence in the estimated EC_{05}, however, is limited because the comparison involves extrapolation to doses that are lower than the experimental doses.

As discussed in Section 4.1.2.5.2, plant absorption of aminocyclopyrachlor methyl ester is greater than plant absorption of aminocyclopyrachlor acid (Bukun et al. 2009, 2010), and this difference may account for the greater toxicity of the ester. On the other hand, differences in absorption are not correlated with differences in sensitivity among some target plants (Bell et al. 2011).

As noted in Section 4.3.2.5, the EPA reviewed and accepted the plant studies on aminocyclopyrachlor methyl ester (U.S. EPA/OPP 2010b). In the meantime, the vegetative vigor study conducted with the acid (Porch and Kendall 2010b) was submitted to the EPA; however the review is not currently available. Nonetheless, a full copy of this study was provided by DuPont™ for the conduct of the current Forest Service risk assessment. Since this study was not obtained from the EPA, it cannot be shared with the peer reviewers of this risk assessment. This limitation is common with any FIFRA CBI study.

SERA reviewed the vegetative vigor study by Porch and Kendall (2010b) on aminocyclopyrachlor acid in the conduct of the current Forest Service risk assessment; however, the nature of SERA's review is less detailed than reviews conducted by U.S. EPA/OPP. In the preparation of a DER on Tier II plant toxicity studies, the EPA typically contracts a full reanalysis of the raw data submitted by the registrant; moreover, the reanalysis goes through several stages of additional review by the EPA. It is not uncommon for the EPA to modify both EC_{25} and NOAEC values reported in registrant-submitted studies. This level of review and reanalysis is beyond the scope of the current effort. Notwithstanding the limited nature of the current review, the study by Porch and Kendall (2010b) is reported in great detail (156 pages) and appears to have been conducted properly.

The NOAECs reported in the vegetative vigor study by Porch and Kendall (2010b) are used in the current risk assessment because this study involves a formulation that will be used by the Forest Service. As discussed previously, DuPont™ is not commercializing formulations of aminocyclopyrachlor methyl ester. Moreover, U.S. EPA/OPP (2010b) expresses concern with the extrapolated EC_{05} for sensitive species of dicots, and the magnitude of the difference between the acid and the ester is substantial—i.e., the ester appears to be more toxic by a factor of about 56. In the event that the U.S. EPA/OPP review of the Porch and Kendall (2010b) study results in substantially different NOAECs than those reported in the study, the current Forest Service risk assessment should be modified to accept the NOAECs derived by U.S. EPA/OPP.

Following the above approach, the NOAECs for foliar exposure are taken as 0.000044 lb a.e./acre for sensitive species (based on sensitive dicots), and the corresponding NOAEC for tolerant species (based on tolerant monocots) is taken as 0.36 lb a.e./acre.

4.3.2.5.2. Seedling Emergence

Selecting toxicity values for soil exposures involves issues similar to those for selecting toxicity values for foliar exposures. EPA reviewed the registrant-submitted seedling emergence study conducted with aminocyclopyrachlor ester; however, it has not reviewed the full study on seedling emergence conducted with aminocyclopyrachlor acid (Porch and Kendall 2010a), which was available to SERA for the conduct of the current risk assessment.

Unlike the case with the vegetative vigor studies, the relationship of the toxicity of the acid and ester of aminocyclopyrachlor is not consistent. As summarized in Table 23 and detailed in Appendix 4 (Table A4-2), dicots are much more sensitive to the ester than to the acid; however, this pattern is not apparent in monocots. For sensitive species of monocots, the seedling emergence assays indicate that the acid (NOAEC=0.0028 lb a.e./acre for onions) is more toxic than the ester (NOAEC=0.0394 lb a.e./acre for onions) by a factor of about 14 [$0.0394 \div 0.0028 \approx 14.0714$]. There is no apparent reason for onions to be more sensitive to the acid than to the ester form of aminocyclopyrachlor.

In the current Forest Service risk assessment, rationale for the selection of toxicity values for seedling emergence is identical to that for vegetative vigor. While there are reservations about using the study by Porch and Kendall (2010a) because it has not been reviewed by the U.S. EPA/OPP, the study appears to have been conducted properly, is well-documented, and involves a form of aminocyclopyrachlor that will be used in Forest Service programs. Thus, the NOAECs for soil exposure are taken as 0.00018 lb a.e./acre for sensitive species (based on sensitive dicots) and 0.35 lb a.e./acre for tolerant species (based on tolerant monocots). Like the toxicity values for foliar exposures, the toxicity values for soil exposures should be modified to accept any potential changes to the NOAECs as a result of the U.S. EPA/OPP review of the study.

4.3.2.5.3. Toxicity to Conifers

As discussed in Section 4.1.2.5.3, applications of Imprelis®, a 25% a.i. liquid formulation of the potassium salt of aminocyclopyrachlor, are associated with damage to conifers, particularly Norway spruce (*Picea abies*) and white pine (*Pinus strobus*). While standardized toxicity studies for pines are not available, it is possible to at least crudely estimate application rates for soil exposures to aminocyclopyrachlor that might cause minimal (NOAEL) and detectable (LOAEL) effects.

As discussed in Section 4.1.2.5.3, the only reasonably detailed study regarding the toxicity of aminocyclopyrachlor to conifers is Roten (2011), which examines the effects of an aminocyclopyrachlor acid formulation on loblolly pine (*Pinus taeda*). This study focuses on assessing the efficacy of aminocyclopyrachlor for site preparation rather than on evaluating the toxicity of aminocyclopyrachlor to pine. Nonetheless, crude estimates of the toxicity of aminocyclopyrachlor to pine can be made based on reports of injury to pine.

At an application rate of 64 g a.e./ha (≈0.057 lb a.e./acre), Roten (2011) noted minor effects on pine seedling (i.e., a statistically insignificant increase in dead leaders) planted 3 to 5 months after application. At 128 g a.e./ha (≈0.114 lb a.e./acre), damage to pines leaders was statistically significant. As summarized in Table 9, the reported half-lives of aminocyclopyrachlor in soil range from about 114 to 433 days. These half-lives correspond to degradation rates [$\ln(2) \div T_{50}$] of about 0.0016 to 0.006 day^{-1}. Taking 4 months (120 days) as the average interval between aminocyclopyrachlor application and seedling planting, the proportion of aminocyclopyrachlor remaining in the soil after 120 days can be estimated as about 0.48 to 0.83 [$e^{-0.0016 \text{ to } 0.006 \times 120 \text{ days}} \approx$ 0.04821 to 0.82523]. Based on these proportions, the effective application rate associated with a NOAEL for pine can be estimated at 0.027 to 0.047 lb a.e./acre [0.057 lb a.e./acre x 0.48 to 0.83]. Similarly, the effective application rate associated with a LOAEL for pine can be estimated at 0.055 to 0.094 lb a.e./acre [0.114 lb a.e./acre x 0.48 to 0.83].

By comparison to the standard bioassays for seedling emergence (Table 23), the estimated NOAECs for pine of 0.027 to 0.047 lb a.e./acre are most closely related to the NOAEC of 0.045 lb a.e./acre for tolerant species of dicots. As indicated in Table 24, which summarizes the toxicity values used in the ecological risk assessment, the NOAEC of 0.045 lb a.e./acre is used in the risk characterization (Section 4.4.2.5.2) to describe potential effects on pines.

4.3.2.6. Terrestrial Microorganisms

The toxicity of aminocyclopyrachlor to terrestrial microorganisms (Section 4.1.2.6) is not addressed in the available literature. Consequently, a dose-response assessment cannot be made for soil microorganisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish

The dose-response assessment for fish is straightforward. As discussed in Section 4.1.3.1 and summarized in Appendix 5 (Table A5-1), concentrations of 120 to 129 mg a.e./L technical grade aminocyclopyrachlor in three acute bioassays failed to cause signs of toxicity in two species of freshwater fish. In the current risk assessment, 120 mg a.e./L is used as an acute NOAEC and is applied to tolerant species of fish.

In an early life-stage study with rainbow trout, measured concentrations of up to 11 mg a.e./L, (the highest concentration tested) of technical grade aminocyclopyrachlor did not adversely affect survival, behavior, or growth. Consequently, the NOAEC of 11 mg a.e./L is used to assess risks to tolerant species of fish associated with longer-term exposures to aminocyclopyrachlor.

All of the NOAECs are free-standing (i.e., concentrations of aminocyclopyrachlor that cause adverse effects in fish have not been determined). While the NOAECs are applied to presumably tolerant species of fish, it is not clear that other species of fish would be substantially more sensitive to aminocyclopyrachlor. The lack of demonstrated effect levels in fish has no impact on the risk assessment. As discussed in Section 4.4.3.1 (risk characterization for fish), all acute and longer-term exposures of fish to aminocyclopyrachlor are substantially below the corresponding NOAECs.

4.3.3.2. Amphibians (Aquatic-Phase)

As noted in Section 4.1.3.2, no information is available on the toxicity of aminocyclopyrachlor to aquatic-phase amphibians. Consequently, no dose-response assessment is proposed for this group of organisms. Following the approach taken in U.S. EPA/OPP (2010b), risks to aquatic-phase amphibians are characterized based on risks to fish.

4.3.3.3. Aquatic Invertebrates

4.3.3.3.1. Acute Exposures

Unlike the case with fish, adverse effects were observed in aquatic invertebrates in some standard studies on aminocyclopyrachlor. In terms of acute toxicity, *Daphnia magna*, a freshwater invertebrate, is clearly more sensitive than two saltwater species, the eastern oyster (*Crassostrea virginica*) and a mysid shrimp (*Americamysis bahia*). These are the only three species on which acute toxicity studies have been conducted; thus, generalizations concerning the relative sensitivities of freshwater and saltwater invertebrates are not justified.

In the absence of additional information, the acute NOAEC of 3.7 mg a.e./L for mortality and signs of sublethal toxicity in *Daphnia magna* (Gallagher et al. 2007b) is taken as the toxicity value for sensitive aquatic invertebrates. The NOAEC of 122 mg a.e./L (Gallagher et al. 2008b), also based on mortality and signs of sublethal toxicity, is taken as the toxicity value for tolerant species of aquatic invertebrates.

4.3.3.3.2. Longer-term Exposures

The chronic toxicity data in aquatic invertebrates is limited to two standard reproduction studies in *Daphnia magna* (Gallagher et al. 2008e; Minderhout et al. 2011). As noted in U.S. EPA/OPP (2010b) and discussed in Section 4.1.3.3.2 of the current risk assessment, the usefulness of the earlier study by Gallagher et al. (2008e) is questionable, because relatively high rates of parental mortality (i.e., 30 to 40%) were observed at mean measured concentrations of 0.37 (8/20), 0.73 (6/20), and 1.5 mg a.e./L (8/20) but only 10% mortality was observed in the control group (2/20) and the two higher concentrations (1/10) (i.e., mean measured concentrations of 3 and 6 mg a.e./L). No reproductive effects, including time to first brood, total body lengths, and total mean dry weight were observed at any concentration. The mortality rates at low concentration are not statistically significant, based on Fisher's Exact test (i.e., a *p*-value of 0.076039 for response rates of 4/10 vs 2/20), and there is clearly no concentration-response relationship. Nonetheless, the DER for the Gallagher et al. (2008e) study classifies 0.37 mg a.e./L as a LOAEC but expresses concern for the health of the test organisms. Because of concerns with the lack of a concentration-response relationship and concerns for the health of the test organism, the EPA classifies Gallagher et al. (2008e) as *Supplemental* rather than *Acceptable* or *Guideline*.

In response to the U.S. EPA/OPP review of the Gallagher et al. (2008e) study, DuPont™ conducted a second reproduction study in *Daphnia magna* (Minderhout et al. 2011). This study has been submitted to the U.S. EPA/OPP; however, an evaluation of this study by U.S. EPA/OPP is not currently available. Nonetheless, DuPont™ provided SERA with a full copy of Minderhout et al. (2011), which appears to have been conducted properly and is well documented. Consistent with the acute toxicity data in *Daphnia magna*, no adverse effects on survival, growth or reproductive parameters were observed at mean measured concentrations of up to 4.9 mg a.e./L, and the LOAEL is defined as 9.9 mg a.e./L, based on adult growth—i.e., a slight (5.5%) but statistically significant decrease in mean body length (study Table 4, p. 29)—and survival. As with the earlier study by Gallagher et al. (2008e), no effects were noted on the number of offspring.

As with the studies by Porch and Kendall (2010a,b) on seedling emergence and vegetative vigor (discussed in Section 4.3.2.5.2), there are concerns with using studies that have not been reviewed and accepted by the U.S. EPA/OPP. Nonetheless, given the concerns with the earlier study by Gallagher et al. (2008e), the more recent study by Minderhout et al. (2011) is used to define a chronic NOAEC of 4.9 mg a.e./L for aquatic invertebrates. This experimental chronic NOAEC of 4.9 mg a.e./L is somewhat greater than the acute NOAEC of 3.7 mg a.e./L discussed in Section 4.3.3.3.1. This difference, however, simply reflects the differences in the experimental concentrations used in the acute and chronic studies. Because it is not sensible to use a chronic NOAEC that is higher than an acute NOAEC, the acute NOAEC of 3.7 mg a.e./L is applied to both acute and chronic exposures. This approach may be viewed as overly conservative in that it would be equally sensible to apply the chronic NOAEC to acute exposures. As discussed further in Section 4.4.3.4, however, this conservative approach has no impact on the risk characterization.

As discussed in Section 4.3.3.3.1, *Daphnia magna* are more sensitive than two saltwater species to aminocyclopyrachlor. In this respect, *Daphnia magna* may be viewed as a sensitive species in terms of acute toxicity. Given the limited data available on the acute toxicity of aminocyclopyrachlor on other freshwater organisms and the availability of chronic studies on only one species of aquatic invertebrates, the NOAEC of 3.7 mg a.e./L is used for potentially tolerant species of aquatic invertebrates. The longer-term hazard to other potentially more sensitive species of aquatic invertebrates is considered qualitatively in Section 4.4.3.4.

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

As discussed in Section 4.1.3.4.1 and summarized in Appendix 7 (Table A7-1), standard acute assays in algae are available for three freshwater species and one marine species. The most sensitive NOAECs for freshwater algae are 1.11 mg a.e./L (*Anabaena flos-aquae* based on biomass), 14 mg a.e./L (*Navicula pelliculosa*, biomass), and 15.3 mg a.e./L (*Pseudokirchneriella subcapitata*, cell density and biomass). A much higher NOAEC of 120 mg a.e./L (*Skeletonema costatum*, all endpoints) is reported for the marine species.

Because of the reasonably substantial range of sensitivities in freshwater species—i.e., a factor of about 14 [15.3 mg a.e./L ÷ 1.11 mg a.e./L ≈ 13.784]—and because most forestry uses of aminocyclopyrachlor will not be conducted in close proximity to saltwater, the NOEAC of 1.11

mg a.e./L is used as the toxicity value for sensitive species of freshwater algae and the NOAEC of 15.3 mg a.e./L is used as the toxicity value for tolerant species of freshwater algae. Based on the single assay in a saltwater species, saltwater algae may be less sensitive than freshwater algae to aminocyclopyrachlor. As discussed in Section 4.4.3.4.1, this difference has no impact on the risk characterization, because tolerant freshwater algae do not appear to be at risk from exposures to aminocyclopyrachlor even in the accidental spill scenario. Thus, there is no basis for asserting that saltwater species of algae will be at risk.

4.3.3.4.2. Macrophytes

As discussed in Section 4.1.3.4.2 and summarized in Appendix 7 (Table A7-2), only a single standard bioassay on aminocyclopyrachlor acid is available: the study by Porch et al. (2008e) on a species of duckweed (*Lemna gibba*). This study defines an NOAEC of 3.75 mg a.e./L for all endpoints (frond number, biomass, frond growth rate). In the absence of data on other species of aquatic macrophytes, this NOAEC is applied to potentially tolerant species of aquatic macrophytes.

As also discussed in Section 4.1.3.4.2, an efficacy study on aquatic applications of both the acid and methyl ester of aminocyclopyrachlor suggest that low surface application rates (≈0.0009 to 0.03 lb a.e./acre) may be effective for the control of aquatic weeds (Israel 2011). This study, however, does not provide sufficient information to estimate the concentrations of aminocyclopyrachlor in water. Consequently, this study is not used quantitatively to estimate NOAELs or LOAELs for other potentially sensitive species of aquatic macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

Aminocyclopyrachlor is an effective herbicide for terrestrial vegetation. Under some conditions, the terrestrial application of aminocyclopyrachlor could damage nontarget terrestrial vegetation either by offsite drift, offsite losses associated with runoff, or the misuse of contaminated surface water for irrigation. Offsite losses associated with the transport of contaminated soil by wind are less likely than drift, runoff, and irrigation water to damage nontarget terrestrial vegetation.

The current risk assessment is concerned with the reports of damage to conifers following applications of one aminocyclopyrachlor formulation, Imprelis®, to turf. While Imprelis® will not be used in Forest Service programs, the incidents of conifer damage following applications of Imprelis® to turf raise concerns that damage to conifers might occur in applications of other aminocyclopyrachlor formulations. The reasons for the atypically frequent and severe reports of damage to conifers following applications of Imprelis® to turf are not clear.

As detailed in Section 2.2.2.1, the revised product labels for DuPont™ Method® 50SG (DuPont™ 2012a) and DuPont™ Method® 240SL (DuPont™ 2012b) contain cautionary language concerning the potential for runoff following applications of aminocyclopyrachlor. Based on the Gleams-Driver modeling conducted as part of the current Forest Service risk assessment, damage due to runoff losses appears to be plausible under conditions that are conducive to high rates of runoff (i.e., soils saturated with water or soils such as hard clay with very low porosity and sites in which runoff would occur from a relatively large treated area to a smaller area that contains conifers). At sites with low rainfall and/or well-drained soils, damage to conifers due to runoff would not be anticipated.

There is no basis for asserting that applications of aminocyclopyrachlor will lead to significant or even detectable signs of toxicity in terrestrial animals, aquatic animals, or aquatic algae. Based on a single efficacy study in which aminocyclopyrachlor was evaluated as an aquatic herbicide, damage to sensitive species of nontarget aquatic macrophytes cannot be ruled out.

The risk characterization for aminocyclopyrachlor must be qualified in terms of the small number of species on which data are available, relative to the numerous species which could be exposed to aminocyclopyrachlor. This type of reservation is common in many pesticide risk assessments, particularly new pesticides, such as aminocyclopyrachlor, for which the open literature is scant.

While the risk characterization for aminocyclopyrachlor focuses on the potential for direct toxic effects, there is potential for secondary effects in virtually all groups of nontarget organisms. Terrestrial applications of any effective herbicide, including aminocyclopyrachlor, are likely to alter vegetation within the treatment area. This alteration could have secondary effects on terrestrial or aquatic animals, including changes in food availability and habitat quality. These secondary effects may be beneficial to some species and detrimental to others; moreover, the magnitude of secondary effects is likely to vary over time. While these concerns are acknowledged, they are not specific to aminocyclopyrachlor or herbicide applications in general. Any effective method for vegetation management, including mechanical methods which do not

involve aminocyclopyrachlor or any other herbicide, is likely to lead to secondary effects on both nontarget animals and vegetation.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

4.4.2.1.1. Aminocyclopyrachlor

The risk characterization for mammals exposed to aminocyclopyrachlor is summarized in Worksheet G02a of Attachment 1, the EXCEL workbook for aminocyclopyrachlor. None of the HQs exceed the level of concern. The highest HQs are associated with consumption of contaminated short grass by a small mammal—i.e., HQs of 0.1 (0.01 to 0.6) for acute exposures and 0.08 (0.009 to 0.4) for longer-term exposures. As noted in Table 15, short grass is the standard food item from Fletcher et al. (1997) with the highest residue rates. As discussed in Section 4.2.2.3, this scenario assumes that the small mammal will consume nothing but contaminated grass following a direct spray. While this activity may occur in some instances, most small mammals have a more diverse diet, particularly in a forest environment, and residues on contaminated short grass will often be diminished by foliar interception. Thus, this scenario should be viewed as an extreme worst-case—i.e., the Most Exposed Individual as discussed in Section 3.2.3.1.1.

Notwithstanding the above discussion, the Most Exposed Individual approach is carried over to the ecological risk assessment, because of the numerous species that may be exposed to pesticides applied by broadcast application and the wide range of materials these species might consume. The HQs for this exposure scenario suggest that mammals are not likely to be at risk following applications of aminocyclopyrachlor.

4.4.2.1.2. Cyclopropanecarboxylic acid

The risk characterization for mammals associated with exposures to cyclopropanecarboxylic acid following applications of aminocyclopyrachlor is summarized in Worksheet G02a of Attachment 2, the EXCEL workbook for cyclopropanecarboxylic acid. As discussed in Section 4.2.2.4.1, the exposure scenarios for cyclopropanecarboxylic acid are limited to surface water. All of the resulting HQs are substantially below the level of concern. The highest upper bound HQ is 0.04 (i.e., below the level of concern by a factor of 25), and this hazard quotient is associated with the consumption of contaminated fish by a canid following an accidental spill of aminocyclopyrachlor. The highest upper bound HQ of the non-accidental exposure scenarios is 0.002 (i.e., below the level of concern by a factor of 500). This HQ applies to both acute and longer-term scenarios for the consumption of contaminated fish by a canid following an accidental spill of aminocyclopyrachlor.

The HQs for mammals are based on the study by Ulrich et al. (1994) conducted with panadiplon. As discussed in Section 4.3.2.1.2, it seems likely that the U.S. EPA/OPP will adjust the NOAEC for cyclopropanecarboxylic acid upward by a factor of about 40 to 1 mg/kg bw/day based on the more recent subchronic gavage study in rats by Carpenter (2012). This adjustment would lower the HQs for cyclopropanecarboxylic acid but would have no impact on the qualitative risk characterization: No risks to mammals are apparent from exposure to cyclopropanecarboxylic acid as a degradate of aminocyclopyrachlor.

4.4.2.2. Birds

The risk characterization for birds exposed to aminocyclopyrachlor is summarized in Worksheet G02b of Attachment 1, the EXCEL workbook for aminocyclopyrachlor. As with mammals, none of the HQs associated with accidental or acute non-accidental exposures exceed the level of concern. Also as with mammals, the highest HQs for acute exposure scenarios are associated with the consumption of contaminated short grass—i.e., HQs of 0.05 (0.005 to 0.2). This is a common pattern in the foliar application of pesticides, because of the high residue rates for short grass from Fletcher et al. (1997).

Unlike the case with mammals, some of the longer-term HQs for birds do modestly exceed the level of concern (HQ>1). As illustrated in Figure 6, the upper bounds of HQs for a small bird exceed the level of concern for the consumption of broadleaf foliage [HQs= 0.4 (0.04 to 1.9)], tall grass [HQs= 0.3 (0.03 to 1.6)], and short grass [HQs= 0.7 (0.08 to 3)].

A major reservation in the interpretation of these HQs involves the nature of the chronic toxicity data in birds. As discussed in Section 4.3.2.2.2, U.S. EPA/OPP (2010b) classifies both of the available reproduction studies in birds as *Invalid*. Appropriately, the EPA does not use studies classified as *Invalid* for risk characterization. The chronic HQs for birds are given in the current Forest Service risk assessment simply because the reproduction studies in birds represent the only data that are available.

An additional and perhaps more important reservation with interpreting the modestly high HQs for a small bird is that none of the available studies in birds demonstrates any signs of toxicity. As discussed in Section 4.1.2.2, the reproductive NOAEL of 100.9 mg a.e./kg bw/day is the highest dose in the quail study by Temple et al. (2008b), and acute doses of up to 2423 mg a.e./kg bw failed to induce any signs of the toxicity in birds (Hubbard et al. 2007a). Consequently, the upper bound HQs for birds that modestly exceed the level of concern are cited in the current Forest Service risk assessment as a matter of transparency. These upper bound HQs should not be interpreted as an indication that adverse effects in birds are plausible.

As noted in Section 4.4.2.1.2, the risk assessment for mammals indicates that exposures to cyclopropanecarboxylic acid following applications of aminocyclopyrachlor are substantially below the level of concern. The lack of toxicity data in birds for cyclopropanecarboxylic acid precludes the development of a quantitative risk characterization. Nonetheless, the low HQs for mammals suggest that risks to birds associated with exposures to cyclopropanecarboxylic acid are not a substantial concern.

4.4.2.3. Reptiles and Amphibians (Terrestrial Phase)

Risks to reptiles and terrestrial phase amphibians cannot be characterized directly because of the lack of data on the toxicity of aminocyclopyrachlor to this group of organisms. Based on the risk characterization for birds, as well as all other groups of terrestrial animals for which data are available, there is no basis for assuming that reptiles or terrestrial-phase amphibians are likely to be at risk from exposures to aminocyclopyrachlor. The extension of the risk characterization for birds to the risk characterization for reptiles and terrestrial-phase amphibians is adopted for amphibians in the recent EPA ecological risk assessment of aminocyclopyrachlor (U.S. EPA/OPP 2010b, pp. 34).

As discussed in Section 4.1.2.3, amphibians may be more sensitive to some pesticides because their skin is more permeable to pesticides, relative to mammalian skin. Thus, it is not clear that the risk characterization for other groups of terrestrial animals is applicable to amphibians. This limitation may also apply to reptiles. As discussed in Section 4.4.2.2, issues with the quality of the chronic toxicity data on birds limits the risk characterization for longer-term exposures of birds to aminocyclopyrachlor. By extension, this limitation applies to the risk characterization for longer-term exposures of reptiles and terrestrial-phase amphibians to aminocyclopyrachlor.

4.4.2.4. Terrestrial Invertebrates

4.4.2.4. Terrestrial Invertebrates

As discussed in Section 4.2.3, three sets of exposure scenarios are developed for terrestrial invertebrates following terrestrial foliar applications of aminocyclopyrachlor: direct spray and spray drift (Section 4.2.3.1), the consumption of contaminated vegetation or prey (Section 4.2.3.2), and exposure to contaminated soil (Section 4.2.3.3). As detailed in the following subsections, none of these exposure scenarios lead to HQs that reach a level of concern (HQ=1).

4.4.2.4.1. Contaminated Vegetation

HQs for herbivorous insects based on the consumption of contaminated vegetation are summarized in Worksheet G08b of Attachment 1. As discussed in Section 4.3.2.4.1, the toxicity value used for the HQs is an oral NOAEL in honeybees of 460 mg a.e./kg bw with a corresponding LOAEL of about 860 mg/kg bw based on incoordination. As discussed in Section 4.2.3.2, the exposure values used in the HQs are based on estimates of food consumption by insects and the residue rates from Fletcher et al. (1997) that were used in the corresponding scenarios for mammals and birds (Table 15).

The upper bounds of the HQs range from 0.02 (the consumption of fruit or large insects) to 0.3 (the consumption of short grass), and there is no basis for suggesting that herbivorous insects are likely to be at risk from the consumption of contaminated vegetation. This risk characterization is limited by the nature of toxicity data on terrestrial invertebrates—i.e., standard acute bioassays in honeybees. This limitation is common for many herbicides, particularly new herbicides for which the open literature is limited and only standard EPA-required studies are available.

4.4.2.4.2. Direct Spray and Spray Drift

Risks associated with direct spray or spray drift are summarized in Worksheet G09 of Attachment 1 (the EXCEL workbook on aminocyclopyrachlor), based on the direct spray of a honeybee. At the maximum application rate of 0.28 lb a.e./acre, the HQ for the direct spray with no foliar interception is 0.02, below the level of concern by a factor of 50. Considerations of foliar interception as well as reduced deposition on to the insect at various distances downwind from the application site lead to lower HQs ranging from $7x10^{-7}$ (below the level of concern by about 1.4 million) to 0.01 (below the level of concern by a factor of 100). Given these very low HQs, there is no basis for asserting that terrestrial insects would be at risk due to the deposition of aminocyclopyrachlor. Given the generally low direct toxicity of herbicides to insects, this risk characterization for aminocyclopyrachlor is common to many herbicides.

4.4.2.4.3. Contaminated Soil

HQs for contact with or the consumption of contaminated soil are not typically derived in either U.S. EPA/OPP or Forest Service risk assessments. For aminocyclopyrachlor, however, a soil

toxicity study in earthworms is available for the methyl ester of aminocyclopyrachlor, and the NOAEL for a 14-day duration is 203 mg a.e./kg dry weight soil (U.S. EPA/OPP 2010b, pp. 12). As discussed in Section 4.2.3.3, the GLEAMS modeling for the current risk assessment indicates that concentrations of aminocyclopyrachlor in the top 12 inches of soil would be about 0.057 (0.045 to 0.097) mg a.e./kg dw soil. Taking the soil concentrations as the numerator and the earthworm NOAEL as the denominator, the corresponding HQs for the earthworm would be 0.0003 (0.0002 to 0.0005). The upper bound HQ is below the level of concern (HQ=1) by a factor of 2000.

The major limitation of these HQs is that the toxicity value is based on a 14-day study using aminocyclopyrachlor methyl ester rather than the acid. As discussed by U.S. EPA/OPP (2010b, p. 12), however, the methyl ester of aminocyclopyrachlor degrades to aminocyclopyrachlor acid in soil so rapidly that a half-life could not be calculated. Thus, the use of a soil toxicity study on the methyl ester to characterize risks associated with exposure to aminocyclopyrachlor acid seems reasonable. With this minor limitation, the very low HQs for earthworms suggest that these organisms will not be at risk following applications of aminocyclopyrachlor.

4.4.2.5. Terrestrial Plants

4.4.2.5.1. Direct Spray and Spray Drift

The HQs for sensitive and tolerant species of terrestrial plants are summarized in Worksheet G05a (fine droplets) and Worksheet G05b (coarse droplets) of Attachment 1 (the EXCEL workbook for aminocyclopyrachlor). These worksheets are customized to reflect the use of three sets of values for drift: aerial application, ground high-boom broadcast application, and ground low-boom broadcast application. Backpack applications are considered only in Worksheet G05b (coarse droplets). As detailed in Section 4.2.4.2, all estimates of drift are based on AgDRIFT (Teske et al. 2002). As detailed in Section 4.3.2.5 and summarized in Table 24, all HQs are based on NOAELs from studies on vegetative vigor (foliar applications)—i.e., a NOAEL of 0.000044 lb a.e./acre for sensitive species and a NOAEL of 0.36 lb a.e./acre for tolerant species. The HQs for direct spray and drift based on all four application methods discussed above are summarized in Table 25, which is taken from Worksheets G05a and G05b of Attachment 1.

Aminocyclopyrachlor is an effective herbicide and is particularly toxic to dicots. If sensitive species of dicots are directly sprayed with aminocyclopyrachlor at the maximum application rate of 0.28 lb a.e./acre, the plants will die (HQ=6364). Some monocots, however, are highly tolerant of aminocyclopyrachlor. For a tolerant monocot, it is possible that no adverse effects would be evident even if the plant were sprayed directly (HQ=0.8).

Based on estimates of drift using AgDRIFT, risks to sensitive species of plants will remain above the level of concern at distances of up to 900 feet downwind from the application site. The risks will be greatest with aerial applications (HQ=79 for fine droplets and 20 for coarse droplets) and least with backpack applications (HQ=2). These HQs, however, should be viewed as only crude (Tier 1) approximations. As discussed in Section 4.2.4.2, AgDRIFT is a relatively sophisticated model, and numerous site- and application-specific parameters can be used to refine the estimates of potential risk summarized in Table 25. In the assessment of any planned application of aminocyclopyrachlor, it would be prudent to use AgDRIFT with site- and application-specific parameters to refine the HQs given in Table 25.

4.4.2.5.2. Soil Exposures by Runoff

Risks to nontarget vegetation associated with runoff and sediment losses to a field adjacent to the treated site are estimated in Worksheet G04 (Attachment 1). For tolerant species of plants, the HQs are 0.04 (0.0004 to 0.7). For sensitive species of plants, the HQs are 40 (0.4 to 70). As with the estimates of drift, the estimates of offsite transport in runoff and sediment should be regarded as only crude approximations. The upper bound HQs represent estimates of exposure levels which may not be applicable to many site-specific applications made in Forest Service programs.

For sensitive species of plants, the extreme range of the HQs reflects the nature of the generic (non-site-specific) Gleams-Driver modeling on which the exposure assessment is based. As detailed in Section 3.2.3.4.3 and summarized in Table 8, Gleams-Driver simulations are conducted for nine different locations encompassing extremes of temperature and rainfall. For each of these nine sites, three separate sets of simulations are conducted for soils that consist predominantly of clay, loam, and sand. As detailed in Section 4.2.4.3, with respect to runoff, the estimated exposures of nontarget plants adjacent to the application site are taken as a composite (i.e., a central estimate and a range) for all of the simulations combined. Consequently, the range of HQs for sensitive species does not apply to any specific location but is a composite of HQs that might be seen nationally.

Appendix 8, Table A8-1 should be consulted in any consideration of the consequences of potential risks to sensitive species of nontarget vegetation in a site-specific application. In areas with predominantly sandy soils, the runoff of aminocyclopyrachlor following foliar applications should be negligible and risks to nontarget plants should also be negligible. Conversely, risks will be greatest in areas with predominantly clay soils and moderate to high rates of rainfall. Risks may also be relatively high in cool locations with predominantly loam soils. Further generalizations do not appear to be warranted, because the modeling conducted for the current risk assessment is inherently conservative and a number of site-specific conditions could reduce, and perhaps substantially reduce, estimates of risks to nontarget vegetation.

4.4.2.5.3. Contaminated Irrigation Water

The HQs for nontarget plants associated with using aminocyclopyrachlor contaminated surface water for irrigation are summarized in Worksheet G06a of Attachment 1—HQs of 144 (0.7 to 2,018) for sensitive species and 0.02 (0.00009 to 0.2) for tolerant species of terrestrial plants.

As detailed in Section 4.2.4.4, the conditional registration for aminocyclopyrachlor requires all product labels for aminocyclopyrachlor to include language restricting the use of water contaminated with aminocyclopyrachlor for irrigation (U.S. EPA/OPP 2010k, p. 22). As also discussed in Section 4.2.4.4, consideration of risks associated with this scenario reflects a misuse rather than an expected event.

As with the HQs for runoff, the HQs associated with irrigation water for tolerant species of plants do not require elaboration. The key variables in this exposure scenario are the expected concentrations in ambient water (Section 3.2.3.4.6.1) and the amount of irrigation water applied, which is assumed to be 1 (0.25 to 2) inches. Taking into account reasonable variations that might be made in the exposure scenario, there is little basis for asserting that tolerant species of plants will be at risk.

The apparent risks to sensitive plants are substantial at the central estimates and upper bounds of exposures. As with the runoff estimates discussed in the previous section, expected concentrations of aminocyclopyrachlor in surface water are taken from the Gleams-Driver modeling and adjusted for the maximum application rate of 0.28 lb a.e./acre. As detailed in Section 3.2.3.4.3, the expected concentrations in surface water are a composite of all sites and soils considered in the Gleams-Driver modeling. Site- or region-specific Gleams-Driver simulations may be used to derive more relevant HQs. Given the label language discussed above, however, the use of aminocyclopyrachlor contaminated surface water for irrigation is not an anticipated event—i.e., the use of contaminated water for irrigation is contrary to the cautionary language on the formulation labels.

4.4.2.5.4. Wind Erosion

The HQs associated with the exposures of terrestrial plants due to wind erosion of contaminated soil are summarized in Worksheet G06b of Attachment 1. The HQs for sensitive species of plants are 0.4 (0.09 to 0.9), and the corresponding HQs for tolerant species of plants are 0.00005 (0.00001 to 0.0001). As detailed in Section 4.2.4.5, substantial uncertainties are associated with this exposure scenario, and the expected loss rates for soil are intended to represent forestry applications. Much higher loss rates could occur if aminocyclopyrachlor were to be applied inadvertently to fallow soil. Within this limitation, the HQs for both sensitive and tolerant species indicate that wind erosion is a minor concern relative to other routes of exposure.

4.4.2.5.5. Special Note on Conifers, Other Trees, and Shrubs

The current risk assessment is concerned with the reports of damage to conifers following applications of Imprelis®. While Imprelis® will not be used in Forest Service programs, the incidents of conifer damage following applications of Imprelis® to turf raise concerns that damage to conifers might occur in applications of other aminocyclopyrachlor formulations. As discussed in Section 4.1.2.5.3, the reason(s) for the atypical rates and severity of damage to conifers following the application of aminocyclopyrachlor by certified pesticide applicators is not clear. Damage to conifers could occur from direct treatment of turf slightly beyond the drip line of the conifer or from herbicide runoff into soil that lies within the extent of the root system of the conifers (Purdue Extension 2011; Reicher 2011). As detailed in Section 2.2.2.1, concern for runoff is expressed on the revised product labels for DuPont™ Method® 50SG (DuPont™ 2012a) and DuPont™ Method® 240SL (DuPont™ 2012b).

As noted in Section 4.4.2.5.2, the HQs for sensitive species of dicots associated with runoff are substantial—i.e., HQs are 40 (0.4 to 70). Based on the scant available information on the toxicity of aminocyclopyrachlor to conifers (Section 4.3.2.5.3), it appears that conifers are more tolerant than sensitive dicots and that the potential potency of aminocyclopyrachlor to conifers may be better approximated by tolerant species of dicots. Consequently, the NOAEC of 0.045 lb a.e./acre for tolerant species of dicots is used in the risk characterization for conifers.

Worksheet G04 of Attachment 1 is modified to include HQs based on the NOAEC of 0.045 lb a.e./acre for tolerant species of dicots as a surrogate for conifers. As indicated in this worksheet, the estimated HQs for conifers are 0.3 (0.003 to 6). As also discussed in Section 4.3.2.5.3, the estimated LOAELs for pine are 0.055 to 0.094 lb a.e./acre. The lower bound of the LOAELs corresponds to an HQ of about 1.2 [0.055 lb a.e./acre ÷ 0.045 lb a.e./acre ≈ 1.2]. Based on this

admittedly crude dose-response assessment, HQs of greater than 1 might be associated with adverse effects in pine.

As with the other HQs for runoff (Section 4.4.2.5.2), the exposure components of the HQs for conifers are based on a composite (i.e., a central estimate and a range) from all of the Gleams-Driver simulations detailed in Section 3.2.3.4.3.1. In practical terms, the estimated HQs for conifers suggest that damage due to runoff is plausible only under conditions that favor high rates of runoff (i.e., soils such as hard clay with very low porosity and sites in which relatively large treated areas would drain into smaller areas that contain conifers). At sites with low rainfall and well-drained soils in which runoff is not favored, damage to conifers would not be expected. Many species of pine will not grow well in clay soils (e.g., Kansas Forest Service 2011; Pollock et al. 1995; USDA 2011). The extent to which this may reduce the likelihood of damage to pine in naturally forested areas is not clear.

4.4.2.6. Terrestrial Microorganisms

The toxicity of aminocyclopyrachlor to terrestrial microorganisms is not addressed in the available literature (Section 4.3.2.6). Consequently, no risk characterization for this group of organisms is developed.

4.4.3. Aquatic Organisms

An overview of the HQs for aquatic organisms is given in Figure 7. Based on expected peak and longer-term concentrations, there is no basis for asserting that applications of aminocyclopyrachlor will damage either aquatic animals or plants. Based on the accidental spill scenario, the upper bound of the HQ for sensitive species of aquatic algae modestly exceeds the level of concern (HQ=2). Details of the risk characterization for aquatic organisms are discussed further in the following sections.

4.4.3.1. Fish

The risk characterization for fish is simple and unambiguous: there is no basis for asserting that adverse effects on fish are plausible for any exposure scenarios, including the accidental spill. The upper bound HQs for fish are 0.02 for the accidental spill, 0.002 for expected peak concentrations, and 0.009 for longer-term concentrations.

The major reservation with this benign risk characterization involves the limited toxicity data on fish—i.e., two acute bioassays on freshwater fish (rainbow trout and bluegills), one acute bioassay on saltwater fish (sheepshead minnow), and one early life stage bioassay on rainbow trout. Given that numerous fish species may be exposed to aminocyclopyrachlor, it is not possible to rule out the existence of more sensitive species. Nonetheless, trout, bluegills, and minnows are standard test species required by the U.S. EPA/OPP for pesticide registration and these studies consistently indicate that aminocyclopyrachlor is essentially non-toxic to fish (Section 4.1.3.1). The lack of toxicity data on numerous species of fish is a common concern for any newly registered pesticide.

4.4.3.2. Amphibians (Aquatic-Phase)

As with risks to terrestrial-phase amphibians (Section 4.4.2.3), risks to aquatic-phase amphibians cannot be characterized directly, due to the lack of toxicity data on amphibians. In the absence of toxicity data on aquatic-phase amphibians, U.S. EPA/OPP (2010b) uses data on fish to

characterize risks to aquatic phase amphibians. Based on the risk characterization for fish and all other groups of aquatic and terrestrial animals for which data are available, there is no basis for assuming that aquatic-phase amphibians are likely to be at risk from exposures to aminocyclopyrachlor. Nonetheless, a reasonably definitive risk characterization for aquatic-phase amphibians (i.e., one based on experimental data on amphibians) cannot be developed.

4.4.3.4. Aquatic Invertebrates

Qualitatively, the risk characterization for aquatic invertebrates is essentially identical to that for fish: there is no basis for asserting that adverse effects on aquatic invertebrates are plausible for any exposure scenarios, including the accidental spill. As with fish, data are available on relatively few species—i.e., acute and chronic studies on *Daphnia magna* and acute studies on two species of saltwater invertebrates (an oyster and a shrimp). Based on these limited data, *Daphnia magna* (a freshwater species) appear to be more sensitive than the saltwater species. The upper bound HQs for *Daphnia magna* are 0.7 for the accidental spill, 0.05 for expected peak concentrations, and 0.03 for longer-term concentrations.

While *Daphnia magna* appears to be the most sensitive species based on acute toxicity data, the current risk assessment takes the conservative position of assuming that *Daphnia magna* may be a tolerant species in terms of chronic effects (Section 4.3.3.3.2). This assumption has little impact on the risk characterization, in that a sensitive species, in terms of chronic effects, would need to be about 30 times more sensitive than *Daphnia magna* [1÷0.03≈33.33…] for the HQ to reach a level of concern.

4.4.3.4. Aquatic Plants

4.4.3.4.1. Algae

While aminocyclopyrachlor is an effective terrestrial herbicide, it does not appear to be remarkably toxic to algae or, as discussed below, aquatic macrophytes. The NOAEC for sensitive species of algae (1.11 mg a.e./L) is not substantially less than the acute NOAEC for sensitive aquatic invertebrates (3.7 mg a.e./L). As with fish and aquatic invertebrates, HQs for sensitive species of algae based on expected concentrations do not exceed the level of concern (HQ=1) for either acute exposures [HQ = 0.03 (0.0005 to 0.2)] or chronic exposures [HQ = 0.02 (0.0002 to 0.09)]. For the accidental spill scenario, the HQs modestly exceed the level of concern at the upper bound [HQ = 0.6 (0.03 to 2)] for sensitive species but not for tolerant species [HQ = 0.04 (0.0004 to 0.2)].

Qualitatively, the most reasonable interpretation of the HQs is that no substantial or even detectable effects on aquatic algae appear to be likely, except in the event of an accidental spill. For the spill scenario considered in the current risk assessment, the magnitude of adverse effects on algae would not be substantial.

4.4.3.4.2. Macrophytes

The risk characterization for aquatic macrophytes is limited in that the dose-response relationship is limited to a standard test species of duckweed, *Lemna gibba* (Section 4.3.3.4.2). The NOAEC for duckweed (3.75 mg a.e./L) is virtually identical to the acute NOAEC for sensitive aquatic invertebrates (3.75 mg a.e./L). Consequently, the HQs for macrophytes are virtually identical to those for aquatic invertebrates and indicate that no adverse effects would be anticipated based on

an accidental spill, expected peak concentrations, or longer-term concentrations of aminocyclopyrachlor in surface water.

As discussed in Section 4.1.3.4.2, the efficacy study by Israel (2011) suggests that aminocyclopyrachlor may be effective in the control of some aquatic weeds, including alligator weed, creeping water primrose, parrot feather, and water hyacinth, at surface application rates as low as 0.0009 lb a.e./acre. Worksheet B04c of Attachment 1 is customized to indicate functional surface application rates to a small pond that might be associated with drift following aerial, high boom ground spray, low boom ground spray, and backpack applications at the maximum application rate of 0.28 lb a.e./acre. As indicated in this worksheet, the functional application rates could exceed 0.0009 lb a.e./acre at distances of up to 900+ feet for aerial applications, 500 feet for high boom ground applications, 300 feet for low boom ground applications, and 50 feet for backpack applications. Consequently, the observations from Israel (2011) suggest that damage to some species of aquatic macrophytes cannot be ruled out if substantial drift of aminocyclopyrachlor to surface water were to occur.

5. REFERENCES

NOTE: The initial entry for each reference in braces {} simply specifies how the reference is cited in the text. The final entry for each reference in brackets [] indicates the source for identifying the reference.

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ClrRev	**Cleared reviews at** http://www.epa.gov/pesticides/foia/reviews.htm**. None available as of May 12, 2012.**
DuPont™01	**Initial Set of Data Evaluation Records (DERs) from DuPont™ [n=72].**
DuPont™02	**Full studies or study summaries from DuPont™ [n=10].**
DuPont™03	**Summary of subchronic study on cyclopropanecarboxylic acid.**
DuPont™04	**Supplemental information from DuPont™.**
E-Docket01	**Selected documents from** www.regulations.gov**, EPA-HQ-OPP-2009-0789 as of February 11, 2012.**
FOIA01	**Initial Freedom of Information Act request on February 11, 2012 (HQ-FOI-00749-12).**
PeerRev	**Papers added in response to peer review.**
ProgDesc	**From comments on initial program description.**
Sec	**Studies taken from secondary sources in open literature.**
SecEPA	**Studies taken from U.S.EPA reports or summaries.**
Set00	**Preliminary/supplemental scoping.**
Set01	**Toxline literature search.**
Std	**Standard references used in most Forest Service risk assessments**
Sundry	**Personal communications and related material.**

Note: Standard reference books that are copyrighted are not on the CD that accompanies this risk assessment.

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Table 1: Chemical and Physical Properties of Aminocyclopyrachlor

All values for acid unless otherwise noted.

Property	Value	Reference[1]
	Identifiers	
Common name:	Aminocyclopyrachlor	
IUPAC Name	6-amino-5-chloro-2-cyclopropylpyrimidine-4-carboxylic acid	Wood 2012
CAS Name	6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid	Wood 2012
Synonyms	DPX-MAT28 (acid)	Bell et al. 2011
	DPX-KJM44 (methyl ester)	Bell et al. 2011
CAS No.	**Form** / **CAS No.** Acid / 858956-08-8 K-Salt / 858956-35-1 Methyl ester / 858954-83-3	PubChem 2012
Molecular formula	$C_8H_8ClN_3O_2$ (acid)	Wood 2012
SMILES Notation	`C1(=NC(=C(Cl)C(=N1)N)C(O)=O)C2CC2` (acid)	http://iaspub.epa.gov/apex/pesticides/

Canonical SMILES Notation	Acid:
	`C1CC1C2=NC(=C(C(=N2)N)Cl)C(=O)O`
	K-Salt:
	`C1CC1C2=NC(=C(C(=N2)N)Cl)C(=O)[O-].[K+]`
	Methyl Ester:
	`COC(=O)C1=C(C(=NC(=N1)C2CC2)N)Cl`
		PubChem 2012

Structures	See Figure 1	
U.S. EPA/OPP PC Codes	**Form** / **PC Code** Acid / 288008 K-Salt / 288009 Methyl ester / 288010	U.S. EPA/OPP 2010d
	Physical Properties	
Henry's Law Constant	**Form** / **(atm m^3/mol** Acid / 3.47×10^{-12}	MRID 475598-20 (acid)
K_{ow}	Acid 0.076 [Log Kow of -1.12 at pH4] 0.0033 [Log Kow of - 2.48 at pH 7]	MRID 475598-15 from U.S. EPA/OPP 2010b, p. 10
K_{ow}	**Form** / **$\log_{10} K_{ow}$** / **Kow** Acid / 0.9 / 7.9 Methyl ester / 1.2 / 15.8 Based on anti-log10 of computation of octanol−water partition coefficients	PubChem 2012
K_{ow}	**Form** / **$\log_{10} K_{ow}$** / **Kow** Acid / 0.5502 / 3.5 Methyl ester / 1.2418 / 17.5	EPI-Suite 2011, Version 4.1
Molecular weights	**Form** / **MW (g/mole)** Acid / 213.62102 K-Salt / 251.71138 Methyl ester / 227.6476	PubChem 2012

Table 1: Chemical and Physical Properties of Aminocyclopyrachlor

All values for acid unless otherwise noted.

Property	Value	Reference[1]
a.i. to a.e. conversion	**Form (Abbrev)** / **Factor** Acid: 1 K-Salt: 0.849 Methyl ester: 0.938 a.i. to a.e. calculated as MW of acid ÷ MW of specified form rounded to three significant digits.	See entry for Molecular Weights
pKa Value	Acid: 4.65 at 20°C	MRID 475598-14
	Potassium salt: pKa = 4.63 ± 0.14 @ 20 ±1 °C within 2 to 7 minutes	MRID 478909-01
Vapor pressure	Acid: 3.7×10^{-8} torr at 25°C	MRID 475598-18
Water solubility	**Form** / **Condition** / **mg/L** Acid / pH 4 / 3130 / pH 7 / 4200 / pH 9 / 3870 / Milli-Q purified water / 2810	MRID 475598-16
Environmental Properties **See Table 2 for description of degradates including IN-LXT69 and IN-V0977.**		
Aerobic aquatic metabolism half-life	Sand-Water and Silt-loam-Water: > 100 days (duration of study) Extrapolated Half-times: Water/Sand System Water: ≈430 to 462 days. Sediment: No degradation detected. Water/Loam System Water: ≈150 to 165 days. Sediment: No degradation detected. Metabolites: IN-LXT69: 1 to 1.2% in sediment, 2.3 to 2.4% in total system. IN-LXT69 found in test standard – i.e., it appears to be a contaminant rather than transformation product. Carbon dioxide: Small amounts (0.7% for sand and 0.2% for silt-loam formed over 100 days study period.	McCorquodale 2008b , MRID 475602-16, Supplemental due to length of study observations versus apparent rates of degradation.
Anaerobic aquatic metabolism half-life	Acid Half-times (EPA calc., nonlinear): Total System: 6,932 days. Water: 578 days. Sediment: no degradation observed. Metabolites: IN-LXT69: 2.2% in water, 1.0% in sediment, and 2.2% in total system. Carbon dioxide: Small amounts (0.7% for sand and 0.2% for silt-loam formed over 100 days study period. **Working Note: A half-time of 1733 days (stable) is given in U.S. EPA/OPP (2010b). The values summarized above are from the DER.**	McCorquodale 2008a , MRID 475602-17, Acceptable

Table 1: Chemical and Physical Properties of Aminocyclopyrachlor

All values for acid unless otherwise noted.

<table>
<tr><th>Property</th><th>Value</th><th>Reference[1]</th></tr>
<tr><td>Aqueous photolysis half-life</td><td>Acid:
<table>
<tr><th colspan="2">Acid</th></tr>
<tr><th>Condition</th><th>Half-life, [Observed DT_{50}] (days)</th></tr>
<tr><td>Natural water, pH 6.2, at 20°C</td><td>1.2 [≈29]</td></tr>
<tr><td>Buffer, pH 4</td><td>7.8 [≈168]</td></tr>
</table>
Metabolites:
At pH 4, degrades to IN-LXT69, 16.1%, Degrades to IN-QFH57 in pH 4 buffer (13.8%) and natural water (maximum of 33.1%).
Degrades to IN-V0977 in pH 4 buffer (maximum of 12.4%) and natural water (maximum of 14.6%).
IN-YY905, maximum of 8% at pH 4 and 11.7% in natural water.</td><td>MRID 475602-11 from U.S. EPA/OPP 2010b, p. 24.</td></tr>
<tr><td>Aqueous photolysis half-life</td><td>Ester:
$t_{1/2}$ = 4.1 days; DT_{50} > 2 days
Metabolites:
IN-LXT69: Maximum 9.3% of applied at 2 days (study duration).
IN-Q3007: Maximum 7.8% of applied at 2 days (study duration).</td><td>MRID 475602-12 from U.S. EPA/OPP 2010b, p. 29.</td></tr>
<tr><td>Bioconcentration Factor (BCF)</td><td>
<table>
<tr><th>Form</th><th>BCF</th><th>Log_{10} BCF</th></tr>
<tr><td>Acid</td><td>3.162</td><td>0.5</td></tr>
<tr><td>Ester</td><td>3.064</td><td>0.486</td></tr>
</table></td><td>EPI-Suite 2011, Version 4.1</td></tr>
<tr><td rowspan="4">Field Dissipation half-life , acid</td><td>Canada Bare Soil: 0-5 cm, $t_{1/2}$: 126 days; DT_{50}: ≈31 days</td><td>MRID 475602-24</td></tr>
<tr><td>California Bare Soil: possible leaching, detected at 70 to 90 cm</td><td>MRID 475751-02</td></tr>
<tr><td>Georgia turf: 0-5 cm, $t_{1/2}$: 27 days; DT_{50}: ≈10.8 days
Possible leaching, detected at 15-30 cm.</td><td>MRID 475602-22</td></tr>
<tr><td>Canada turf: 0-5 cm, $t_{1/2}$: 38 days; DT_{50}: ≈21 days
Possible leaching, detected at 50-70 cm.</td><td>MRID 475602-23</td></tr>
<tr><td rowspan="4">Field Dissipation half-life , ester</td><td>Canada Bare Soil: 0-5 cm, $t_{1/2}$: 7.7 days; DT_{50}: ≈4.6 days</td><td>MRID 475602-24</td></tr>
<tr><td>California Bare Soil: 0-5 cm, $t_{1/2}$: 3.8 days; DT_{50}: ≈1.2 days</td><td>MRID 475751-02</td></tr>
<tr><td>Georgia turf: 0-5 cm, $t_{1/2}$: 5.5 days; DT_{50}: ≈1 day</td><td>MRID 475602-22</td></tr>
<tr><td>Canada Turf: 0-5 cm, $t_{1/2}$: 48 days; DT_{50}: ≈1 day</td><td>MRID 475602-23</td></tr>
<tr><td>Hydrolysis half-life</td><td>Acid:
Stable at pH 4, 7, and 9.</td><td>Manjunatha 2008a, MRID 475602-10, Supplemental</td></tr>
</table>

Table 1: Chemical and Physical Properties of Aminocyclopyrachlor

All values for acid unless otherwise noted.

<table>
<tr><th>Property</th><th>Value</th><th>Reference[1]</th></tr>
<tr><td>Hydrolysis half-life</td><td>Methyl Ester
<table>
<tr><th>pH</th><th>Temperature</th><th>Half-life (days)</th><th>Maximum % acid</th></tr>
<tr><td>4</td><td>40°C</td><td>26.9</td><td>48.6</td></tr>
<tr><td>4</td><td>50°C</td><td>15.8</td><td>20.1</td></tr>
<tr><td>4</td><td>60°C</td><td>7.9</td><td>82.8</td></tr>
<tr><td>7</td><td>20°C</td><td>51.7</td><td>31.7</td></tr>
<tr><td>7</td><td>30°C</td><td>7.9</td><td>89.4</td></tr>
<tr><td>7</td><td>50°C</td><td>0.6</td><td>97.5</td></tr>
<tr><td>9</td><td>10°C</td><td>1.0</td><td>20.1</td></tr>
<tr><td>9</td><td>20°C</td><td>0.3</td><td>60.3</td></tr>
<tr><td>9</td><td>50°C</td><td><1 hour</td><td>99.9</td></tr>
</table>
The methyl ester hydrolyzed to the acid.</td><td>Manjunatha 2008c , MRID 478357-01, supplemental</td></tr>
<tr><td>Kd/Koc [2]</td><td>Acid
<table>
<tr><th>Soil Type</th><th>%Clay</th><th>% OC</th><th>K_d</th><th>K_{oc}</th></tr>
<tr><td>Loam</td><td>15</td><td>0.5</td><td>0.03</td><td>5.2</td></tr>
<tr><td>Sandy Loam</td><td>13</td><td>1.2</td><td>0.27</td><td>22</td></tr>
<tr><td>Sandy Loam</td><td>7</td><td>1.3</td><td>0.03</td><td>2.0</td></tr>
<tr><td>Silty Clay</td><td>45</td><td>1.6</td><td>0.05</td><td>3.2</td></tr>
<tr><td>Clay Loam</td><td>31</td><td>3.8</td><td>0.98</td><td>26</td></tr>
<tr><td></td><td></td><td>Average:</td><td>0.272</td><td>11.68</td></tr>
</table>
Freundlich adsorption Kd and Koc values were close to the reported Kd and Koc values – i.e., the simple Koc model appears to apply reasonably well.</td><td>Manjunatha 2008b, MRID 475602-19, Supplemental</td></tr>
<tr><td>Kd/Koc</td><td>Acid: Brazilian soils
<table>
<tr><th>Soil Code</th><th>Soil Texture</th><th>% OC</th><th>K_d</th><th>K_{oc}</th></tr>
<tr><td>BRA1</td><td>Clay</td><td>1.60</td><td>0.62-0.67</td><td>39-42</td></tr>
<tr><td>BRA10</td><td>Clay</td><td>1.79</td><td>0.48-0.51</td><td>27-29</td></tr>
<tr><td>BRA13</td><td>Clay</td><td>1.63</td><td>1.07-1.09</td><td>15-16</td></tr>
<tr><td>BRA5</td><td>Clay</td><td>1.83</td><td>0.5-0.53</td><td>27-29</td></tr>
<tr><td>BRA7</td><td>Clay</td><td>2.05</td><td>1.09-1.17</td><td>53-57</td></tr>
<tr><td>BRA8</td><td>Clay</td><td>2.17</td><td>0.85</td><td>39</td></tr>
<tr><td>BRA14</td><td>Loamy-sand</td><td>0.64</td><td>0.12</td><td>19-22</td></tr>
<tr><td>BRA3</td><td>Loamy-sand</td><td>0.5</td><td>0.05-0.07</td><td>10-14</td></tr>
<tr><td>BRA4</td><td>Loamy-sand</td><td>1.02</td><td>0.34-0.39</td><td>33-38</td></tr>
<tr><td>BRA11</td><td>Sandy-loam</td><td>1.06</td><td>0.50-0.51</td><td>47-48</td></tr>
<tr><td>BRA6</td><td>Sandy-loam</td><td>0.90</td><td>0.28-0.29</td><td>32</td></tr>
<tr><td>BRA12</td><td>Sand</td><td>0.61</td><td>0.09</td><td>15-16</td></tr>
<tr><td>BRA2</td><td>Sand</td><td>0.68</td><td>0.23-0.26</td><td>32-39</td></tr>
<tr><td>BRA9</td><td>Sand</td><td>0.65</td><td>0.06-0.07</td><td>9-11</td></tr>
</table>
Freundlich 1/n values ranged from 0.9 to 1.0 – i.e., the simple Koc model appears to apply reasonably well. Ranges reflect central estimates at concentrations of 0.047 and 1.41 µmol/L. See Table 3 of Oliveira et al. 2011 for details.</td><td>Oliveira et al. 2011</td></tr>
<tr><td>Sediment/water half-life</td><td>See Aerobic aquatic metabolism half-life</td><td></td></tr>
</table>

Table 1: Chemical and Physical Properties of Aminocyclopyrachlor

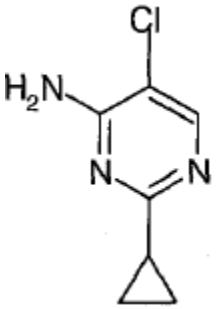
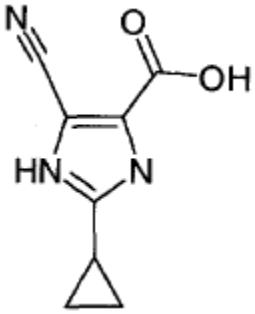
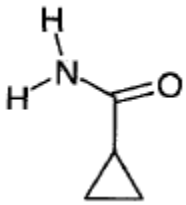
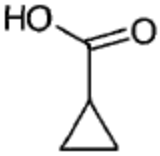
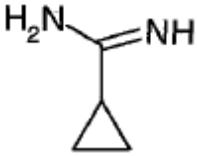
All values for acid unless otherwise noted.

<table>
<tr><th>Property</th><th>Value</th><th>Reference[1]</th></tr>
<tr><td rowspan="3">Soil half-life, aerobic</td><td>Ester on Sassafras
Half-life = 315 days
Metabolites:
IN-LXT69: maximum of 2.9% of applied amount after 3 days (260 days study duration).
Carbon dioxide: maximum of 23.1% of applied amount at Day 360 (study duration).</td><td>MRID 475602-14</td></tr>
<tr><td>Acid:
<table>
<tr><th>Soil Type</th><th>$t_{1/2}$ (days)</th><th>DT_{50} (days)</th></tr>
<tr><td>Nambsheim</td><td>433</td><td>>120</td></tr>
<tr><td>Tama</td><td>114</td><td>≈100</td></tr>
<tr><td>Drummer</td><td>126</td><td>≈100</td></tr>
<tr><td>Average:</td><td>224</td><td></td></tr>
</table>
Metabolites:
IN-LXT69: Maximum of 4 to 6.%, all on Day 0 of 120 day study.</td><td>MRID 475602-21</td></tr>
<tr><td>Methyl Ester:
Too rapid to estimate at half-life. Converted rapidly to acid.</td><td>MRID 475602-14</td></tr>
<tr><td>Soil half-life, anaerobic</td><td>6932 days (stable)
DT_{50} > 365 days</td><td>MRID 475602-15</td></tr>
<tr><td>Soil photolysis half-life</td><td>129 days at 20°C
Metabolites:
IN-LXT69, 4.9% of applied amount after 7 days.</td><td>MRID 475602-13</td></tr>
<tr><td>Vegetation half-life</td><td>Acid
Georgia turf, Grass: 22.4 days; DT_{50}: ≈4.3 days
Ester
Georgia turf, Grass: 1.3 days; DT_{50}: ≈1.2 days</td><td>MRID 475602-22</td></tr>
<tr><td></td><td>Acid
Canada turf, Grass:
22.2 days; DT_{50}: ≈5.4 days
7.2 days; DT_{50}: ≈3.3 days
Ester
Canada turf, Grass:
5.6 days; DT_{50}: ≈1 day</td><td>MRID 475602-23</td></tr>
</table>

[1] Data referenced to MRID numbers taken from U.S. EPA/OPP 2010d unless otherwise specified.

[2] Manjunatha (2008d, MRID 475602-20), a soil sorption study, is classified by U.S. EPA/OPP as unacceptable. Given the availability of other acceptable studies (Manjunatha 2008b), Manjunatha (2008d) is not summarized in this table.

Table 2: Major Degradates of Aminocyclopyrachlor

Code	Structure	Identifiers
IN-LXT69		IUPAC Name: 5-Chloro-2-cyclopropyl-pyrimidin-4-ylamine Smile Notation: `c1(C2CC2)ncc(CL)c(N)n1`
IN-QFH57		IUPAC Name: 4-Cyano-2-cyclopropyl-1H-imidazole-5-carboxylic acid Smile Notation: `N#CC(N=C1C2CC2)=C(N1)C(O)=O`
IN-Q3007		IUPAC Name: Cyclopropanecarboxamide CAS No.: 6228-73-5 Smile Notation: `O=C(N)C1CC1`
IN-V0977		IUPAC Name: Cyclopropanecarboxylic acid CAS No.: 1759-53-1 Smile Notation: `C1(C(O)=O)CC1`
IN-YY905		IUPAC Name: Cyclopropanecarboximid-amide CAS No.: 54070-74-5 or 57297-29-7 [www.chemspider.com] Smile Notation: `[N@H]=C(N)C1CC1`

Source: Modified from U.S. EPA/OPP 2010d, Table 3.5, pp. 31-32 and Appendix E.

Table 3: List of formulations for aminocyclopyrachlor

EPA Product Name[1,2]	EPA Reg. No.	Common Product Name	% a.i.
Parent Acid (CAS No. 858956-08-8)			
DPX-MAT28 Technical Herbicide	352-782	DuPont™ Aptexor® Technical	89.3
DPX-MAT28 10% Manufacturing Concentrate	352-796	DuPont™ Aptexor® Manufacturing Concentrate	10.0
DPX-MAT28 50SG Herbicide	**352-787**	**DuPont™ Method® 50SG**	**50.0**
DPX-MAT28 50SG Turf Herbicide	352-794	Same as EPA Product name	50.0
Potassium Salt (CAS No. 858956-35-1)			
DPX-MAT28 240SL Herbicide	**352-786**	**DuPont™ Method® 240SL**	**25.0**
DPX-MAT28 240SL Turf Herbicide [3]	352-793[3]	DuPont™ Imprelis® [3]	25.0
Methyl Ester (CAS No. 858954-83-3)			
DPX-KJM44 Technical Herbicide	352-783	N/A (technical a.i. only)	95.6
DPX-KJM44 80 MUP Herbicide	352-784	Same as EPA Product name	80.0
DPX-KJM44 10% Manufacturing Concentrate	352-795	Same as EPA Product name	10.0
DPX-KJM44 80XP Herbicide	**352-785**	**Same as EPA Product name**	**80.0**
DPX-KJM44 80XP Turf Herbicide	352-792	Same as EPA Product name	80.0

[1] Formulations in bold font are labeled for the control of leafy spurge. See Table 4 for additional details.
[2] Excludes turf and lawn formulations that contain fertilizer.
[3] A stop sale, use, and distribution order issued by the U.S. EPA on August 11, 2011(U.S. EPA/OPP 2011a)

Source: Modified from U.S. EPA/OPP (2010k), pp. 5-6

See Section 2.2 for discussion

Table 4: Aminocyclopyrachlor Formulations Labeled for Leafy Spurge and Other Weeds

Information	Formulation		
	DuPont™ Method® 50SG	**DuPont™ Method® 240SL**	**DPX-KJM44 80XP**
Active Ingredient	Parent Acid	K-Salt	Methyl Ester
EPA Reg. No.	352-787	352-786	352-785
% Active ingredient	50%	25 %	80%
% Acid equivalents	50%	21.225 %	75.04%
Physical state	Soluble granules	Soluble liquid	Dispersible granules
lb a.e./gallons	N/A	2 lb a.e./gallon	N/A
Maximum Annual Application Rate	9 oz formulation/acre ≈0.28 lb a.e./acre	18 fl oz formulation/acre ≈0.28 lb a.e./acre	6 oz formulation/acre ≈0.28 lb a.e./acre
Application Rate for Leafy Spurge	4 to 9 oz formulation/acre ≈ 0.125-0.28 lb a.e./acre	8 to 18 fl oz formulation/acre ≈ 0.125-0.28 lb a.e./acre	2.5 to 6 oz formulation/acre 0.115 to 0.28 lb a.e./acre
Application timing	Preemergence or early postemergence		
Recommended Adjuvants	Methylated seed oils and vegetable oils at 1% v/v (1 gallon per 100 gallons of spray solution) Non-ionic surfactants (at least 70%) at a minimum of 0.25%. Invert emulsions (water-in-oil)		
Application methods	Aerial, fixed-wing or helicopter. Volume Median Diameter (VMD)>350µ. No more than 10 feet above ground or canopy. Wind speed ≤ 10 mph. Application volumes of 15 to 25 gallons/acre. Ground Broadcast, VMD>350µ. No more than 4 feet above ground. Wind speed ≤ 10 mph. Application volume of at least 10 to 20 gallons/acre (ULV), 20 to 50 gallons/acre (low volume), or 100 to 400 gallons/acre (high volume). Spot Application, calibrated boom sprayer, a boom-less sprayer, or a handheld or backpack sprayer. Application volumes of 13 to 130 gallons per acre. Cut Stump or Cut Stubble. Application volume of at least 20 gallons/acre. Penetrating agent at 5% v/v. Basal Bark (Method® 240 SL Only). 10 to 20 gallons of Method® 240 SL in enough basal oil to make 100 gallons of spray mixture – i.e., 10 to 20% mixture.		
Target Vegetation	broadleaf weeds, woody plants, invasive and/or noxious weeds		
Application sites	non-agricultural areas (e.g., utility rights-of-way, wildlife openings, and wildlife habitats) including intermittently flooded areas up to the water's edge.		
Label Source	EPA Draft Label dated 8/30/2010	EPA Draft Label dated 8/30/2010	EPA Draft Label dated 8/30/2010
Inerts	None specified on MSDS.	None specified on MSDS.	No information available.
MSDS Source	DuPont™ MSDS Method® 50 SG, Version 2.1, MSDS No. 130000044335	DuPont™ Method® 240SL Herbicide, Version 2.4, MSDS No. 130000044135	MSDS not located

Table 5: Formulations of Aminocyclopyrachlor with Other Herbicides			
Formulation	**Ingredients**	**%**	**Comment**
Perspective®	Aminocyclopyrachlor acid CAS No. 858956-08-8	39.5	Dispersible granule mixed with water. Ground application only (except helicopter applications on rights-of-way). Labeled for broadleaf weeds including many terrestrial and riparian invasive and noxious weeds.
	Chlorsulfuron CAS No. 64902-72-3	15.8	
	inerts	44.7	
Streamline®	Aminocyclopyrachlor acid CAS No. 858956-08-8	39.5	Dispersible granule mixed with water. Aerial or grounds applications. Labeled for broadleaf weeds including many terrestrial and riparian invasive and noxious weeds.
	Metsulfuron methyl CAS No. 74223-64-6	12.6	
	inerts	47.9	
Viewpoint®	Aminocyclopyrachlor acid CAS No. 858956-08-8	22.8	Dispersible granule mixed with water. Aerial (helicopter only) or ground applications. Labeled for broadleaf weeds including many terrestrial and riparian invasive and noxious weeds.
	Imazapyr CAS No. 81334-34-1	31.6	
	Metsulfuron methyl CAS No. 74223-64-6	7.3	
	inerts	38.3	

Table 6: Worker Exposure Rates for Standard Terrestrial Application Methods

Worker Group	Central	Lower	Upper
Absorbed Dose Rates	**mg/kg bw/day per lb applied**		
Directed foliar	0.003	0.0003	0.01
Broadcast foliar	0.0002	0.00001	0.0009
Aerial	0.00003	0.000001	0.0001
Treatment Rate	**Acres Treated per Day**		
Directed foliar	4.4	1.5	8.0
Broadcast foliar	112	66	168
Aerial	490	240	800

See Section 3.2.2.1 for discussion.

Table 7: Precipitation, Temperature and Classifications for Standard Test Sites

Location	Precipitation	Temperature	Average Annual Rainfall (inches)	Average Annual Temperature (◦F)
HI, Hilo	Wet	Warm	126.06	73.68
WA, Quillayute [1]	Wet	Temperate	95.01	49.14
NH, Mt. Washington	Wet	Cool	98.49	27.12
FL, Key West	Average	Warm	37.68	77.81
IL, Springfield	Average	Temperate	34.09	52.79
MI, Sault Ste. Marie	Average	Cool	32.94	40.07
AR, Yuma Test Station	Dry	Warm	3.83	73.58
CA, Bishop	Dry	Temperate	5.34	56.02
AK, Barrow	Dry	Cool	4.49	11.81

[1] Based on composite estimation in WEPP using a latitude of 47.94 N and a longitude of -124.54 W. See SERA (2006c) for details.

Table 8: Field and Waterbody Parameters Used in Gleams-Driver Modeling

Field Characteristics	Description	Pond Characteristics	Description
Type of site and surface (FOREST)	Field (0)	Surface area	1 acre
Treated and total field areas	10 acres	Drainage area:	10 acres
Field width	660 feet	Initial Depth	2 meters
Slope	0.1 (loam and clay) 0.05 (sand)	Minimum Depth	1 meter
Depth of root zone	36 inches	Maximum Depth	3 meters
Cover factor	0.15	Relative Sediment Depth	0.02
Type of clay	Mixed		
Surface cover	No surface depressions		

Stream Characteristics	Value
Width	2 meters
Flow Velocity	6900 meters/day
Initial Flow Rate	710,000 liters/day

GLEAMS Crop Cover Parameters[3]	Description	Value
ICROP	Weeds	78
CRPHTX	Maximum height in feet.	3
BEGGRO	Julian day for starting growth	32
ENDGRO	Julian day for ending growth	334

Application, Field, and Soil Specific Factors [1]	Code[3]	Clay	Loam	Sand
Percent clay (w/w/):	CLAY	50%	20%	5%
Percent silt (w/w/):	SILT	30%	35%	5%
Percent sand (w/w/):	N/A	20%	45%	90%
Percent Organic Matter:	OM	3.7%	2.9%	1.2%
Bulk density of soil (g/cc):	BD	1.4	1.6	1.6
Soil porosity (cc/cc):	POR	0.47	0.4	0.4
Soil erodibility factor (tons/acre):	KSOIL	0.24	0.3	0.02
SCS Runoff Curve Number [2]:	CN2	83	70	59
Evaporation constant (mm/d):	CONA	3.5	4.5	3.3
Saturated conductivity below root zone (in/hr):	RC	0.087	0.212	0.387
Saturated conductivity in root zone (in/hr)	SATK	0.087	0.212	0.387
Wilting point (cm/cm):	BR15	0.28	0.11	0.03
Field capacity (cm/cm):	FC	0.39	0.26	0.16

[1] The qualitative descriptors are those used in the QuickRun window of Gleams-Driver. Detailed input values for the soil types are given in the sub-table below which is adapted from SERA (2007b, Tables 2 and 3). All fields are run for about 6 months before the pesticide is applied in early summer.

[2] From Knisel and Davis (Table H-4), *Clay*: Group D, Dirt, upper bound; *Loam*: Group C, woods, fair condition, central estimate; *Sand*: Group A, meadow, good condition, central estimate.

[3]Codes used in documentation for GLEAMS (Knisel and Davis 2000) and Gleams-Driver (SERA 2007a)

Table 9: Aminocyclopyrachlor GLEAMS inputs

Parameter	Value	Note/Reference
Half-lives (days) Aquatic Sediment	6,932	Based on total system half-life from McCorquodale (2008a). This is not substantially different from the U.S. EPA/OPP (2010g, Table 2) assumption that aminocyclopyrachlor is stable in aquatic sediment.
Foliar	93	No vegetation half-lives have been encountered. Use relationship from Juraske et al. (2006), divide the soil half-life by 4 and round to the nearest day – i.e., 373÷4=93.25.
Soil	373 (114 to 433)	Central estimate Identical to value used by U.S. EPA/OPP (2010g, Table 2) from MRID 475602-14. Range is based on soil half-lives of 114, 126, and 433 days are reported in MRID 475602-21.
Water	150	Based on an experimental photolysis half-life of 1.2 days from natural water, pH 6.2 from MRID 475602-11. This differs substantially from U.S. EPA/OPP (2010g). See Section 3.2.3.4.3.1.2 for discussion.
Soil $K_{o/c}$, mL/g	12 (2 to 25)	Average value and range (rounded to nearest integer) of K_{oc} values from Manjunatha 2008b. The central estimate is identical to that used by U.S. EPA/OPP (2010g, Table 2).
Sediment K_d, mL/g	0.27 (0.03 to 0.98)	Average value and range (rounded to two significant digits) of K_d values from Manjunatha (2008b).
Water Solubility, mg/L	2810	The U.S. EPA/OPP (2010g) uses a value of 2810 mg/L at 20°C for highly purified water from MRID 475598-16.
Foliar wash-off fraction	0.9	No foliar washoff fraction is available. Based on analogy to other pesticides with similar water solubility. See Section 3.2.3.4.3.1.2 for discussion.
Coefficient of transformation (COFTRN)	0.40	Molecular weight of cyclopropanecarboxylic acid (86.09) divided by molecular weight of aminocyclopyrachlor (213.62) rounded to 2 significant places.
Plant Uptake	1	Herbicide is absorbed by plants.
Fraction applied to foliage	0.5	Default value used for applications of liquid solutions of herbicides.
Depth of incorporation	1 cm	Standard incorporation depth used for surface applications

See Section 3.2.3.4.3 for discussion.

Table 10: Physical and chemical properties of aminocyclopyrachlor degradates

Property	Degradate				
	IN-LXT69	**IN-Q3007**	**IN-QFH57**	**IN-V0977[2]**	**IN-YY905**
CAS Number [6]	N/A	N/A	N/A	**1759-53-1**	N/A
Molecular weight	169.61	85.11	177.16	**86.09**	84.12
Water solubility (mg/L)	8,453	262,300	6,030	**149,540**	79,050
Hydrolysis	N/A	N/A	N/A	**N/A**	N/A
Biodegradation [4]	Very slow	3.9 days 3.0 weeks	Rapid	**Rapid**	3.73 day 3.01 weeks
Log Kow	1.0113	-0.37	0.83	**0.63***	-1.72
Kow	10.26	0.42	6.76	**4.27***	0.019
Koc (L/kg)	169.3	5.208	25.43[3]	**3.193**	0.89 to 70.64
Bioconcentration factor	2.2	3.162	3.162	**1.259**	3.162
Volatilization Half-life					
River	132.8 yr	7.1 yr	142,000 yr	**217.7 days**	95.66 days
Lake	1449 yr	77.4 yr	1,549,000 yr	**2379 days**	1047 days
Soil half-life (days)[5]	75	30	75	**17**	30
Sediment half-life (days) [5]	340	140	340	**78**	140
Water half-life (days) [5]	38	15	38	**8.7**	15

[1] Values based on experimental measurements indicated with an asterisk (*). All other values are based on QSAR estimates using EPI Suite (2011).
[2] Cyclopropanecarboxylic acid, a metabolite of concern. See Section 3.1.15.1 for toxicity.
[3] Koc may be sensitive to pH.
[4] Where available, biodegradation rates given as a range based on expert surveys.
[5] Values adjusted from hours in EPI-Suite output to days and rounded to 2 significant digits.
[6] CAS numbers from ChemIDplus (http://chem.sis.nlm.nih.gov/chemidplus/).

See Section 3.2.3.4.3.1.3 for discussion.
See Table 2 for illustration of structures.

Table 11: Cyclopropanecarboxylic acid (IN-V0977) GLEAMS inputs

Parameter	Value	Note/Reference
Half-lives (days)		
Aquatic Sediment	78	Based on QSAR using EPI Suite (2011). See Table 6..
Foliar	4	No vegetation half-lives have been encountered. Use relationship from Juraske et al. (2006), divide the soil half-life by 4 and round to the nearest day – i.e., 17÷4=4.25.
Soil	17	Based on QSAR using EPI Suite (2011). See Table 6.
Water	8.7	Based on QSAR using EPI Suite (2011). See Table 6.
Soil $K_{o/c}$, mL/g	2.7 to 3.2	Lower bound based on U.S. EPA/OPP (2010g) using KOCWIN Version 2.0 (2.735) rounded to 2 significant places. Upper bound based on EPI Suite (2011), 3.193 (Table 6) also rounded to 2 significant places.
Sediment K_d, mL/g	0.014 to 0.15	Based on Koc (above) multiplied by proportions of organic carbon in soils (0.005 to 0.038) from Manjunatha (2008b) – i.e., identical to the approach used for aminocyclopyrachlor – rounded to 2 significant places.
Water Solubility, mg/L	149,540	Based on QSAR using EPI Suite (2011). See Table 6. Identical to value used by U.S. EPA/OPP (2010g).
Foliar wash-off fraction	0.95	Approximation for highly water soluble compound.
Coefficient of transformation (COFTRN)	1	This value has no impact on the modeling because metabolites of cyclopropanecarboxylic acid are not modeled.
Fraction applied to foliage	0.5	Default value used for applications of liquid solutions of herbicides.
Depth of incorporation	1 cm	Section 2.3.1.
Irrigation after application	None	Section 2.3.1.

Note: U.S. EPA/OPP (2010g) did not explicitly model cyclopropanecarboxylic acid. Rather, they assumed that the maximum concentration of cyclopropanecarboxylic acid would be a molar ratio of 0.146 based on MRID 475602-11. The concentration of cyclopropanecarboxylic acid in mg/L were adjusted for the ratio of the molecular weight of the metabolite and parent (COFTRN above). Thus, the concentrations were estimated as:

Aminocyclopyrachlor (mg/L) x 0.146 x 0.4

See Section 3.2.3.4.3 for discussion.

Table 12: Aminocyclopyrachlor – Modeled Concentrations in Surface Water

Scenario	Concentrations (ppb a.e. or µg a.e./L per lb/acre application rate)	
	Peak	**Long-Term Average**
MODELING FOR THIS RISK ASSESSMENT (1 lb a.e./acre)		
Direct Spray and Spray Drift		
Pond, Direct Spray (Section 3.2.3.4.2) [a]	112	N/A
Pond, drift at 25 feet (Section 3.2.3.4.2) [a]	0.9 to 25	N/A
Stream, Direct Spray (Section 3.2.3.4.2) [a]	91	N/A
Stream, drift at 25 feet (Section 3.2.3.4.2) [a]	0.7 to 20	N/A
Gleams-Driver		
Broadcast Foliar, Single Application (see Appendix 8 for details)		
Pond, Section 3.2.3.4.4	137 (2.04 to 720)	62.9 (0.9 to 350) (annual)
Stream, Section 3.2.3.4.4	81.7 (2.42 to 700)	2.3 (0.0155 to 10.6) (annual)
Other Modeling (1 lb a.e./acre)		
U.S. EPA/OPP 2010g (Drinking water assessment)		
FIRST (Reservoir model) [b]	90.3	56.1 (annual)
SCIGROW (Ground water) [c]	124	124 (annual)
GENEEC (Farm pond) [d]	59.4	58.2 (90-day)
Monitoring		
No monitoring studies on aminocyclopyrachlor in water have been encountered. See Section 3.2.3.4.5.		

[a] Section 3.2.3.4.2 discusses expected concentrations in terms of the nominal application rate of 1 lb a.e./acre. The values for direct spray and drift are taken from Worksheet B04c (direct spray and drift as 25 feet for a pond) and Worksheet B04d (direct spray and drift as 25 feet for a stream). The ranges for drift reflect the different application methods – lowest for backpack and highest for aerial.

[b] FIRST modeling from U.S. EPA/OPP 2010g, Table 1, p. 3, non-crop aerial application. Modeled at an application rate of 0.284 lb/acre. Peak concentration of 25.576 µg/L and annual average concentration of 15.943 µg/L. Values in table normalized for an application rate of 1 lb/acre. Results for non-crop ground applications are virtually identical.

[c] SCIGROW modeling from U.S. EPA/OPP 2010g, Table 1, p. 3. Non-crop aerial application. Modeled at an application rate of 0.284 lb/acre. Peak and annual average concentration of 35.2 µg/L. Values in table normalized for an application rate of 1 lb/acre.

[d] GENEEC modeling from U.S. EPA/OPP 2010b, p. 67, non-crop aerial application. Modeled at an application rate of 0.284 lb/acre. Peak concentration of 16.86 µg/L and 90-day average maximum concentration of 16.53 µg/L. Results for non-crop ground applications are virtually identical.

Note: The maximum application rate for aminocyclopyrachlor is 0.28 lb a.e./acre. This table, however, summarizes estimated concentrations in surface water for a normalized application rate of 1 lb a.e./acre.

See Section 3.2.3.4.3.2.1 for discussion.

Table 13: Cyclopropanecarboxylic acid – Modeled Concentrations in Surface Water

Scenario	Concentrations (ppb a.e. or µg a.e./L)	
	Peak	Long-Term Average
MODELING FOR THIS RISK ASSESSMENT (1 aminocyclopyrachlor lb a.e./acre)		
Direct Spray and Spray Drift		
Pond, Direct Spray (Section 3.2.3.4.2) [a]	2.1	N/A
Pond, drift at 25 feet (Section 3.2.3.4.2) [a]	0.46	N/A
Stream, Direct Spray (Section 3.2.3.4.2) [a]	1.7	N/A
Stream, drift at 25 feet (Section 3.2.3.4.2) [a]	0.37	N/A
Gleams-Driver		
Broadcast Foliar, Single Application (see Appendix 9 for details)		
Pond, Section 3.2.3.4.4	0.57 (0.0017 to 4.9)	0.085 (0.000225 to 0.7) (annual)
Stream, Section 3.2.3.4.4	0.76 (0.00265 to 6.7)	0.0248 (0.000065 to 0.2) (annual)
Other Modeling		
U.S. EPA 2005c (RED)		
FIRST (Reservoir model) [b]	89.1	63.8
Monitoring		
No water monitoring studies on cyclopropanecarboxylic acid associated with applications of aminocyclopyrachlor have been encountered. See Section 3.2.3.4.5.		

[a] Section 3.2.3.4.2 discusses expected concentrations in terms of the nominal application rate of 1 lb a.e./acre. The values for direct spray and drift are taken from Worksheet B04c (direct spray and drift as 25 feet for a pond) and Worksheet B04d (direct spray and drift as 25 feet for a stream). The ranges for drift reflect the different application methods – lowest for backpack and highest for aerial.

[b] FIRST modeling from U.S. EPA/OPP 2010g, Table 1, p. 3, non-crop aerial application. Modeled at an "application rate" of 0.017 lb/acre. Peak concentration of 1.515 µg/L and annual average concentration of 1.084 µg/L. Values in table normalized for an application rate of 1 lb/acre. Results for non-crop ground applications are virtually identical.

See Section 3.2.3.4.3.2.2 for discussion.

Table 14: Concentrations in Surface Water Used in This Risk Assessment

	Water contamination rate in mg/L per lb/acre applied [a]	
Aminocyclopyrachlor	**Peak**	**Longer-term**
Central	0.1	0.06
Lower	0.002	0.0009
Upper	0.7	0.35
Cyclopropanecarboxylic acid	**Peak**	**Longer-term**
Central	0.0007	0.00005
Lower	0.000002	0.0000002
Upper	0.007	0.0007

[a] Water contamination rates – concentrations in units of mg a.i./L expected at an application rate of 1 lb aminocyclopyrachlor/acre. Units of mg a.i./L are used in the EXCEL workbook that accompanies this risk assessment.

See Section 3.2.3.4.6 for discussion.

Table 15: Estimated residues in food items per lb a.e. applied

Food Item	Concentration in Food Item (ppm per lb a.e./acre)		
	Central [a]	Lower [b]	Upper [a]
Broadcast Foliar Applications			
Short grass	85	30	240
Tall grass	36	12	110
Broadleaf/forage plants and small insects	45	15	135
Fruits, pods, seeds, and large insects	7	3.2	15

[a] From Fletcher et al. (1994).
[b] Central values × (Central Value ÷ Upper Value).

See Section 3.2.3.6 for discussion.

Table 16: Aminocyclopyrachlor, Human Health Dose-Response Assessment

Duration	Derivation of RfD	Reference	Comment
Acute – single exposure			
NOAEL Dose		N/A	The U.S. EPA/OPP (2010a) did not derive an acute RfD for aminocyclopyrachlor. *No acute endpoint was identified because no toxicity was observed at the limit dose in acute oral studies.* (U.S. EPA/OPP 2010a, p. 19)
LOAEL Dose			
LOAEL Endpoint(s)			
Species, sex			
Uncertainty Factor		U.S. EPA/OPP 2010a	
RfD	None derived		
Chronic – lifetime exposure			
NOAEL Dose	350 mg/kg bw/day	Anand 2008a MRID 47573403 Anand 2008b MRID 47560007	This chronic RfD was derived for the conditional registration of aminocyclopyrachlor (U.S. EPA/OPP 2010k). Since the conditional registration was issued, chronic studies on aminocyclopyrachlor have been submitted to the U.S. EPA/OPP – i.e., Han 2010; Huh 2010; Moon 2010. It is likely that the RfD will increase at some point. See Sections 3.1.5 and 3.3 for discussion.
LOAEL Dose	1045 mg/kg bw/day		
Species, sex	Rats, male and female		
LOAEL Endpoint(s)	Decreased body weight, weight gain, food consumption, and food efficiency.		
Uncertainty Factor	1000	U.S. EPA/OPP 2010a	
RfD	0.35 mg/kg bw/day		
Incidental Oral Exposure (Short- and Intermediate-Term)			
NOAEL Dose	350 mg/kg bw/day	Anand 2008a MRID 47573403 Anand 2008b MRID 47560007	In the absence of an acute RfD, this toxicity value is used in the current Forest Service risk assessment to characterize risks associated with acute exposures.
LOAEL Dose	1045 mg/kg bw/day		
LOAEL Endpoint	Decreased body weight, weight gain, food consumption, and food efficiency.		
Species, sex	Rats, male and female		
Uncertainty Factor/MOE	100	U.S. EPA/OPP 2010a	
Equivalent RfD	3.5 mg/kg bw/day		

See Section 3.3.2 for discussion.

Table 17: Cyclopropanecarboxylic acid, Human Health Dose-Response Assessment			
Duration	**Derivation of RfD**	**Reference**	**Comment**
Acute – single exposure			
NOAEL Dose	Not determined	Ulrich et al. 1994	Toxicity study on panadiplon. Dose equivalent of 2.55 mg/kg bw/day calculated based on molar conversion of 10 mg/kg bw/day x 14 days dose of panadiplon. Standard uncertainty factors. See text for discussion.
LOAEL Dose	2.55 mg/kg bw/day		
LOAEL Endpoint(s)	Hepatic steatosis		
Species, sex	Rabbits		
Uncertainty Factor	1000	U.S. EPA/OPP 2010a	
RfD	0.0026 mg/kg/day		
Chronic – lifetime exposure			
NOAEL Dose	Not determined	Ulrich et al. 1994	EPA used only a 3x uncertainty factor for extrapolating from a 14 day exposure to a chronic exposure.
LOAEL Dose	2.55 mg/kg bw/day		
Species, sex	Rabbits		
LOAEL Endpoint(s)	Hepatic steatosis		
Uncertainty Factor	3000	U.S. EPA/OPP 2010a	
RfD	0.00087 mg/kg bw/day		

See Section 3.3.3 for discussion.

Table 18: Risk Characterization for Workers (0.28 lb a.e./acre)

Scenario	Receptor	Hazard Quotients		
		Central	Lower	Upper
Accidental/Incidental Exposures				
Contaminated Gloves, 1 min.	Worker	2E-07	2E-09	1E-06
Contaminated Gloves, 1 hour	Worker	9E-06	1E-07	7E-05
Spill on Hands, 1 hour	Worker	2E-05	3E-07	2E-04
Spill on lower legs, 1 hour	Worker	6E-05	6E-07	6E-04
General Exposures				
Backpack Applications:		1E-02	4E-04	6E-02
Ground Broadcast Applications:		2E-02	5E-04	0.1
Aerial Applications:		1E-02	2E-04	6E-02

Taken from Attachment 1, Worksheet E02.
See Section 3.4.2 for discussion.

Table 19: Aminocyclopyrachlor Risk Characterization for the General Public

Application Rate:	0.28	lb a.e./acre		
Scenario	**Receptor**	**Hazard Quotients**		
		Central	**Lower**	**Upper**
Accidental Acute Exposures (dose in mg/kg/event)				
Direct Spray of Child, whole body	Child	9E-04	1E-05	9E-03
Direct Spray of Woman, feet and lower legs	Adult Female	9E-05	1E-06	9E-04
Water consumption (spill)	Child	1E-02	8E-05	8E-02
Fish consumption (spill)	Adult Male	1E-03	1E-05	5E-03
Fish consumption (spill)	Subsistence Populations	6E-03	6E-05	3E-02
Non-Accidental Acute Exposures (dose in mg/kg/event)				
Vegetation Contact, shorts and T-shirt	Adult Female	9E-05	2E-05	4E-04
Contaminated Fruit	Adult Female	9E-04	4E-04	1E-02
Contaminated Vegetation	Adult Female	1E-02	9E-04	0.1
Swimming, one hour	Adult Female	3E-09	2E-11	9E-08
Water consumption	Child	6E-04	7E-06	6E-03
Fish consumption	Adult Male	6E-05	1E-06	4E-04
Fish consumption	Subsistence Populations	3E-04	6E-06	2E-03
Chronic/Longer Term Exposures (dose in mg/kg/day)				
Contaminated Fruit	Adult Female	7E-03	3E-03	0.1
Contaminated Vegetation	Adult Female	9E-02	7E-03	0.8
Water consumption	Adult Male	1E-03	1E-05	1E-02
Fish consumption	Adult Male	2E-05	3E-07	1E-04
Fish consumption	Subsistence Populations	2E-04	3E-06	1E-03

Taken from Attachment 1, Worksheet E04.
See Section 3.4.3.1 for discussion.

Table 20: Cyclopropanecarboxylic Acid Risk Characterization for the General Public

Aminocyclopyrachlor Application Rate:	0.28	lb a.e./acre		
Scenario	**Receptor**	**Hazard Quotients**		
		Central	**Lower**	**Upper**
Accidental Acute Exposures (dose in mg/kg/event)				
Direct Spray of Child, whole body	Child	No exposure assessment		
Direct Spray of Woman, feet and lower legs	Adult Female	No exposure assessment		
Water consumption (spill)	Child	0.3	2E-03	**2**
Fish consumption (spill)	Adult Male	1E-02	1E-04	5E-02
Fish consumption (spill)	Subsistence Populations	6E-02	6E-04	0.3
Non-Accidental Acute Exposures (dose in mg/kg/event)				
Vegetation Contact, shorts and T-shirt	Adult Female	No exposure assessment		
Contaminated Fruit	Adult Female	No exposure assessment		
Contaminated Vegetation	Adult Female	No exposure assessment		
Swimming, one hour	Adult Female	3E-05	5E-08	6E-04
Water consumption	Child	6E-03	1E-05	9E-02
Fish consumption	Adult Male	2E-04	6E-07	2E-03
Fish consumption	Subsistence Populations	1E-03	3E-06	1E-02
Chronic/Longer Term Exposures (dose in mg/kg/day)				
Contaminated Fruit	Adult Female	No exposure assessment		
Contaminated Vegetation	Adult Female	No exposure assessment		
Water consumption	Adult Male	5E-04	1E-06	8E-03
Fish consumption	Adult Male	3E-06	1E-08	4E-05
Fish consumption	Subsistence Populations	2E-05	9E-08	3E-04

Taken from Attachment 2, Worksheet E04.
See Section 3.4.3.2 for discussion.

Table 21: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption	Other
MAMMALS[1]					
Small mammal	Mice	20	$2.514\ W^{0.507}$ [Eq 3-48]	$0.099\ W^{0.9}$ [Eq 3-17]	
Larger mammal	Squirrels	400	$2.514\ W^{0.507}$ [Eq 3-48]		
Canid	Fox	5,000	$0.6167\ W^{0.862}$ [Eq 3-47]		
Large Herbivorous Mammal	Deer	70,000	$1.518\ W^{0.73}$ [Eq 3-46]		
Large Carnivorous Mammal	Bear	70,000	$0.6167\ W^{0.862}$ [Eq 3-47]		
BIRDS[2]					
Small bird	Passerines	10	$2.123\ W^{0.749}$ [Eq 3-36]	$0.059\ W^{0.67}$ [Eq 3-17]	
Predatory bird	Owls	640	$1.146\ W^{0.749}$ [Eq 3-37]		
Piscivorous bird	Herons	2,400	$1.916\ W^{0.704}$ [Eq 3-38]		
Large herbivorous bird	Geese	4,000	$1.146\ W^{0.749}$ [Eq 3-37]		
INVERTEBRATES[3]					
Honey bee	*Apis mellifera*	0.000116	≈2 (1.2 to 4)[6]	Not used	SA[7]: 1.42 cm^2
Herbivorous Insects	Various	Not used	1.3 (0.6 to 2.2)	Not used	

[1] Sources: Reid 2006; U.S. EPA/ORD 1993.
[2] Sources: Sibley 2000; Dunning 1993; U.S. EPA/ORD 1993.
[3] Sources: Humphrey and Dykes 2008; Reichle et al. 1973; Winston 1987
[4] Body weight in grams.
[5] For vertebrates, based on allometric relationships estimating field metabolic rates in kcal/day for rodents (omnivores), herbivores, and non-herbivores. For mammals and birds, the estimates are based on Nagy (1987) as adapted by U.S. EPA/ORD (1993). The equation numbers refer to U.S. EPA/ORD (1993). See the following table for estimates of caloric content of food items. For herbivorous insects, consumption estimates are based on fractions of body weight (g food consumed/g bw) from the references in Note 3.
[6] For honeybees, food consumption based on activity and caloric requirements. Used only when estimates of concentrations in nectar and/or pollen can be made, which is not the case in the current risk assessment.
[7] Based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

See data on food commodities in following table.
See Sections 4.2.2 and 4.2.3.2 for discussion.

Table 22: Metabolizable Energy of Various Food Commodities

Food Item	Animal Group	Caloric Value [1] (kcal/g dw)	Water Content [2]	Comment/Source(s)
Fruit	Mammals	1.1	0.77	See Footnote 3
	Birds	1.1	0.77	See Footnote 4
Fish	Mammals	4.47	0.70	Water content from Ali et al. (2005)
	Birds	3.87	0.70	
Insects	Mammals	4.47	0.70	Water contents from Chapman 1998 (, p. 491). Typical ranges of 60-80%.
	Birds	4.30	0.70	
Vegetation (NOS)	Mammals	2.26	0.85	
	Birds	2.0	0.85	See Footnote 5

[1] Metabolizable energy. Unless otherwise specified, the values are taken from U.S. EPA/ORD (1993), Table 3-1, p. 3-5 as adopted from Nagy 1987.

[2] From U.S. EPA/ORD (1993), Table 4-2, p. 4-14 unless otherwise specified.

[3] Based on a gross caloric value of 2.2 kcal/g dw (U.S. EPA/ORD 1993, Table 4-2). An assimilation factor for mammals eating fruit not identified. Use estimate for birds (see below).

[4] Based on a gross caloric value of 2.2 kcal/g dw (U.S. EPA/ORD 1993, Table 4-2) and an assimilation factor for the consumption of fruit by birds of 51% [2.2 kcal/g dw x 0.51 ≈ 1.1 kcal/g dw]

[5] Based on a gross caloric value of 4.2 kcal/g dw for dicot leaves (U.S. EPA/ORD 1993, Table 4-2) and an assimilation factor for the consumption leaves by birds of 47% [4.2 kcal/g dw x 0.47 = 1.974 kcal/g dw]

See Sections 4.2.2.3 for discussion.

Table 23: Summary of Terrestrial Plant Toxicity Studies of Acid and Ester

Receptor	Susceptibility	NOAEC (lb a.e./acre) Aminocyclopyrachlor acid (50SG) [1]	NOAEC (lb a.e./acre) Aminocyclopyrachlor ester (76.5%) [2]
Vegetative Vigor			
Monocot	Most sensitive	0.022 (Corn)	0.0028 (Onion)
	Most tolerant	0.36 (Ryegrass)	0.335 (Onion)
Dicot	Most sensitive	0.000044 (Bean)	0.00000078 (Bean) [3]
	Most tolerant	0.00078 (Cucumber)	0.00035 (Sugarbeet and tomato)
Seedling Emergence			
Monocot	Most sensitive	0.0028 (Onion)	0.0394 (Corn, Onion, and Ryegrass)
	Most tolerant	0.35 (Ryegrass)	0.355 (Oat)
Dicot	Most sensitive	0.00018 (Soybean and Sugarbeet)	0.000012 (Soybean) [3]
	Most tolerant	0.045 (Cucumber)	0.00439 (Oilseed Rape, Sugarbeet, and Tomato)

[1] Porch and Kendall 2010a,b as detailed in Appendix 4.
[2] MRID 47560132 and MRID 47560133 as summarized in U.S. EPA/OPP 2010b.
[3] Extrapolated EC_{05} rather than NOAEC. U.S. EPA/OPP (2010b) notes that confidence in the extrapolated value is limited.

See Appendix for details and references to studies.
See Section 4.3.2.5.1 (Vegetative Vigor) and 4.3.2.5.2. (Seedling Emergence for discussion.

Table 24:Summary of toxicity values used in ecological risk assessment

Group/Duration	Organism	Endpoint	Toxicity Value (a.e.)	Reference
Terrestrial Animals				
Acute				
	Mammals (non-canid)	Subchronic NOAEL	350	Section 4.3.2.1.1
	Canids	Use value for other mammals	350	
	Birds	Gavage NOAEL	2075	Section 4.3.2.2
	Herbivorous Insects	Oral NOAEL	460	Section 4.3.2.4.1
	Honey Bee (contact)	Contact NOAEL	862	Section 4.3.2.4.2
Longer-term				
	Small Mammal	Subchronic NOAEL	350	Section 4.3.2.1.1
	Bird	Chronic NOAEL	100.9	Section 4.3.2.2.
Terrestrial Plants				
Soil	Sensitive	NOAEC, bean (dicot)	0.00018	Section 4.3.2.5.2
	Tolerant	NOAEC, cucumber (monocot)	0.35	
	Conifer	NOAEC (use tolerant dicot)	0.045	Section 4.3.2.5.3
Foliar	Sensitive	NOAEC, bean (dicot)	0.000044	Section 4.3.2.5.1
	Tolerant	NOAEC, ryegrass (monocot)	0.36	
Aquatic Animals (mg/L)				
Acute				
Amphibians	Sensitive	No toxicity data.	N/A	Section 4.3.3.2
	Tolerant	No toxicity data.	N/A	
Fish	Sensitive	None identified	N/A	Section 4.3.3.1
	Tolerant	NOAECs, several species	120	
Invertebrates	Sensitive	NOAEC, *Daphnia magna*	3.7	Section 4.3.3.3
	Tolerant	NOAEC, mysid shrimp	122	Section 4.3.3.3
Longer-term				
Amphibians	Sensitive	No toxicity data.	N/A	Section 4.3.3.2
	Tolerant	No toxicity data.	N/A	
Fish	Sensitive	None identified	N/A	Section 4.3.3.1
	Tolerant	NOAEC, trout early life-stage	11	
Invertebrates	Sensitive	Not clearly identified	N/A	Section 4.3.3.3
	Tolerant	Use acute daphnid value	3.7	
Aquatic Plants				
Algae	Sensitive	NOAEC, blue-green	1.11	Section 4.3.3.4.1
	Tolerant	NOAEC, marine diatom [3]	15.3	
Macrophytes	Sensitive	None identified	N/A	Section 4.3.3.4.2
	Tolerant	NOAEC, *Lemna gibba*	3.75	

Table 25: Hazard Quotients for Terrestrial Plants from Direct Spray or Drift

Distance Downwind (feet)	Hazard Quotients Based on Drift for the Specified Application Methods			
	Aerial	**High Boom Ground Broadcast**	**Low Boom Ground Broadcast**	**Backpack**
FINE DROPLETS (Extreme)				
	Sensitive Species			
Direct Spray	**6,364**	**6,364**	**6,364**	N/A
25	**1,419**	**662**	**223**	N/A
50	**1,088**	**318**	**113**	N/A
100	**623**	**158**	**60**	N/A
300	**199**	**48**	**22**	N/A
500	**122**	**25**	**13**	N/A
900	**79**	**11**	**7**	N/A
	Tolerant Species			
Direct Spray	0.8	0.8	0.8	N/A
25	0.2	8E-02	3E-02	N/A
50	0.1	4E-02	1E-02	N/A
100	8E-02	2E-02	7E-03	N/A
300	2E-02	6E-03	3E-03	N/A
500	1E-02	3E-03	2E-03	N/A
900	1E-02	1E-03	8E-04	N/A
COARSE DROPLETS (Anticipated)				
	Sensitive Species			
Direct Spray	**6,364**	**6,364**	**6,364**	**6,364**
25	**902**	**105**	**80**	**53**
50	**472**	**53**	**47**	**28**
100	**231**	**28**	**28**	**15**
300	**58**	**10**	**12**	**6**
500	**35**	**6**	**8**	**4**
900	**20**	**3**	**4**	**2**
	Tolerant Species			
Direct Spray	0.8	0.8	0.8	0.8
25	0.1	1E-02	1E-02	6E-03
50	6E-02	6E-03	6E-03	3E-03
100	3E-02	3E-03	3E-03	2E-03
300	7E-03	1E-03	1E-03	7E-04
500	4E-03	7E-04	9E-04	5E-04
900	2E-03	3E-04	5E-04	2E-04

Attachment 1, Worksheet G05a (fine droplets) and G05b (coarse droplets).
See Section 4.4.2.5.1 for discussion.

Table 26: Plants with Demonstrated Sensitivity to Aminocyclopyrachlor

Conifers	Deciduous Trees	Ornamental Shrubs
Douglas fir	Aspen	Arborvitae
Norway spruce	Chinese tallow	Burning bush
Ponderosa pine	Cottonwood	Crape myrtle
White Pine	Honey locust	Forsythia
	Magnolia	Hydrangea
	Poplar species	Ice plant
	Redbud	Magnolia
	Silver maple	Purple plum
	Willow species	Yew

Source: Modified from DuPont™ 2012c
See Section 4.1.2.5.3 for discussion.

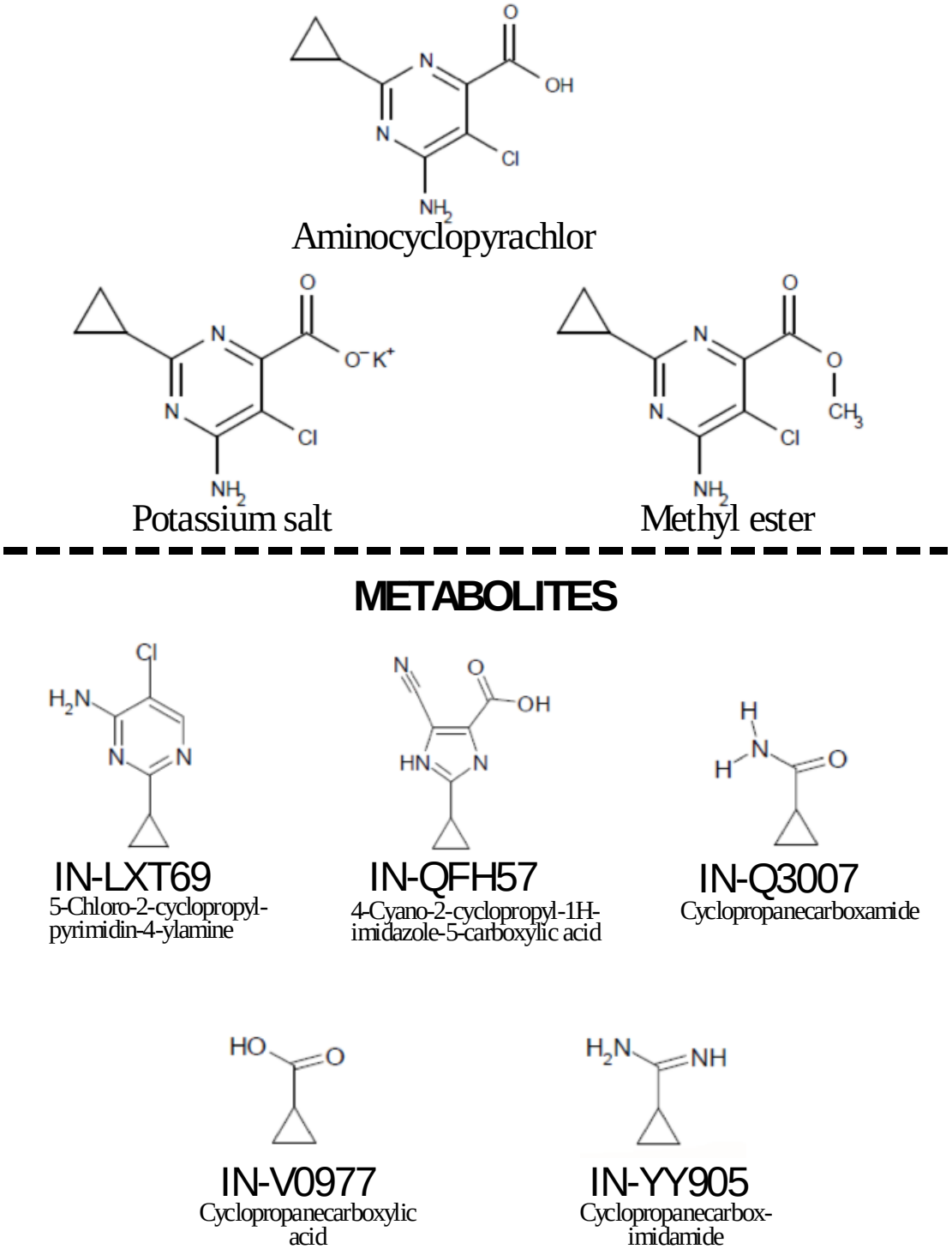


Figure 1: Forms of Aminocyclopyrachlor and Aminocyclopyrachlor Degradates

Source: Modified from U.S. EPA/OPP (2010d)

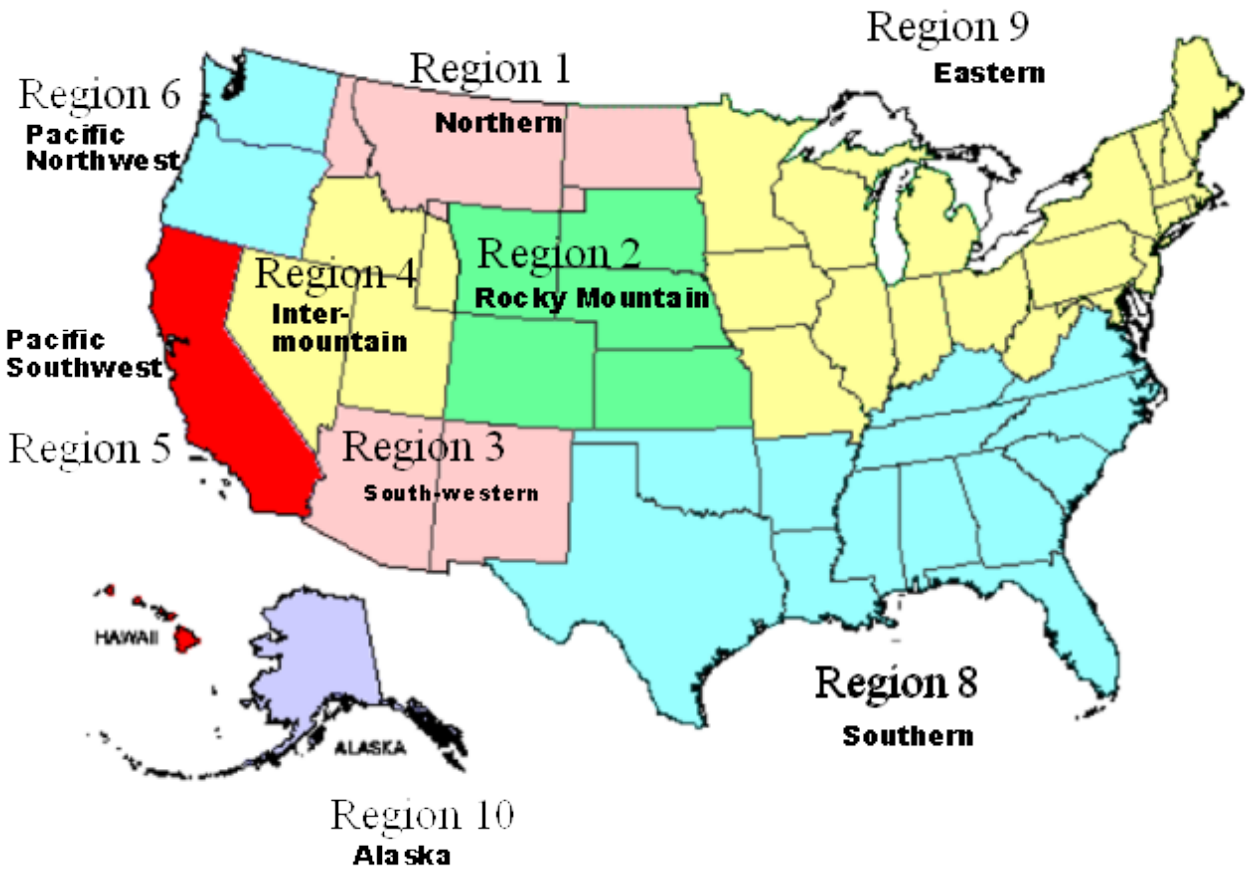


Figure 2: Designated Regions in the Forest Service

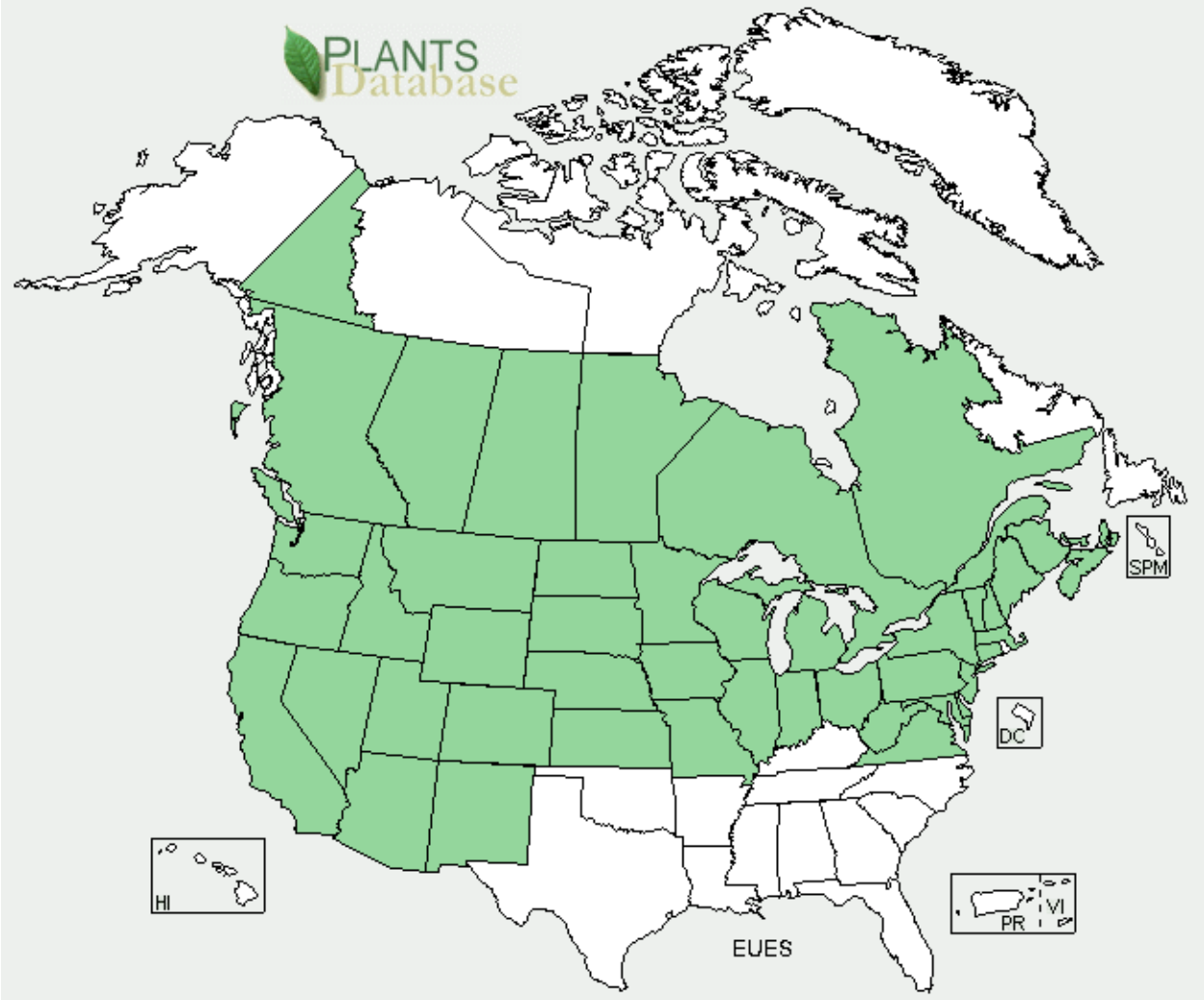


Figure 3: Distribution of Leafy Spurge in North America

Source: http://plants.usda.gov/java/profile?symbol=EUES

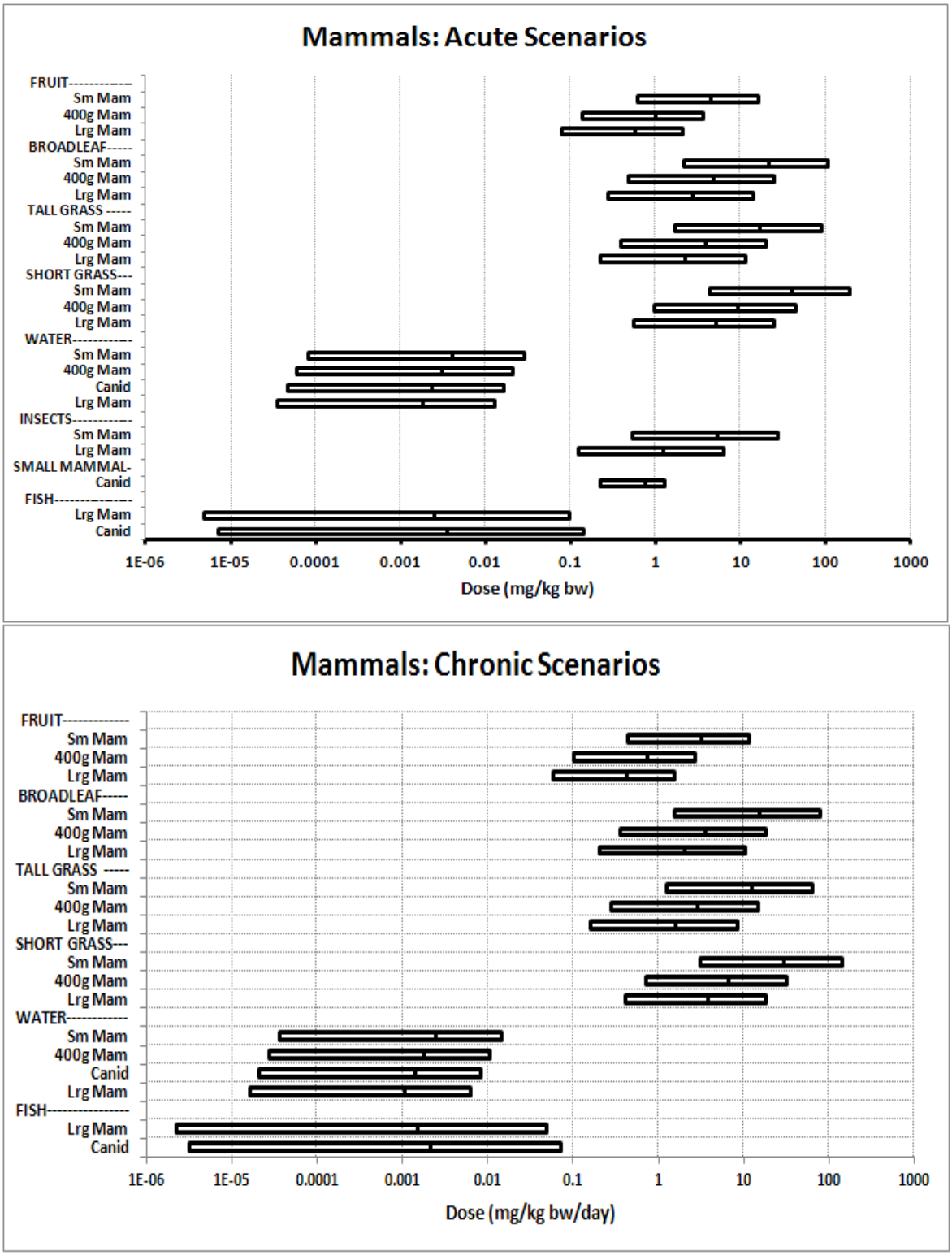


Figure 4: Overview of Exposure Assessments for Mammals

See Section 4.2.1 for discussion.
See Attachment 1, Worksheet G01a for details.

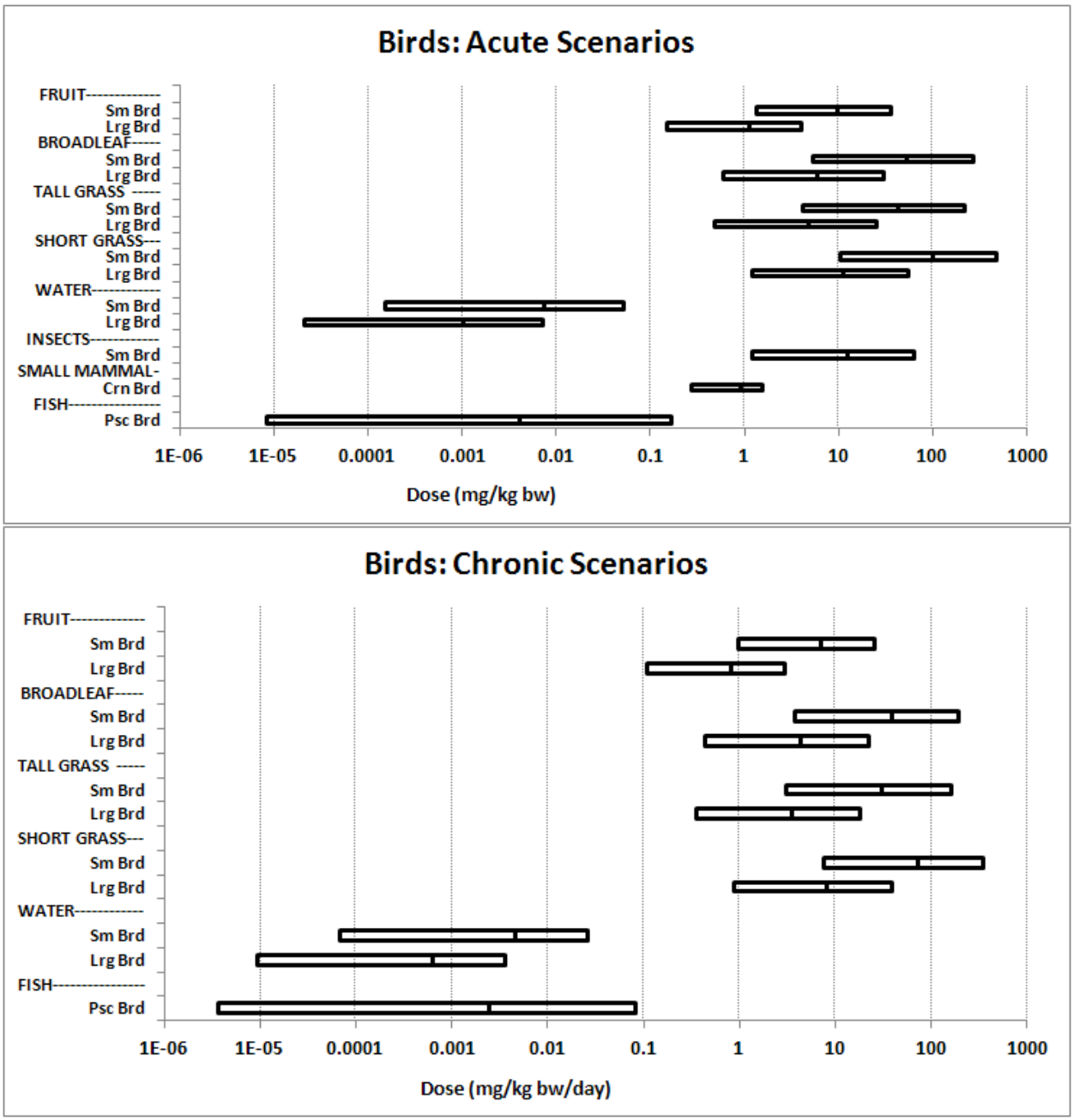


Figure 5: Overview of Exposure Assessments for Birds

See Section 4.2.1 for discussion.
See Attachment 1, Worksheet G01b for details.

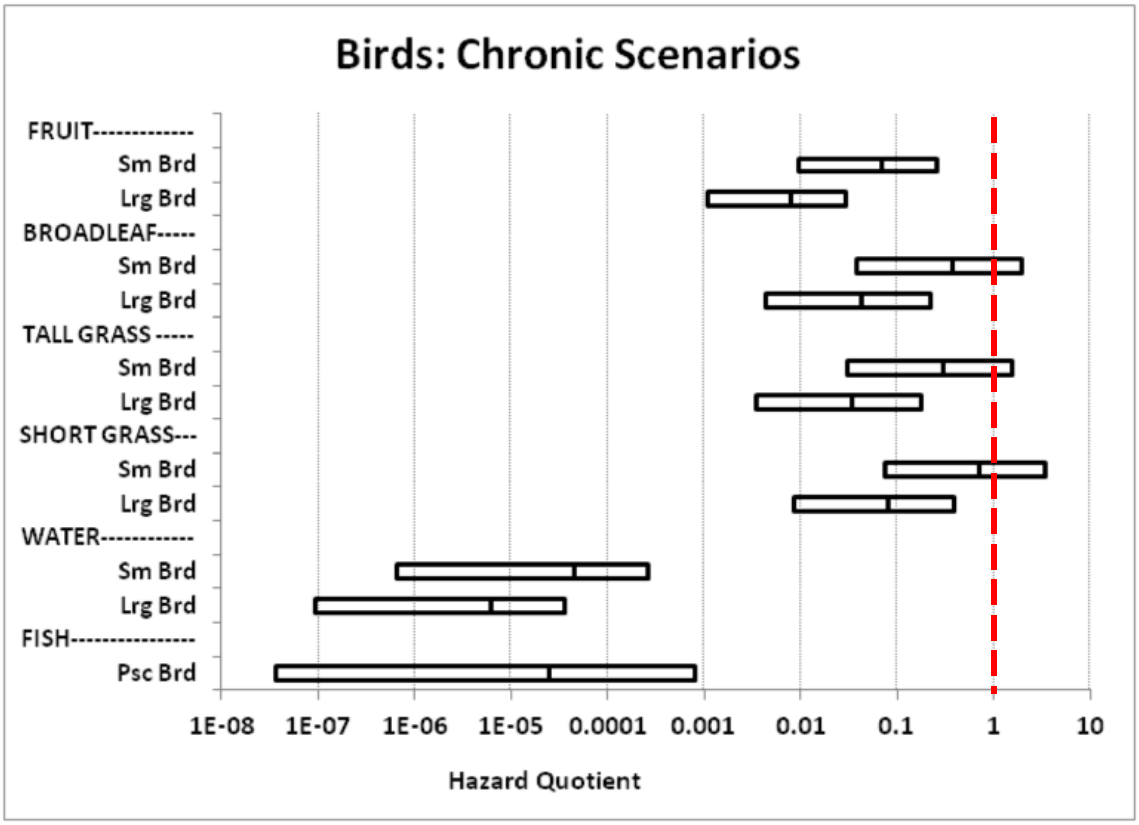


Figure 6: Risk Characterization for Birds, Chronic Scenarios

See Section 4.4.2.2 for discussion.
See Attachment 1, Worksheet G02b for data.

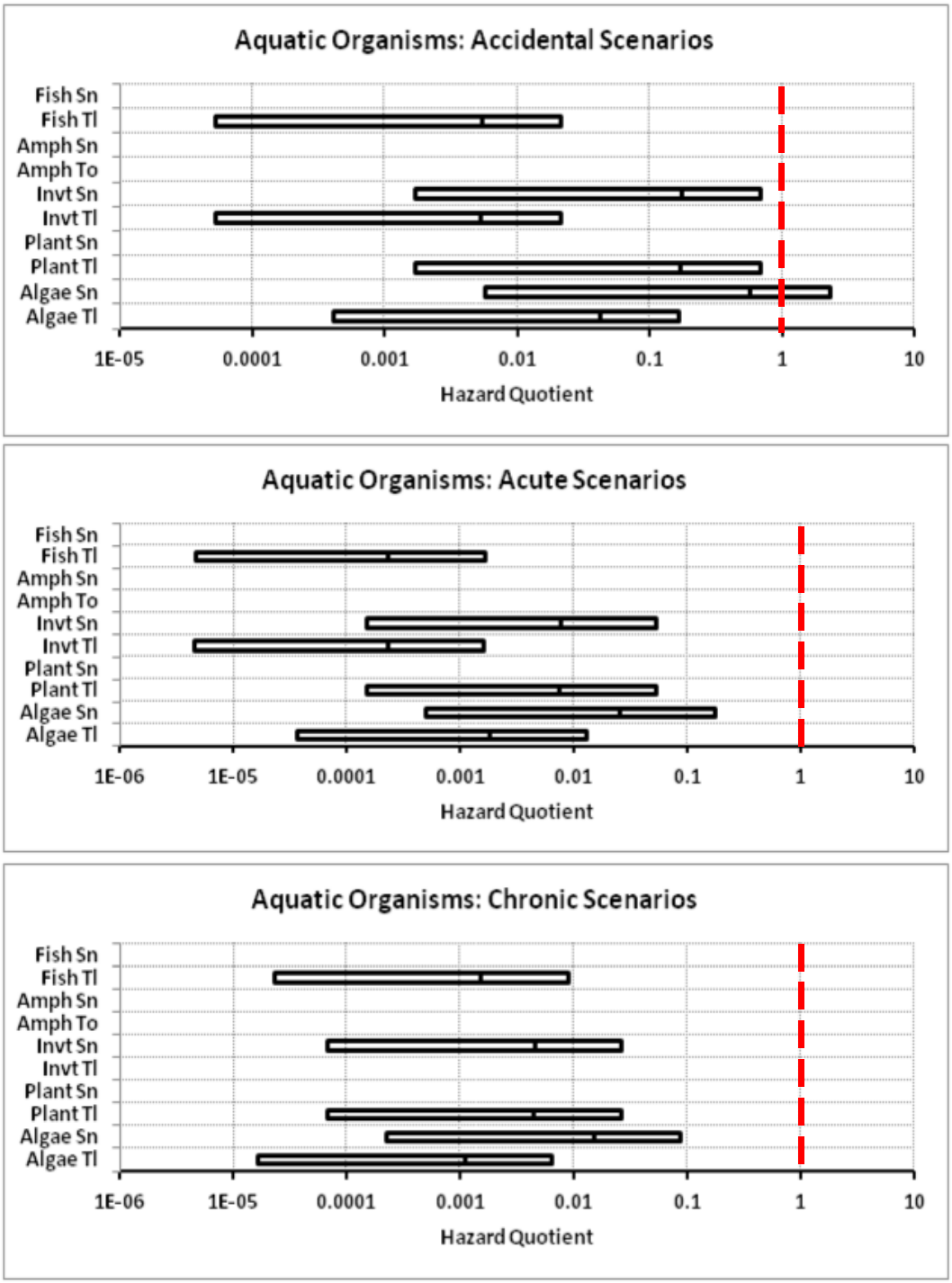


Figure 7: Overview of Risk Characterization for Aquatic Organisms

See Section 4.4.3 for discussion
See Attachment 1, Worksheet G03, for data.

Appendix 1: Toxicity to Mammals

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A1 Table 1: Acute Oral Toxicity

Species	Exposure	Response	Reference
Gavage			
Rat, three fasted females, 10- or 11-weeks-old, 210.3-230.6 g,	5000 mg a.e./kg-bw Aminocyclopyrachlor acid (92.2% a.i.) suspended in deionized water by gavage; observation period of 14 days Limit Test.	Day following exposure, one rat had diarrhea but recovered by the next day; there were no mortalities or clinical signs of toxicity, and necropsies performed at the end of the study did not show gross lesion. All animals gained weight throughout the study. LD_{50} >5000 mg/kg Technical grade aminocyclopyrachlor classified as EPA Toxicity Category IV: (Practically non-toxic). *Study classified as Acceptable*	Carpenter (2007c) MRID 47559934
Rat, three fasted females, 10- or 11-weeks-old, 231.4-235.4 g,	5000 mg /kg-bw aminocyclopyrachlor (22.4% a.e.) [DPX-MAT28 240 g/L SL] single oral gavage dose Note: This material is identical to DuPont™ Method® 240SL, a formulation that will be used by the Forest Service. The dose is equivalent to 1200 mg a.e./kg bw. Limit Test	Day following exposure, one rat had diarrhea but recovered by the next day; there were no mortalities or clinical signs of toxicity, and necropsies performed at the end of the study did not show gross lesion. All animals gained weight throughout the study. LD_{50} >5000 mg formulation/kg or >1120 mg a.e./kg bw. The formulation is classified as EPA Toxicity Category IV: (Practically non-toxic). *Study classified as Acceptable*	Carpenter (2008b) MRID 47560040
Rat, Sprague Dawley, (F), 11-weeks-old, 211-215 g, n=3	5000 mg/kg (limit dose) aminocyclopyrachlor [(DPX-MAT28) 50SG (49.80%) in distilled water, single oral gavage dose. Observation period of 14 days. Note: This material is identical to DuPont™ Method® 50SG, a formulation that will be used by the Forest Service. The dose is equivalent to 2490 mg a.e./kg bw.	All animals survived, gained body weight and appeared active and healthy during the study. There were no clinical signs of toxicity or abnormal behavior. No gross abnormalities were noted at necropsy. Oral LD_{50} >5000 mg formulation /kg bw or >2490 mg a.e./kg bw.	Moore (2008a) MIRD 47560111

A1 Table 1: Acute Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Rat, Sprague Dawley (M,F), approx. 6-weeks-old, 267.4-273.3 g (males), 199.8-205.4 g (females) 10/sex/dose group	0, 200, 1000, or 2000 mg/kg bw (limit dose) aminocyclopyrachlor (acid) (92.2% a.i.) in 0.5%carboxymethylcellulose. Gavage dosing.	**Acute Neurotoxicity** No treatment-related effects on mortality, clinical signs of toxicity, body weight, food consumption, brain weight, body weight gain, gross pathology, or neuropathology No neurological effects observed in either sex at any dose level. NOAEL = 2000 mg/kg (limit dose) No acute neurotoxicity.	Barnett (2009a) MRID 47725702
Mouse Crl:CD1(ICR), (M,F), approx.. 6- to 8-weeks-old, 25.8-29.7 g (males), 20.8-25.7 g females, 5/sex/dose group	Single gavage dose of 0, 500, 1000, or 2000 mg/kg (limit dose) aminocyclopyrachlor (acid) (92.2% a.i.) in sterile water. Bone marrow cells harvested at 24 and 48 hours post-dosing. 5 mice/sex were treated with cyclophosphamide (50 mg/kg) and marrow cells were harvested at 24 hours post-dosing.	**Mouse bone marrow erythrocyte micronucleus test** No mortality or clinical signs of toxicity observed at any dose level. No significant decrease in polychromatic erythrocyte to normochromatic erythrocyte rations, indicating that test material was not toxic to bone marrow.	Krsmanovic and Huston (2007) MRID 47560022

A1 Table 2: Subchronic and Chronic Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Subchronic oral			
Mice, CD-1 (M,F)	0, 300, 1000, 3000, or 7000 ppm aminocyclopyrachlor (92.2%) in the diet for 90 days (equivalent to 0/0, 47/61, 154/230, 459/649, or 1088/1623 mg/kg/day)	No treatment-related mortality; small (↓4-8%), statistically significant decreases in male body weights on day 49 through the end of the study at 1000, 3000, and 7000 ppm; significant decreases (↓8-11%) in female body weights at 1000, 3000, and 7000 ppm; significant decreases (↓12-27%) in male body weight gains from day 0-91 at 1000 and 7000 ppm; decreases in female body weight gains were not significant; no effects on food consumption observed for either sex; overall food efficiency (days 0-91) significantly decreased (↓24%) in males at 7000 ppm and (↓28-36%) in females at 1000 and 7000 ppm (but not 3000 ppm); statistically significant decrease (p<0/05) in number of reticulocytes (by 15%) in females at 7000 ppm, relative to controls, was not considered adverse. IN-IXT69 metabolite was not detected any plasma samples, although the plasma concentration of the parent compound was increased in all treated groups and slightly higher in males at all doses. NOAEL= 7000 ppm (1088/1623 mg/kg/day M/F, limit dose) LOAEL = not established.	Anand (2008c,d) MRID 47560010 47560011

A1 Table 2: Subchronic and Chronic Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Rat, Crl:CD (Sprague Dawley, (M/F), approx 51-days-old, 253-256 g (males), 174-180 g (females),weight variation did not exceed ±20% of mean weight/sex 15/sex/dose	0, 600, 2000, 6000, or 18,000 ppm aminocyclopyrachlor (acid) (92.2% a.i.) in the diet for 13 weeks (94-95 days in males and 96-97 days in females). Doses (adjusted for purity) equivalent to 0/0, 34.8/44.8, 114.3/145.7, 349.4/448.0, or 1044.6/1424.9 mg/kg/day (M/F)	No treatment-related mortality (one control male and one 6000 ppm female were accidentally killed during blood collection just prior to necropsy). No adverse effects on organ weights, ophthalmology, hematology, coagulation, clinical chemistry or urinalysis in males or females at any dose level. NOAEL (systemic effects) = 6000 ppm (349.4/448.0 mg/kg/day M/F) LOAEL (systemic effects) = 18,000 ppm (1044.6/1424.9 mg/kg/day M/F), based on decreased body weights, body weight gains, food consumption, and food efficiency in both sexes. Neurobehavioral assessment (functional observational battery [FOB] and motor activity testing) was performed prior to treatment and during Weeks 4, 8, and 13 on 10 rats/sex/group. No treatment-related effects on brain weighs or gross or microscopic neuropathology in either sex at any dose level. No differences between controls and high-dose groups in histopathological evaluation of brain, spinal cord, and peripheral nerves, NOAEL(neurotoxicity) = 18,000 ppm (limit dose) (1044.6/1424.9 mg/kg/day M/F) One metabolite (IN-LXT69 in Table 2) was identified suggesting decarboxylation. **This is the study on which the chronic RfD is based. Uncertainty Factor(s): 1000X [10X interspecies x 10X intraspecies x 10 X subchronic to chronic]**	Anand (2008a,b) MRID 47573403 47560007
Dog, beagle, (M/F), approx. 8- to-10-weeks-old, 9.8-10.8 kg (males), 8.6-9.3 (females), 4/sex/group	0, 250, 1250, 5000, or 15,000 ppm technical grade aminocyclopyrachlor (92.2% a.i.) in the diet (equivalent to **0/0, 6.5/7.0, 33/38, 126/124, 426/388 mg/kg /day in males/females**) for 13 weeks	No treatment-related effects observed on mortality, clinical signs, neurological evaluations, body weight, body weight gains, food consumption, food efficiency, hematology, clinical chemistry, urinalysis, organ weights, or gross microscopic pathology. Increased incidence of skin scaling on feet (severity of effect not noted/foot pads not biopsied) was dose related, affecting 4/4 males and 2/4 females at the high dose. Effect not considered adverse because it did not impair walking or weight bearing, and no grooming (licking/biting) of the feet was observed. NOAEL = 15,000 ppm (426/388 mg/kg/day M/F) LOAEL = not established.	Luckett (2008a); Luckett and Mawn (2008) MRID 47560012 47560013

A1 Table 2: Subchronic and Chronic Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Rat, Sprague Dawley, (M), 8-weeks-old, 233.0-273.1 g, 10/dose group	0, 600, 6000, or 18,000 ppm technical grade aminocyclopyrachlor (92.2% a.i.) in the diet (equivalent to **0, 42, 407, or 1277 mg/kg/day**) for 28 days An additional group of 5 rats were dosed by intraperitoneal injection (10 mL/kg) with 25 mg/kg cyclophosphamide monohydrate to serve as positive controls.	Treatment did not cause systemic toxicity or have adverse effects on mortality, clinical signs, body weights, body weight gains, food consumption, food efficiency, organ weights or gross pathology at any dose level. No evidence of immunotoxicity. **Systemic** NOAEL= 18,000 ppm (1277 mg/kg/day) **Systemic** LOAEL= not established **Immunotoxicity** NOAEL= 18,000 ppm (1277 mg/kg/day) **Immunotoxicity** LOAEL= not established	Hoban (2008b) MRID 47560025
Mice, CD-1 (Crl:CD[ICR]), (M), 8-weeks-old, 29.4-34.5 g, 10/dose group	0, 300, 3000, or 7000 ppm technical grade aminocyclopyrachlor (92.2% a.i.) in diet (equivalent to 0, 45, 425, or 1056 mg/kg/day) for 28 days An additional group of 5 mice were dosed by intraperitoneal injection (10 mL/kg) with 25 mg/kg cyclophosphamide monohydrate to serve as positive controls.	Treatment did not cause systemic toxicity or have adverse effects on mortality, clinical signs, body weights, body weight gains, food consumption, food efficiency, organ weights or gross pathology at any dose level. No evidence of immunotoxicity. **Systemic** NOAEL= 7000 ppm (1056 mg/kg/day) **Systemic** LOAEL= not established **Immunotoxicity** NOAEL= 7,000 ppm (1056 mg/kg/day) **Immunotoxicity** LOAEL= not established	Hoban (2008c) MRID 47560026
Chronic Oral			
Dog, beagle, (M/F), approx. 8- to 9-months old, 6428-10,273 g (males), 5591-8549 (females), 4/sex/group	0, 1250, 5000, 15,000, or 30,000 ppm technical grade aminocyclo-pyrachlor (88.3% purity) in the diet (equivalent to **mean daily intakes/males: 0, 37.9, 178.0, 465.1, or 1076.7 mg/kg bw; mean daily intakes/females: 0, 46.9, 174.6, 542.1 or 1072.5 mg/kg/ bw)** for 53 weeks.	No mortality; no treatment-related effects on body weight, body weight gain, food consumption, food efficiency, clinical signs, ophthalmology, coagulation, clinical chemistry, urinalysis, gross findings, organ weights, or histopathology observed during the course of the study. NOAEL = 30,000 ppm for M/F (concentration equivalent to 1077 mg/kg/day in males and 1073 mg/kg/day in females).	Han 2010
Rat, Crl:CD (SD), (M/F), approx.. 6-weeks-old, 180.4-249.4 g (males), 130.5-186.4 g (females), 80/sex/concentration	0, 600, 2000, 6000, or 18,000 ppm technical grade aminocyclopyrachlor (88.3% purity) in the diet (equivalent to **mean daily intakes/males: 0, 27, 97, 270, or 892 mg/kg bw; mean daily intakes/females: 0, 29, 100, 309, or 957 mg/kg bw)** for 2 years	Treatment-related adverse effects included decreases in body weight parameters and food efficiency parameters in males and females at 18,000 ppm. No other treatment-related effects were observed in the course of the study. No evidence of carcinogenicity. NOAEL = 6000 ppm (based on body weight and food efficiency parameters in males and females) (concentration equivalent to 279 mg/kg/day in males and 309 mg/kg/day in females).	Moon 2010
Mice, Crlj:CD-1 (ICR), (M/F), approx.. 6-weeks-old, 27.5-38.4 g (males), 20.7-28.1 g (females), 60/sex/concentration.	0, 300, 1000, 3000, or 7000 ppm technical grade aminocyclo-pyrachlor (88.3% purity) in the diet (equivalent to **mean daily intakes/males: 0, 38.7, 132.7, 393.1, 876.2 mg/kg bw; mean daily intakes/females: 0, 49.9, `70.6, 526.8, or 1190.0 mg/kg bw)** for 18 months.	No mortality or carcinogenicity; no treatment-related effects on body weight parameters, food intake parameters, hematology, organ weights, gross pathology, or neoplastic/non-neoplastic changes observed in either sex or at any concentration during the course of the study. NOAEL = 7000 ppm for M/F (concentration equivalent to 876 mg/kg/day in males and 1190 mg/kg/day in females).	Huh 2010

A1 Table 3: Reproductive and Developmental Studies			
Species	**Exposure**	**Response**	**Reference**
Reproduction			
Rat, Sprague Dawley, (M/F), approx. 56-days-old, 247-306 g (males), 167-219 g (females) 28/sex/dose group	0, 500, 1500, 5000, or 17,000 ppm aminocyclopyrachlor (90.9-92.2% a.i.) (equivalent to 0/0, 36/41, 109/125, 363/416, or 1285/1454 mg/kg bw/day in males and females during pre-mating) for two successive generations with one litter per generation. The P (parental) generation animals were fed the test diets for at least 10 weeks prior to mating to produce the F1 litters. The F1litters were culled on post-natal day (PND) 4 to eight pups/litter (four/sex where possible). On PND 21, one pup/sex/litter (where possible) was selected and fed the same test diet concentration as the dam. These animals were fed the test diets for at least 10 weeks prior to mating (at 13 weeks of age) to produce the F2 litters.	No treatment-related effects on mortality, clinical signs, or macroscopic or microscopic findings. **Pre-mating period**: Adverse effects included significantly ($p \leq 0.05$) decreased bodyweights (↓6-15%) and decreased body weight gains (↓7-16%) in P and F1 males at ≥5000 ppm. Food efficiency was decreased (↓8-15% at ≥1500 ppm). In P and F1 females bodyweights were decreased (↓6-14%) at 17,000 ppm). Body weight gains and food efficiency were decreased only at 17,000 ppm (↓12-16%). **Gestation**: Adverse effects included significant decreases in body weights (↓8-12%) in P females only at 17,000 ppm; decreases in food consumption (↓10%) and food efficiency (↓20%) were also observed. Terminal body weights were significantly ($p \leq 0.05$) decreased at 17,000 ppm for P males and females (↓6-7%) and F1 males (↓16%). At 5000 ppm, terminal body weight was decreased (↓9%) for F1 males only. There were significant decreases (↓4-5%) in absolute (but not relative) brain weights for P and F1 females at 17,000 ppm. At 5000 ppm, decreases in absolute brain weights were observed for P females only (↓4%). There were no correlating microscopic findings. At 17,000 ppm, a significant decrease (13-31%) was noted in spleen weights in F1 weanlings but this effect was not significant in F1 adults. **Parental Systemic** NOAEL = 5000 ppm (363/416 mg/kg/day M/F) **Parental Systemic** LOAEL = 17,000 ppm (1285/1454 mg/kg/day M/F) based on decreased body weights. **Reproduction** NOAEL = 17,000 ppm (1285/1454 mg/kg/day M/F) **Reproduction** LOAEL was not established. **Offspring** NOAEL = 5000 ppm (363/416 mg/kg/day) **Offspring** LOAEL = 17,000 ppm (1285/1454 mg/kg/day M/F) based on decreased body weights in F1 and F2 pups. *Study classified as Acceptable*	Lewis (2008a) MRID 47575101
Developmental			
Rat, Sprague Dawley, (F), approx. 67=days-old, 222-270 g (time-mated presumed pregnant), 25/dose group	Aminocyclopyrachlor (92.9%) in 0.5% methylcellulose by gavage daily at doses of 0, 30, 100, 300, or 1000 mg/kg/day on gestation days 6-20	No abortions, premature deliveries, late resorptions, complete litter resorptions , or dead fetuses. No treatment-related effects on litter numbers, live fetuses, or early resorptions. **Maternal** NOAEL = 1000 mg/kg/day LOAEL = not established. No treatment-related external, visceral or skeletal variations or malformations. Incidental findings included fused cervical vertebrae at 300 mg/kg/day, anophthalmia and eye bulge in one 300 mg/kg/day fetus, and a protruding tongue in another 300 mg/kg/day fetus. **Developmental** NOAEL= 1000 mg/kg/day LOAEL = not established. No effects on body weight or food consumption.	Lewis (2008b) MRID 47560016

A1 Table 3: Reproductive and Developmental Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbit, New Zealand white, (F), (time-mated presumed pregnant), 22/dose group	Aminocyclopyrachlor (92.9% a.i.) in 0.5% methylcellulose by gavage daily at doses of 0, 100, 300, 500, or 1000 mg/kg/day on gestation days 7-28 Dose volume = 4 mL/kg	**At 1000 mg/kg/day**: one treatment-related maternal death on gestation day 13 (signs of toxicity included increased respiration 1 hour after dosing on gestation day 7 and rales and decreased defecation during gestation days 9-13); two animals aborted (one on gestation day 10 and the other on gestation day 26) and abortions may be secondary to body weight loss >10%. Clinical signs of toxicity included body weight losses of 636-643 g (17-19%) from gestation day 7 through the day of abortion. These maternal effects corresponded with reduced food consumption, generally ≤17 g/day from gestation day 13 or 17 through the day of abortion. Decreased food consumption was statistically significant only in the 1000 mg/kg/day group (consistently about 30% after gestation days 14-15 through the end of the study. **500 mg/kg bw/day:** No adverse effects on dams or offspring. **100 mg/kg bw/day**: Death in one dam. The cause of death was not identified. **Maternal** NOAEL = 500 mg/kg/day LOAEL = 1000 mg/kg/day based on mortality and abortion and decreased body weight gains and food consumption. No effects of treatment on mean numbers of live fetuses, early resorptions, or late resorptions. Fetal body weights, sex ratio, and post-implantation losses in the treated groups were comparable to controls. No treatment-related external, visceral, or skeletal malformations or variations **Developmental** NOAEL = 1000 mg/kg/day (limit dose) LOAEL = not established. Study classified as Acceptable/Guideline	Fleeman 2008, MRID 47560015

A1 Table 4: Acute and Subchronic Dermal Toxicity			
Species	**Exposure**	**Response**	**Reference**
ACUTE			
Rat, Sprague Dawley (M,F), approx.. 9- to 10-weeks-old, 275.3-301.9 g (males), 223.4-227.5 g (females), 5/sex/group	**Technical grade aminocyclopyrachlor** Dermal exposure to 5000 mg/kg technical grade aminocyclopyrachlor acid (92.2% a.i.), which was applied to clipped lumbar region for 24 hours. The rats were wrapped with stretch gauze bandage and self-adhesive bandage. After the exposure period, the excess test material was removed with warm water and the skin was dried. Dermal effects were scored according to the Draize Scale (1959).	No mortality; all animals gained weight throughout the study. No clinical signs of toxicity were observed; no gross abnormalities were noted at necropsy. Two males had stained fur/skin or ocular discharge which was not related to the test material. One female had hair loss on forelimb on days 11 through 14. Ulceration was noted on four males on Day 1. Erythema was noted on four males and five females on Day 1 with recovery by Day 2. The study author stated that erythema and ulceration may have been due to the gauze pads adhering to the test sites at the time of washing. LD_{50} >5000 mg a.e./kg Technical aminocyclopyrachlor classified as EPA Toxicity Category IV.	Carpenter (2007b) MRID 47559935
Rat, Sprague Dawley (M,F), approx.. 9-weeks-old, 273.9-307.1 g (males), 204.6-218.4 g (females), 5/sex/group	**DuPont™ Method® 240SL** Dermal exposure to 5000 mg/kg aminocyclopyrachlor (22.4%) [DPX-MAT28 240 g/L SL], which was applied to clipped lumbar region for 24 hours. The rats were wrapped with stretch gauze bandage and self-adhesive bandage. After the exposure period, the excess test material was removed with warm water and the skin was dried. Dermal effects were scored according to the Draize Scale (1959).	No mortality; no clinical signs of toxicity during the study, no body weight losses. Observed effects included, red nasal and oral discharge on day 1 after exposure and stained fur/skin up to 6 days after exposure (1/5 males) and erythema (score 2) but no edema in 1/5 males on the day after exposure. No dermal irritation was observed in the remaining rats. Dermal LD_{50} >5000 mg formulation/kg bw (equivalent to 1120 mg a.e./kg bw Based on the LD_{50}, aminocyclopyrachlor (22.4%) [DPX-MAT28 240 g/L SL] is classified as EPA Toxicity Category IV (not and irritant).	Carpenter (2008e) MRID 47560101
Rat, Sprague Dawley, (M,F), 8- to-9-weeks-old, 244-260 g (males), 183-202 g (females), 5/sex/dose group	**DuPont™ Method® 50SG** 24-hour dermal application of 5000 mg/kg aminocyclopyrachlor [(DPX-MAT28) 50SG (49.80%) 85% w/w mixture in distilled water on an area of approx 10% of the total body surface area on the clipped dorsal trunk. After the exposure period, the pads were removed and the test sites were gently cleansed of any residual test material. Observations made 1 and 6 hours after application and least once/day for 14 days.	No mortality, no effects on body weight gain, no clinical signs of toxicity, no dermal irritation or abnormal behavior, and no gross abnormalities observed at necropsy. LD_{50} >5000 mg formulation/kg bw (equivalent to 2490 mg a.e./kg bw EPA Toxicity Category IV.	Moore (2008f) MRID 47560106

A1 Table 4: Acute and Subchronic Dermal Toxicity			
Species	**Exposure**	**Response**	**Reference**
SUBCHRONIC			
Rat, Sprague Dawley, (M,F), 8- to-9-weeks-old, 243-267 g (males), 175-199 g (females), 10/sex/dose group	**Technical grade aminocyclopyrachlor** Aminocyclopyrachlor (90.9% a.i.) applied to shaved intact skin at dose levels (adjusted for purity) of 0, 150, 400, or 1000 mg/kg/day 6 hours/day for 28 consecutive days	No treatment-related mortality. Only clinical sign observed was limited and barely perceptible erythema/edema (score of 1 on a scale of 4.4 being severe) in three males: one at 400 mg/kg/day (day 28); one at 1000 mg/kg/day (day 3) and one at 1000 mg/kg/day (day 28). No treatment-related effects on body weight, body weight gain, food consumption, food efficiency, clinical chemistry, hematology, gross pathology, or histopathology. Female Rats: Statistically significant changes in adrenal gland (15% increase) and ovary weights (20% decrease) in 1000 mg/kg/day females and a decrease in kidney weights (10% relative brain weights) in females at 150 mg/kg/day. These effects were not considered treatment-related due to a lack of corroborating microscopic lesions. Male Rats: No changes in organ weights. NOAEL = 1000 mg/kg/day LOAEL = not established.	Merkel 2008 MRID 47560014

A1 Table 5: Acute Inhalation Studies			
Species	**Exposure**	**Response**	**Reference**
Rat (M,F), 8-weeks-old, 244.1-271.0 g (males), 185.7-196.6 g (females), 5/sex	**Technical grade aminocyclopyrachlor** Nose-only exposure to 5.4 mg/L aminocyclopyrachlor (acid), technical (92.2%) for 4 hours followed by 14-day observation period.	No mortality, all animals gained weight during the study. No gross lesions at necropsy. LD_{50} >5.4 mg/L (M,F) EPA Toxicity Category IV.	Anand (2007a) MRID 47560001
Rat (M,F), 9 to 10-weeks-old, 331-339 g (males), 242-257 g (females), 5/sex	**Test Material: Method 240 SL** (potassium salt) Nose-only exposure to 6.9 mg/L DPX-MAT28 21.9SL 22.4% a.e.), technical (92.2%) for 4 hours followed by 14-day observation period.	No mortality and normal body weight gain. Gross pathology noted pale kidneys in one female and dark red area on the thymus of one female. LD_{50} >6.9 mg/L (M,F), >1.54 mg a.e./L EPA Toxicity Category IV.	Wineberg 2008a, MRID 47560102

A1 Table 6: Skin Irritation Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbit, New Zealand white, young adult males, 2830-3024 g, (n=3)	**Technical grade aminocyclopyrachlor** Dermal exposure to 0.5 g aminocyclopyrachlor acid (technical grade) (92.2% a.i.) for 4 hours: Moistened test material was applied to a 6 cm^2 area of the shaved skin from the scapular to the lumbar region of the back and covered with a gauze pad and held in place with non-irritating tape. The trunk was wrapped with porous tape and secured with waterproof tape. After exposure period, excess material was removed with warm water and skin was patted dry. Individual test sites were scored according to the Draize Scale (1959) at approximately 1, 24, 48, and 72 hours after patch removal.	Well-defined erythema (score 2) observed in one rabbit immediately after patch removal, which decreased to very slight erythema (score 1) by 1 hour and cleared completely by 24 hours. The formulation was slightly irritating based on the Primary Irritation Index (PII) = 0.08. Aminocyclopyrachlor technical is classified as EPA Toxicity Category IV (not an irritant) for primary dermal irritation**.**	Carpenter (2007a) MRID 47560003
Rabbit, New Zealand white, young adult males, 2590-2867 g, (n=3)	**DuPont™ Method® 240SL** Dermal exposure to 0.5 g aminocyclopyrachlor (22.4%) [DPX-MAT28 240 g/L SL] for 4 hours. Moistened test material was applied to a 6 cm^2 area of the shaved skin from the scapular to the lumbar region of the back and covered with a gauze pad and held in place with non-irritating tape. The trunk was wrapped with porous tape and secured with waterproof tape. After exposure period, excess material was removed with warm water and skin was patted dry. Individual test sites were scored according to the Draize Scale (1959) at approximately 1, 24, 48, and 72 hours after patch removal.	No dermal irritation or clinical signs of toxicity were observed and no body weight loss occurred. In this study, the formulation was non-irritating. Aminocyclopyrachlor (22.4%) [DPX-MAT28 240 g/L SL] is classified as EPA Toxicity Category IV (not an irritant) for primary dermal irritation. Primary Dermal Irritation Index (PDII) = 0.0.	Carpenter (2008f) MRID 47560104
Rabbit, New Zealand white, young adult males, 2128-2614 g, (n=3)	**DuPont™ Method® 50SG** Dermal exposure to 0.59g aminocyclopyrachlor [(DPX-MAT28) 50SG (49.80%) for 4 hours. Ground test material moistened with distilled water to achieve a dry paste by preparing an 85% w/w mixture was placed onto a gauze pad and applied to one 6-cm^2 intact dose site on each animal. The pad and entire trunk of each animal were then wrapped with semi-occlusive tape to avoid dislocation of the pad. Elizabethan collars were placed on each rabbit. Individual dose sites were scored according to the Draize scoring system (1944) at approximately 30-60 minutes, 24, 48 and 72 hours after patch emoval.	At 1 hour post patch removal, very slight (score 1, 2/3 rabbits) to well-defined (score 2, 1/3 rabbits) erythema was observed at all three treated sites, and two sites showed slight (score 1) edema. All dermal irritation resolved by 48 hours post treatment. Primary Dermal Irritation Index (PDII) = 1.17. DPX-MAT28-034 was slightly irritating and is classified as EPA Toxicity Category IV (not an irritant).	Moore (2008h) MRID 47560109

A1 Table 7: Skin Sensitization Studies			
Species	**Exposure**	**Response**	**Reference**
Mice, CBA/JHsd (F), approx. 9-weeks-old, 21.3-23.2 g, 5/dose group	**Technical grade aminocyclopyrachlor** This is a local lymph node assay study. Exposure entailed the topical application of 25 µL of technical grade aminocyclopyrachlor acid (92.2% a.i.) to the dorsal surface of each ear once/day for 3 consecutive days. On day 5, the mice were injected intravenously with 20 µCi of ^{3}H-thymidine/mouse. N,N-dimethylformamide (DMF) was the vehicle. The positive control was α-hexylcinnamaldehyde (HCA) in DMF. Working Note: Table A.2.1. on page 44/76 in U.S. EPA/OPP (2010a) indicates that this study was conducted on guinea pigs. This appears to be an error. The DER as well as the bibliography from EPA indicates that this study was conducted in mice.	No statistically significant increases in cell proliferation measurements, relative to controls; no dermal sensitization response observed in mice.	Carpenter (2007e) MRID 47560004
Mice, CBA/JHsd (F), approx. 9-weeks-old, 21.1-22.4 g, 5/dose group	**DuPont™ Method® 240SL** Exposure entailed the topical application of 25 µL of aminocyclopyrachlor (22.4% a.i.) [DPX-MAT28 240 g/L SL] to the dorsal surface of each ear once/day for 3 consecutive days. On day 5, the mice were injected intravenously with 20 µCi of ^{3}H-thymidine/mouse. N,N-dimethylformamide (DMF) was the vehicle. The positive control was α-hexylcinnamaldehyde (HCA) in DMF.	No statistically significant differences in body weights or body weight gains, relative to control; no treatment-related clinical signs of toxicity; no statistically significant increases in cell proliferation measurements, relative to controls. Aminocyclopyrachlor (22.4%) not considered to a dermal sensitizer	Carpenter 2008c MRID 47560105
Mice, CBA/JHsd (F), approx. 11-weeks-old, 23.3-24.5 g, 5/dose group	**DuPont™ Method® 50SG** Exposure entailed the topical application of 25 µL of Aminocyclopyrachlor 50SG (49.80% a.i.) to the dorsal surface of each ear once/day for 3 consecutive days. On day 5, the mice were injected intravenously with 20 µCi of ^{3}H-thymidine/mouse. N,N-dimethylformamide (DMF) was the vehicle. The positive control was α-hexylcinnamaldehyde (HCA) in DMF.	No statistically significant differences in body weights or body weight gains, relative to control; no treatment-related clinical signs of toxicity; no statistically significant increases in cell proliferation measurements, relative to controls. Aminocyclopyrachlor 50SG did not produce dermal sensitization response in mice.	Carpenter (2008a) MRID 47560110

A1 Table 8: Eye Irritation Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbit, white New Zealand (M), young adults, 3167-3610 g (n=3)	**Technical grade aminocyclopyrachlor** 0.1 mL (approximately 86 mg) aminocyclopyrachlor acid (92.2% a.i.) instilled into the conjunctival sac of the right eye; untreated eye served as control. Treated and control eyes remained unwashed and ocular irritation was evaluated according to Draize et al. (1959) at 1, 24, 48, and 72 hours after exposure.	No corneal opacity observed in any treated animals. Adverse effects included: Iritis (score 1): 1/3 rabbits up to 48 hours post treatment with clearance at 72 hours;, Conjunctival redness (score 2): 3/3 rabbits at 1 hour, in 2/3 rabbits at 24 hours with clearance by 48 hours; Conjunctival chemosis (score 2): 1/3 rabbits at 1 hour. All ocular irritation resolved by 72 hours. Highest maximum mean total score was 8.3 recorded at 1 hour post treatment. Technical grade aminocyclopyrachlor acid is classified as EPA Toxicity Category III: Slightly irritating	Carpenter (2007d) MRID 47560002
Rabbit, white New Zealand (M), young adults, 2934-2936 g (n=3)	**DuPont™ Method® 240 SL** 0.1 mL (approximately 77 mg) aminocyclopyrachlor (22.4%) [DPX-MAT28 240 SL] instilled into the conjunctival sac of the right eye; untreated eye served as control. Treated and control eyes remained unwashed and ocular irritation was evaluated according to Draize et al. (1959) at 1, 24, 48, and 72 hours after exposure.	No corneal opacity, iritis, conjunctival redness, chemosis, or discharge was observed in any of the treated eyes. Since the formulation was non-irritating. DPX-MAT28-011 is classified as EPA Toxicity Category IV (not an irritant) for primary eye irritation.	Carpenter (2008d) MRID 47560103
Rabbit, white New Zealand (M), young adults, 2181-2622 g (n=3)	**DuPont™ Method® 50SG** 0.07g aminocyclopyrachlor [(DPX-MAT28) 50SG (49.80%) instilled into the conjunctival sac of the right eye; untreated eye served as control. Ocular irritation was evaluated using a high-intensity white light in accordance with Draize et al (1944) at 1, 24, 48 and 72 hours and at 4 and 7 days post instillation.	Corneal opacity (score 1) was observed in 2/3 eyes at 1 hour, in 3/3 eyes from 24 to 72 hours, and in 2/3 eyes on Day 4. Iritis (score 1) was observed in 2/3 eyes at 1 hour and in 3/3 eyes from 24 to 72 hours. Conjunctival redness (score 2) was observed in 2/3 eyes at 1 hour, in 3/3 eyes at 24 and 48 hours and in 2/3 eyes at 72 hours and on Day 4. Conjunctival discharge (score 2) was observed in 1/3 eyes at 24 and 48 hours. All ocular irritation was resolved by Day 7. DPX-MAT28-034 is classified as EPA Toxicity Category III (slightly irritating) for primary eye irritation.	Moore (2008g) MRID 47560108

A1 Table 9: Cyclopropanecarboxylic acid Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Gavage			
Rabbits, Dutch-belted, 10/dose group (controls n=9)	0, 10, or 20 mg/kg/day panadiplon [*which is metabolized to cyclopropanecarboxylic acid*] by gavage for 14 days Vehicle: 1.25% low viscosity, micro-crystalline cellulose and sodium Carboxymethyl-cellulose NF, 0.2% polysorbate NF food grade, and 0.1N sodium hydroxide in purified water USP without sorbic acid	LOAEL = 2.55 mg/kg/day based on gross liver lesions and microscopic effects of microvesicular hepatic steatosis (fatty degeneration) and necrosis. NOAEL not observed. RfD = 0.00087 mg/kg/day **(For chronic dietary exposures, an additional 3X uncertainty factor was added for extrapolation from a 14 day study to chronic exposure)**	Ulrich et al. 1994, MRID 47916803 (discussed in U.S. EPA/OPP 2010j)
Note on Ulrich et al. 1994: The LOAEL for panadiplon ($LOAEL_P$) was converted to a LOAEL for CPCA ($LOAEL_C$) based on molecular weight and mole fraction, assuming a metabolic conversion of panadiplon to cyclopropanecarboxylic acid. $LOAEL_P$ = 10 mg/kg/day x [(86.09 g CPCA/mole) / (337.35 g panadiplon/mole)] x [1 mole CPCA/mole panadiplon]= 2.55 mg/kg/day = $LOAEL_C$. See Section 3.1.15.1 for discussion.			
Rats, Crl:CD(SD), 10/sex/group.	Gavage doses of 0, 2, 10, 30, and 60 mg/kg bw/day approximately 90 days – i.e., 92-93 days for males and 93/94 days for females.	No mortality, signs of toxicity, or effects on body weight. 60 mg/kg bw/day: Increase (*mild*, NOS) in absolute neutrophil and monocyte counts in male rats. Increase in absolute neutrophil counts in female rats. Increase in aspartate aminotransferase and bile acids in both sexes. Histopathological changes in liver (fatty changes), thymus (lymphoid necrosis), pancreas (decreased zymogen in actinar cells) and heart (myocardial vacuolation, cardiomyopathy). Increase in liver and kidney weights (both sexes). Liver weight increase associated with fatty changes. No kidney pathology. 30 mg/kg bw/day: Increased aspartate aminotransferase (females only). Histopathological changes in liver and heart (see above). Increase in liver and kidney weights (females). Liver weight increase associated with fatty changes. No kidney pathology. 2 and 10 mg/kg bw/day: No effects. Working Note: Study summary does not give data on the magnitude of the changes in liver or kidney weight.	Carpenter 2012 Summary provided by DuPont™.

Appendix 2: Toxicity to Birds

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A2 Table 1: Acute Oral/Gavage Toxicity to Birds

Species	Exposure	Response	Reference[1]
Bobwhite Quail (*Colinus virginianus*), (M,F), 20-weeks-old, 179-221 g (males), 168-219 g (females), 10/sex/dose group	Technical grade aminocyclopyrachlor (92.2% purity) by gavage for 14 days Nominal dose levels: 0 (vehicle control), 269, 448, 747, 1245, or 2075 mg a.e./kg bw Measured concentrations were not verified.	No mortality or sublethal effects observed; no signs of toxicity or effects on body weight or food consumption: LD_{50} >2075 mg a.e./kg-bw NOAEC = 2075 mg a.e./kg-bw *Practically Non-toxic* *Acceptable*	Gallagher and Beavers (2007) MRID 47560118

A2 Table 2: Acute Dietary Toxicity to Birds			
Species	**Exposure**	**Response**	**Reference[1]**
Bobwhite Quail (*Colinus virginianus*), 10-days-old, 18-25 g	Technical grade aminocyclopyrachlor acid (92.2% purity) in diet for 8 days (5 days with treated feed followed by 3 days with untreated feed). Nominal concentrations: 0 (negative control), 562, 1000, 1780, 3160, or 5620 mg a.e./kg diet Mean measured concentrations: <25.0 (<LOD, control), 555, 982, 1790, 3200, and 5290 mg a.e./kg diet Estimated daily dietary doses (using body weight and food consumption data): 129, 212, 389, 719, and 1177 mg a.e./kg bw/day	No mortality or sublethal effects observed; no signs of toxicity or effects on body weight or food consumption: LC_{50} >5290 mg a.e./kg-bw or 1177 mg a.e./kg bw. NOAEC = 1177 mg a.e./kg bw. *Practically Non-toxic Acceptable*	Hubbard et al. (2007b) MRID 47560120
Mallard duck (*Anas platyrhynchos*), 10-days-old, 132-178 g,	Technical grade aminocyclopyrachlor acid (92.2% purity) in diet for 8 days (5 days with treated feed followed by 3 days with untreated feed). Nominal concentrations: 0 (negative control), 562, 1000, 1780, 3160, or 5620 mg a.e./kg diet Mean measured concentrations: <25.0 (<LOD, control), 555, 982, 1790, 3200, and 5290 mg a.e./kg diet Estimated daily dietary doses (using body weight and food consumption data): 208, 439, 779, 1530,and 2423 mg a.e./kg bw/day	No mortality or sublethal effects observed; no signs of toxicity or effects on body weight or food consumption: LC_{50} >5290 mg a.e./kg-diet, equivalent to 2423 mg a.e./kg bw. NOAEC = 2423 mg a.e./kg bw. *Practically Non-toxic Acceptable*	Hubbard et al. (2007a) MRID 47560119

A2 Table 3: Reproductive Toxicity in Birds

Species	Exposure	Response	Reference[1]
Bobwhite Quail (*Colinus virginianus*), 20-weeks-old, 179-233 g (males), 180-202 g (femlaes), 16 pairs/dose group	Technical grade aminocyclopyrachlor acid (92.2% purity) in diet for 22 weeks. Nominal concentrations: 0 (control), 160, 400, or 1000 mg a.i/kg dw diet (adjusted for purity). Duration: 11 weeks pre-laying and 11 weeks during egg-laying. Mean measured concentrations: <LOD (control), 159, 382, or 994 mg a.e./kg diet Average daily doses based on measured food consumption and body weights: 0, 16.1, 40.0, and 100.9 mg/kg bw/day.	No treatment related effects on signs of toxicity, food consumption, body weight, or reproductive parameters. Study is classified as ***invalid***: cages were 6 times smaller than recommended in guideline which may have contributed to the seven incidental deaths. Other adverse effects attributed to the inadequate cage size include, bruising, fractures and necrotic lesions. See Section 4.1.2.2.3 for discussion. *DER indicates: Due to the timing of the mortalities, the lack of a concentration response, and the nature of lesions observed at necropsy, none of the deaths were considered to be treatment related. The NOAEC =1000 mg a.i /kg diet.*	Temple et al. (2008b) MRID 47560121
Mallard duck (*Anas platyrhynchos*), (M, F), 21-weeks-old, 976-1302 g (males), 856-1205 g (females), 16 pairs/dose group	Technical grade aminocyclopyrachlor acid (92.2% purity) in diet for 22 weeks. Nominal concentrations: 0 (control), 160, 400, or 1000 mg a.i/kg dw diet (adjusted for purity). Duration: 11 weeks pre-laying and 11 weeks during egg-laying. Mean measured concentrations: <LOD (control), 159, 382, or 994 mg a.e./kg diet Average daily doses based on measured food consumption and body weights: 0, 18.7, 47.7, and 126.7 mg a.e./kg bw/day.	No treatment related effects on signs of toxicity, food consumption, body weight, or reproductive parameters. Study is classified as I***nvalid***: cages were 3 times smaller than recommended in guideline which may have contributed to the three incidental deaths in the control group and two in the lower treatment groups. *Additionally, sixteen hens in the control and treatment groups were observed to be non-productive (less than ten eggs laid). Necropsy showed that egg yolk peritonitis was apparent in the non-laying hens. Although this endpoint may not be treatment related, the health of the birds is questionable* (U.S. EPA/OPP 2010b, p. 42). See Section 4.1.2.2.3 for discussion. DER indicates: *No other mortalities occurred during the study. Due to the timing of the mortalities, the lack of a concentration response, and the nature of lesions observed at necropsy, none of the deaths were considered to be treatment related. NOAEC = 1000 mg a.e./kg diet.*	Temple et al. (2008a) MRID 47560122

Appendix 3: Toxicity to Terrestrial Invertebrates.

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A3 Table 1: Honeybees

Species	Exposure	Response	Reference
Honey bee (*Apis mellifera*), young adult female worker bees (50 bees per dose)	Aminocyclopyrachlor acid (92.2%) in **contact toxicity** study Nominal doses: 0 (negative control), 6.25, 12.5, 25, 50, or 100 µg a.e./bee. Negative control: tap water with anesthetization. Observation period: 4, 24 and 48 hours after application. Body weights not reported. For dose conversion, an average body weight of 116 mg is used from Winston (1987).	No mortality or sublethal effects observed after 48 hours: LC_{50} >100 µg a.e./bee NOAEL = 100 µg a.e./bee LOAEL >100 µg a.e./bee *Practically non-toxic* *Acceptable* Based on an average body weight of 116 mg, the NOAEL dose is estimated at 862 mg a.e./kg bw [0.1 mg a.e. ÷ 0.000116 kg bw ≈ 862.069 mg/kg bw].	Warmers (2007a) MRID 47560131

A3 Table 1: Honeybees

Species	Exposure	Response	Reference
Honey bee (*Apis mellifera*)), young adult female worker bees (50 bees per dose)	Aminocyclopyrachlor acid (92.2%) in **oral toxicity** study Nominal doses: 0 (negative control), 6.25, 12.5, 25, 50, or 100 µg a.e./bee Measured doses: 0 (negative control), 7,39, 13.84, 28.09, 53.86, or 123.03 µg a.e./bee Negative control: 50% sucrose solution Observation period: 4, 24 and 48 hours after application. Body weights not reported. For dose conversion, an average body weight of 116 mg is used from Winston (1987).	No significant mortality; sublethal effects observed at 24 hours but not at 48 hours, included one apathetic bee at the 28.09 µg a.e./bee (1/50) treatment level and eight bees with coordination problems at the 112.03 µg a.e./bee treatment level (8/50). Using the Fisher Exact test, the p-value for the 1/50 response is 0.5. The p-value for the 8/50 response is 0.0002885. LC_{50} >112.03 µg a.e./bee NOAEL = 112.03 µg a.e./bee LOAEL >112.03 µg a.e./bee Based on an average body weight of 116 mg and measured dose, the estimated mg/kg bw dose for high group dose (100 µg/bee nominal dose) is estimated at 966 mg/kg bw [0.11203 mg a.e. ÷ 0.000116 kg bw ≈ 965.7759 mg/kg bw]. For the 50 µg/bee nominal dose, the estimated mg/kg bw dose for is estimated at 464 mg/kg bw [0.05386 mg ÷ 0.000116 kg ≈ 464.31 mg/kg bw].	Warmers (2007a) MRID 47560131

A3 Table 2: Earthworms

Species	Exposure	Response	Reference
Earthworm (*Eisenia fetida*)	Aminocyclopyrachlor methyl ester. Soil concentrations of 123, 203, 334, 551, and 909 mg a.e./kg-dw soil for 14 days	NOAEC: 203 mg a.e./kg soil. LOAEC: 334 mg a.e./kg soil based on decreased body weights.	MRID 475602-08 as summarized in U.S. EPA/OPP 2010b, p. 44

Appendix 4: Toxicity to Terrestrial Plants

A4 Table 1: Vegetative Vigor 186
A4 Table 2: Seedling Emergence 188

Note on nomenclature: This appendix summarizes studies submitted to OECD (Porch and Kendall 2010a,b). These studies use terms that are different from those used in most reports submitted to U.S. EPA/OPP. To maintain consistency with the original studies, the OECD terms are used in the following tables. The OECD terms are defined below with the corresponding terms from EPA:

NOER: No Observed Effect Rate, equivalent to EPA NOAEC.
ER_{25}: Rate associated with a 25% response, equivalent to EPA EC_{25}.

The "R" in NOER and ER_{25} refers to the application Rate. In the main body of this risk assessment, on the EPA terminology is used.

A4 Table 1: Vegetative Vigor

Form	Exposure	Species/Response	Reference
Monocots			
	Aminocyclopyrachlor 50SG (formulation containing 50% a.i) foliar application (at rates ranging from 0.012 to 400 g a.e./ha) to seedling plants. Applications were made with a track sprayer calibrated to apply approximately 400 L water/ha. Test duration was 21 days.	Summary from OECD DuPont™-28150 Species / End-point (NOER) / **g a.e./ha** NOER / ER_{25} Corn (**most sensitive monocot**) / Shoot Height and Dry Weight / 25 / 58.4 Oat / All endpoints / 100 / 149 Onion / Survival / 50 / 73.6 Ryegrass / All endpoints / 400 / >400 Note: OECD report expresses results in **g a.e./ha.** Summary below in lb a.e./acre. **Most Sensitive Species:** Corn, NOER: 0.022 lb a.e./acre, ER_{25}: 0.052 lb a.e./acre. **Most Tolerant Species:** Ryegrass, NOER: 0.36 lb a.e./acre, ER_{25}: not determined.	Porch and Kendall 2010b No MRID Assigned. No review from EPA available.
	Aminocyclopyrachlor (76.5%) *ester formulation*	Summary from U.S. EPA/OPP 2010b, p. 46 Species / End-point / lb a.e./acre NOAEC / EC_{25} Corn / Shoot Height / 0.012 / 0.096 Oat / Dry Weight / 0.033[1] / 0.16 Onion* / Dry Weight / 0.0028 / **0.0058** Ryegrass / None / 0.355 / **>0.355** [1] EC05 rather than NOAEC. Extrapolated value.	MRID 47560133 (summarized in U.S. EPA/OPP 2010b)

A4 Table 1: Vegetative Vigor

Form	Exposure	Species/Response	Reference
Dicots			
	Aminocyclopyrachlor 50SG (formulation containing 50% a.i) foliar application (at rates ranging from 0.012 to 400 g a.e./ha) to seedling plants. Applications were made with a track sprayer calibrated to apply approximately 400 L water/ha. Test duration was 21 days. `Working Note: NOER determined with Jonckheere-Terpstra or Dunnett's test. ER25s determined with non-linear regression. Thus, in some cases, the estimated ER25 may be lower than the NOER.`	Summary from OECD DuPont™-28150 Species / End-point (NOER) / **g a.e./ha** NOER / ER_{25} Bean (**most sensitive dicot**) / Shoot Height / 0.049 / 0.0246 Cucumber / Shoot Dry Weight / 0.78 / 1.33 Oilseed Rape / Shoot Height / 0.049 / 0.384 Soybean / Shoot Height / 0.20 / 0.706 Sugarbeet / Shoot Dry Weight / **0.78** / **0.896** Tomato / Shoot Dry Weight / 0.049 / 0.461 Note: OECD report expresses results in **g a.e./ha.** Summary below in lb a.e./acre. **Most Sensitive Species:** Bean, NOER: 0.000044 lb a.e./acre, ER_{25}: 0.000022 lb a.e./acre. **Most Tolerant Species:** Cucumber, NOER: 0.00078 lb a.e./acre, ER_{25}: **0.0012 lb a.e./acre.**	Porch and Kendall 2010b No MRID Assigned. No review from EPA available.
	Aminocyclopyrachlor (76.5%) *ester formulation*	Summary from U.S. EPA/OPP 2010b, p. 46 Species / End-point / lb a.e./acre NOAEC / EC_{25} Bean* / Shoot Height / **0.00000078**[1] / 0.000075 Cucumber / Dry Weight / 0.00035 / **0.00098** Oilseed Rape / Shoot Height / 0.00035 / 0.0004 Soybean / Dry Weight / 0.000068 / 0.00064 Sugarbeet / Dry Weight / 0.00018 / 0.00056 Tomato / Dry Weight / 0.00018 / 0.00073	MRID 47560133 (summarized in U.S. EPA/OPP 2010b)

[1]In cases where there was not a definitive NOAEC, the EC_{05} is presented; however, there is very little confidence in these values, as they were outside the range of treatment concentrations (U.S. EPA/OPP 2010b)
*Species with the lowest EC_{25}; used for risk quantification in U.S. EPA/OPP (2010b)

A4 Table 2: Seedling Emergence

Form	Exposure	Species/Response	Reference
Monocots			
	Aminocyclopyrachlor 50SG (formulation containing 50% a.i) soil surface application (at rates ranging from 0.0051 to 400 g a.e./ha) to planted seeds prior to emergence. Applications were made with a track sprayer calibrated to apply approximately 400 L water/ha. Test duration was 21 days.	Summary from OECD DuPont™-28149 Species / End-point (NOER) / **g a.e./ha** NOER / ER_{25} Corn / Survival / 200 / >400 Oat / Survival / 100 / >400 Onion (**most sensitive monocot**) / Shoot Dry Weight / 3.1 / 21.6 Ryegrass / Shoot Dry Weight / 400 / 396 Note: OECD report expresses results in **g a.e./ha.** Summary below in lb a.e./acre. **Most Sensitive Species:** Onion, NOER: 0.0028 lb a.e./acre, ER_{25}: 0.019 lb a.e./acre. **Most Tolerant Species:** Ryegrass, NOER: 0.36 lb a.e./acre, ER_{25}: 0.35 lb a.e./acre.	Porch and Kendall 2010a No MRID Assigned. No review from EPA available.
	Aminocyclopyrachlor (76.5%) *ester formulation*	Summary from U.S. EPA/OPP 2010b, pp. 45-46 Species / End-point / lb a.e./acre NOAEC / EC_{25} Corn / Shoot Height / 0.0394 / 0.15 Oat / None / 0.355 / >0.355 Onion* / Shoot Height / 0.0394 / 0.048 Ryegrass / Dry Weight / 0.0394 / 0.075	MRID 47560132 (summarized in U.S. EPA/OPP 2010b)

Note: Seedling Emergence Assays for dicots on following page.

A4 Table 2: Seedling Emergence

Form	Exposure	Species/Response	Reference
Dicots			
	Aminocyclopyrachlor 50SG (formulation containing 50% a.i) soil surface application (at rates ranging from 0.0051 to 400 g a.e./ha) to planted seeds prior to emergence. Applications were made with a track sprayer calibrated to apply approximately 400 L water/ha. Test duration was 21 days. `Working Note: NOER determined with Jonckheere-Terpstra or Dunnett's test. ER25s determined with non-linear regression. Thus, in some cases, the estimated ER25 may be lower than the NOER.`	Summary from OECD DuPont™-28149 Species / End-point (NOER) / **g a.e./ha** NOER / ER_{25} Bean (**most sensitive dicot**) / Shoot Height / 0.39 / 0.250 Cucumber / Shoot Dry Weight and Survival / 50 / 41.4 Oilseed Rape / Shoot Dry Weight / 6.3 / 6.88 Soybean / Shoot Height / 0.20 / 8.88 Sugarbeet / Shoot Dry Weight / 0.20 / 1.66 Tomato / Shoot Dry Weight / 11 / 16.2 Note: OECD report expresses results in **g a.e./ha.** Summary below in lb a.e./acre. **Most Sensitive Species:** NOAEC: Soybean and Sugarbeet, 0.00018 lb a.e./acre. ER25, Bean,: 0.00022 lb a.e./acre. **Most Tolerant Species:** Cucumber, NOER: 0.045 lb a.e./acre, ER_{25}: 0.037 lb a.e./acre.	Porch and Kendall 2010a No MRID Assigned. No review from EPA available.
	Aminocyclopyrachlor (76.5%) *ester formulation*	Summary from U.S. EPA/OPP 2010b, pp. 45-46 Species / End-point / lb a.e./acre NOAEC / EC_{25} Bean / Dry Weight / 0.00147 / 0.0053 Cucumber / Dry Weight / 0.0131 / 0.032 Oilseed Rape / Dry Weight / 0.00439 / 0.0025 Soybean / Dry Weight / 0.000012[1] / 0.00077 Sugarbeet* / Shoot Height / 0.000439 / 0.00053 Tomato / Dry Weight / 0.00439 / 0.0047	MRID 47560132 (summarized in U.S. EPA/OPP 2010b)

[1]In cases where there was not a definitive NOAEC, the EC_{05} is presented; however, there is very little confidence in these values, as they were outside the range of treatment concentrations (U.S. EPA/OPP 2010b)

*Species with the lowest EC_{25}; used for risk quantification in U.S. EPA/OPP (2010b)

Appendix 5: Toxicity to Fish.

A5 Table 1: Acute Toxicity 190
A5 Table 2: Longer-term Exposures..... 191

A5 Table 1: Acute Toxicity

Species	Exposure	Response	Reference
Freshwater			
Rainbow trout *(Oncorhynchus mykiss)*, wet weight: 1.0 (0.67-1.5) g, total length: 4.6 (4.2-5.3) cm, 10/dose group	Nominal concentrations of 0 (negative control), 7.5, 15, 30, 60, or 120 mg a.i. /L [mean-measured concentrations: <0.0210 (<LOD, control), 7.6, 15, 30, 62, or 122 mg a.i./L] aminocyclopyrachlor acid (92.2%) under static conditions for 96 hours.	No mortality or sublethal effects: LC_{50}: > 122 mg a.i./L NOAEC: 122 mg a.i./L *Practically Non-toxic Acceptable*	Palmer et al. (2007a) MRID 47560123
Bluegill sunfish (*Lepomis macrochirus*), juvenile, mean wet weight: 0.09 (0.05-0.13) g; mean total length: 2.1 (1.9-2.3) cm, 10/replicate	Technical grade (92.2%) aminocyclopyrachlor acid in static/flow-through test for 96 hours at measured concentrations of 0 (negative control), 7.5, 15, 30, 60, or 120 mg a.i./L. Observations made at 4, 24, 48, 72, and 96 hours of exposure.	No mortality or signs of sublethal effects: LC_{50}: >120 mg a.i./L (95% C.I. N/A) NOAEC: 120 mg a.i./L *Practically Non-toxic Acceptable*	Gallagher et al. (2007a) MRID 47560124
Marine			
Sheepshead minnow (*Cyprinodon variegatus*), juvenile, mean wet weight: 0.18 (0.13-0.26) g; mean total length: 2.2 (1.0-2.5) cm, 10/replicate w/3 replicates	Aminocyclopyrachlor acid (92.2%) in limit test study with nominal concentrations of 0 (negative control) and 120 mg a.i./L; measured concentrations of <0.0294 (LOD; control) and 120 mg a.i./L for 96 hours under static conditions. . Observations made at 4.5, 24, 48, 72, and 96 hours of exposure.	No observed mortality or treatment-related effects: 96-hr LC_{50}: > 129 mg a.i./L NOAEC: 129 mg a.i./L *Practically Non-toxic Acceptable*	Gallagher et al. (2008a) MRID 47560125

A5 Table 2: Longer-term Exposures			
Species	**Exposure**	**Response**	**Reference**
Rainbow trout (*Oncorhynchus mykiss*), early life stage: fertilized eggs/embryos, <24-hours-old), 120/test concentration, 4 replicates	Aminocyclopyrachlor acid (92.2%) at nominal concentrations of 0 (negative control), 0.75, 1.5, 3.0, 6.0, or 12 mg a.e./L; measured concentrations (identical to TWA concentrations): <0.00245 (<LOD, control), 0.69, 1.5, 2.9, 5.8, or 11 mg a.e./L for 90 days under flow-through conditions	No treatment-related effects observed on hatching success, time to hatch, post-hatch survival, time to swim-up or growth at any treatment level: LC/EC_{50} >11 mg a.e./L NOAEC: 11 mg a.e./L LOAEC: > 11 mg a.e./L *Acceptable*	Gallagher et al. (2008c) MRID 47560130

Appendix 6: Toxicity to Aquatic Invertebrates

A6 Table 1: Acute Toxicity 192
A6 Table 2: Chronic toxicity 193

A6 Table 1: Acute Toxicity

Species	Exposure	Response	Reference
Freshwater			
Water flea (*Daphnia magna*), 1st instar (<24-hours old), 5/replicate w/4 replicates	Aminocyclopyrachlor (acid) (92.2% a.e.) at nominal concentrations of 0 (negative control), 3.8, 7.5, 15, 30, 60 or 120 mg a.e./L (mean-measured concentrations of <LOD (control), 3.7, 7.4, 15, 30,59 or 120 mg a.e./L for 48 hours under static conditions (no solvent) Observations made at 5, 24, and 48 hours.	Lethargy observed in all but the lowest treatment group: LC_{50} = 39.7 mg a.e./L (95% CI = 27.2-65.6 mg a.e./L NOAEC = 3.7 mg a.e./L (based on mortality and sublethal effects (i.e., lethargy) *Slightly toxic* *Acceptable*	Gallagher et al. (2007b) MRID 47560126
Marine			
Eastern Oyster (*Crassostrea virginica*), initial length: 43.6 (37.7-49.8) mm, 20/treatment level	Aminocyclopyrachlor acid (92.2%) in shell deposition study at nominal concentrations of 0 (negative control), 7.5, 15, 30, 60 or 120 mg a.e./L; mean-measured concentrations: <0.0184 (<LOD, control), 8.2, 14, 33, 67, or 118 mg a.e./L (93-112% of nominal) for 96 hours under flow-through conditions.	Significant reduction in shell deposition observed only in highest dose group: IC_{50} >118 mg a.e./L LC_{50} > 118 mg a.e./L EC_{50} > 118 mg a.e./L NOAEC = 67 mg a.e./L *Practically Non-toxic* *Acceptable*	Gallagher et al. (2008d) MRID 47560127
Mysid shrimp (*Americamysis bahia*), juveniles (<24 hours old), 20/treatment level, equally divided among two replicates.	Aminocyclopyrachlor acid (92.2% a.e.) at nominal concentrations of 0 (negative control), 7.5, 15, 30, 50 or 120 mg a.e./L; mean-measured concentrations: <0.0181 (<LOD; control), 7.5, 15, 30, 60, or 122 mg a.e./L under static conditions for 96 hours. No solvent used. Observations made every 24 hours.	No significant treatment-related effects: LC_{50} >122 mg a.e./L (95% C.I. N/A) NOAEC = 122 mg a.e./L *All toxicity values were visually determined based on the mean-measured concentrations.* *Practically Non-toxic* *Acceptable*	Gallagher et al. (2008b) MRID 47560128

A6 Table 2: Chronic toxicity			
Species	**Exposure**	**Response**	**Reference**
Water flea (*Daphnia magna*), 1st instar, <24-hours-old, 1/replicate, 10 replicates.	Technical grade aminocyclo-pyrachlor acid (92.2%) at nominal concentrations of 0, (negative control), 0.38, 0.75, 1.5, 3.0, or 6.0 mg a.e./L**; mean-measured concentrations**: <0.00215 (<LOD, control) 0.37, 0.73, 1.5, 3.0, or 6.0 mg a.e./L for 21 days under static renewal conditions	LC_{50} >6.0 mg a.e./L NOAEC: N/A (less than the lowest concentration tested) LOAEC: 0.37 mg a.e./L EPA commentary: *This study is classified as **Supplemental**: no dose-response mortalities were observed in 0.37 mg a.e. /L (40%), 0.73 mg a.e. /L (30%), and 1.5 mg a.e./L (40%) exposure groups. Additionally, immobility was observed in all treatment levels of the second range-finding test; however, data for the range-finding tests were not provided. Finally, in the acute water flea study (MRID 475601-26), sublethal effects and mortality provided a NOAEC of 3.7 mg a.e./L; **this comparison suggests a possible issue with the health of the test organisms in this chronic study.*** `Working Note: Only 10% mortality was noted at 3 and 6 mg a.e./L.`	Gallagher et al. (2008e) MRID 47560129
Water flea (*Daphnia magna*), 1st instar, <24-hours-old, 1 daphnid/ test chamber, 10 neonates/concentration, 10 replicates	Technical grade aminocyclo-pyrachlor acid (88.4%) at nominal concentrations: dilution water control, 0.63, 1.3, 2.5, 5.0 or 10 mg a.e./L; corresponding mean, **measured concentrations**: ND (limit of detection of 0.000228) 0.61, 1.3, 2.4, 4.9 or 9.9 mg a.e./L in unaerated, static-renewal conditions for 21 days.	No statistically significant differences in survival or reproduction noted in any of the aminocyclopyrachlor treatment groups, compared with controls. A small but statistically significant difference in mean adult body length observed in the 9.9 mg a.s./L treatment group, compared with controls. 21-day NOEC = 4.9 mg a.e./L (based on adult growth) 21-day LOEC = 9.9 mg a.e./L (based on adult growth) 21 day EC_{50} > 9.9 mg a.e./L (based on mobility) 21 day EC_{50} > 9.9 mg a.e./L (based on reproduction)	Minderhout et al. 2011

Appendix 7: Toxicity to Aquatic Plants

A7 Table 1: Algae 194
A7 Table 2: Macrophytes 196

A7 Table 1: Algae

Species	Exposure	Response	Reference
Freshwater blue-green algae (*Anabaena flos-aquae*), 3 replicates	Technical grade aminocyclopyrachlor acid (92.2%) for 96 hours under static conditions Nominal concentrations: 0 (negative control), 0.36, 1.1, 3.7, 12, 38, or 120 mg a.e./L Mean-measured concentrations: <0.0273 (<LOD, control), 0.0358, 1.11, 3.57, 11.3, 30.9, and 119 mg a.e./L	Endpoints affected included cell density (1-76% inhibition), growth rate (3-22% inhibition), and biomass (-3-73%). Biomass was the most sensitive endpoint. EC_{50} = 7.4 mg a.e./L (biomass) NOAEC = 1.11 mg a.e./L (biomass) No differences in cell morphology between the treated and control groups. *Acceptable*	Porch et al. (2008a) MRID 47560201
Marine diatom (*Skeletonema costatum*), 3 replicates	Technical grade aminocyclopyrachlor acid (92.2%) for 96 hours under static conditions Nominal concentrations: 0 (negative control 7.5, 15, 30, 60, or 120 mg a.e./L Mean-measured concentrations: <0.0281 (<LOD, control), 7.85, 15.5, 28.9, 60.0, or 120 mg a.e./L	No differences in cell morphology between the treated and control groups. Inhibitions for all endpoints were extremely low or nonexistent: cell density (-6.3-5.5%) biomass (-11-0.4%), growth (-1.8-1.5%) most sensitive endpoint not determined. EC_{50} >120 mg a.e./L NOAEC = 120 mg a.e./L *Acceptable*	Porch et al. (2008b) MRID 47560202

A7 Table 1: Algae

Species	Exposure	Response	Reference
Freshwater green algae (*Pseudokirchneriella subcapitata*) , 3 replicates	Technical grade aminocyclopyrachlor acid (92.2%) for 72 hours under static conditions Nominal concentrations: 0 (negative control) 7.5, 15, 30, 60, or 120 mg a.e./L Mean-measured concentrations: <0.0165 (<LOD, control), 7.35, 15.3, 30.1, 59.1, or 120 mg a.e./L `Working Note: The 72 hour exposure period is compliant with OECD guidelines but EPA requires a 96 hour assay. EPA, however, will accept a 72 hour assay for Tier 1 screening.`	No differences in cell morphology between the treated and control groups; no flocculation, aggregation, or adherence occurred in any dose group; no endpoint inhibited by more than 50%: EC_{50} >120 mg a.e./L Growth rate endpoint: EC_{05} = 93 mg a.e./L NOAEC = 59.1 mg a.e./L Cell density and biomass endpoints: EC_{05} = 62 mg a.e./L NOAEC = 15.3 mg a.e./L *Acceptable* [Tier 1 only]	Porch et al. (2008c) MRID 47560203
Freshwater diatom (*Navicula pelliculosa*), 4 replicates	Technical grade aminocyclopyrachlor acid (92.2%) for 96 hours under static conditions Nominal concentrations: 0 (negative control) 7.5, 15, 30, 60, or 120 mg a.e./L Mean-measured concentrations: <0.0149 (<LOD, control), 7.2, 14, 29, 60, or 1119 mg a.e./L	No differences in cell morphology between the treated and control groups, no flocculation, aggregation, or adherence occurred in any dose group. Inhibitions of 96-99% observed for all three endpoints; biomass was the most sensitive endpoint: Cell density endpoint: EC_{50} = 38 mg a.e./L (95% C.I. = 24-61 mg a.e./L) NOAEC : 29 mg a.e./L LOAEC: 60 mg a.e./L Growth rate endpoint: EC_{50} = 39 mg a.e./L (95% C.I. = 27-58 mg a.e./L) NOAEC : 29 mg a.e./L LOAEC: 60 mg a.e./L Biomass endpoint: EC_{05} = 18 mg a.e./L (95% C.I. = 11-29 mg a.e./L) EC_{50} = 38 mg a.e./L (95% C.I. = 30-48 mg a.e./L) NOAEC = 14 mg a.e./L Probit Slope: 5.07 ± 1.02 *Acceptable*	Porch et al. (2008d) MRID 47560204

A7 Table 2: Macrophytes			
Species	**Exposure**	**Response**	**Reference**
Duckweed *(Lemna gibba)*, 3 fronds/plant, 4 plants/replicate,	Technical grade aminocyclopyrachlor acid (92.2%) for 96 hours under static renewal conditions Nominal concentrations: 0 (negative control 0.36, 1.1, 3.7, 12, 38, or 120 mg a.e./L Mean-measured concentrations: <0.0067 (<LOD, control), 0.37, 1.1, 3.7, 12, 38, or 122 mg a.e./L	Most sensitive endpoint not determined since inhibition was not greater than 50%. By termination date, investigators observed isolated incidence of chlorosis, necrosis, and dead fronds observed in all but the highest test level. In the highest test level, some or all of the fronds were small, curled, and/or some or all of the colonies were coagulating (not breaking apart). Frond number: EC_{05} = 21 mg a.e./L (95% C.I. = 9.9-47 mg a.e./L) EC_{50} >122 mg a.e./L NOAEC = 3.75 mg a.e./L Probit Slope: 1.95 ± 0.431 Frond number yield: EC_{05} = 21 mg a.e./L (95% C.I. = 9.6-45 mg a.e./L) EC_{50} >122 mg a.e./L NOAEC = 3.75 mg a.e./L Probit Slope: 2.05 ± 0.447 Biomass: EC_{05} >122 mg a.e./L EC_{50} = >122 mg a.e./L NOAEC = 122 mg a.e./L Growth rate based on frond number: EC_{05} = 38 mg a.e./L (95% C.I. = 22-63 mg a.e./L) EC_{50} >122 mg a.e./L NOAEC = 3.75 mg a.e./L Probit Slope: 1.79 ± 0.381 *Acceptable*	Porch et al. (2008e) MRID 47560134

Aminocyclopyrachlor

Table 1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.000125	0	0
	(0 - 0.00186)	(0 - 1.05E-05)	(0 - 0)
Dry and Temperate	0.000096	6.00E-08	0
Location	(0 - 0.0038)	(0 - 0.00113)	(0 - 0.0005)
Dry and Cold Location	0.163	0.068	0.042
	(0.069 - 0.276)	(0.0303 - 0.128)	(0.0209 - 0.064)
Average Rainfall and	0.0046	2.18E-05	0
Warm Location	(0.00033 - 0.0257)	(3.08E-07 - 0.00054)	(0 - 0)
Average Rainfall and	0.0047	0.000147	1.27E-05
Temperate Location	(0.00076 - 0.027)	(1.56E-05 - 0.00134)	(0 - 0.00029)
Average Rainfall and Cool	0.0048	0.000119	3.90E-06
Location	(0.00091 - 0.0212)	(3.50E-06 - 0.00056)	(0 - 0.000077)
Wet and Warm Location	0.0048	4.60E-06	0
	(0.00035 - 0.0146)	(7.20E-08 - 0.00041)	(0 - 0)
Wet and Temperate	0.00275	7.80E-06	0
Location	(0.000135 - 0.0136)	(1.06E-07 - 0.000309)	(0 - 0)
Wet and Cool Location	0.65	0.215	0.08
	(0.4 - 0.91)	(0.101 - 0.38)	(0.046 - 0.136)
		Average of Central Values:	0.0459
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.91
		Summary of Values:	0.046 (0 - 0.91)

Note: Effective offsite application rate is calculated as the amount of pesticide lost in runoff divided by the treatment area of the adjacent (offsite) field under the assumption that the treated field is the same size as the adjacent non-treated field into which the runoff is transported.

Aminocyclopyrachlor

Table 2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.265 (0.196 - 0.33)	0.246 (0.167 - 0.298)	0.224 (0.148 - 0.278)
Dry and Temperate Location	0.32 (0.232 - 0.37)	0.282 (0.202 - 0.33)	0.237 (0.187 - 0.298)
Dry and Cold Location	0.39 (0.35 - 0.42)	0.37 (0.34 - 0.39)	0.33 (0.273 - 0.36)
Average Rainfall and Warm Location	0.249 (0.235 - 0.286)	0.225 (0.212 - 0.253)	0.223 (0.205 - 0.228)
Average Rainfall and Temperate Location	0.254 (0.235 - 0.288)	0.225 (0.216 - 0.246)	0.223 (0.192 - 0.226)
Average Rainfall and Cool Location	0.269 (0.244 - 0.313)	0.228 (0.22 - 0.257)	0.223 (0.21 - 0.226)
Wet and Warm Location	0.24 (0.237 - 0.24)	0.225 (0.222 - 0.225)	0.224 (0.217 - 0.225)
Wet and Temperate Location	0.239 (0.233 - 0.24)	0.224 (0.219 - 0.225)	0.224 (0.209 - 0.225)
Wet and Cool Location	0.153 (0.09 - 0.232)	0.195 (0.16 - 0.222)	0.205 (0.192 - 0.223)
		Average of Central Values:	0.2486
		25th Percentile of Lower Bounds:	0.194
		Maximum Value:	0.42
		Summary of Values:	0.249 (0.194 - 0.42)

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Table 3: Concentrations (mg/kg) in the top 36 inches of soil.

Site	Clay	Loam	Sand
Dry and Warm Location	0.088 (0.066 - 0.11)	0.082 (0.057 - 0.099)	0.075 (0.052 - 0.095)
Dry and Temperate Location	0.108 (0.079 - 0.124)	0.097 (0.069 - 0.113)	0.084 (0.063 - 0.102)
Dry and Cold Location	0.131 (0.117 - 0.141)	0.125 (0.117 - 0.132)	0.118 (0.104 - 0.128)
Average Rainfall and Warm Location	0.097 (0.087 - 0.109)	0.087 (0.075 - 0.101)	0.077 (0.071 - 0.095)
Average Rainfall and Temperate Location	0.107 (0.096 - 0.116)	0.093 (0.08 - 0.104)	0.077 (0.072 - 0.09)
Average Rainfall and Cool Location	0.116 (0.103 - 0.125)	0.102 (0.087 - 0.116)	0.08 (0.074 - 0.096)
Wet and Warm Location	0.081 (0.08 - 0.088)	0.075 (0.075 - 0.076)	0.075 (0.075 - 0.075)
Wet and Temperate Location	0.08 (0.078 - 0.086)	0.075 (0.073 - 0.075)	0.075 (0.073 - 0.075)
Wet and Cool Location	0.061 (0.044 - 0.087)	0.067 (0.059 - 0.082)	0.071 (0.067 - 0.074)
		Average of Central Values:	0.089
		25th Percentile of Lower Bounds:	0.068
		Maximum Value:	0.141
		Summary of Values:	0.089 (0.068 - 0.141)

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Table 4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	18 (8 - 30)	12 (8 - 30)	12 (8 - 36)
Dry and Temperate Location	24 (12 - 36)	18 (8 - 36)	24 (8 - 36)
Dry and Cold Location	30 (12 - 36)	36 (18 - 36)	36 (24 - 36)
Average Rainfall and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
		Average of Central Values:	31.8
		25th Percentile of Lower Bounds:	15
		Maximum Value:	36
		Summary of Values:	31.8 (15 - 36)

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Table 5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.5	0	0
	(0 - 4.8)	(0 - 0.04)	(0 - 0)
Dry and Temperate	0.4	0.00023	0
Location	(0 - 12.4)	(0 - 10.4)	(0 - 72)
Dry and Cold Location	261	120	84
	(129 - 520)	(60 - 261)	(45 - 139)
Average Rainfall and	15.7	29.5	107
Warm Location	(2.62 - 39)	(2.22 - 103)	(29.9 - 217)
Average Rainfall and	15.8	33	85
Temperate Location	(5.4 - 43)	(5.9 - 76)	(34 - 172)
Average Rainfall and Cool	17.9	42	90
Location	(4.7 - 39)	(18.9 - 80)	(39 - 204)
Wet and Warm Location	35	68	164
	(23.5 - 56)	(41 - 121)	(122 - 238)
Wet and Temperate	35	61	129
Location	(25.7 - 55)	(42 - 105)	(67 - 213)
Wet and Cool Location	450	181	180
	(360 - 700)	(116 - 320)	(137 - 257)
		Average of Central Values:	81.7
		25th Percentile of Lower Bounds:	2.42
		Maximum Value:	700
		Summary of Values:	81.7 (2.42 - 700)

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Table 6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0015	0	0
	(0 - 0.017)	(0 - 0.00011)	(0 - 0)
Dry and Temperate	0.0014	6.0E-07	0
Location	(0 - 0.04)	(0 - 0.07)	(0 - 0.4)
Dry and Cold Location	1.92	0.9	0.6
	(0.9 - 3.3)	(0.4 - 1.52)	(0.3 - 0.9)
Average Rainfall and	0.18	0.6	2.23
Warm Location	(0.016 - 1)	(0.015 - 2.81)	(0.4 - 4.5)
Average Rainfall and	0.23	0.8	1.96
Temperate Location	(0.06 - 1.05)	(0.08 - 2.58)	(0.6 - 4.6)
Average Rainfall and Cool	0.3	1.47	4
Location	(0.08 - 1.18)	(0.4 - 3.4)	(2.06 - 6.3)
Wet and Warm Location	3.8	4.2	5.4
	(2.85 - 5.4)	(3.11 - 6.5)	(3.5 - 7.5)
Wet and Temperate	4	3.9	4.4
Location	(3.04 - 5.5)	(2.55 - 6.2)	(1.93 - 6.8)
Wet and Cool Location	5.2	7.5	8.6
	(3.9 - 7.3)	(5.5 - 9.4)	(5.3 - 10.6)
		Average of Central Values:	2.3
		25th Percentile of Lower Bounds:	0.0155
		Maximum Value:	10.6
		Summary of Values:	2.3 (0.0155 - 10.6)

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Table 7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.14	0	0
	(0 - 2.09)	(0 - 0.014)	(0 - 0)
Dry and Temperate	0.13	0.00007	0
Location	(0 - 4.8)	(0 - 10)	(0 - 96)
Dry and Cold Location	134	57	36
	(56 - 264)	(25 - 113)	(18.4 - 64)
Average Rainfall and	23	77	293
Warm Location	(1.93 - 138)	(2.14 - 410)	(57 - 690)
Average Rainfall and	32	103	238
Temperate Location	(5.8 - 133)	(6.9 - 313)	(59 - 570)
Average Rainfall and Cool	31.1	132	330
Location	(7 - 101)	(31.4 - 300)	(159 - 540)
Wet and Warm Location	167	320	570
	(92 - 370)	(147 - 560)	(390 - 720)
Wet and Temperate	86	101	222
Location	(53 - 178)	(62 - 250)	(104 - 510)
Wet and Cool Location	172	275	312
	(138 - 246)	(148 - 410)	(187 - 540)
		Average of Central Values:	137
		25th Percentile of Lower Bounds:	2.04
		Maximum Value:	720
		Summary of Values:	137 (2.04 - 720)

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Table 8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.05	0	0
	(0 - 0.7)	(0 - 0.006)	(0 - 0)
Dry and Temperate	0.05	0.000027	0
Location	(0 - 2.01)	(0 - 5.1)	(0 - 45)
Dry and Cold Location	67	27.4	18.3
	(27.5 - 120)	(11.3 - 51)	(9 - 30.8)
Average Rainfall and	10.5	38	153
Warm Location	(0.8 - 50)	(1 - 168)	(22.1 - 340)
Average Rainfall and	14	44	113
Temperate Location	(2.93 - 60)	(3.4 - 166)	(38 - 279)
Average Rainfall and Cool	13.3	62	199
Location	(3.8 - 49)	(16.8 - 166)	(88 - 330)
Wet and Warm Location	88	125	200
	(43 - 190)	(66 - 263)	(122 - 350)
Wet and Temperate	47	37	50
Location	(20 - 98)	(14.9 - 81)	(20.2 - 140)
Wet and Cool Location	76	141	175
	(47 - 122)	(86 - 216)	(96 - 284)
		Average of Central Values:	62.9
		25th Percentile of Lower Bounds:	0.9
		Maximum Value:	350
		Summary of Values:	62.9 (0.9 - 350)

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Table 1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	2.64E-07 (0 - 1.71E-06)	0 (0 - 1.78E-09)	0 (0 - 0)
Dry and Temperate Location	2.44E-07 (0 - 2.63E-05)	0 (0 - 0.000005)	0 (0 - 3.30E-06)
Dry and Cold Location	0.00046 (0.000165 - 0.00132)	0.000166 (0.00005 - 0.00052)	0.000108 (3.15E-05 - 0.00035)
Average Rainfall and Warm Location	3.80E-06 (1.14E-06 - 1.14E-05)	9.60E-09 (0 - 7.50E-08)	0 (0 - 0)
Average Rainfall and Temperate Location	4.90E-06 (1.59E-06 - 0.000027)	2.07E-08 (0 - 6.40E-06)	0 (0 - 4.50E-09)
Average Rainfall and Cool Location	3.30E-06 (7.10E-07 - 1.17E-05)	5.90E-09 (0 - 5.60E-07)	0 (0 - 8.90E-10)
Wet and Warm Location	2.86E-06 (8.10E-07 - 8.70E-06)	1.78E-09 (0 - 3.03E-08)	0 (0 - 0)
Wet and Temperate Location	2.11E-06 (4.40E-07 - 8.80E-06)	3.50E-09 (0 - 2.50E-08)	0 (0 - 0)
Wet and Cool Location	5.20E-06 (5.20E-08 - 0.000203)	1.07E-06 (1.52E-07 - 0.000042)	3.06E-07 (3.80E-08 - 1.83E-05)
		Average of Central Values:	0.00002808
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.00132
		Summary of Values:	0.0000281 (0 - 0.00132)

Note: Effective offsite application rate is calculated as the amount of pesticide lost in runoff divided by the treatment area of the adjacent (offsite) field under the assumption that the treated field is the same size as the adjacent non-treated field into which the runoff is transported.

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Table 2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0032 (0.00213 - 0.0054)	0.003 (0.00178 - 0.0049)	0.00256 (0.00145 - 0.0041)
Dry and Temperate Location	0.00281 (0.00178 - 0.0044)	0.00241 (0.00136 - 0.0042)	0.00181 (0.00099 - 0.0033)
Dry and Cold Location	0.0039 (0.00271 - 0.0079)	0.0036 (0.00261 - 0.0074)	0.00245 (0.00173 - 0.0052)
Average Rainfall and Warm Location	0.00283 (0.00202 - 0.0055)	0.00247 (0.00164 - 0.0044)	0.00199 (0.00135 - 0.0039)
Average Rainfall and Temperate Location	0.00249 (0.00177 - 0.0052)	0.00208 (0.00147 - 0.0045)	0.0017 (0.00096 - 0.0038)
Average Rainfall and Cool Location	0.00255 (0.00176 - 0.0048)	0.00199 (0.00135 - 0.0038)	0.00148 (0.00069 - 0.00301)
Wet and Warm Location	0.00233 (0.00162 - 0.005)	0.00196 (0.00126 - 0.0042)	0.0015 (0.00068 - 0.00313)
Wet and Temperate Location	0.00206 (0.00142 - 0.0045)	0.00183 (0.00116 - 0.004)	0.00139 (0.00062 - 0.003)
Wet and Cool Location	1.12E-05 (5.20E-06 - 0.00142)	1.18E-05 (6.60E-06 - 0.00132)	1.07E-05 (6.40E-06 - 0.00087)
		Average of Central Values:	0.00209
		25th Percentile of Lower Bounds:	0.000975
		Maximum Value:	0.0079
		Summary of Values:	0.00209 (0.000975 - 0.0079)

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Table 3: Out_Site01_SOIL36

Site	Clay	Loam	Sand
Dry and Warm Location	0.00107 (0.00071 - 0.00181)	0.00101 (0.00066 - 0.00162)	0.00085 (0.00055 - 0.00138)
Dry and Temperate Location	0.00096 (0.00061 - 0.00154)	0.00081 (0.00051 - 0.00146)	0.00063 (0.00037 - 0.00118)
Dry and Cold Location	0.00131 (0.0009 - 0.00263)	0.00123 (0.00088 - 0.00262)	0.00106 (0.00067 - 0.00233)
Average Rainfall and Warm Location	0.00121 (0.00084 - 0.00219)	0.00111 (0.00066 - 0.00202)	0.00086 (0.00054 - 0.00167)
Average Rainfall and Temperate Location	0.00118 (0.00067 - 0.00234)	0.00096 (0.00061 - 0.00189)	0.00068 (0.00042 - 0.00139)
Average Rainfall and Cool Location	0.00124 (0.00082 - 0.00262)	0.00102 (0.00051 - 0.00207)	0.00067 (0.000304 - 0.00143)
Wet and Warm Location	0.00098 (0.00073 - 0.00194)	0.00088 (0.00062 - 0.0018)	0.00074 (0.0004 - 0.00168)
Wet and Temperate Location	0.00074 (0.00053 - 0.00163)	0.0007 (0.00045 - 0.00156)	0.00061 (0.000294 - 0.0015)
Wet and Cool Location	4.50E-06 (2.23E-06 - 0.00095)	5.20E-06 (3.16E-06 - 0.00082)	4.60E-06 (2.67E-06 - 0.00048)
		Average of Central Values:	0.000834
		25th Percentile of Lower Bounds:	0.00041
		Maximum Value:	0.00263
		Summary of Values:	0.00083 (0.00041 - 0.00263)

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Table 4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	18 (8 - 30)	12 (8 - 30)	12 (8 - 36)
Dry and Temperate Location	24 (12 - 36)	18 (8 - 36)	24 (8 - 36)
Dry and Cold Location	24 (12 - 36)	30 (18 - 36)	36 (24 - 36)
Average Rainfall and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
		Average of Central Values:	31.3
		25th Percentile of Lower Bounds:	15
		Maximum Value:	36
		Summary of Values:	31.3 (15 - 36)

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Table 5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0008	0	0
	(0 - 0.007)	(0 - 0.000005)	(0 - 0)
Dry and Temperate Location	0.0009	0	0
	(0 - 0.06)	(0 - 0.4)	(0 - 1.49)
Dry and Cold Location	0.5	0.21	0.16
	(0.19 - 1.48)	(0.09 - 0.7)	(0.06 - 0.8)
Average Rainfall and Warm Location	0.16	1	2.43
	(0.01 - 0.6)	(0.03 - 2.23)	(0.12 - 5.4)
Average Rainfall and Temperate Location	0.15	0.9	1.5
	(0.013 - 1)	(0.026 - 2.24)	(0.025 - 4.6)
Average Rainfall and Cool Location	0.24	1.22	1.66
	(0.004 - 1.09)	(0.008 - 2.6)	(0.014 - 4.4)
Wet and Warm Location	0.9	1.83	3.2
	(0.6 - 1.49)	(1.25 - 3.5)	(1.75 - 6.7)
Wet and Temperate Location	0.8	1.42	2.16
	(0.5 - 1.61)	(0.8 - 3.6)	(0.3 - 5.2)
Wet and Cool Location	0.007	0.007	0.014
	(0.0013 - 1.08)	(0.005 - 2.02)	(0.01 - 2.51)
		Average of Central Values:	0.758
		25th Percentile of Lower Bounds:	0.00265
		Maximum Value:	6.7
		Summary of Values:	0.76 (0.00265 - 6.7)

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Table 6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	2.9E-06	0	0
	(0 - 0.000021)	(0 - 2.3E-08)	(0 - 0)
Dry and Temperate	0.000004	0	0
Location	(0 - 0.00017)	(0 - 0.0024)	(0 - 0.012)
Dry and Cold Location	0.005	0.0018	0.0013
	(0.0019 - 0.011)	(0.0006 - 0.004)	(0.0005 - 0.007)
Average Rainfall and	0.0014	0.018	0.04
Warm Location	(0.00007 - 0.019)	(0.00031 - 0.06)	(0.0008 - 0.11)
Average Rainfall and	0.0016	0.016	0.029
Temperate Location	(0.00013 - 0.024)	(0.00026 - 0.07)	(0.00018 - 0.1)
Average Rainfall and Cool	0.004	0.04	0.07
Location	(0.00006 - 0.04)	(0.00016 - 0.14)	(0.00027 - 0.18)
Wet and Warm Location	0.08	0.09	0.09
	(0.04 - 0.16)	(0.04 - 0.18)	(0.04 - 0.2)
Wet and Temperate	0.06	0.06	0.06
Location	(0.03 - 0.13)	(0.022 - 0.14)	(0.003 - 0.17)
Wet and Cool Location	0.00024	0.0005	0.0006
	(0.00011 - 0.1)	(0.00031 - 0.12)	(0.0003 - 0.07)
		Average of Central Values:	0.02479
		25th Percentile of Lower Bounds:	0.000065
		Maximum Value:	0.2
		Summary of Values:	0.0248 (0.000065 - 0.2)

Cyclopropanecarboxylic acid

Table 7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.00026	0	0
	(0 - 0.0019)	(0 - 2.6E-06)	(0 - 0)
Dry and Temperate Location	0.00023	0	0
	(0 - 0.023)	(0 - 0.28)	(0 - 1)
Dry and Cold Location	0.17	0.07	0.05
	(0.06 - 0.5)	(0.026 - 0.16)	(0.015 - 0.27)
Average Rainfall and Warm Location	0.08	0.7	1.9
	(0.004 - 0.6)	(0.017 - 1.96)	(0.06 - 4.4)
Average Rainfall and Temperate Location	0.11	0.7	1.15
	(0.006 - 1.11)	(0.028 - 2.07)	(0.011 - 3.5)
Average Rainfall and Cool Location	0.12	0.9	1.35
	(0.0026 - 0.9)	(0.005 - 2.3)	(0.01 - 3.5)
Wet and Warm Location	0.7	1.55	2.42
	(0.4 - 1.27)	(0.9 - 2.69)	(1.22 - 4.9)
Wet and Temperate Location	0.5	1.05	1.75
	(0.3 - 1.15)	(0.5 - 2.93)	(0.21 - 4.1)
Wet and Cool Location	0.002	0.005	0.008
	(0.0009 - 0.7)	(0.0025 - 1.3)	(0.005 - 1.21)
		Average of Central Values:	0.566
		25th Percentile of Lower Bounds:	0.0017
		Maximum Value:	4.9
		Summary of Values:	0.57 (0.0017 - 4.9)

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Table 8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.000011	0	0
	(0 - 0.00008)	(0 - 1.0E-07)	(0 - 0)
Dry and Temperate Location	0.000012	0	0
	(0 - 0.001)	(0 - 0.016)	(0 - 0.06)
Dry and Cold Location	0.012	0.005	0.003
	(0.004 - 0.04)	(0.0015 - 0.012)	(0.0011 - 0.02)
Average Rainfall and Warm Location	0.008	0.1	0.23
	(0.0004 - 0.09)	(0.0018 - 0.32)	(0.004 - 0.5)
Average Rainfall and Temperate Location	0.009	0.08	0.14
	(0.0006 - 0.11)	(0.0019 - 0.4)	(0.0008 - 0.5)
Average Rainfall and Cool Location	0.015	0.16	0.25
	(0.00026 - 0.15)	(0.0006 - 0.5)	(0.0011 - 0.7)
Wet and Warm Location	0.19	0.31	0.4
	(0.1 - 0.4)	(0.16 - 0.7)	(0.14 - 0.7)
Wet and Temperate Location	0.09	0.12	0.17
	(0.04 - 0.2)	(0.04 - 0.3)	(0.01 - 0.6)
Wet and Cool Location	0.0004	0.0008	0.001
	(0.00019 - 0.14)	(0.0005 - 0.23)	(0.0005 - 0.11)
		Average of Central Values:	0.085
		25th Percentile of Lower Bounds:	0.000225
		Maximum Value:	0.7
		Summary of Values:	0.085 (0.000225 - 0.7)