SERA TR-052-24-02a

Imazamox

Human Health and Ecological Risk Assessment

Final Report

Submitted to:
Paul Mistretta, COR
USDA/Forest Service, Southern Region
1720 Peachtree RD, NW
Atlanta, Georgia 30309

USDA Forest Service Contract: **AG-3187-C-06-0010**
USDA Forest Order Number: **AG-43ZP-D-09-0033**
SERA Internal Task No. **52-24**

Submitted by:
Patrick R. Durkin
Syracuse Environmental Research Associates, Inc.
8125 Solomon Seal
Manlius, New York 13104

December 10, 2010

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
ALS	acetolactate synthase
APHIS	Animal and Plant Health Inspection Service
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
ChE	cholinesterase
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
DER	data evaluation record
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
EHE	2-ethylhexyl ester
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide 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
IARC	International Agency for Research on Cancer
IRED	Interim Reregistration Eligibility Decision
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)
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MSMA	monosodium methanearsonate
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
NIOSH	National Institute for Occupational Safety and Health
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
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
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
T.G.I.A.	Technical grade active ingredient
TIPA	Triisopropanolamine
TRED	Tolerance Reassessment Eligibility Decision
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
WHO	World Health Organization

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

Imazamox is a herbicide under consideration for use in Forest Service vegetation management programs. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the human health and environmental consequences of using this herbicide. Only one formulation of imazamox, Clearcast, is labeled for forestry and other non-crop applications. Clearcast is currently registered to BASF. Imazamox may be used for either terrestrial or aquatic weed control. The maximum application rate for terrestrial applications is 0.5 lb a.e./acre and the maximum target concentration for aquatic applications is 0.5 mg a.e./L. The current risk assessment is based on the maximum application rates. The quantitative risk characterization in both the human health and in the ecological risk assessments is based on the hazard quotient (HQ), which is defined as the anticipated exposure divided by the toxicity value.

Imazamox is an effective herbicide for the control of both terrestrial and aquatic vegetation. Under some conditions, terrestrial applications of imazamox could damage nontarget terrestrial vegetation. Effective aquatic applications of imazamox will most certainly damage aquatic macrophytes and may damage some species of algae. While imazamox is an effective terrestrial herbicide, the exposure scenarios developed for terrestrial plants in the current risk assessment lead to a very wide range of HQs, some of which are far below the level of concern and others substantially above the level of concern. This apparent ambiguity relates to the attempt made in the exposure assessments to encompass a wide range of potential exposures associated with different weather patterns and other site-specific variables. Thus, for applications of imazamox to areas in which potential effects on nontarget plants are a substantial concern, refinements to the exposure scenarios for nontarget plants could be justified.

While adverse effects on plants may be anticipated, there is no basis for asserting that applications of imazamox will pose any substantial risk to humans or other species of animals. For humans and mammalian wildlife, confidence in the risk characterization is high. Imazamox has been subject to a standard and relatively extensive series of acute, subacute, and chronic studies in mammals. There is little doubt that imazamox is practically nontoxic to mammals. No anticipated exposures of humans or mammalian wildlife to imazamox raise concern. Data on the toxicity of imazamox to birds are less extensive but include both acute toxicity and reproduction studies that fail to identify any potential hazards to birds. For other groups of animals, including amphibians, terrestrial invertebrates, fish, and aquatic invertebrates, the toxicity data are very limited or, in the case of amphibians, nonexistent. While the available studies on these groups of organisms fail to suggest any hazards, confidence in the risk characterization for these groups of organisms is less than that in the risk characterization for humans, mammalian wildlife, and birds.

Terrestrial or aquatic applications of any effective herbicide, including imazamox, are likely to alter vegetation within the treatment area, which may lead to secondary effects on terrestrial or aquatic animals as a result of changes in food availability and habitat quality. These secondary effects, the magnitude of which is likely to vary over time, may be beneficial to some species and detrimental to others. These types of secondary effects could occur after any form of vegetation management whether or not herbicides are used.

1. INTRODUCTION

Imazamox is a herbicide under consideration for use in Forest Service vegetation management programs. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the human health and environmental consequences of using this herbicide.

The Forest Service has not conducted a previous risk assessment on imazamox. The toxicology and environmental fate of imazamox has been reviewed by various government organizations within and outside of the United States (e.g., California EPA 2000; European Commission 2002; Health Canada 2008; National Registration Authority, Australia 2000; NYDEC 2003; U.S. EPA/OPP 1997a,b, 2001a,b,c,d, 2002, 2008a,b). The U.S. E-Docket (www.regulations.gov) contains 70 items at least peripherally related to imazamox; however, the list does not include risk assessments prepared by the U.S. EPA or other organizations in the U.S. government. Imazamox is considered a *reduced risk* pesticide, which means that it is one of the pesticides which U.S. EPA … *believes pose less risk to human health and the environment than existing alternatives* (U.S. EPA/OPP 1998).

The published literature on imazamox was identified using TOXLINE (http://toxnet.nlm.nih.gov/) and AGRICOLA (http://agricola.nal.usda.gov/), and additional information on imazamox was identified through standard Internet search engines and databases (e.g., HSDB 2010; PAN 2010). As summarized in Section 5 (References), the open literature on imazamox is sparse; most publications relate to efficacy or environmental fate, and very few publications pertain to the toxicity of imazamox (e.g., Cedergreen et al. 2005; Fragiorge et al. 2008). Imazamox is not included in the U.S. EPA IRIS database (http://www.epa.gov/IRIS/), WHO INCHEM series (http://www.inchem.org/), the EXtension TOXicology NETwork series (http://extoxnet.orst.edu/), or the USDA/ARS Pesticide Properties Database (http://www.ars.usda.gov/Services/docs.htm?docid=14199). USGS (2003a) provides information on the agricultural use of imazamox; however, monitoring data are not included in the USGS (2003b) National Water Quality Assessment Program.

While the open literature on imazamox is limited, the U.S. EPA requires a relatively standard set of studies for pesticide registration. In the preparation of this risk assessment, a Freedom of Information Act (FOIA) request, HQ-FOI-00787-10, was submitted to the U.S. EPA for a complete bibliography of all the registrant-submitted studies on imazamox, which included two hundred and six submissions. In Appendix 1, these submissions are organized by *Guideline Number*, which refers to the type of study required by the U.S. EPA for pesticide registration. The study guidelines relevant to imazamox are summarized in Table 1.

As indicated in Table 1, the studies submitted to the U.S. EPA in support of the registration of imazamox include toxicity studies in mammals and ecological receptors which are highly relevant to the current Forest Service risk assessment. Consequently, this risk assessment is and must be based almost exclusively on the registrant-submitted studies. Generally, these studies are classified as *Confidential Business Information* (CBI), and they are not released or made available to individuals outside of the U.S. EPA Office of Pesticides.

The list of registrant-submitted studies was reviewed in the preparation of this risk assessment, and 66 EPA study summaries/evaluations were provided by BASF, the current registrant for imazamox. As discussed below, the EPA study summaries/evaluations are referred to as Data Evaluation Records (DERs), which are cited in the current risk assessment by author and date (e.g., Blaszcak 1995). These citations are included in the reference list (Section 5). DERs are not available for all registrant-submitted studies; nonetheless, all studies submitted to the U.S. EPA are identified by a Master Record Identification Number (MRID) and are summarized in various U.S. EPA documents. Citations for information taken from EPA documents on studies for which no DER is available are identified by MRID number (e.g., MRID 43193218).

The Forest Service is sensitive to concerns about risk assessments based chiefly on registrant-submitted studies. The general concern can be expressed as follows:

> *If the study is paid for and/or conducted by the registrant, the study may be designed and/or conducted and/or reported in a manner that will obscure any adverse effects that the compound may have.*

This concern is largely unfounded because although any study (published or unpublished) can be falsified, concerns with the design, conduct, and reporting of studies submitted to the U.S. EPA for pesticide registration are minor. Studies submitted for pesticide registration are designed in accordance with guidelines regarding the manner in which the studies are conducted and reported. These guidelines are developed by the U.S. EPA and not by the registrants. Full copies of the guidelines for these studies are available at http://www.epa.gov/opptsfrs/home/guidelin.htm. All studies are conducted under Good Laboratory Practices (GLPs). GLPs are an elaborate set of procedures that involve documentation and independent quality control and quality assurance, which substantially exceed the levels typically seen in open literature publications. Furthermore, the EPA reviews each of the submitted studies for adherence to the relevant study guidelines. These reviews most often take the form of Data Evaluation Records (DERs). While the nature and complexity of DERs will vary with the nature and complexity of the studies, each DER involves an independent assessment of the study to ensure that the EPA Guidelines are followed. In addition, each DER undergoes internal review within the EPA (and sometimes several layers of internal review).

There are legitimate concerns with risk assessments based largely on registrant-submitted studies; however, the concerns are based on the nature and diversity of the available studies, and not data quality or data integrity. The studies required by the U.S. EPA are based on a relatively narrow set of studies in a relatively small subset of species. For some pesticides (e.g., picloram, clopyralid, and triclopyr), the number of published studies is substantial, many of which are generated by academics who have a fundamental interest in understanding both the toxicology of a compound as well as underlying biological principles (e.g., physiology, biochemistry, ecology, etc.). Such studies tend to be non-standard but highly creative and can substantially contribute to or even form the basis of a risk assessment. For imazamox, however, the information available in the open literature is clearly limited; therefore, it is likely that as the open literature on imazamox develops, the risk assessment will be updated.

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 associated with imazamox, 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 and it 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 2007a). 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.

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. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations, most of which are relatively simple. They are included in the body of the document.

Some of the calculations, however, are cumbersome. For those calculations, EXCEL workbooks (sets of EXCEL worksheets) are included as attachments to this risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. Documentation for the use of these workbooks is presented in SERA (2009). For imazamox, two EXCEL workbooks are provided, one for terrestrial applications (Attachment 1) and the other for aquatic applications (Attachment 2).

The EXCEL workbooks are an integral part of the risk assessment. The worksheets contained in these workbooks are designed to isolate the large number of calculations from the risk assessment narrative. In general, all calculations of exposure scenarios and quantitative risk characterizations (i.e., hazard quotients) are derived and contained in the worksheets. The rationale for the calculations as well as the interpretation of the hazard quotients are contained in this risk assessment document.

2. PROGRAMS DESCRIPTION

2.1. Overview

Imazamox is an imidazolinone herbicide labeled for the control of numerous terrestrial and aquatic weeds. Imazamox is not currently used, or at least is not used extensively, in Forest Service programs; moreover, the specific types of applications to be used in Forest Service programs are not well defined. Currently, the Forest Service uses two other imidazolinone herbicides, imazapic and imazapyr, to control various grasses, broadleaf weeds, vines, and brush species, as well as for site preparation and conifer release, and rights-of-way maintenance. Accordingly, it is likely that the Forest Service would use imazamox for similar types of applications.

Only one formulation of imazamox, Clearcast, is labeled for forestry and other non-crop applications. Clearcast is currently registered to BASF. In both terrestrial and aquatic applications, Clearcast is applied at rates of 0.125-0.5 lb a.e./acre. In aquatic applications, the maximum application rate for Clearcast is also limited by water depth, and the maximum target concentration is 500 ppb (equivalent to 500 µg/L or 0.5 mg/L). In broadcast applications, Clearcast is labeled for both ground and aerial (fixed wing or helicopter) applications. Other forestry-specific application methods include foliar spot, hack and squirt, cut stump, and basal bark applications. In aquatic applications, Clearcast may be applied either to the water surface for the control of emergent weeds or below the water surface for the control of submersed vegetation.

2.2. Chemical Description and Commercial Formulations

Imazamox is the common name for (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-(methoxymethyl)-3-pyridinecarboxylic acid. An overview of the physical and chemical properties of imazamox is provided in Table 2.

Imazamox is a member of the imidazolinone class of herbicides which also includes imazapic, imazapyr, imazethapyr, imazamethabenz, and imazaquin. Previous Forest Service risk assessments have been prepared on imazapyr (SERA 2004a) and imazapic (SERA 2004b). As illustrated in Figure 1, imazamox is structurally identical to imazapic, except that the methyl group on the pyridine ring of imazapic is replaced with a dimethyl ether moiety in imazamox. All of the imidazolinone herbicides share a common mechanism of herbicidal action that involves the inhibition of acetolactate synthase (ALS). ALS is an enzyme found in plants and is required for the synthesis of essential branched chain amino acids (i.e., valine, leucine, and isoleucine), all of which are important for plant growth (Tan et al. 2005).

Imazamox was introduced in Europe in 1995, granted a conditional registration in the United States in 1997, and granted an unconditional registration in the United States in 2001 (Tomlin 2004; U.S. EPA/OPP 1997). The conditional registration in the United States was issued to American Cyanamid. Currently, all active formulations in the United States are registered to BASF (http://www.epa.gov/pesticides/pestlabels/index.htm).

The commercial formulations of imazamox are summarized in Table 3. All commercial formulations of imazamox consist of the ammonium salt as the active ingredient (a.i.). The commercial formulations include Beyond, Clearcast, Clearmax, Raptor DG, and Raptor. For

completeness, Table 3 also includes Raptor (technical). This product has an EPA number and EPA label, but consists of imazamox acid and is intended only for reformulation. Thus, Raptor (technical) is not an actual commercial formulation.

As indicated in Table 3, the only formulation labeled for forestry is Clearcast, a liquid formulation that consists of 12.1% imazamox ammonium salt and 87.9% other ingredients. Clearcast contains 1 lb imazamox acid equivalents/gallon (1 lb a.e./gallon). As summarized in Table 1 and detailed in Appendix 1, information on the other ingredients in technical grade imazamox as well as imazamox formulations was disclosed to the U.S. EPA—i.e., Guidelines 61-1, 61-3, 830.1600, 830.1620, 830.1650, and 830.1670. The identity of the other ingredients (formerly referred to as *inerts*) in the imazapic formulations is considered proprietary; therefore, the manufacturer does not identify the other ingredients on the general or supplemental product labels or material safety data sheets (MSDS). Nonetheless, the MSDS for Clearcast does not specify any *toxic* or specially regulated ingredients, which means that none of the other ingredients present at a concentration of 0.1% or greater are classified as hazardous. The potential significance of the other ingredients in imazamox formulations also can be inferred based on differences in the toxicity of the formulations and technical grade imazamox, as discussed further in Section 3.1.14. The potential impact of impurities in technical grade imazamox is discussed in Section 3.1.15.

2.3. Application Methods

2.3.1. Terrestrial Applications

Clearcast is labeled for ground broadcast applications as well as aerial broadcast applications using either fixed wing aircraft or helicopters. In addition, Clearcast is labeled for several specific forestry application methods including foliar spot, hack and squirt, cut stump, and basal bark applications. Applications of Clearcast must be made with an adjuvant that can consist of a nonionic surfactant, methylated seed oil or vegetable oil concentrates or silicone-based surfactants. Clearcast is labeled for the control of numerous terrestrial target species, including ryegrass, Johnsongrass, purple loosestrife, and purple or yellow sedge.

2.3.2. Aquatic Applications

Clearcast is also labeled for aquatic applications, which are considered in the current Forest Service risk assessment. Like terrestrial applications, aquatic applications of Clearcast require the use of adjuvants for the control of either emergent, floating or shore-line vegetation, and the recommended adjuvants are the same as those used in terrestrial applications. To control the emergence of aquatic vegetation, Clearcast can be applied to the water surface using methods analogous to those used in terrestrial applications—i.e., either surface ground broadcast or aerial applications. Clearcast may also be applied below the water surface. The product label for Clearcast does not specify the types of equipment to be used for subsurface applications. These types of applications, however, typically involve specialized equipment for injecting the herbicide directly into the water column. Some aquatic herbicides are labeled for applications to streams. In these types of applications, metering devices are used to inject the herbicides at a fixed rate so that the flow rate in the stream and the rate of injection result in the desired target concentration of the herbicide in water. The product label for Clearcast, however, does not provide information on applications to streams of lotic water bodies. Nonetheless, a Special

Local Need Label for Florida indicates that Clearcast may be applied to flowing waters to control of emergent vegetation.

2.4. Mixing and Application Rates

2.4.1. Terrestrial Applications

Labeled terrestrial broadcast application rates for Clearcast range from 16 to 64 fl. oz/acre. These rates correspond to 0.125- 0.5 lb a.e./acre [128 fl. oz/gallon, 1 lb a.e./gallon]. The lower bound of the labeled application rates is recommended for the control of annual ryegrass and Johnsongrass seedlings. The upper bound of the labeled application rates is recommended for the control of alligator weed, California bulrush, cattail, Chinese tallowtree, giant ragweed, Japanese stiltgrass, Johnsongrass rhizomes, *Phragmites australis*, purple loosestrife, spike rush, *Taro* species, and water primrose.

For this risk assessment, the extent to which a formulation of imazamox is diluted prior to application primarily influences dermal and direct spray scenarios, both of which depend on 'field dilution' (i.e., the concentration of imazamox in the applied spray). In all cases, the higher the concentration of imazamox (i.e., equivalent to the lower dilution of imazamox), the greater is the risk. For terrestrial applications, the product label for Clearcast does not specify minimum or maximum application volumes. As discussed in the following subsection on aquatic applications, the minimum application volume specified on the product label is 5 gallons/acre, but the minimum recommended application volume for "best results" is 20 gallons/acre. The maximum application volume specifically noted on the product label is 30 gallons/acre, although it appears that greater application volumes may sometimes be used.

As discussed further in Section 2.5, information on the use of imazamox by the Forest Service is not available. In the absence of this information, the EXCEL workbook for terrestrial applications is based on the maximum labeled application rate of 0.5 lb a.e./acre with application volumes of 10 (5 to 30) gallons per acre. The impact of using lower application rates and differing application volumes is discussed in the risk characterization for human health effects (Section 3.4) and ecological effects (Section 4.4).

2.4.2. Aquatic Applications

Rates for aquatic applications of herbicides may be expressed as lb a.e./acre of surface water for emergent vegetation or as target concentrations for submerged vegetation. As noted in Section 2.3.2, the product label for Clearcast supports both types of applications. For either surface or subsurface applications of Clearcast, the maximum application rate is expressed as a target concentration of 500 ppb (µg/L).

The product label for Clearcast provides a table for converting surface application rates, in units of fluid ounces of formulation, to target concentrations in units of ppb based on the average depth of the water in feet for a 1 acre area of water surface.

This table appears to be based on the general algorithm:

$$TC_{ppb} = \frac{N\,oz_{Form} \times \frac{1\,gal}{128\,oz} \times \frac{1\,lb\,a.e.}{gal_{Form}} \times \frac{453592.37\,\text{mg}}{lb} \times \frac{1000\,\mu g}{mg}}{D_{feet} \times acre \times \frac{43560\,\text{ft}^3}{\text{acre - foot}} \times \frac{28.32\,\text{L}}{\text{ft}^3}} \qquad \text{(Eq. 1)}$$

where *TC* is the target concentration in ppb (µg/L), *N* is the ounces of formulation required to achieve the target concentration for 1 acre area of water surface where the average water depth is *D* in units of feet. The other terms in Equation 1 are simply conversion factors taken from Budavari (1989).

Equation 1 can also be rearranged to solve for the number of ounces of formulation (*N*):

$$N_{oz\,Form} = \frac{TC_{\mu g/L} \times D_{feet} \times acre \times \frac{43560\,\text{ft}^3}{\text{acre - foot}} \times \frac{28.32\,\text{L}}{\text{ft}^3}}{\frac{1\,gal}{128\,oz} \times \frac{1\,lb\,a.e.}{gal_{Form}} \times \frac{453592.37\,\text{mg}}{lb} \times \frac{1000\,\mu g}{mg}} \qquad \text{(Eq.2)}$$

For example, the table in the product label for Clearcast specifies that 207 fluid ounces of formulation should be applied for a water depth of 6 feet and a target concentration of 100 ppb. Using Equation 1 above, the target concentration achieved by adding 207 fluid ounces of Clearcast to a 1 acre-foot of water is 99.1046 µg/L. Using Equation 2, the number of ounces of Clearcast required to achieve a target concentration of 100 µg/L is 208.87 oz. These discrepancies between the above algorithms and table in the product label are clearly based on differences in rounding in some of the conversion factors. More importantly, these discrepancies are insubstantial.

For emergent weeds, the recommended application rates for Clearcast vary from 16 to 64 fl. oz/acre. These rates are equivalent to the application rates recommended for terrestrial applications (i.e., 0.125-0.5 lb a.e./acre). Notwithstanding these labeled application rates, the product label for Clearcast indicates that no more than 173 fl. oz of Clearcast can be applied per acre-foot of water (i.e., the target concentration cannot exceed 500 ppb a.e.). Note that solving the above equation using the conversion factors in the equation results in an estimate of 174.099 oz of formulation to reach a target concentration of 500 ppb a.e. This minor difference is insubstantial and is probably due to the use of different conversion factors (i.e., fewer significant digits) in preparing the product label.

For the current Forest Service risk assessment, the EXCEL workbook for aquatic applications is based on the maximum labeled target concentration of 500 ppb. As with terrestrial applications, application volumes of 10 (5 to 30) gallons/acre are used. Also as with terrestrial applications, the impacts of using lower target concentrations and differing application volumes are discussed in the risk characterization for human health effects (Section 3.4) and ecological effects (Section 4.4).

2.5. Use Statistics

Most Forest Service risk assessments attempt to characterize the use of an herbicide or other pesticide in Forest Service programs relative to the use of the herbicide or other pesticide in agricultural applications. The 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://ca.water.usgs.gov/pnsp/ pesticide_use_maps/) and/or detailed pesticide use statistics compiled by the state of California (http://www.calepa.ca.gov/).

Apparently, imazamox has not been used or at least not used extensively in Forest Service programs, since its use is not documented in the pesticide use reports. In addition, a screening of various Forest Service web sites did not identify recent Forest Service programs in which imazamox was used. As illustrated in Figure 2, agricultural uses of imazamox are predominant in mid-west and the north central region of the United States, primarily in Ohio, Indiana, Illinois, Iowa, southern Minnesota, and the eastern areas of the Dakotas. The areas of major agricultural use are primarily in Forest Service Region 1 (referred to as the Eastern Region by the Forest Service) with lesser amounts in Forest Service Region 2 (including South Dakota) and Forest Service Region 3 (including North Dakota). Lesser amounts of imazamox are used in the west, and very little imazamox is used in the northeast and southeast states. Based on the 2002 statistics from USGS (2003a), the great majority of imazamox use is for soybeans (82.81%) with lesser amounts used for alfalfa (12.58%).

More recent use statistics are available for California (CDPR 2008). The greatest agricultural use of imazamox in California is on alfalfa (about 98.6% of total use in 2007). The only forestry related use listed in the California statistics is rights of way maintenance, which accounts for only about 0.03% of total use (i.e., 1.08 lbs a.i. applied in 2007).

It is unclear, however, if the forestry uses of imazamox would parallel the locations of agricultural applications. The Pacific Northwest Weed Management Handbook (covering Forest Service Region 6) notes the efficacy of imazamox in controlling weeds in a number of agricultural commodities as well as in controlling aquatic weeds. Only the latter use would likely be relevant to Forest Service activities.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

Virtually all of the available information on the toxicity of imazamox to mammals comes from standard studies submitted to the U.S. EPA/OPP in support of the registration of imazamox. Full copies of these studies, which are considered proprietary, were not available for the preparation of the current Forest Service risk assessment. As noted in Section 1, however, the studies relating to the hazard identification of potential human health effects are adequately summarized in various EPA risk assessments and related documents (U.S. EPA/OPP 1997a,b, 2001a,b,c,d, 2002). Furthermore, BASF, the registrant for imazamox, kindly provided U.S. EPA/OPP reviews (i.e., DERs) of many key studies on imazamox.

As discussed further in the ecological risk assessment (Section 4), imazamox is an effective herbicide, and its mechanism of action in plants is well characterized. In terms of the human health risk assessment, however, mechanism of action may not be a meaningful concept, because imazamox does not appear to cause detectable signs of toxicity in mammals even at very high doses. Based on standard acute oral toxicity studies, the LD_{50} of imazamox 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. Similarly, imazamox does not cause any signs of toxicity in chronic dietary studies at doses greater than 1000 mg/kg bw/day in mice, rats, and dogs. The only seemingly adverse effects noted in repeated dose toxicity studies are decreases in body weight and food consumption noted in reproduction studies at gavage doses of 600 mg/kg bw/day in rabbits and 500 mg/kg bw/day in rats. Gavage dosing—i.e., direct instillation of the test material into the stomachs of the test animals —is an inherently stressful procedure that often leads to animal responses unlikely to be observed in studies involving more typical and relevant routes of exposure—i.e., dietary or drinking water studies.

No remarkable signs of toxicity are reported in standard toxicity studies involving dermal, ocular, or inhalation exposure. For each of these routes of exposure, studies are available on both technical grade imazamox and an 11.83% imazamox formulation. In these studies, neither technical grade imazamox nor the imazamox formulation caused serious effects. Technical grade imazamox causes a somewhat greater degree of eye irritation and respiratory tract irritation, compared with the imazamox formulation; however, the relatively modest differences may be due to the fact that technical grade imazamox was tested as a powder, whereas the formulation is a liquid. It is not uncommon for powders to cause modest levels of eye and respiratory irritation due to general particulate exposure rather than specific toxicity.

The only reservation with the largely benign hazard identification for imazamox involves the nature of the available data. All of the toxicity data on imazamox come from studies submitted to the U.S. EPA in support of the registration of imazamox. While these studies appear to have been appropriately designed and conducted and were accepted by the U.S. EPA/OPP, the available information on imazamox 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

As noted in Section 2.2 and discussed further in Section 4.1.2.5, the mechanism for the phytotoxicity of imazamox as well as other imidazolinone herbicides, the inhibition of acetolactate synthase (ALS) is well understood. Since the ALS enzyme is found only in plants and microorganisms (e.g., Bernasconi et al. 1995), its inhibition is not relevant to potential adverse effects in humans and other mammals. As summarized in Appendix 2 and discussed further in the following subsections, imazamox does not appear to cause any specific signs of toxicity in mammals. In the few acute toxicity studies that note any responses associated with treatment, the observed effects may be attributable to the physical response associated with gross over-exposures or irritant effects. In other words, imazamox does not appear to have a specific mechanism of action in mammals. This determination is reflected in the EPA hazard identification for imazamox (U.S. EPA/OPP 2001b, p. 13) in which no toxicological endpoints of concern are identified for acute or chronic dietary exposures as well as occupational or residential exposures.

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 imazamox 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.

In addition to the general consideration about how imazamox behaves in the body, another consideration is the behavior of imazamox in the environment and the extent to which the metabolism of imazamox in the environment must be considered quantitatively in the risk assessment. The consideration of environmental metabolites is discussed in Section 3.1.15.1.

3.1.3.1. General Considerations

For pesticide registration, the U.S. EPA/OPP generally requires a relatively standard metabolism study in rats in which the compound is administered by both intravenous and oral routes. One such study (Chiu 1995a, MRID 43876218) is available for imazamox. In the intravenous phase of this study, ^{14}C-labelled imazamox was administered at a single dose of 10 mg/kg bw. The oral administrations consisted of single doses of 10 or 1000 mg/kg bw as well as pretreatment with unlabelled imazamox at 10 mg/kg bw/day for 14 days followed by a single oral dose of ^{14}C-labelled imazamox. In both the intravenous and oral studies, imazamox was excreted rapidly with estimated whole-body half-lives of less than 6 hours. On intravenous administration, about 85-90% of the radioactivity was recovered in the urine with only about 2- 3% recovered in the feces. On oral administration, imazamox was eliminated primarily in urine (about 70-80%) with about 12-24% recovered in feces. The greater amount of imazamox in feces following oral administration suggests incomplete absorption following oral dosing. Very little imazamox was recovered in tissue with most assays of tissue radioactivity being below the level of detection. In a few animals, detectable levels of imazamox were noted the lung tissue (0.007% of the administered dose) and uterus (0.001% of the administered dose).

The metabolites of imazamox assayed in the study by Chiu (1995a) are illustrated in Figure 3. Most of the administered dose was excreted unchanged in the urine (93%) and feces (73%). The primary metabolic pathway involved demethylation to 5-(hydroxymethyl)-2-(4-isopropyl-4-methyl-5-oxo-2-imazazolin-2-yl) nicotinic acid (CL 263,284) which accounted for 1% of the radioactivity in the urine and 9% of the radioactivity in the feces. The CL 263,284 metabolite was oxidized to 2-(4-isopropyl-4-methyl-5-oxo-2-imadazqlin-2-yl)-3,5-pyridine-dicarboxylic acid (CL 312,622), which accounted for 0.2-0.3% of the radioactivity in the urine and 3% of the radioactivity in the feces. As illustrated in Figure 3, trace amounts of an O-methyl ester were detected in the urine and trace amounts of an N-methyl metabolite were detected in the feces.

The only other metabolism study on imazamox is a relatively standard dietary study in lactating goats summarized in U.S. EPA/OPP (1997a, MRID 43193235). Metabolism studies in lactating goats are designed to assess the potential for the contamination of milk in ruminants consuming food treated with pesticides. In this study, ^{14}C-labelled imazamox was administered by capsules to lactating goats for 7 days at doses equivalent to dietary concentrations of 2.08 and 11.6 ppm. Detectable concentrations were not found in milk or body tissue except for the kidneys which evidenced imazamox concentrations of 0.02 ppm at the low dose and 0.06 ppm at the high dose. As in the metabolism study in rats, most of the radioactivity was excreted in the urine.

3.1.3.2. 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 to 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 imazamox 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 (2007a), 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 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.

In the absence of experimental data, quantitative structure activity relationships, detailed in SERA (2007a), are used to estimate dermal absorption rates. For estimating the dermal permeability coefficient, U.S. EPA/ORD (1992, 2007) developed an algorithm based on the K_{ow} and molecular weight. Using a K_{ow} of 5.37 and the molecular weight of 205.34 for imazamox (Table 2), the estimated dermal permeability coefficient is 0.00034 cm/hour with a 95% confidence interval of 0.00020-0.00056 cm/hour. These estimates are used in all exposure assessments based on Fick's first law. The calculations for these estimates are presented in Worksheet B05 in the EXCEL workbooks that accompany this risk assessment.

As discussed in SERA (2007a, Section 3.1.3.2, Eq. 3-3), a similar algorithm, also based on molecular weight and K_{ow}, has been developed for estimating first-order dermal absorption rates.

Applying the above values for the molecular weight and K_{ow} of imazamox, the estimated first-order dermal absorption rate coefficient for imazamox is estimated at 0.0033 $hour^{-1}$ with a 95% confidence interval of 0.0013-0.0079 $hour^{-1}$. The calculations for these estimates are presented in Worksheet B06 in the EXCEL workbooks that accompany this risk assessment.

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 is not possible for imazamox 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).

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). The concentration of the chemical in the body after a series of doses (X_{Inf}) over an infinite period of time can be estimated based on the body burden immediately after a single dose, X_0, by the relationship:

$$\frac{X_{Inf}}{X_0} = \frac{1}{1 - e^{-kt*}}$$

where ***t**** is the interval between dosing and k is the first-order excretion rate.

As discussed in Section 3.1.3.1, the available metabolism study with rats indicates that imazamox is excreted rapidly with a whole-body half-life of less than 6 hours. Taking 6hours (0.25 days) as a conservative estimate of the whole-body half-life, the whole-body excretion rates for imazamox would be about 2.8 day^{-1} [ln(2)/0.25 days ≈ 2.773]. Thus, after repeated daily doses of imazamox, body burden would increase by a factor of about 1.1 [$1 \div (1\text{-}e^{-2.8/day \times 1\ day}) \approx 1.064$]. In other words, there is no basis for asserting that long-term exposures to imazamox will have a substantial impact on body burden.

3.1.4. Acute Oral Toxicity

Like all of the available toxicity data on imazamox, the acute oral toxicity data are available only from studies conducted as part of the registration process. Appendix 2 provides details of all of the toxicity studies discussed in this hazard identification.

The standard acute oral toxicity studies are typically used to determine LD_{50} values—i.e., the treatment dose estimated to be lethal to 50% of the animals. LD_{50} values are not used directly to derive toxicity values as part of the dose-response assessment in Forest Service risk assessments. Even so, comparing the LD_{50} values for the active ingredient to the LD_{50} values for the formulations, may be useful in assessing the potential impact of inerts in pesticide formulations

As summarized in Appendix 2, Table A2-1, the rat LD_{50} is >5000 mg/kg bw for both imazamox and an 11.83% imazamox formulation. It is not clear that the 11.83% imazamox formulation is identical to Clearcast, which is a 12.1% formulation of the ammonium salt of imazamox (Table 2). After correcting for the conversion of the ammonium salt to the acid equivalent of imazamox, Clearcast contains about 11.45% imazamox a.e. [12.1% x 0.947 = 11.4587%].

Toxicity studies on pesticide formulations often report concentrations of the active ingredient or acid equivalents that vary slightly from the nominal concentrations. In any event, both imazamox and the 11.83% imazamox formulation would be classified as Category IV for acute oral toxicity based on the classification scheme typically used for product labeling (e.g., SERA 2007a, Table 3-2).

One potential area of confusion in the acute oral toxicity data on imazamox concerns the study by Lowe and Bradley (1995a), designated as MRID 43876212. As summarized in Appendix 2, Table A1, this study reports LD_{50} values of about 2200 mg/kg bw. According to the DER for this study, these LD_{50} values are based on a bioassay of CL 354,825, a soil metabolite of imazamox; however, in the recent EPA ecological risk assessment of imazamox, these LD_{50} values are reported for imazamox rather than the soil metabolite (U.S. EPA/OPP 2008b, p. 30). In the absence of the full study, which was not available for the preparation of the current Forest Service risk assessment, the discrepancy between the DER and the summary in U.S. EPA/OPP (2008b) cannot be resolved.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

As discussed in SERA (2007a, 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-effect levels (NOAELs) for the identified endpoints as well as levels associated with adverse effects—i.e., lowest-observed-effect-levels (LOAELS).

Appendix 2 summarizes the subchronic toxicity studies (Table A2-9) and chronic toxicity studies (Table A2-10) on imazamox. Standard 90-day subchronic dietary toxicity studies were conducted in dogs (Kelly 1994) and rats (Fischer 1992c) and chronic dietary toxicity studies were conducted in dogs (Kelly 1995a), mice (Kelly 1995b), and rats (MRID 43891001). Except for the chronic study in rats, DERS are available for all of the subchronic and chronic studies. The most consistent and remarkable finding in all of these studies is the lack of overt toxicity or tissue pathology at doses of up to about 1600 mg/kg bw/day—i.e., the subchronic NOAEL in rats (Fischer et al. 1992c). As discussed further in Section 3.1.9.2, the lack of a dietary LOAEL is also confirmed in a multi-generation reproduction study conducted at doses equivalent to more than 1500 mg/kg bw/day (Schroeder 1955).

All of the available subchronic and chronic toxicity studies on imazamox were reviewed and accepted by the EPA (U.S. EPA/OPP 1997a, 2001a). As noted in U.S. EPA/OPP (2001a), … *no hazard was seen at the Limit-Dose in animal studies via the oral and dermal routes, either following subchronic or chronic exposures*. While not explicitly discussed in their risk assessments, the EPA uses the term *limit-dose* to designate the highest dose required in toxicity studies.

As discussed further in Section 3.1.9.2, the only effects observed in multiple dose studies are decreased food consumption and decreased body weight gain in studies that involved gavage administration of imazamox, as opposed to dietary exposure.

3.1.6. Effects on Nervous System

For potential neurotoxins, the U.S. EPA may require a number specialized neurotoxicity studies for pesticide registration (U.S. EPA/OCSPP 2010). None of these studies were required for the registration of imazamox. As noted in U.S. EPA's hazard identification for imazamox:

> *There was no evidence of neurotoxic effects observed in acute, sub-chronic, developmental, reproduction or chronic studies. The NOAEL in almost all studies was the limit dose and the LOAEL was not established.*
>
> U.S. EPA/OPP (2001b), p. 8.

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.

With the exception of skin sensitization studies (Section 3.1.11.2), specific studies regarding the effects of pesticides on immune function are not required for pesticide registration. Nonetheless, 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, the subchronic and chronic toxicity studies on imazamox failed to note any adverse effects in blood or other tissue. Thus, there is no basis for suggesting that imazamox has an adverse effect on immune function.

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, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). The U.S. EPA/OPP has developed a battery of screening assays for endocrine disruption (i.e., http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series890.htm). Imazamox was not selected as one of the pesticides for which the screening assays are required (U.S. EPA/OPP 2009).

Inferences concerning the potential for endocrine disruption can sometimes be made from responses seen in standard toxicity tests—i.e., changes in the structure of major endocrine glands (i.e., the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis) or changes in growth rates. As with effects on the nervous system and immune function, however, no effects on organs associated with endocrine function are noted in standard toxicity studies on imazamox. As discussed further in Section 3.1.9.1, developmental toxicity studies involving gavage exposures note decreases in body weight gain; however, these effects are associated with corresponding decreases in food consumption. Thus, there is no basis for asserting that the decreases in weight gain might be associated with effects on the endocrine system.

In terms of effects that have important public health implications, effects on endocrine function would be expressed as diminished reproductive performance. As detailed in Section 3.1.9.2, however, adverse effects on reproduction are not noted in rats exposed to imazamox in the standard 2-generation reproduction study.

In considering the available toxicity data on imazamox, the U.S. EPA/OPP (2001a) notes:

> *Collective organ weight data and histopathological findings from the 2-generation rat reproductive study, as well as from the sub-chronic and chronic toxicity studies conducted in two or more animal species, demonstrate no apparent estrogenic effects or effects on the endocrine system. There is no information available that suggests that imazamox would be associated with endocrine effects.*
>
> U.S. EPA/OPP 2001a, p. 8

In other words, there is no basis for asserting that imazamox is likely to have an adverse effect on endocrine function.

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 the registration of pesticides. Very 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 2, Table A2-7, standard developmental toxicity studies were conducted in rabbits (Hoberman 1995) and rats (Foss 1994). Unlike all of the other repeated dosing studies in mammals, these developmental toxicity studies were conducted using gavage administration. Gavage administration involves the use of a specialized device (an intubation syringe) to directly insert the test compound into the stomach of the test organisms. Generally, gavage dosing leads to signs of toxicity at lower doses than observed in dietary exposures, and this pattern is evident with imazamox.

In the developmental study in rabbits, gavage doses of 600 mg/kg bw/day were associated with decreases in food consumption (14% to 22%) and corresponding decreases in body weight (19% to 21%). No effects, however, were noted in rabbits at gavage doses of 300 mg/kg bw/day (Hoberman 1995). Similarly, in the developmental study in rats, the only adverse effect noted was a decrease in body weight (97% of controls) and body weight gain (77% of controls), which was also accompanied by a decrease in food consumption (98% of controls). The only statistically significant ($p<0.05$) effect was the decrease in body weight gain at a dose of 1000 mg/kg bw/day. No effects were seen in rats at a dose of 500 mg/kg bw/day. Furthermore, no effects were noted in the offspring of either rabbits or rats at the highest doses tested—i.e., 900 mg/kg bw/day for rabbits and 1000 mg/kg bw/day for rats.

The U.S. EPA/OPP (1997a) uses the NOAEL of 300 mg/kg bw/day as the basis of the RfD for imazamox. As discussed in U.S. EPA/OPP (2001b), however, a subsequent review of the developmental studies in rats and rabbits resulted in a reclassification of the LOAELs to NOAELs because … *decreased body weight gain was not considered biologically significant and thus not appropriate for endpoints of concern for regulatory purposes* (U.S. EPA/OPP 2001b, p. 4). The use of these studies in the current Forest Service risk assessment is discussed further in Section 3.3 (Dose-Response Assessment).

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). During these types of studies, standard observations for gross signs of toxicity are made. 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 2, Table A2-8, a single 2-generation reproduction study in rats (Schroeder 1955) was submitted to and accepted by the U.S. EPA/OPP. A DER for this study is available. In this study, rats were fed diets containing imazamox at concentrations of 0, 1000, 10,000, or 20,000 ppm. As in the standard subchronic and chronic dietary studies (Section 3.1.5), no adverse effects were noted in either P or F_1 adults, and no signs of reproductive toxicity were noted at any exposure level. The dietary concentration of 20,000 ppm is considered a NOAEL and a limit dose by U.S. EPA/OPP. Based on measured food consumption and body weights, this exposure level corresponds to a dose of about 1500 mg/kg bw in male rats and 1700 mg/kg bw in female rats.

3.1.10. Carcinogenicity and Mutagenicity

As reviewed by U.S. EPA/OPP (2001b, pp. 6-7), imazamox has been subject to several standard assays for mutagenicity using both bacterial and mammalian cell cultures as well as an *in vivo* micronucleus assay in mice. All of these assays were accepted by the U.S. EPA/OPP, and none of the assays evidenced any mutagenic activity.

One study on the potential mutagenicity of imazamox was encountered in the open literature. Fragiorge et al. (2008) assayed imazamox and several other imidazolinone herbicides using a strain of fruit flies (*Drosophila melanogaster*) that are trans-heterozygous for the specific types of wing mutations. In this assay system, larvae were fed imazamox or other herbicides at various dietary concentrations. According to this assay system, imazamox tested positive for one type of mutation—i.e., large single spots on the wing—at a dietary concentration of 20.0 mM (≈ 6100 mg/L). While not providing specific details, Fragiorge et al. (2008) note that the high concentrations of imazamox were also associated with toxicity to the larvae.

In terms of a quantitative significance to the human health risk assessment, carcinogenicity is an issue only if the data are adequate to support the derivation of a cancer potency factor. A cancer

potency factor is typically derived based on a dose-related increase in malignant tumors from a chronic toxicity study in mammals that encompasses a significant portion of the test animals' lifespan. As summarized in Appendix 2, chronic dietary exposures were conducted over a substantial portion of the lifespan of mice and rats. No signs of carcinogenicity were observed in either of these bioassays. Based on the lack of carcinogenicity in these two bioassays, the EPA hazard identification for imazamox (U.S. EPA/OPP 2001b, p. 6) states: *Imazamox is classified as a "not likely to be a human carcinogen" based on the lack of evidence for carcinogenicity in mice and rats*.

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 2010). For all three endpoints, the U.S. EPA/OPP uses a ranking system for response ranging from Category I (most severe response) to Category IV (least severe response). These studies are summarized in Appendix 2: Table A2-4 for skin irritation, Table A2-5 for skin sensitization, and Table A2-6 for eye irritation. Furthermore, these endpoints are addressed in the EPA hazard identification for imazamox (U.S. EPA/OPP 2001b), and DERs are available for all studies. For each endpoint, assays are available on both technical grade imazamox and an 11.83% formulation of imazamox. As discussed in Section 3.1.4, it is not clear that the 11.83% formulation is identical to Clearcast, a 12.1% formulation.

3.1.11.1. Skin Irritation

Standard skin irritation studies were conducted on both technical grade imazamox (Fischer 1992b) as well as an 11.83% formulation of imazamox (Boczon 1994b). In both skin irritation studies, only minimal effects were noted: slight erythema in one of six rabbits at 1 hour after exposure to the imazamox formulation and barely perceptible irritation in two of six rabbits at 24 hours after exposure to technical grade imazamox. Based on these studies, U.S. EPA/OPP (2001a, p. 12) classifies imazamox as Category IV for skin irritation—i.e., non-irritating to the skin.

3.1.11.2. Skin Sensitization

Standard assays for skin sensitization in guinea pigs were conducted on both technical grade imazamox (Boczon 1994c) as well as an 11.83% formulation of imazamox (Glaza 1992), and both of these studies are classified as acceptable by the U.S. EPA/OPP. Skin sensitization was not observed in either study.

3.1.11.3. Ocular Effects

Standard assays for eye irritation in rabbits were conducted on technical grade imazamox (Fischer 1992a) as well as an 11.83% formulation of imazamox (Boczon 1994). No eye irritation was noted with the formulation (Category IV); however, technical grade imazamox caused moderate eye irritation (Category III).

3.1.12. Systemic Toxic Effects from Dermal Exposure

As summarized in Appendix 2, Table A2-2, acute dermal toxicity studies were conducted on both technical grade imazamox (Fischer 1994) and an 11.83% formulation of imazamox. In addition, a standard subchronic toxicity study is available on technical grade imazamox (Blaszcak 1995). In the two acute toxicity studies, no mortality or gross signs of toxicity were

observed at doses of 4000 mg/kg bw. In the acute assay using the imazamox formulation, porphyrin secretion into tears as well as slight dermal irritation and blood around the noses of some of the rats was observed from Day 3 to Day 11 of the study. In the subchronic study with technical grade imazamox, no signs of toxicity were observed at doses of up to 1000 mg/kg bw/day over the 4 week period of dosing.

3.1.13. Inhalation Exposure

As summarized in Appendix 2, Table A2-3, two inhalation toxicity studies are available, one on technical grade imazamox (Hoffman 1994a) and the other on the 11.83% formulation of imazamox (Hoffman 1994b). The EPA classifies both studies as acceptable.

Both of these studies, like the acute dermal toxicity studies (Section 3.1.12), are limit tests, each involving a 4-hour period of exposure to a single nominal air concentration of 6.3 mg/L of technical grade imazamox or 12 mg/L of the formulation. The study on technical grade imazamox appears to have involved whole-body exposures to the material as a dust with a median diameter of 4.8 µM. The assay on the formulation involved nose-only exposures—i.e., an inhalation tube connected to the nose of the exposed animal. As summarized in Table A2-3, a number of clinical signs indicative of stress were observed during a 2-hour period following the whole-body exposures to imazamox dust (Hoffman 1994a). In the nose-only exposures to the formulation, animals in both the control and test groups evidenced signs of stress associated with the exposure method. Over the 2-week post-exposure observation periods, no mortality and no signs of systemic toxicity were noted in either of the two bioassays.

Based on these two acute inhalation toxicity studies, the U.S. EPA classifies imazamox (both the a.e. and the formulation) as Category IV, the minimal classification for acute inhalation toxicity.

3.1.14. Other Formulation Ingredients and Adjuvants

3.1.14.1. Other Formulation Ingredients

U.S. EPA is responsible for regulating both the active ingredients (a.i.) in pesticide formulations as well as any other chemicals that may be 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.

The identities of inerts in pesticide formulations are generally considered trade secrets and need not be disclosed to the general public. Nonetheless, all inert ingredients as well as the amounts of the inerts in the formulations are disclosed to and reviewed by the U.S. EPA as part of the registration process. Some inerts are considered potentially hazardous and are identified as such on various lists developed by the federal government and state governments. The identity of these inerts must be listed on the Material Safety Data Sheet for the formulation. No hazardous substances are listed on the MSDS for Clearcast (BASF 2008), the only formulation of imazamox likely to be used in Forest Service programs.

As discussed in previous subsections, several standard acute toxicity studies are available on both imazamox and an 11.83% imazamox formulation. Occasionally, comparisons of studies on the active ingredient with corresponding studies on a formulation may be useful in inferring whether other ingredients in the formulation substantially contribute to the toxicity of the formulation. This is not the case with imazamox, because both the active ingredient and the formulation have very low toxicities. In both the eye irritation studies (Section 3.1.11.3) and the inhalation toxicity studies (Section 3.1.13), imazamox appeared to be modestly more toxic than the formulation. In both sets of bioassays, however, this difference may be related to the composition of the test material: imazamox in granular form vs. the liquid formulation. In other words, both the greater degree of eye irritation and the observed effects of inhalation exposure may be due to the irritant effects of the particles rather than the toxic effect of imazamox.

3.1.14.2. Adjuvants

As summarized in Table 3, adjuvants including nonionic surfactants (0.25% v/v), methylated seed oils, or vegetable oil concentrates are recommended in both terrestrial and aquatic applications of Clearcast. For some herbicides such as glyphosate, studies are available suggesting that at least some nonionic surfactants may be much more toxic than the herbicide itself (e.g., SERA 1997, 2003). Although the use of adjuvants will clearly enhance the efficacy of imazamox—i.e., toxicity to target species (e.g., Nelson et al. 1998), there is no information, regarding the impact of adjuvants in combination with imazamox or imazamox formulations on humans or other mammals.

Methylated seed oils and vegetable oil concentrates are somewhat vague terms, but there is no basis for asserting that these adjuvants are likely to enhance the toxicity of imazamox 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 imazamox in combination with various nonionic surfactants, it is not possible to generalize about potential health effects. As discussed further in the ecological risk assessment, some nonionic surfactants are much more toxic than imazamox to aquatic species (Section 4.1.3.5).

3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

Whereas the *in vivo* mammalian metabolism of imazamox is considered in Section 3.1.3, this section concerns the metabolism of imazamox in the environment. The environmental metabolism of a pesticide is considered quantitatively, if the metabolites are more toxic and more persistent than the parent compound.

As discussed in U.S. EPA/OPP (2002, p. 78232), the plant metabolites of imazamox are identical to the mammalian metabolites observed in treated rats (Figure 3), and these metabolites do not appear to be toxicologically significant.

The aqueous photolysis of imazamox has been examined in some detail, and there are proposed pathways for the photodecomposition of imazamox (Harir et al. 2007; Quivet et al. 2006). The degradates formed by aqueous photolysis differ from the mammalian and plant metabolites of

imazamox. No toxicity data, however, have been encountered on the photodegradates of imazamox. As discussed in U.S. EPA/OPP (2008a, p. 25), laboratory measurements of the photolysis of imazamox indicate half-lives of about 6.8 hours, but there are no field studies available on the aquatic dissipation of imazamox. Accordingly, the extent to which photodegradates might form in the environment is unclear. Given the lack of toxicity data on the photodegradates of imazamox and uncertainties in the quantitative significance of photolysis under field conditions, the surface water modeling conducted in the current Forest Service risk assessment (Section 3.2.3.4.3) does not incorporate photodegradation into the modeling. Functionally, this approach treats photodegradation byproducts of imazamox as if the degradates were the parent compound. In the absence of toxicity data on the photodegradates, no alternative approach to considering the potential hazards of the photodegradates is apparent.

3.1.15.2. Impurities

There is no published information regarding the impurities in technical grade imazamox or any of its commercial formulations. As indicated in Appendix 1, information on the impurities in technical grade imazamox were disclosed to the U.S. EPA (MRIDs 43193201, 43193204, 43876205, 43876233). This information is considered proprietary and has not been available in the conduct of the current Forest Service risk assessment. Nonetheless, all of the toxicology studies on imazamox involve technical grade imazamox, which is presumed to be the same as or comparable to the active ingredient in the formulation used by the Forest Service. Thus, any toxic impurities present in the formulated product are likely to be encompassed by the available toxicity studies conducted with technical grade imazamox.

3.1.16. Toxicological Interactions

No information is available on the interactions of imazamox with other compounds. As discussed above, there is remarkably little information suggesting that imazamox will have substantial toxicological effects on mammals. Consequently, there is no basis for inferring toxicological interactions of imazamox with other agents.

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 terrestrial applications and Attachment 2 for aquatic applications. These workbooks contain a set of worksheets that detail each exposure scenario discussed in this risk assessment as well as summary worksheets for both workers (Worksheet E01) and members of the general public (Worksheet E02). Documentation for these worksheets is presented in SERA (2009). All exposure assessments associated with terrestrial applications are based on the maximum application rate of 0.5 lb a.e./acre. All exposure assessments for aquatic applications are based on the maximum target concentration of 0.5 mg a.e./L.

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 imazamox, central estimates of exposure for workers are approximately 0.007 mg/kg/day for aerial and backpack workers and about 0.01 mg/kg/day for broadcast ground spray workers. Upper ranges of exposures are approximately 0.04 mg/kg/day for backpack and aerial workers and 0.08 mg/kg/day for broadcast ground spray workers. Aquatic applications of imazamox are associated with doses of 0.006 (0.003 to 0.013) mg/kg bw/day, which are similar to the doses estimated for terrestrial applications. All of the accidental exposure scenarios for workers involve dermal exposures. The accidental exposure scenarios lead to dose estimates that are comparable to the general exposure levels estimated for workers. For terrestrial applications, the upper bound estimate of the absorbed dose is about 0.08 mg/kg bw if contaminated gloves are worn for 1 hour. The scenario for wearing contaminated gloves for 1hour during aquatic applications leads to higher levels of exposures with an upper bound dose estimate of about 0.8 mg/kg bw.

For the general public (Worksheet E03), acute non-accidental exposure levels associated with terrestrial applications range from minuscule (e.g., $1x10^{-9}$ mg/kg/day) to about 0.7 mg/kg bw at the maximum application rate of 0.5 lb a.e./acre. The upper bound of exposure, 0.7 mg/kg bw, is associated with the consumption of contaminated vegetation. The other acute exposure scenarios lead to lower and often much lower dose estimates. The lowest acute exposure levels are associated with swimming in or drinking contaminated water. Of the accidental exposure scenarios, the greatest exposures are associated with the consumption of contaminated water by a small child, for which the upper bound dose is about 1 mg/kg bw/day. For aquatic applications, the consumption of contaminated vegetation is not a relevant route of exposure. The highest non-accidental exposure scenario for aquatic applications is associated with the consumption of contaminated water for which the upper bound of the estimated dose is about 0.06 mg/kg bw/day.

The chronic or longer-term exposure levels are much lower than the estimates of corresponding acute exposures. For terrestrial applications, the highest longer-term exposure levels are associated with the consumption of contaminated vegetation, and the upper bound for this scenario is about 0.2 mg/kg/day, which is followed by the scenario for the longer-term consumption of contaminated fruit with an upper bound of 0.03 mg/kg/day. As with the acute exposures, the lowest longer-term exposures are associated with the consumption of surface

water. For aquatic applications, the highest longer-term exposure level is about 0.01 mg/kg bw/day, the upper bound of the estimated dose associated with 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 terrestrial application rate of 0.5 lb a.e./acre (Attachment 1) and the maximum aquatic target concentration of 0.5 mg a.e./L. 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

3.2.2.1.1. Terrestrial Applications

As described in SERA (2007a), 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, taken from Table 3-3 in SERA (2007a), are summarized in Table 4 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. Estimates of the number of acres per day that a worker might treat are also given in Table 4. 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 2.3.1, other application methods may be used for imazamox, including foliar spot, hack and squirt, cut stump, and basal bark applications. Exposure rates for these application methods are not available. In the evaluation of Forest Service programs that use these application methods, the most prudent approach would be to calculate the amount of imazamox that a worker would apply in a single day and use the exposure rates for backpack applications given in Table 4.

For some pesticides, either the product label or standard Forest Service practice will require the use of personal protective equipment (PPE). This is not the case with imazamox. The product label for Clearcast recommends the use of chemical-resistant gloves, long-sleeved shirts, long

pants, and shoes and socks. 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 4. 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 use of extraordinary PPE does not have an impact the risk characterization.

Typical occupational exposures involve multiple routes of exposure (i.e., 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.

3.2.2.1.2. Aquatic Applications

The literature on imazamox does not include data regarding absorbed doses in workers involved in aquatic applications. This situation is similar to that encountered in Forest Service risk assessments on fluridone (SERA 2008a) and rotenone (SERA 2008b). In the fluridone and rotenone risk assessments, a study on worker exposure rates associated with aquatic applications of 2,4-D (Nigg and Stamper 1983) is used as a surrogate study for worker exposure. The study involved the application of a liquid formulation of 2,4-D by airboat handguns to control water hyacinths. The absorbed doses of 2,4-D were assayed in four workers as total urinary elimination over a 24-hour period. The estimated occupational exposure rates for the workers applying 2,4-D were 0.0009 (0.0004-0.002) mg/kg body weight per lb handled.

In the more recent Forest Service risk assessment on endothall (SERA 2010), much lower worker exposure rates are used—i.e., 0.000039 (0.000033 to 0.000054) mg/kg bw per lb a.i. handled. As detailed in the endothall risk assessment, these lower worker exposure rates are based on an occupational exposure rate developed by U.S. EPA/OPP (2005) which considers the severe dermal irritant effects of endothall. As noted in Section 3.1.11.1, however, imazamox causes only minimal skin irritation. Consequently, the higher worker exposure rates of 0.0009 (0.0004-0.002) mg/kg body weight per lb handled are used to estimate exposure levels for workers involved in aquatic applications of imazamox.

As shown in Worksheet A01 of Attachment 2 (EXCEL workbook for aquatic applications of imazamox), the amount handled is calculated as the product of the target application rate and the volume of water to be treated. For the current risk assessment, the target application rate is taken as the highest labeled rate, 500 ppb (equivalent to 0.5 mg/L). The volume of water is taken as 6,000,000 liters. The water volume is based on assumptions used by the U.S. EPA in a recent occupational exposure assessment for rotenone (U.S. EPA/OPP 2006). This is the same water volume used in the Forest Service risk assessments on fluridone (SERA 2008a) and rotenone (SERA 2008b).

In the evaluation of any specific Forest Service application, the target application rate as well as the volume of water to be treated would be adjusted in Worksheet A01 to reflect the anticipated application of imazamox at a specific site. As discussed further in Section 3.4.2 (risk characterization for workers), the HQs for workers involved in aquatic applications of imazamox

are far below the level of concern; furthermore, variations in the volume of water to be treated are not likely to have an impact on the risk characterization for workers.

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), the 11.83% formulation of imazamox does not appear to be an eye irritant, and the Clearcast label does not specifically note the use of protective eye wear.

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 workbooks that accompany this risk assessment. Additionally, Worksheet E01 references other worksheets in which the calculations of each exposure assessment are detailed.

Exposure scenarios involving direct contact with solutions of imazamox 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 imazamox 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 10 gallons/acre with a range of 5-30 gallons per acre, which encompasses the potential range of applications to be used in ground and aerial treatments (Section 2.4.1). At an application rate of 0.5 lb/acre, the estimated concentrations in a field solution are 6 mg/mL with a range of 2 to 12 mg/mL (Worksheet A01 in Attachment 1). For aquatic applications, Clearcast may be applied without dilution. Based on the bulk density of Clearcast and the percent a.e. of imazamox in Clearcast, the concentration of imazamox in undiluted field solutions of Clearcast is taken as 120 mg a.e./L. Details of these calculations are given in Worksheet A01 of Attachment 2.

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 on, or 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 could be exposed to imazamox in Forest Service applications involving the treatment of recreational areas, including campgrounds, picnic areas, and trails. 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 (2007a, 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 M*aximum 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 imazamox 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 workbooks that accompany this risk assessment. 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).

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 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. 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 imazamox at the maximum application rate of 0.5 lb a.e./acre for terrestrial applications or the maximum target concentration of 0.5 mg a.e./L for aquatic applications. 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 (MEI) as well as the most sensitive individual. As detailed in Section 3.1.9.1, the only adverse effects associated with exposure to imazamox, albeit at very high doses, are those noted in developmental toxicity studies. Consequently, the exposures 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 are provided in documentation for the worksheets (SERA 2009).

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 imazamox. This 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 imazamox. This is 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

In the EXCEL workbooks that accompany this risk assessment, three exposure scenarios are given for the consumption of contaminated water: the consumption of contaminated water by a small child following an accidental spill (Worksheet D05), the consumption of contaminated water by a small child, based on expected peak imazamox concentrations in water (Worksheet D06), and the consumption of contaminated water by an adult male, based on expected longer-term water concentrations of imazamox (Worksheet D07). Details of the accidental spill scenario are provided in Section 3.2.3.4.1. The development of the expected peak and longer-term imazamox concentrations of imazamox in water are developed in the remaining subsections, and these concentrations are summarized in Section 3.2.3.4.6.

3.2.3.4.1. Accidental Spill

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 specifics of this scenario are 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, it 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, and the amount of contaminated water consumption. 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.

For terrestrial applications, spill volumes of 100 gallons with a range of 20-200 gallons are used to reflect plausible spill events. These spill volumes are used in all Forest Service risk assessments involving terrestrial applications. The imazamox concentrations 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 imazamox in a small pond ranges from about 0.15 to about 9 mg/L, with a central estimate of about 2.3 mg/L (Attachment 1, Worksheet D05).

For aquatic applications, the spill volumes of 20 to 200 gallons of formulation are not sensible. As discussed in Section 3.2.2.1.2, aquatic applications are assumed to involve the treatment of 6,000,000 liters of water at the target application rate of 0.5 mg/L. As detailed in Worksheet A01 of Attachment 2 (the EXCEL workbook for aquatic applications), this treatment scenario involves the use of about 6.6 lbs a.e. of imazamox. Clearcast, the formulation of imazamox considered in this risk assessment, contains imazamox at a concentration of 1 lb a.e./gallon. Thus, the maximum volume of a spill associated with the amount of water treated by a single worker would be about 6.6 gallons. The volume of a spill, however, could be greater than 6.6 gallons in the case of a crew of workers treating a body of water with a volume greater than 6,000,000 liters. For example, a 10 acre pond (≈40,470 m^2) with an average depth of 2 meters would have a volume of 40,470 m^3 or about 40 million liters. To reach a target concentration of 0.5 mg/L, this body of water would be treated with about 44 pounds of imazamox [40,470,000 L x 0.5 mg a.e./L = 20,235,000 mg a.e. ≈ 20.2 kg a.e. ≈ 44.44 lbs a.e.]. Thus, for this larger pond, about 44 gallons of Clearcast would be used. This type of situational variability is extremely difficult to address analytically. For the current risk assessment, the volume of a spill for an aquatic application is assumed to range from 6.6 gallons (the amount used by a single worker) to 45 gallons (the amount needed to treat a relatively large pond). The central estimate of the spill volume is taken as 20 gallons—i.e., the geometric mean of 6.6 and 45 rounded to one significant digit. Based on these assumptions, the estimated concentration of imazamox in a small pond ranges from about 3 to about 20 mg/L, with a central estimate of about 9 mg/L (Attachment 2, Worksheet D05).

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

Estimates of imazamox concentrations in ponds and streams due to drift are developed only for terrestrial applications (Attachment 1). 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 imazamox at the maximum application rate of 0.5 lb a.e./acre, the peak concentration in the pond would be about 0.0561 mg/L (Worksheet D10a). This concentration is a factor of about 160 below the upper bound of the peak concentration of 9 mg/L after the accidental spill (Section 3.2.3.4.1, Worksheets D05). Worksheet D10a also models

concentrations at distances of 25-900 feet down wind based on standard values adapted from AgDrift and assuming aerial application (SERA 2009). Based on these estimates, imazamox concentrations in a small pond contaminated by drift would range from about 0.0007 to 0.01 mg/L. Drift from aerial application is used in Worksheet 10a, because of all the application methods, aerial applications are associated with the greatest drift rates.

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 0.05 mg/L. Much lower concentrations, ranging from about 0.0006 to 0.01 mg/L are estimated based on drift at distances of 25-900 feet (Worksheet D10b).

3.2.3.4.3. GLEAMS Modeling

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 was used in the current risk assessment to model imazamox concentrations in a small stream and a small pond.

The generic site parameters used in the Gleams-Driver runs are summarized in Table 5, 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. As summarized in Table 6, nine locations are used in the Gleams-Driver 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 pesticide losses to surface water from 100 modeled applications at a unit application rate of 1 lb a.e./acre, and each of the simulations was followed for a period of more than 1½ years post application.

Table 7 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 to the parameters used by U.S. EPA/OPP (2008b) in PRZM/EXAMS modeling of imazamox. The EPA modeling efforts are discussed below (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 7 indicate the sources of the chemical-specific values used in the GLEAMS modeling effort.

Two of the chemical specific parameters used in Gleams-Driver modeling, soil K_{oc} and sediment K_d, are based on distributions rather than single values, and this approach differs from the approach used in the modeling done by U.S. EPA/OPP (2008b). This approach is taken because the binding of imazamox to soil does not follow the simple K_{oc} model in which the K_{oc} should be relatively constant because, under the K_{oc} model, soil binding is directly proportional to the organic carbon in the soil (e.g., Winegardner 1996). As summarized in Table 2, soil K_{oc} and sediment K_d values for imazamox are highly variable ranging from about 2 to 374. In addition to this variability, all of the soil binding studies on imazamox (Kuhn 1995; Mangels 1994b; Sakaliene et al. 2007) note that the binding of imazamox to soil does not correlate well with soil organic carbon, soil pH, cation exchange capacity, or any other soil parameters. Because of the apparent lack of correlation between soil binding and organic carbon, the K_{oc} and sediment K_d values are not specified by soil type. Instead, these values are represented by triangular distributions which are identical for each of the three soils modeled. The K_{oc} values are modeled with a mode of 67 and a range of 2 to 374. These values are based on the summary of K_{oc} values for imazamox given in the review by the European Commission (2002). As summarized in Table 2, these K_{oc} values are consistent with and encompass K_{oc} values reported in U.S. soils. The K_d values are modeled with a mode of 0.5 and a range of 0.05 to 3. These values are a composite of the K_d values reported in open literature publication of Sakaliene et al. (2007) and registrant submitted study by Mangels (1994b).

The above values for K_{oc} and K_d are substantially different from the modeling by U.S. EPA/OPP (2008b). U.S. EPA/OPP (2008b, p. 13) reports that a K_d of 159 mL/g was used in the PRZM/EXAMS modeling. This K_d is attributed to MRID 43193242, which is the study by Mangels (1994b), and the K_d of 159 mL/g is cited as the average K_d. As summarized in Table 2, the average K_d from the study by Mangels (1994b) is 0.81 mL/g and the average K_{oc} is 59.2 mL/g. U.S. EPA/OPP (2008b, p. 35-36) provides a copy of the input file used in the PRZM/EXAMS modeling which indicates that a K_{oc} (not a K_d) of 159 mg/L was used. The units of mg/L are incorrect. While somewhat speculative, it appears that U.S. EPA/OPP (2008b) used a K_{oc} of 159 mL/g in the PRZM/EXAMS modeling and that the use of 159 mL/g rather than 59 mL/g was an input error. The results of the PRZM/EXAMS modeling are discussed below in Section 3.2.3.4.4.

The only other noteworthy component of the K_{oc} inputs for Gleams-Driver involves the open literature publication of Celis et al. (1999) which reports K_{oc} values for imazapic ranging from essentially zero (no binding to soil) to over 1000. This study, however, involves the treatment of various clay soils with synthetic hydroxides to assess the potential use of synthetically modified clay soils to serve as binding agents in the restoration of contaminated water. The K_{oc} values from such modified soils are not germane to modeling concentrations of imazamox in water following applications to natural soils.

Details of the results for the Gleams-Driver runs are provided in Appendix 8. A summary of the results for the Gleams-Driver runs are presented in Table 8, along with a summary of other modeling efforts which are discussed further in the following subsection. The uses of all of the

available data in developing the exposure assessments for the current risk assessment are discussed in Section 3.2.3.4.6.

3.2.3.4.4. Other Modeling Efforts

Other efforts to model imazamox concentrations in surface water are summarized in Table 8, which also summarizes the surface water modeling conducted for the current risk assessment. To estimate concentrations of a pesticide in ambient water, the U.S. EPA will typically use either Tier 1 screening models (e.g., GENEEC, FIRST, and SCIGROW) or PRZM/EXAMS, a more refined Tier 2 modeling system. In the EPA's most recent risk assessment on imazamox, U.S. EPA/OPP (2008b), PRZM/EXAMS was used to model applications of imazamox using the Florida turf scenario at an application rate of about 0.5 lb a.e./acre. As discussed in Section 3.2.3.4.3, the chemical-specific input parameters used in U.S. EPA/OPP (2008b) are also used in Gleams-Driver with the exception of the values for the soil K_{oc} and sediment K_d.

As summarized in Table 8, the average surface water concentrations modeled in U.S. EPA/OPP (2008b) are lower than the average concentrations modeled using Gleams-Driver by a factor of about 3 based on peak exposures (about 3 vs 10 ppb) and 10 based on longer-term exposures (about 0.5 vs 5 ppb). In addition, upper bound concentrations from Gleams-Driver are much higher than the upper bound concentration modeled in U.S. EPA/OPP (2008b)—i.e., upper bound peak concentrations of 190 ppb using Gleams-Driver vs 4.8 ppb from PRZM/EXAMS and upper bound longer-term concentrations of about 100 ppb using Gleams-Driver vs 0.66 ppb using PRZM/EXAMS. This is not an unusual situation in comparisons of a single PRZM/EXAMS simulation by U.S. EPA/OPP and the standard Gleams-Driver simulations in Forest Service risk assessments. The U.S. EPA/OPP (2008b) conducted a single 20-year simulation at a site in Florida. As discussed in Section 3.2.3.4.3, the Gleams-Driver simulations involve nine different locations, as specified in Table 6, and three different soil textures (clay, loam, and sand) were used for a total of 27 simulations with each simulation involving 100 replicates. Thus, the greater variability noted in the Gleams-Driver simulations relative to the single PRZM/EXAMS simulation probably reflects the more variable and extreme conductions used in the Gleams-Driver simulations.

As also summarized in Table 8, the earlier EPA risk assessment (U.S. EPA/OPP 1997a) reports a 1-year average concentration of 1 ppb modeled in GENEEC. While GENEEC is a conservative Tier 1 model, the Gleams-Driver pond simulations of a small pond yielded an average concentration of about 5 ppb and a peak concentration of about 100 ppb. Again, the somewhat higher average and much higher peak concentrations modeled with Gleams-Driver reflect the more variable and extreme conditions used in the Gleams-Driver modeling.

3.2.3.4.5. Monitoring Data

There are no monitoring data regarding concentrations of imazamox in surface water. USGS (2003a) provides data on the agricultural uses of imazamox; however, USGS (2003b) does not include imazamox in the survey of pesticides in streams and groundwater.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

For terrestrial applications, the surface water concentrations of imazamox used in the current risk assessment are summarized in Table 9. 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 8, units of exposure are expressed as ppb or µg/L, as a matter of convenience. In Table 9, 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 B04 in Attachment 1 (the EXCEL workbook for terrestrial applications). The values in Worksheet B04 are linked to the appropriate scenario-specific worksheets in the EXCEL workbooks.

As discussed in the previous subsections and summarized in Table 8, the Gleams-Driver simulations of the small pond provided the highest estimates of imazamox concentrations in surface water. Consequently, the Gleams-Driver simulations serve as the basis for the water concentrations of imazamox used in the current risk assessment.

As summarized in Table 9, the peak concentrations are taken as 0.011 (0.00004 to 0.19) mg a.e./L. The central estimate of 0.011 mg/L is based on the central estimate of 10.5 ppb (i.e., equivalent to 10.5 µ/L) from the Gleams-Driver modeling of the small pond rounded upward to 11 ppb (11 µg/L) or 0.011 mg/L. The upper bound of 0.19 mg/L is simply a unit conversion of the upper bound concentration of 190 ppb from the Gleams-Driver pond simulations. The lower bound of 0.00004 mg/L is based on the lower bound of the peak concentrations in a small pond for a wet and warm location with sandy soil. As indicated in Appendix 8, Table A8-7, this concentration is 0.04 ppb (0.04 µg/L or 0.00004 mg/L). Lower concentrations could be selected but would have no impact on the risk assessment.

As also summarized in Table 9, the longer-term concentrations are taken as 0.0051 (0.000002 to 0.104) mg a.e./L. The central estimate and upper bound are the central estimate of 5.1 ppb and the upper bound of 104 ppb converted to units of mg/L. Both of these values could be rounded down to a single significant digit and the failure to round is not intended to suggest a high degree of precision. Downward rounding is avoided simply to maintain slightly more conservative estimates of exposure. The lower bound of 0.000002 mg/L is based on the modeled concentration of 0.0023 ppb, the lower bound of the annual average concentration in a pond at a wet and temperate location with predominantly sandy soil. As with the lower bound of the peak concentrations, a lower concentration could be selected but would have no impact on the risk assessment.

All of the concentrations given in Table 9 apply only to terrestrial applications and are used only in Attachment 1, the EXCEL workbook for terrestrial applications. For aquatic applications, the peak concentration in surface water is taken as 0.5 mg a.e./L, the maximum target application rate. Longer-term concentrations are modeled based on an assumed dissipation half-life of 90 days. This 90-day value is admittedly arbitrary. The actual dissipation of imazamox in surface water could vary remarkably, depending on the site-specific conditions for the body of water that is being treated. As discussed further in Section 3.4 (risk characterization for human health), peak concentrations of imazamox are far below the level of concern, and the dissipation half-life for imazamox has no impact on the human health risk assessment. Similarly and as discussed in Section 4.4 (risk characterization for ecological effects), assumptions concerning the dissipation half-life of imazamox have no impact on the ecological risk assessment for aquatic applications of imazamox.

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).

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 imazamox 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 (2007).

Imazamox has a relatively low potential for bioconcentration. As summarized in Appendix 5, Table A5-2, the bioconcentration study by Johnson (1995) notes bioconcentration factors in inedible fish tissue ranging from 0.054 to 0.066 over a 28-day exposure of bluegill sunfish to C^{14}-labeled imazamox. These estimates of bioconcentration, however, are based on total radioactivity rather than the identification of imazamox residues. Consequently, the apparent bioconcentration reflects the binding of imazamox, imazamox metabolites, including mineralized carbon, to fish tissue. Concentrations of imazamox in edible fish tissue were below the limit of quantification.

For the current risk assessment, the bioconcentration factor of 0.1 is used to estimate dietary exposure to fish. This is the maximum bioconcentration factor of 0.066 for the inedible fish tissue from Johnson (1995) rounded to one significant place. This value will overestimate likely exposures for humans, because individuals generally consume only the edible portion of the fish. As discussed further in Section 3.4.3, this approach has no impact on the current risk assessment because the estimated exposures are substantially below the level of concern.

The scenarios associated with consumption of contaminated fish are based on the same concentrations of imazamox in water used for the accidental spill scenario (Section 3.2.3.4.1.) and the drinking 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 (Worksheet D11). 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).

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 imazamox 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 imazamox 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 applications of imazamox and are omitted from the EXCEL workbook for aquatic applications of imazamox (Attachment 2).

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 imazamox (U.S. EPA/OPP 2008b, p. 19).

The residue rates recommended by Fletcher et al. (1994) are given in Table 10 of the current Forest Service 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 imazamox 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. This data gap is somewhat unusual for an herbicide.

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 (Knissel and Davis 2000) suggests that soil half-lives are usually much greater than foliar half-lives.

As summarized in Table 7, a soil half-life 81 days is used for Gleams-Driver modeling, based on studies reviewed and accepted by the EPA (U.S. EPA/OPP 2008b). This estimated soil half-life is quite conservative. As summarized in Table 2, soil half-lives for imazamox are reported to range from 12 days (European Commission 2002) to 30 days (Ta 1994).

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-life by 4. Thus, the half-life for total residues on contaminated vegetation or fruit are taken as 20 days—i.e., 81 days divided by 4 and rounded to the nearest day.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

The dose-response assessment for imazamox is highly atypical because endpoints of concern for imazamox cannot be identified. In other words, imazamox does not appear to be toxic to mammals, and potential hazards to humans cannot be identified. U.S. EPA/OPP (1997a) proposes an RfD of 3 mg/kg bw/day for imazamox based on a developmental study in rabbits, which is essentially rescinded in U.S. EPA/OPP (2008b). The doses of 600 and 900 mg/kg bw from the developmental study in rabbits which are classified as LOAELs in U.S. EPA/OPP (1997a) are reclassified as NOAELs in U.S. EPA/OPP (2008b). Although it appears that the reclassification by U.S. EPA/OPP is appropriate, the current risk assessment uses the RfD of 3 mg/kg bw/day proposed in U.S. EPA/OPP (1997a) as a tool to quantitatively characterize risks by developing HQs. Limitations with the use of the 3 mg/kg bw/day dose as an RfD are discussed in the Risk Characterization (Section 3.4).

3.3.2. Chronic RfD

The U.S. EPA has not derived an agency-wide chronic RfD for imazamox—i.e., there is no RfD for imazamox 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 (1997a) discussed below, no exposure criteria are available.

U.S. EPA/OPP (1997a) uses the NOAEL of 300 mg/kg bw/day from the developmental toxicity study in rabbits (Hoberman 1995) with an uncertainty factor of 100 to derive a chronic RfD of 3 mg/kg bw/day. The uncertainty factor of 100 was derived as a multiple of a factor of 10 for animal-to-human extrapolation and a factor of 10 for potentially sensitive individuals in the human population. As discussed in Section 3.1.9.1 and summarized in Appendix 2, Table A2-7, the NOAEL of 300 mg/kg bw/day is associated with a LOAEL of 600 mg/kg bw/day. The only effect observed at the dose of 600 mg/kg bw/day was a decrease in food consumption. At a dose of 900 mg/kg bw/day, the only effects observed by Hoberman (1995) were a decrease in food consumption and a corresponding decrease in body weight. The NOAEL of 300 mg/kg bw/day in rabbits is supported by a NOAEL of 500 mg/kg bw/day in rats with a corresponding LOAEL (also based on decreases in body weight) of 1000 mg/kg bw/day (Foss 1994).

In a subsequent review of developmental studies in both rabbits (Hoberman 1995) and rats (Foss 1994), U.S. EPA/OPP (2001b) reclassifies the LOAELs in rabbits and rats as NOAELs. As noted in Section 3.1.9.1, this reclassification is based on the determination that … *decreased body weight gain was not considered biologically significant and thus not appropriate for endpoints of concern for regulatory purposes* (U.S. EPA/OPP 2001b, p. 4). In other words, U.S. EPA/OPP (2001b) essentially rescinds the chronic RfD of 3 mg/kg bw/day and the rationale for this approach is stated concisely and completely as follows:

> *No toxicity was seen at doses exceeding the Limit-Dose in long-term studies in mice (NOAEL=1053 mg/kg/day), rats (NOAEL= 1068 mg/kg/day), dogs (NOAEL= 1156 mg/kg/day) and 2-generation reproduction study in rats (NOAEL 1469 mg/kg/day). No developmental or maternal toxicity was observed in rats (NOAEL 1000 mg/kg/day) and rabbit developmental (NOAEL 900 mg/kg/day) toxicity study. No suitable*

> *end point of concern was observed in any of the available oral studies. No quantification of risk is required since no hazard is identified.*
>
> U.S. EPA/OPP 2001b, p. 4

As noted in Section 3.1.5, the term *limit-dose* is used to designate the highest dose required by the EPA in toxicity studies.

While the position taken in U.S. EPA/OPP (2001b) is reasonable, the current risk assessment maintains the RfD of 3 mg/kg bw/day originally proposed in U.S. EPA/OPP (1997a). This approach does not imply any disagreement with the EPA determination expressed in U.S. EPA/OPP (2001b), as quoted above. Instead, the RfD of 3 mg/kg bw/day is maintained simply as a tool to develop quantitative risk characterizations—i.e., hazard quotients or HQs —as detailed further in Section 3.4. It is noted that a higher RfD of up to about 10 mg/kg bw/day could be justified based on the NOAELs summarized above by U.S. EPA/OPP (2001b). This argument is not given further consideration because the RfD of 3 mg/kg bw/day does not lead to any HQs that exceed the level of concern (HQ=1).

3.3.3. Acute RfD

The U.S. EPA/OPP will sometimes derive acute RfDs for some 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.

As discussed in the previous subsection on the chronic RfD, endpoints of concern that might be associated with a single dose of imazamox are not identified in the available toxicity studies. Consequently, the chronic RfD of 3 mg/kg bw/day proposed in U.S. EPA/OPP (1997a) is used to characterize risks associated with acute exposures to imazamox.

3.3.4. Dose-Severity Relationships

Most Forest Service risk assessments of pesticides consider dose-severity relationships as an effort to more fully characterize potential risks in exposure scenarios where the doses exceed the RfD. For imazamox, however, endpoints of concern cannot be identified and dose-severity relationships are not relevant. In addition, as discussed in Section 3.4, there are no exposure scenarios, including accidental exposure scenarios, that result in dose estimates that exceed the chronic RfD.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

The quantitative risk characterization in both the human health and in the ecological risk assessment is based on the hazard quotient (HQ), which is defined as the anticipated exposure divided by the toxicity value. For both workers and members of the general public, the chronic RfD of 3 mg a.e./kg bw/day is used to characterize risks associated with both acute and longer-term exposures. As discussed in the exposure assessment (Section 3.2.2), all exposure assessments for terrestrial applications are based on the application of Clearcast at the maximum application rate of 0.5 lb a.e./acre. For aquatic applications, all exposure assessments are based on the maximum target concentration of 0.5 mg a.e./L.

In most Forest Service risk assessments, an HQ of 1 is defined as the level of concern. As discussed in the dose-response assessment (Section 3.3), imazamox is somewhat unusual in that doses of imazamox that may cause adverse effects have not been determined. Thus, the interpretation of HQs that exceed a value of 1 would be unclear. This is not a practical concern in this risk assessment on imazamox because none of the HQs exceed a value of 1. There is no basis for asserting that imazamox is likely to pose any identifiable risk to either workers or members of the general public.

3.4.2. Workers

The quantitative risk characterization for workers is summarized in Table 11. The HQs given in this table are taken from Worksheets E02 in Attachment 1 (terrestrial applications) and Attachment 2 (aquatic applications).

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 imazamox. The highest HQ for general exposures—i.e., exposure levels anticipated in the normal use of imazamox—is 0.03, the upper bound of the HQ for workers involved in ground broadcast applications of imazamox. If the RfD of 3 mg/kg bw/day is taken as the level of concern, this HQ is below the level of concern by a factor of over 30. The highest accidental HQ is 0.3, the upper bound of the HQ for a worker involved in aquatic applications wearing contaminated gloves for 1 hour.

3.4.3. General Public

The quantitative risk characterization for members of the general public is summarized in Table 12 for terrestrial applications and Table 13 for aquatic applications. The HQs given in these tables are taken from Worksheets E04 in Attachment 1 (terrestrial applications) and Attachment 2 (aquatic applications).

The risk characterization for members of the general public is essentially identical to the risk characterization for workers: there is no basis for asserting that members of the general public are likely to be at risk due to applications of imazamox. Based on the RfD of 3 mg/kg bw/day, the highest HQs are those associated with an accidental spill of imazamox into a small pond and the subsequent consumption of contaminated water by a small child. For this exposure scenario the HQs are 0.06 (0.003 to 0.3) for terrestrial applications and 0.2 (0.05 to 0.8) for aquatic applications. For most pesticides, HQs in the range of 0.3 to 0.8 might be characterized as … *approaching a level of concern*. This is not the case for imazamox. As discussed in the dose-

response assessment, the dose of imazamox that might actually pose a risk to humans has not been determined. The RfD of 3 mg/kg bw/day may be regarded as a dose that will not lead to adverse effects in humans; however, the same may be said for higher doses of imazamox. The RfD of 3 mg/kg bw/day is used as a convenience to quantitatively illustrate that the use of imazamox is not likely to pose any identifiable risk to humans.

The highest HQ for members of the general public associated with expected (i.e., non-accidental) exposure scenarios is 0.2, the upper bound of the acute HQ for the consumption of contaminated vegetation. For any pesticide that is applied directly to vegetation, this is an extraordinarily conservative exposure scenario which typically leads to HQs that exceed the level of concern. For imazamox, no risks can be identified.

3.4.4. Sensitive Subgroups

No hazards to members of the general population associated with exposure to imazamox have been identified (Section 3.1). Because no mechanism of toxicity for imazamox in humans can be identified, subgroups within the human population that might be sensitive to imazamox cannot be identified.

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 use of imazamox.

As discussed in detail in Sections 3.1.14 (Inerts and Adjuvants) and 3.1.15 (Impurities and Metabolites), imazamox formulations contain inert components, and the metabolism of imazamox involves the formation of other compounds. Given the low HQs associated with non-accidental exposure scenarios and the generally conservative assumptions on which these HQs are based, there does not appear to be a plausible basis for suggesting that inerts, impurities, or metabolites 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 current risk assessment to address adjuvants in detail. This is a general issue in all Forest Service risk assessments.

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 imazamox) and other agents that may cause the same effect or effects by the same or a similar mode of action.

As noted by the U.S. EPA/OPP:

> *Because of the low toxicity of imazamox and its metabolic degradates, there is no concern regarding the potential for cumulative effects of imazamox and its degradates with other substances with a common mode of action. Imazamox belongs to the imidazolinone class of chemistry. The herbicidal activity of the imidazolinones is due to the inhibition of acetohydroxy acid synthase (AHAS), an enzyme only found in plants. AHAS is part of the biosynthetic pathway leading to the formation of branched-chain amino acids. Animals lack AHAS and this biosynthetic pathway. This lack of AHAS contributes to the low toxicity of imazamox in mammals. We are aware of no information to indicate or suggest that imazamox has any toxic effects on mammals that would be cumulative with those of any other chemical.*
>
> U.S. EPA/OPP 2002, p. 78232.

Given the low toxicity of imazamox, concern for cumulative effects is minimal.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Just as the human health risk assessment of imazamox is limited by the available data, which fail to demonstrate any significant or substantial association between imazamox exposure and toxicity, so is the ecological risk assessment constrained in identifying the potential hazards to terrestrial or aquatic animals exposed to imazamox. Compared with the large number of animal species that might be exposed to imazamox, toxicity studies are available on only a few animal species. Furthermore, the data regarding the potential effects of imazamox on aquatic animals are limited to standard acute toxicity studies and brief summaries of longer-term studies in fish and aquatic invertebrates that apparently were not submitted to or evaluated by the U.S. EPA/OPP. Consequently, the longer-term studies in fish and invertebrates are only marginally useful for hazard identification. Nevertheless, within the context of these admittedly substantial reservations, imazamox appears to be essentially nontoxic to terrestrial and aquatic animals.

The toxicity of imazamox to terrestrial plants is relatively well characterized. Like other imidazolinone herbicides and sulfonylurea herbicides, imazamox inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. Based on standard toxicity studies involving both foliar applications and studies on seedling emergence, imazamox is about equally effective in both post-emergent and pre-emergent applications. As with many other imidazolinone herbicides, populations of plants may develop resistance to imazamox by developing less sensitive forms of acetolactate synthase (ALS) and/or through their ability to metabolize and detoxify imazamox more rapidly.

Relatively few bioassays are available on the toxicity of imazamox to aquatic plants. As with some other imidazolinone herbicides, imazamox appears to be more toxic to aquatic macrophytes than to algae. The data on algae, however, are marginal and consist of a single study on four algal species assayed at a single concentration that is below anticipated levels of exposure, particularly for aquatic applications of imazamox. The data on aquatic macrophytes consist of only a two studies on two species of duckweed.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

The toxicity studies used to assess the potential hazards of imazamox to humans (Appendix 2) can also be applied to the risk assessment for mammalian wildlife. While the toxicity of imazamox to plants is understood relatively well (Section 4.1.2.4), it is not clear what, if any, specific toxicity imazamox may cause in mammalian wildlife. As discussed in Section 3.1 and summarized in Appendix 2, acute, subchronic, and chronic toxicity studies on imazamox do not demonstrate adverse effects that are clearly attributable to exposure.

As discussed in Section 3.1.4, there is some confusion concerning the study by Lowe and Bradley (1995a)—i.e., MRID 43876212—which reports LD_{50} values of about 2200 mg/kg bw. In the EPA ecological risk assessment (U.S. EPA/OPP 2008a), these LD_{50} values are attributed to imazamox; however, in the DER for this study, the LD_{50} values seem to be attributed to a soil metabolite of imazamox. Nonetheless, the acute oral toxicity study conducted by Fischer (1993) indicates an LD_{50} >5000 mg a.e./kg bw for imazamox, and according to the classification system applied in ecological risk assessments conducted by U.S. EPA/OPP, any LD_{50} of greater than 2000 mg/kg bw results in a designation of *practically nontoxic* (U.S. EPA/OPP 2001, p. 27). Thus, the uncertainty regarding the LD_{50} values reported in Lowe and Bradley (1995a) has a relatively minor impact on the risk assessment for imazamox.

The lack of information on dose levels of imazamox that cause adverse effects in mammals may be considered an uncertainty. Nonetheless, this uncertainty has a relatively minor impact on the risk assessment because the reasonably complete set of available toxicity studies—chronic studies in three mammalian species (dogs, rats, and mice) and several reproduction studies in two mammalian species (rats and rabbits) indicate that relatively high dose levels of imazamox are not likely to be associated with adverse effects in mammals.

4.1.2.2. Birds

As summarized in Appendix 3, a relatively standard set of toxicity studies, including acute gavage studies (Appendix 3, Table A3-1), acute dietary studies (Appendix 3, Table A3-2), and reproduction studies (Appendix 3, Table A3-3) in both quail and mallards, was submitted to the U.S. EPA. DERs are available for all of these studies with the exception of the acute gavage study in mallards (MRID 43193226, summarized in U.S. EPA/OPP 2008a). In addition, the EPA classifies each of these studies as acceptable (U.S. EPA/OPP 2008a,b).

Like the acute and chronic studies in mammals (Section 3.1), the available avian studies on imazamox, all of which were conducted at limit doses, do not report any signs of toxicity. For instance, a gavage dose of 1846 mg/kg (the highest dose tested) was not associated with mortality or signs of toxicity in quail. As noted above, a DER for the gavage study in mallards (MRID 43193226) is not available. The EPA ecological risk assessments (U.S. EPA/OPP (2008a,b), which do not summarize this study in detail, report an acute gavage LD_{50} of >1950 mg/kg bw in mallards; however, no signs of toxicity or observations on the lack of toxicity in the exposed mallards are discussed in the risk assessments.

In the acute dietary study in mallards (Campbell 1994d), no mortality or signs of toxicity were noted at mean measured dietary concentrations of 5572 ppm. Although the DER indicates that body weights and food consumption rates were determined in this study, they are not reported. Based on data from a feeding study on aminopyralid, another relatively nontoxic herbicide, mallard consume food at a rate of about 42% of their body weight per day (SERA 2007c). Using this food consumption factor, the dietary concentration of 5572 ppm corresponds to a daily dose of about 2300 mg/kg bw [5572 mg/kg food x 0.42 kg food/kg bw ≈ 2340 mg/kg bw].

Acute dietary exposure to 2041 ppm imazamox caused mortality in 4 of 12 quail; however, there was no morality in the control group, in the three lower dietary exposure groups, or in the 5572 ppm dietary exposure group (Campbell et al. 1994c). Using the Fisher Exact test, a response of 4/12, relative to the control response of 0/12, is marginally significant (p=0.046584). These

deaths, however, are discussed in the DER, and they are not attributed to imazamox. The DER attributes three of the deaths to *vent picking* (i.e., cannibalism) by a pen mate and the other death to mechanical injury associated with dropping a pen onto the floor. Given these explanations and the lack of mortality in the 5572 ppm exposure group, there is no basis for attributing the mortality in the 2041 ppm exposure group to imazamox toxicity. The DER indicates that body weights and food consumption were determined but, as with the acute dietary study in mallards, these values are not reported. Again using surrogate data on aminopyralid, the daily food consumption rate for quail during a subacute dietary study is taken as 30% of body weight per day. Using this food consumption factor, the dietary concentration of 5572 ppm corresponds to a daily dose of about 1700 mg/kg bw [5572 mg/kg food x 0.3 kg food/kg bw ≈ 1671.6 mg/kg bw].

As in the developmental studies in mammals (Section 3.1.9.1), in both of the avian reproduction studies (Gagne et al. 1995a,b), slight decreases in food consumption and body weight were noted at various times during the studies and considered incidental to exposure. There is no indication from the information provided in the DERs that the observed changes in body weights were associated with imazamox toxicity. Thus, the NOAEL in both studies is 2000 ppm. The DERs for these studies report both terminal adult body weights as well as average daily food consumption. Based on these values, the daily food consumption rates as a percentage of body weight were about 9.4% for quail and 11% for mallards. For quail, the dietary NOAEL of 2000 ppm corresponds to an average dose of about 190 mg/kg bw/day [2000 mg/kg food x 0.094 kg food/kg bw = 188 mg/kg bw/day]. For mallards, the dietary NOAEL of 2000 ppm corresponds to an average dose of 220 mg/kg bw/day [2000 mg/kg food x 0.11 kg food/kg bw].

4.1.2.3. Reptiles and Amphibians (Terrestrial-Phase)

There is no information in the imazamox literature regarding its toxicity to reptiles or terrestrial-phase amphibians. Neither the database maintained by Pauli et al. (2000) nor the open literature includes information on the toxicity of imazamox to reptiles or terrestrial-phase amphibians. Moreover, according to the EPA ecological risk assessments on imazamox (U.S. EPA/OPP 2008a,b) data on the toxicity of imazamox to terrestrial-phase amphibians or reptiles were not submitted as part of the registration process. As standard practice, U.S. EPA/OPP (2008b, p. 21) notes that … *birds were used as a surrogate for reptiles and terrestrial-phase amphibians.*

4.1.2.4. Terrestrial Invertebrates

In the United States, the registration requirements for testing the effects of herbicides on terrestrial invertebrates are relatively modest, and registrants typically submit only tests on honey bees. For imazamox, a standard contact bioassay in bees is available (Parrish et al. 1994). In this study, imazamox in acetone was applied to abdominal region of honeybees at doses of 0.25, 2.5, or 25 µg/bee. Observations of mortality and other signs of toxicity were made at 1, 2, 4, 24, and 48 hours. Although the DER for this study does not provide details of the mortality rates, the DER notes that mortality was low in all dose groups of bees (from 0 to <5%) and that no dose-response relationship for mortality or any other effect was apparent. The DER also notes abnormal behavior, characterized as bees … *clustered together in the bottom of the recovery cage with little or no movement*. This response was noted in both control and treatment groups and was not attributed to imazamox. The cause or causes of the clustering behavior could not be determined; however, the DER notes that the temperature under which the bees were held (27 °C) was lower than typical temperatures within a bee colony (30 to 35 °C). Despite these

unusual observations, the study by Parrish et al. (1994) is classified as *core*, a term synonymous with acceptable.

The DER for the study by Parrish et al. (1994) does not specify the body weights of the bees. Honeybee body weights are somewhat variable, with typical body weights of worker bees ranging from about 81 to 151 mg (Winston 1987, p. 54). Taking a typical body weight as 100 mg (0.1 g or 0.0001 kg), the contact dose of 25 µg/bee (0.025 mg/bee) would correspond to a dose of about 250 mg/kg bw [0.025 mg ÷ 0.0001 kg].

The study by Parrish et al. (1994) is the only study on terrestrial invertebrates cited in the EPA ecological risk assessments (U.S. EPA/OPP 2008a,b), however imazamox review by the Office of the Health and Consumer Protection Directorate-General of the European Commission provides very brief summaries of toxicity studies in both honeybees and earthworms (European Commission 2002). It is not uncommon for registrants to submit studies to European regulatory groups that are not required by U.S. EPA/OPP. European Commission (2002), however, does not provide full references for the toxicity studies on honeybees or earthworms. The 48-hour LD_{50} values for honeybees are reported as > 40 µg a.s./bee for oral exposure and >58 µg a.s./bee for contact exposures. The meaning of the abbreviation "*a.s.*" is not specified in European Commission (2002) but presumably refers to the *active substance* (i.e., the term appears to be synonymous with *a.i*). Under the assumption that the dose of 40 µg a.s./bee is synonymous with 40 µg a.i./bee, the dose would correspond to about 39 µg a.e./bee [40 µg a.i./bee x 0.947 a.e./a.i. = 38.88 µg a.e.] or about 390 mg a.e./kg bw [0.039 mg a.e. ÷ 0.0001 kg]

In addition to the toxicity values for honeybees, European Commission (2002, p. 18) reports an acute LC_{50} for earthworms of > 901 mg a.s./kg soil as well as reproductive NOECs for earthworms. The reproductive NOECs are reported as 13.4 mg RLF 12270/kg soil, 0.963 mg CL 312,622/kg soil, and 0.963 mg CL 354,825/kg soil. RLF 12270 is defined in European Commission (2002, p. 16) as an emulsifiable concentrate of 16.7 g/L imazamox and 250 g/L pendimethaline (another herbicide). CL 312,622 and CL 354,825 refer to soil metabolites of imazamox. As with the honeybee studies on bees, the European Commission (2002) report does not provide citations for the earthworm toxicity studies.

The European Commission (2002, p.) report also provides toxicity data for other terrestrial arthropods exposed to a 40 g/L formulation of imazamox referenced as SF 09464. As summarized in Table 2, Clearcast contains imazamox at a concentration of 1 lb a.e./gallon, which is equivalent to 456.3 g/3.785 L or 120 g/L. Thus, SF 09464 and Clearcast do not appear to be reasonably similar formulations of imazamox. Moreover, since the European Commission (2002) report does not provide experimental details of the toxicity studies, and the reported study results do not suggest a hazard to terrestrial arthropods, they are not given further consideration in the current risk assessment.

4.1.2.5. Terrestrial Plants (Macrophytes)

The mechanism of action of imazamox in plants is well characterized. Imazamox inhibits acetolactate synthase (ALS), also referred to as acetohydroxyacid synthase (AHAS). Acetolactate synthase is an enzyme found in the chloroplasts of plants and is required for the synthesis of essential branched chain amino acids, valine, leucine, and isoleucine (Kuk and Burgos et al. 2007; Nadler-Hassar et al. 2009; Sala et al. 2008; Tan et al. 2005). This mode of

phytotoxic action is common to all imidazolinone and sulfonylurea herbicides (Osuna et al. 2003).

The testing requirements for the effects of herbicides on terrestrial plants are relatively rigorous, since terrestrial vegetation is the usual target of herbicides. The testing requirements include bioassays for vegetative vigor (i.e., post-emergence applications) and bioassays for seedling emergence (i.e., pre-emergence applications). As summarized in Appendix 4, both sets of studies were submitted to the EPA in support of the registration of imazamox, including a vegetative vigor bioassay (Chetram and Canex 1995 as summarized in Table A4-1) and a seedling emergence bioassay (Chetram et al. 1995 as summarized in Table A4-2). Each of these submissions amounts to a series of plant bioassays on six dicots (cabbage, cucumber, lettuce, radish, soybean, and tomato) and four species of monocots (corn, onion, ryegrass, and oats). DERs are available for both of these submissions, which were accepted by U.S. EPA/OPP and are classified as core. The summaries of these studies in Appendix 4 include both the analyses of the data by the study authors as well as the statistical reanalysis by U.S. EPA/OPP which derives both EC_{25} values and NOAECs. The two sets of analyses do not differ remarkably, but only the U.S. EPA/OPP analysis is used in the current Forest Service risk assessment.

As discussed further in Section 4.3.2.5, the dose response assessment for terrestrial plants is based on the NOAEC values, because the Forest Service prefers to use NOAECs rather than defined effect levels like EC_{25} values. Defined effect levels are preferable, however, for comparisons among species; accordingly, the following discussion focuses on EC_{25} values. In both the vegetation vigor assays (Chetram and Canex 1995) and the seedling emergence assays (Chetram et al. 1995), the most sensitive and tolerant species were dicots. The most sensitive species overall was tomato with an EC_{25} of 0.0008 lb a.e./acre in the vegetative vigor assay. The most sensitive species in the seedling emergence assays was cabbage with an EC_{25} of 0.0018 lb a.i./acre. The most tolerant species were lettuce (EC_{25} of 0.048 lb a.i./acre) in the vegetative vigor assay and soybean (EC_{25} of >0.048 lb a.i./acre) in the seedling emergence assay. The most sensitive species of monocot was oats with an EC_{25} of 0.002 lb a.i./acre in both the vegetative vigor and seedling emergence assays. The most tolerant species of monocot was onion in the vegetative vigor assay (EC_{25} of 0.01 lb a.i./acre) and corn in the seedling emergence assay (EC_{25} of 0.013 lb a.i./acre).

Various efficacy studies involving the use of imazamox for weed control are summarized in Appendix 4, Table A4-3. Although efficacy is not a primary concern in the current risk assessment, these studies are included because differences in the sensitivities of target species (i.e., weeds) may relate to potential differences in the sensitivities of nontarget species. Several studies suggest that imazamox offers effective control for several species of grasses and broadleaf weeds at application rates from about 0.006 to about 0.06 lb a.e./acre (Ball et al. 1999; Blackshaw 1998; Nelson and Renner 1998; Rao and Reddy; Sprague et al 1999; Unland et al. 1999).

The lowest effective application rate cited in the open literature is from Blackshaw (1998). In this study, an application of 7 g a.i./acre (the lowest application rate assayed) of an unspecified imazamox formulation reduced the growth of redroot pigweed (*Amaranthus retroflexus*), assayed as shoot biomass, by about 90% at in the first of 2 years during which imazamox was applied to

cultivated peas. Blackshaw (1998) does not report an EC_{25}—i.e., comparable to the analyses by U.S. EPA/OPP—but does indicate that the dose-response relationship was adequately fit (r^2=0.99) by an exponential model,

$$\boldsymbol{Y} = 2608\ e^{-0.442\,\boldsymbol{d}},$$

where ***Y*** is the shoot biomass in g/m^2 and ***d*** is the dose – i.e., the application rate in g a.i./ha. Setting Y to a 25% reduction in shoot biomass [2608 x 0.75 = 1956] and rearranging to solve for ***d*** (i.e., the application associated with a 25% reduction in shoot biomass) the EC_{25} is estimated at about 0.65 g a.i./ha: $\boldsymbol{d} = \text{Ln}(1956 \div 2608) / -0.442 \approx 0.6509$.

As noted above, Blackshaw (1998) does not specify the imazamox formulation used in the study. Assuming that the formulation consisted of the ammonium salt of imazamox, the application rate of 0.65 g a.i./ha is equivalent to about 0.62 g a.e./ha [0.65 g a.i./ha x 0.947 a.e./a.i. ≈ 0.616 g a.e./ha] or about 0.00055 lb a.e./acre [0.00062 kg a.e./ha x 0.892 lb/ac per kg/ha]. This estimated EC_{25} is modestly lower than the lowest EC_{25} in the standard phytotoxicity studies submitted to the U.S. EPA/OPP—i.e., an EC_{50} of 0.0008 lb a.e./acre for tomato in the vegetative vigor bioassay by Chetram and Canex (1995). The apparently greater sensitivity of redroot pigweed to imazamox is discussed further in the dose-response assessment for terrestrial plants (Section 4.3.2.5).

As also indicated in Appendix 4, Table A4-3, other weeds do not appear to be controlled well by imazamox—i.e., witchweeds at about 0.063 lb a.e./acre (Abyo et al. 1998) and cordgrass at up to 0.057 lb a.e./acre (Mateos-Naranjo et al. 2009). These relatively high but ineffective application rates suggest that some types or at least some populations of weeds may be as tolerant or perhaps more tolerant to imazamox, compared with some of the less sensitive species from the registrant-submitted studies (Chetram and Canex 1995; Chetram et al. 1995).

The relative insensitivity of some plant species or at least some plant populations may be due to the development of resistance. As discussed in the Forest Service risk assessment on imazapyr (SERA 2004a), several types of weed species may develop resistance to imidazolinone herbicides. One mechanism for resistance is a modified form of acetolactate synthase (ALS) that is insensitive to imidazolinone herbicides. This type of resistance to imazamox has been demonstrated in resistance populations of ryegrass (Kuk and Burgos et al. 2007), a saltmarsh aster (Osuna et al. 2003), poinsettias (Plaza et al. 2003), *Cyperus difformis* (Ruiz-Santaella et al. 2004), and sunflowers (Sala et al. 2008). Another mechanism of resistance to imidazolinone herbicides, as well as other ALS-inhibiting herbicides like sulfonylurea herbicides, involves an increase in herbicide metabolism (e.g., Christopher et al. 1992). Mateos-Naranjo et al. (2009) suggest that the insensitivity of cordgrass to imazamox may be due to its rapid metabolism of the herbicide.

4.1.2.6. Terrestrial Microorganisms

Studies on terrestrial microorganisms are not required for pesticide registration in the United States, and the EPA ecological risk assessments (U.S. EPA/OPP 2008a,b) do not address effects on terrestrial microorganisms.

The review of imazamox by the European Commission (2002, p. 16) provides a very brief summary of studies on soil microorganisms. As is true of the data on terrestrial invertebrates (Section 4.1.2.4), the source of the toxicity data on soil microorganisms is not specifically referenced by the European Commission (2002). Nevertheless, the report does cite a number of studies conducted by BASF on the metabolism of imazamox in soil, and these studies might be the source of the toxicity data cited by the European Commission (2002). In any event, the report by the European Commission (2002) indicates that imazamox has no effect on nitrogen metabolism or carbon mineralization when applied at rates of 150 g/ha (equivalent to rates of about 0.13 lb a.e./acre).

An open literature study by Huang et al. (2009) indicates that a strain of *Pseudomonas* capable of using imazethapyr as a sole source of carbon was also capable of degrading and using imazamox at a concentration of 50 mg/L as a sole source of carbon in a liquid culture medium.

4.1.3. Aquatic Organisms

4.1.3.1. Fish

Data on the toxicity of imazamox to fish are summarized in Appendix 5. Imazamox appears to be essentially nontoxic to fish in acute exposure assays. LC_{50} values for fish were not determined in the standard acute toxicity studies on imazamox that are required for pesticide registration (Appendix 5, Table A5-1), and the reported acute NOAECs range from 94.2 mg/L in sheepshead minnows (Olivieri et al. 1998a) to 122 mg/L in rainbow trout (Yurk and Wisk 1994b). All of the acute NOAECs are the highest concentrations tested in the acute toxicity studies. Thus, the differences in NOAECs do not imply differences in species sensitivities. Just as mammalian toxicity studies on imazamox fail to determine acutely toxic doses, aquatic toxicity studies fail to determine imazamox concentrations that are acutely toxic to fish—i.e., acute LOAECs.

Chronic toxicity studies in fish are not listed among the registrant-submitted studies on imazamox (Appendix 1), and the EPA ecological risk assessments (U.S. EPA/OPP 2008a,b) note that chronic risks to fish cannot be assessed because chronic toxicity data on fish are not available. This is an unusual situation, particularly for a pesticide that is labeled for aquatic applications. For some herbicides, the U.S. EPA/OPP will waive chronic toxicity studies in fish because of the low acute toxicity of the herbicide to fish. While the acute toxicity of imazamox appears to be very low, there is no explicit indication in the EPA ecological risk assessments (U.S. EPA/OPP 2008a,b) that chronic studies on fish were waived.

The review of imazamox by the European Commission (2002) provides a very brief summary of two longer-term studies in rainbow trout—i.e., a 28-day NOEC of 122 mg/L and a 96-day NOEC of 11.8 mg/L. No further information, including reference citations, for these studies is provided. As noted in Section 4.1.2.4 (Terrestrial Invertebrates), registrants often submit studies to European regulatory groups that are not submitted to the U.S. EPA/OPP. Longer-term studies in fish, however, are typically required by the U.S. EPA/OPP, and it is not clear why these studies appear to have been submitted to the European Commission but not to the U.S. EPA/OPP.

4.1.3.2. Amphibians (Aquatic-Phase)

As is the case for reptiles and terrestrial-stage amphibians (Section 4.1.2.3), there is no information regarding the toxicity of imazamox to aquatic-phase amphibians. In view of this lack of data, U.S. EPA/OPP (2008a,b) follows its standard approach: … *conclusions drawn from studies conducted with fish are assumed applicable to amphibians* (U.S. EPA/OPP 2008a, p. 16).

4.1.3.3. Aquatic Invertebrates

For imazamox, the toxicity data on aquatic invertebrates are similar to the data on fish. As summarized in Appendix 6, there are two standard registrant-submitted acute toxicity studies on aquatic invertebrates, and as with fish, LC_{50} values for imazamox were not determined. At the highest concentrations tested, imazamox caused no mortality and no signs of toxicity in either *Daphnia magna* with an NOAEC of 115 mg a.e./L (Yurk and Wisk 1994c) or mysid shrimp with an NOAEC of 89.3 mg a.e./L (Olivieri et al. 1998b).

Similar again to the fish data on imazamox, chronic toxicity studies in aquatic invertebrates are listed among the registrant-submitted studies on imazamox (Appendix 1), and the EPA ecological risk assessments (U.S. EPA/OPP 2008a,b) note that chronic risks to aquatic invertebrates cannot be assessed because chronic toxicity data are not available. There is no indication in the EPA risk assessments that the requirements for chronic toxicity testing in aquatic invertebrates were waived.

Finally, similar to the situation with the data on fish, the review by the European Commission (2002) notes a 21-day NOAEC for *Daphnia magna* of 137 mg/L. No other study details are provided, including whether the units are in a.i. or a.e., and the source for the information is not cited. It is likely that the 21-day NOAEC is from a standard reproduction study in *Daphnia*.

4.1.3.4. Aquatic Plants

4.1.3.4.1. Algae

While Clearcast is labeled for the control of aquatic macrophytes, it is not specifically labeled for the control of algae. As with imazapyr (SERA 2004a) and imazapic (SERA 2004b), imazamox appears to be less toxic to algae than to aquatic macrophytes. This generalization, however, is somewhat tenuous in that extensive data are not available on the toxicity of imazamox to algae. As summarized in Appendix 7, Table A7-1, one study on the toxicity to algae was submitted to the U.S. EPA in support of the registration of imazamox (Canez et al. 1995). This is a relatively simple study in which imazamox was assayed in four species of algae at a single concentration of 0.040 mg a.i./L, corresponding to about 0.038 mg a.e./L. No growth inhibition was noted in one species (*Navicula pelliculosa*). In the three other species, only slight to moderate growth inhibition was noted—i.e., 3.6 to 11%. A very brief summary of this study is contained in the review by the European Commission (2002). No other information on the toxicity of imazamox to algae was encountered in the open literature.

The limited data on the toxicity of imazamox to algae is noted in the EPA ecological risk assessments on imazamox (U.S. EPA/OPP 2008a,b), which indicate that the maximum application rate for imazamox is 112.5 ppb for aquatic weed control (U.S. EPA/OPP 2008a, p. 20). As detailed in Section 2.4.2, the current maximum target concentration for imazamox in

aquatic weed control is 500 ppb. In any event, current data on the effect of imazamox on algae do not encompass the concentrations of 112.5 ppb or 500 ppb.

4.1.3.4.2. Aquatic Macrophytes

As summarized in Appendix 7, Table A7-2, imazamox appears to be much more toxic to aquatic macrophytes than to algae. As noted in the previous subsection, however, this generalization is based on very limited information. U.S. EPA/OPP (2008a, p. 16) summarizes a standard bioassay in duckweed (*Lemna gibba*) in which the 14-day EC_{50} is reported as 11 µg a.i./L with an NOEC of 4.5 µg a.i./L, equivalent to about 4.3 µg a.e./L. These data are attributed to the registrant-submitted study by Canez (1995), designated as MRID 43876219. As indicated in Appendix 1, the title for this submission indicates that *Lemna gibba* was assayed in this study. The available DER for this study does not summarize the data on duckweed. Consequently, the information on the *Lemna gibba* assay is taken solely from the summary in U.S. EPA/OPP (2008a, p. 16).

Additional information on the toxicity of imazamox to aquatic macrophytes is available in the open literature study by Cedergreen et al. (2005). As also summarized in Appendix 7, Table A7-2, this study assayed *Lemna minor*, another species of duckweed, using pulse exposures and 4- and 7-day exposures to Bolero, a European formulation of imazamox. The results of the 4- to 7-day studies are reasonably consistent with the somewhat longer-term study by Canez (1995). In two assays, Cedergreen et al. (2005) report EC_{50} values equivalent to about 55 and 29 µg a.e./L for 4- and 7-day exposures, respectively.

No data are available on the toxicity of imazamox to genera of aquatic macrophytes other than *Lemna*. This is unfortunate because *Lemna* species, while technically macrophytes, do not have a fully developed vascular system in contrast to the large number of aquatic macrophytes that are targeted for control by Clearcast and that do have a fully developed vascular system.

4.1.3.5. Surfactants

As noted in Section 3.1.14.2, nonionic surfactants, methylated seed oils, or vegetable oil concentrates are recommended in both terrestrial and aquatic applications of Clearcast. It is beyond the scope of the current risk assessment on imazamox to review the toxicity of all the adjuvants recommended for use with Clearcast or their potential impact on aquatic organisms.

Imazamox presents no identified hazards to aquatic animals—i.e., acute exposure to imazamox does not cause signs of toxicity in fish (Section 4.1.3.1) or aquatic invertebrates (Section 4.1.3.3). Nevertheless, at least some of the recommended nonionic surfactants may be more hazardous than imazamox 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 fluridone and glyphosate. The acute toxicity values cover a wide-range from about 1 to >1000 mg/L.

Based on the label instructions for Clearcast, the recommended concentration of a nonionic surfactant is 0.25% v/v. Assuming a density of 1 g/mL for illustration, 0.25% w/v corresponds to a concentration of 2500 mg/L (1% = 10,000 mg/L). Given the very low toxicity of imazamox to both fish and aquatic invertebrates—i.e., NOAECs range from about 10 to 100 mg/L, as discussed in Sections 4.1.3.3 and 4.1.3.3—the use of a relatively toxic nonionic surfactant in an

aquatic application of Clearcast may be viewed as posing a greater risk to aquatic animals than would be anticipated from exposure to imazamox alone.

Notwithstanding the above assertion, there is no basis for asserting that the risks posed by the surfactants would be substantial. The direct application of Clearcast to water may serve as a worst-case example. The concentration of imazamox in Clearcast is 12.1% w/v or about 121,000 mg/L. For aquatic applications, however, the target concentration is 500 ppb or 0.5 mg/L. Thus, the imazamox is diluted by a factor of about 242,000 [121,000 mg/L ÷ 0.5 mg/L]. Therefore, if 2500 mg/L of a surfactant were added to Clearcast, the anticipated concentration of the surfactant in the treated water would be about 0.01 mg/L [2500 mg/L ÷ 242,000 ≈ 0.01033 mg/L]. Using a very toxic surfactant with an LC_{50} of 1 mg/L, the concentration of the surfactant in water would be lower than the LC_{50} by a factor of about 100 [1 mg/L ÷ 0.01033 mg/L ≈ 96.8]. As discussed in the EPA ecological risk assessments on imazamox (U.S. EPA/OPP 2008a,b), the standard criteria used by U.S. EPA as a level of concern for threatened and endangered species is a ratio of the anticipated concentration in water to the acute LC_{50} of 0.05. Using a very toxic surfactant with an acute LC_{50} of 1 mg/L in aquatic applications of Clearcast would result in peak exposures that are below the U.S. EPA/OPP level of concern for threatened and endangered species by a factor of about 5. Thus, there is no basis for asserting that the use of surfactants with Clearcast applications is likely to pose a hazard to aquatic species.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

A standard set of exposure assessments for terrestrial and aquatic organisms is provided in Attachment 1 for terrestrial applications made at the maximum rate of 0.5 lb a.e./acre. A subset of the standard exposure scenarios is provided for aquatic applications (Attachment 2) using the maximum target concentration of 0.5 mg a.e./L. The use of other applications rates is discussed in the risk characterization. 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 and birds are summarized in Worksheet G01 of the EXCEL workbooks that accompany this risk assessment. Accidental exposure scenarios lead to upper bound estimates of exposure ranging from about 0.14 mg/kg bw (the consumption of contaminated fish by a bird after an accidental spill) to about 12 mg/kg bw (dermal exposure for a small mammal after direct spray, assuming 100% absorption). The highest acute non-accidental exposures are associated with the consumption of contaminated insects by a small bird (56 mg/kg bw) and the consumption of contaminated grasses by a large bird (38 mg/kg bw). Scenarios for the consumption of contaminated vegetation also lead to the highest longer-term exposures, up to about 12 mg/kg bw/day for a large bird consuming contaminated grasses. For both acute and chronic exposures, consumption of contaminated water leads to dose estimates far below those associated with consumption of contaminated vegetation. This pattern, which is common in many herbicide exposure assessments, reflects the consequences of direct applications to vegetation.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion, and the use of contaminated irrigation water. Unintended direct spray is expressed simply as the application rate. As with terrestrial animals, all exposure assessments used in the workbooks that accompany this risk assessment are based on a unit application rate of 0.5 lb a.e./acre. The consequences of using other application rates are discussed in the risk characterization. Exposures of aquatic plants and animals to imazamox are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water.

4.2.2. Mammals and Birds

4.2.2.1. Direct Spray

The unintentional direct spray of wildlife during broadcast applications of a pesticide is a plausible 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 (Worksheets F01, F02). The first spray scenario (detailed in Worksheet F01) concerns the direct spray of half of the body surface of a 20 g mammal as the pesticide is being applied. This exposure assessment assumes first-order dermal absorption. The estimates of the first-order dermal absorption rate are identical to those used in the human health risk assessment (Section 3.1.3.2). This scenario is likely to overestimate exposures for most mammals because of fur

which covers the surface of most species of mammalian wildlife. The second exposure assessment (detailed in Worksheet F02) assumes complete absorption over day 1 of exposure. This assessment is included in an effort to encompass the increased exposure due to grooming.

There are no exposure assessments for the direct spray of large mammals, principally because allometric relationships dictate that relative to body weight, the amount of a compound to which large mammals will be exposed as a result of direct spray is less than the amount to which smaller mammals will be exposed. Similarly, there are no exposure scenarios for the direct spray of a small bird. As discussed in Section 4.4.2.1, the direct spray scenario for a small mammal leads to HQs far below the level of concern. In addition, the NOAECs for birds are much higher than the corresponding NOAECs for mammals (Section 4.3.2.2). Thus, there is no need to further elaborate the direct spray scenario to include birds.

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 and dislodgeable foliar residue. Unlike the human health risk assessment, in 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. Given the lower HQs associated with the more severe exposure scenarios for mammals, there is no basis for concern with exposure scenarios involving dermal contact with contaminated vegetation.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

Imazamox may be used in broadcast foliar applications; therefore, the consumption of contaminated vegetation is an obvious concern. Separate exposure assessments are developed for acute and chronic exposure scenarios involving a small mammal (Worksheets F03a, F03b, F04a and F04b), a large mammal (Worksheets F10, F11a, and F11b), and large birds (Worksheets F12, F13a, and F13b). Similarly, the consumption of contaminated insects is modeled for a small bird (Worksheet 14a) and a small mammal (Worksheet 14b). As detailed in the exposure assessment for human health (Section 3.2.3.3), the empirical relationships based on those recommended by Fletcher et al. (1994), as detailed in Table 10, are used to estimate residues in contaminated insects (Worksheets F14a and F14b). A similar set of scenarios is provided for the consumption of small mammals by either a predatory mammal (Worksheet 16a) or a predatory bird (Worksheet 16a). All of these exposure scenarios are relevant only to terrestrial applications; thus, these exposure scenarios are included only in Attachment 1, the EXCEL workbook for broadcast terrestrial applications.

In addition to the consumption of contaminated vegetation, insects, and other terrestrial prey, exposure pathways for imazamox may be associated with ambient water and fish. Thus, a separate scenario is developed for the consumption of contaminated fish by a predatory bird involving acute (Worksheet F08) and chronic (Worksheet F09) exposure, as detailed in the cited worksheets. These exposure scenarios are relevant to both terrestrial and aquatic applications of

imazamox and are included in both Attachment 1 (terrestrial applications) and Attachment 2 (aquatic applications).

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating imazamox concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4). The only major differences in the estimates of exposure involve the weight of the animal and the amount of water consumed. These differences are detailed and documented in the worksheets regarding the consumption of contaminated water for small mammals, canids, large mammals, small birds, and large birds. For each of these five receptors, exposure scenarios are provided for an accidental spill (Worksheets F05a-e), expected peak concentrations (Worksheets F06a-e), and expected longer-term concentrations (Worksheet F07a-e).

As with the human health risk assessment (Section 3.2.3.4.1), somewhat different assumptions are used for the accidental spill scenarios for terrestrial and aquatic applications. The expected peak and longer-term concentrations of imazamox in surface water associated with terrestrial applications are identical to the concentrations summarized in Table 9 and used in the human health risk assessment. As discussed in Section 3.2.3.4.6, the peak concentration of imazamox in surface water is taken as the maximum target concentration of 0.5 mg a.e./L, and the longer-term concentration of imazamox in surface water is modeled based on an assumed dissipation half-life of 90 days. While the actual dissipation half-life of imazamox in water is likely to vary substantially depending on site-specific considerations, assumptions concerning the dissipation half-life of imazamox have no impact on the risk characterization for birds or mammals because of the very low toxicity of imazamox to these receptors (Sections 4.4.2.1 and 4.4.2.2).

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

Estimated levels of exposure associated with broadcast terrestrial applications of imazamox are detailed in Worksheet G02b. 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 G02b are based on Tier 1 aerial estimates from AgDrift (Teske et al. 2002) for distances of 0 (direct spray) to 900 feet downwind of the treated site. Aerial drift estimates are used because estimated drift from aerial applications are greater than estimates for directed foliar or ground broadcast application methods (SERA 2009). As discussed further in Section 4.4.2.4, this modestly conservative approach has no impact on the risk characterization because the hazard quotients for this scenario are far below the level of concern.

In addition to drift, foliar interception of a pesticide may occur. The impact of foliar interception would vary depending on 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) noted 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 G02b, foliar interception rates of 0% (no interception), 50%, and 90% are used. While foliar interception has no impact on the risk characterization for imazamox, the consideration of foliar interception is standard in all Forest Service risk assessments.

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. Thus, the honeybee is used as a surrogate for other insect species.

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

Like terrestrial mammals and birds, terrestrial invertebrates may be exposed to imazamox through the consumption of contaminated vegetation or contaminated prey. For broadcast foliar applications, estimates of residues on contaminated vegetation or prey are identical to the residue rates used in the corresponding exposure assessment for mammals and birds (Section 4.2.2.3).

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 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).

Details concerning estimated exposure levels for the consumption of contaminated vegetation by herbivorous insects are provided in Worksheets G07a, G07b, G07c, and G07d. These levels pertain to the four food items included in the standard residue rates provided by Fletcher et al. (1994). The exposure estimates are included only in the EXCEL workbooks for terrestrial broadcast applications (Attachments 1).

As discussed further in Section 4.3.2.4.1 (Dose-Response Assessment) and Section 4.4.2.4 (Risk Characterization), the major reservation with this exposure scenario is the oral toxicity value for terrestrial invertebrates, for which the documentation is marginal.

4.2.4. Terrestrial Plants

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 likely that 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, as discussed in the following subsection.

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 Worksheet G05 of the EXCEL workbook for terrestrial applications (Attachments 1). Worksheet G05 is manually modified to include drift estimates for aerial, low and high boom ground broadcast, and backpack applications. This manual modification for drift to Worksheet G05 is necessary because the HQs for the direct spray of terrestrial plants differ substantially depending on the application method, and these differences have an impact on the risk characterization for terrestrial plants (Section 4.4.2.5).

The drift estimates 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, and the pesticide formulation. All of these factors cannot be considered in this general risk assessment.

The drift estimates used in the current Forest Service 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 that may be viewed as plausible upper limits of drift. 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 90^{th} percentile values from AgDRIFT.

Drift associated with backpack applications (directed foliar applications) is 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 Forest Service 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 50^{th} percentile estimates of drift (rather than the 90^{th} percentile used for ground broadcast applications).

4.2.4.3. Runoff and Soil Mobility

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 affect non-target plants. Percolation, on the other

hand, represents the amount of the herbicide that is transported below the root zone, and, therefore, may affect water quality but should not affect off-site vegetation. The GLEAMS modeling used to estimate concentrations in water provides data on loss by runoff. As with the estimates of imazamox in surface water, runoff estimates are modeled for clay, loam, and sand at nine sites which are representative of different temperatures and rainfall patterns.

For imazamox, the results of the standard GLEAMS modeling of runoff and sediment losses are summarized in Appendix 8, Table A8-1. It is worth noting that the proportion of runoff as a fraction of the application rate will vary substantially with different types of soils as well as climates—i.e., temperature and rainfall. For this generic risk assessment, the average runoff is taken as 0.0094 which is the average of the central estimates from the 27 Gleams-Driver simulations conducted for the current Forest Service risk assessment. The upper bound of 0.153 is the maximum value for all of the simulations conducted. For imazamox, this maximum is the highest runoff proportion in the 100 individual simulations for an area with predominantly clay soils, cool temperatures, and high rainfall. Several Gleams-Driver runs indicated no runoff loss in sandy soils or other soils with low rainfall rates. The lower bound value of 0.0001 of the application rate is taken as an approximation for relatively dry areas with predominantly loam or sandy soils. Thus, in Worksheet G04, the proportion of the application that is lost to an adjacent field is taken as 0.0094 (0.0001 to 0.153).

The amount of pesticide or pesticide metabolites not washed off in runoff or sediment will penetrate into the soil column, and the depth of penetration will depend on the properties of the chemicals, the properties of the soil, and the amount of rainfall. The GLEAMS model provides estimates of pesticide or metabolite concentrations in soil layers of varying depths. These concentrations are output by GLEAMS in mg pesticide/kg soil (ppm). The minimum non-zero value that GLEAMS will output is 0.000001 mg/kg, equivalent to 1 nanogram/kg soil or 1 part per trillion (ppt). The deepest penetration of imazamox in clay, loam, and sand modeled using GLEAMS is summarized in Appendix 8, Table A8-4. Based on GLEAMS modeling, the average penetration depth of imazamox is estimated at about 40 inches with a range of about 12-60 inches.

4.2.4.4. Contaminated Irrigation Water

Unintentional direct exposure of nontarget plants is possible from the use of contaminated ambient water for irrigation, as observed by Bhandary et al. (1991) for certain herbicides. The levels of exposure associated with this scenario will depend on the pesticide concentration in the ambient water used for irrigation and the amount of irrigation water used. Concentrations in ambient water are generally based on the concentrations modeled in the human health risk assessment (Section 3.2.3.4). 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 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 F15. At the maximum application rate of 0.5 lb a.e./acre, the functional application rate associated with the use of contaminated surface water for irrigation is about 0.00012 (0.0000011 to 0.0043) lb a.e./acre. These rates are

substantially below the rate associated with runoff—i.e., 0.0047 (0.00005 to 0.047) lb a.e./acre, as detailed in Worksheet G04 – and are far below the offsite deposition rates associated with drift—i.e., 0.0002 to 0.11 lb a.e./acre, as detailed in Worksheet G05. Consequently, the risks of contaminated irrigation water are not considered further.

4.2.4.5. Wind Erosion

Wind erosion is 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 contamination of pesticides is likely to be highly site-specific. The amount of imazamox 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 likely that the amount of imazamox transported by the wind would be insubstantial.

For this risk assessment, the potential effects of wind erosion are estimated in Worksheet G06. In this worksheet, it is assumed that imazamox is incorporated into the top 1 cm of soil, which is identical to the depth of incorporation used in GLEAMS modeling. 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 G06, 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 at least partially 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 G06 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 100-300 feet from the application site (G05). All of these 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 plausibility of effects on aquatic species is assessed based on estimated concentrations of imazamox in water which are identical to those used in the human health risk assessment. These values are discussed in Section 3.2.3.4.6 for both terrestrial and aquatic applications of imazamox.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

Table 14 summarizes the toxicity values used in this 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 HQs in the risk characterization, all toxicity values given in Table 14 are expressed as acid equivalents (a.e.). Where necessary, the conversion factor of 0.0.947 a.e./a.i derived in Table 2, is used to convert experimental exposures expressed as a.i. to a.e., based on the ratio of the molecular weight of imazamox acid to the ammonium salt of imazamox.

As with most herbicides labeled for terrestrial applications, the toxicity data on terrestrial plants, including studies submitted to the U.S. EPA/OPP in support of the registration of imazamox as well as studies from the open literature, are reasonably complete and adequate for deriving toxicity values for sensitive and tolerant terrestrial plant species. The toxicity data on aquatic plants, however, are relatively sparse, which is somewhat unusual for a herbicide labeled for aquatic weed control. Because of limitations in the data on both algae and aquatic macrophytes, separate toxicity values cannot be proposed for tolerant and sensitive species. The conservative assumption is made that the available data are representative of tolerant species, and risks to sensitive species of aquatic plants are addressed qualitatively in the risk characterization. As with other imidazolinone herbicides, imazamox appears to be more toxic to macrophytes than to algae.

As with the dose-response assessment for human health effects, the dose-response assessments for both terrestrial and aquatic animals is limited in that adverse effect levels for imazamox have not been defined. Consequently, differences in sensitivity among the various groups of animals considered in this risk assessment cannot be evaluated. Where applicable, the assumption is made that the available toxicity data apply to tolerant rather than sensitive species. This assumption does not imply a serious limitation in the risk assessment for imazamox, since almost all HQs for terrestrial and aquatic animals are far below the level of concern.

4.3.2. Terrestrial Organisms

4.3.2.1. Mammals

In characterizing risk to mammalian wildlife, Forest Service risk assessments generally consider the NOAEL that forms the basis of the RfD. This approach, which is typically the most conservative, is maintained for imazamox. Moreover, the reservations with this approach are essentially identical to the reservations concerning the proposed RfD for imazamox (U.S. EPA/OPP 1997a).

As summarized in the hazard identification for both human health (Section 3.1) and mammalian wildlife (Section 4.1.2.1), the standard array of studies used to assess the acute, subchronic, and chronic toxicity of pesticides, including effects on reproduction and development, does not

identify exposure levels of imazamox likely to cause adverse effects in mammals. For the human health risk assessment, the EPA uses the RfD of 3 mg/kg bw/day, which is based on a NOAEL of 300 mg/kg bw/day with a corresponding LOAEL of 600 mg/kg bw/day from a developmental toxicity study in rabbits (Hoberman 1995), as the basis for risk characterization (U.S. EPA/OPP 1997a). A subsequent reevaluation in U.S. EPA/OPP (2001b), however, suggests that the 600 mg/kg bw/day dose, which had been classified as a LOAEL, did not involve a toxicologically significant response—i.e., a decrease in both food consumption and body weight.

The NOAEL of 300 mg/kg bw/day may be a conservative basis for assessing risks in mammalian wildlife. In addition and as detailed in Appendix 2, doses of up to about 1300 mg/kg bw are not associated with adverse effect in mammals. Nonetheless and as discussed further in the risk characterization for mammalian wildlife, all exposure levels for mammals are substantially below 300 mg/kg bw/day. Consequently, while higher NOAELs may be justified, the NOAEL of 300 mg/kg bw/day is used in the current risk assessment to characterize risks to mammalian wildlife.

4.3.2.2. Birds

Like most toxicity studies of imazamox, avian studies do not identify potentially toxic exposure levels of imazamox (Section 4.1.2.2 and Appendix 3). Adverse effects were not observed in birds after exposure to a single gavage dose of 1846 mg/kg bw (Campbell et al. 1994b). Furthermore, in acute dietary toxicity studies, adverse effects were not observed in quail or mallards exposed to concentrations of up to more than 5000 ppm (Campbell et al. 1994c,d). As discussed in Section 4.1.2.2, these dietary exposures are associated with estimated doses of up to about 2300 mg/kg bw/day in mallards and 1700 mg/kg bw/day in quail. These NOAELs for birds are similar to the NOAELs of up to 1300 mg/kg bw/day for mammals, which are discussed in the previous subsection.

For this risk assessment, the lower dietary NOEL of 1700 mg/kg/day in bobwhite quail (Campbell et al. 1994c) is used to characterize risks associated with acute exposures, because most of the acute exposure scenarios used in this risk assessment involve either dietary exposures or exposures that occur over the course of a day, as opposed to a single event. Given the somewhat higher NOAEL values associated with gavage exposure, it is likely that the true NOAEL for dietary exposure is greater, and perhaps substantially greater, than 1700 mg/kg/day. Because of the remarkably low HQs for acute exposures of birds (Worksheet G02), using the lower acute NOAEL of 1700 mg/kg/day for birds has no impact on the risk characterization.

As with the acute toxicity studies in birds, the longer-term reproduction studies in both quail and mallards (Gagne et al. 1995a,b) fail to define a clear LOAEL at dietary concentrations of up to 2000 ppm. Based on measured body weights and food consumption, the dietary concentration of 2000 ppm corresponds to daily doses of about 190 mg/kg bw/day in quail and 220 mg/kg bw/day in mallards (Section 4.1.2.2). For the current risk assessment, the lower NOAEL of 190 mg/kg bw/day is used to characterize risks to birds from longer-term exposures.

As summarized in Table 14, the acute NOAEL for birds is substantially higher than the acute NOAEL for mammals (1700 mg/kg bw versus 300 mg/kg bw); whereas, the chronic NOAEL in birds is somewhat lower than the chronic NOAEL in mammals (300 mg/kg bw versus 190 mg/kg

bw). These differences do not imply meaningful differences in the underlying sensitivity of birds and mammals to imazamox. Because the available toxicity studies do not define LOAELs for either birds or mammals, the differences in the NOAELs for birds and mammals simply reflect the differences in the dose levels used in the studies. As noted above and discussed in Section 4.3.2.1, doses of up to about 1300 mg/kg bw/day are not associated with adverse effects in mammals. Consequently, there is no basis for asserting that there are differences in the sensitivity of birds and mammals to imazamox.

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. Following the general EPA approach (U.S. EPA/OPP 2008a,b), potential risks to reptiles and terrestrial-phase amphibians are characterized based on the apparent risks to birds.

4.3.2.4. Terrestrial Invertebrates

As discussed in Section 4.1.2.4, the EPA reviewed and accepted the standard contact toxicity study in honeybees (Parrish et al. 1994), as discussed in U.S. EPA/OPP (2008a,c). Furthermore, a DER for this study is available. This study indicates a contact NOAEC of 25 µg/bee, equivalent to about 250 mg/kg bw. Accidental spray is a common exposure scenario for terrestrial invertebrates (Section 4.2.3.1), and the NOAEL of 250 mg/kg bw is used to assess potential risks to terrestrial invertebrates associated with this exposure scenario.

Forest Service risk assessments also 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. As discussed in Section 4.1.2.4, the only source of oral toxicity data for honeybees is a very brief note in the review by the European Commission (2002) indicating that the oral LD_{50} in honeybees is greater than about 390 mg a.e./kg bw.

Unlike the relatively well-documented study by Parrish et al. (1994), the oral toxicity study in bees does not provide experimental details. In particular, it is not clear that the estimated dose of 390 mg a.e./kg bw is an NOAEC. Given the limited documentation available in the European Commission (2002) report, the oral dose of 390 mg a.e./kg bw is not used in the current Forest Service. As an alternative, the somewhat lower and much better documented contact NOAEL of 250 mg/kg bw is used to characterize risks to terrestrial invertebrates that may consume vegetation or prey following terrestrial applications of imazamox.

The apparently low acute toxicity of imazamox to terrestrial invertebrates is consistent with the toxicity data on mammals and birds. No quantitative consideration can be given to other potential subchronic or non-lethal effects, and no information is available on other invertebrate species.

4.3.2.5. Terrestrial Plants (Macrophytes)

As with most herbicides, there are adequate data for the development of 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 imazamox in soil. Studies on vegetative vigor are used to assess risks associated with the deposition of imazamox onto plants as a result of direct spray or spray drift.

The only bioassay involving seedling emergence is the standard study by Chetram et al. (1995) submitted to the U.S. EPA in support of the registration on imazamox. In this study, the most sensitive species is cabbage (dicot) with an NOAEC of 0.0008 lb a.i./acre and an EC_{25} of 0.0018 a.e./acre. The endpoint for the EC_{25} is dry weight. Thus, for the current Forest Service risk assessment, the NOAEC for soil exposures in sensitive species of terrestrial plants is taken as 0.0008 lb a.e./acre. Based on the ratio of the EC_{25} to the NOAEC, an HQ of about 2 [0.0018 a.e./acre ÷ 0.0008 lb a.e./acre 2.25] would be associated with detectable adverse effects on sensitive species of plants.

The selection of the most tolerant species based on the seedling emergence assays is somewhat less direct. As discussed in 4.1.2.5, the soybean is the most tolerant species based on an estimated EC_{25} of >0.048 lb a.e./acre. However, based on the NOAEC, lettuce is the most tolerant species with an NOAEC of 0.012 lb a.e./acre while the NOAEC for soybeans is 0.0015 lb a.e./acre. The Forest Service prefers to base all toxicity values for the ecological risk assessment on NOAECs rather than measures of effective doses such as the EC_{25}. Consequently, for seedling emergence, lettuce is taken as the most tolerant species, and the NOAEC of 0.012 lb a.e./acre is used to characterize risks in tolerant species of plants following soil exposures.

Studies on the effect of foliar applications of imazamox come from both the standard vegetative vigor assay by Chetram and Canex (1995), which is summarized in Appendix 4, Table A4-1 as well as from several field and field simulation studies which are summarized in Appendix 4, Table A4-3. In the vegetative vigor assay by Chetram and Canex (1995), the most sensitive species is the tomato with an EC_{25} of 0.0008 lb a.e./acre and an NOAEC of 0.00075 lb a.e./acre. As discussed in Section 4.1.2.5, the open literature study conducted by Blackshaw (1998) suggests that redroot pigweed (*Amaranthus retroflexus*) is somewhat more sensitive with an estimated EC_{25} of about 0.00055 lb a.e./acre. This EC_{25} is a factor of about 1.5 below the EC_{25} of 0.0008 lb a.e./acre for tomatoes [0.0008 lb a.e./acre ÷ 0.00055 lb a.e./acre ≈ 1.455].

The data in Blackshaw (1998, Figure 2, p. 66) do not define an NOAEC. As noted in Section 4.1.2.5, Blackshaw (1998) fit the response of pigweed to the following exponential model,

$$\boldsymbol{Y} = 2608\ e^{-0.442\ \boldsymbol{d}}.$$

Following the convention commonly used to develop benchmark doses (e.g., Setzer and Kimmel 2003), a response of 10% is used as a surrogate NOAEC. Setting Y to a 10% reduction in shoot biomass [2608 x 0.9 = 2347.2], as a reasonable approximation of a NOAEC, and rearranging to solve for ***d***, the EC_{10} is estimated at about 0.24 g a.i./ha: $\boldsymbol{d}$ = Ln(2347.2÷2608) / -0.442 ≈

0.2384. The application rate of 0.24 g a.i./ha is equivalent to about 0.23 g a.e./ha [0.24 g a.i./ha x 0.947 a.e./a.i. ≈ 0.2273 g a.e./ha] or about 0.0002 lb a.e./acre [0.00023 kg a.e./ha x 0.892 lb/ac per kg/ha ≈ 0.00020516 lb a.e./acre]. This EC_{10} will be used as a surrogate NOAEC for sensitive species of plants following foliar exposure. This surrogate NOAEC is below the NOAEC of 0.00075 lb a.e./acre from the study by Chetram and Canex (1995) by a factor of about 4.

The most tolerant species of plants in the vegetative vigor assay by Chetram and Canex (1995) is lettuce, for which an EC_{25} could not be determined and the NOAEC was 0.048 lb a.e./acre, the highest application rate assayed. Based on the open literature studies by Abyo et al. (1998) and Mateos-Naranjo et al. (2009), some species of weeds are not controlled well at somewhat higher application rates—i.e., in the range of 0.057 to 0.063 lb a.e./acre. These application rates, however, are not substantially higher than the NOAEC was 0.048 lb a.e./acre. Consequently, for tolerant species of plants, the NOAEC of 0.048 lb a.e./acre from Chetram and Canex (1995) is used to characterize risks following foliar application.

4.3.2.6. Terrestrial Microorganisms

As discussed in Section 4.1.2.6, data on the toxicity of imazamox to terrestrial microorganisms is sparse. The most relevant information consists of statements in the report by the European Commission (2002) indicating that an application rate of about 0.13 lb a.e./acre has no effect on nitrogen metabolism or carbon mineralization soil. No information is available on the effects of imazamox on soil microorganisms at the maximum application rate of 0.5 lb a.e/acre. Given the limited information on the toxicity of imazamox to terrestrial microorganisms, no dose-response relationship is proposed for this for this class of organisms and risks are addressed qualitatively in the risk characterization (Section 4.4.2.6).

4.3.3. Aquatic Organisms

4.3.3.1. Fish

The major limitation in the toxicity data on fish is the failure to define toxicity values for imazamox, as is true for the toxicity data on terrestrial animals . As noted in the EPA ecological risk assessments on imazamox (U.S. EPA/OPP 2008a,b), this herbicide is essentially nontoxic to fish.

According to the three acute toxicity studies in fish (Appendix 5, Table A5-1), no mortality or signs of toxicity were observed at concentrations ranging from 89.2 mg a.e./L in sheepshead minnow (Olivieri et al. 1998a) to 115 mg a.e./L in rainbow trout (Yurk and Wisk 1994b). Generally, Forest Service risk assessments attempt to derive toxicity values for sensitive and tolerant species of fish. Because none of the available studies note any signs of adverse effects, the differences in NOAECs do not suggest any differences in species sensitivity, but merely reflect the range of concentrations used in the different acute bioassays. Consequently, the NOAEC of 115 mg a.e./L is used to characterize risks to tolerant species of fish. As discussed further in the risk characterization for fish (Section 4.4.3.1), the available information on the toxicity of imazamox to fish suggests that the concept of sensitive species of fish may not be relevant to imazamox, because imazamox does not appear to be toxic to fish.

As discussed in Section 4.1.3.1, studies involving the longer-term toxicity of imazamox to fish were not submitted to the EPA as part of the registration process, and are not reviewed in U.S.

EPA/OPP (2008a,b). Nonetheless, the European Commission (2002) review states that two NOECs are available in rainbow trout—i.e., a 28-day NOEC of 122 mg/L and a 96-day NOEC of 11.8 mg/L. No details of and no citations for these studies are provided in the European Commission (2002) review. As discussed in the Forest Service risk assessment on imazapyr (SERA 2004a), longer-term NOAECs for imazapyr in fish range from about 43 to 120 mg/L, very close to the range of NOAECs (from 11.8 to 122 mg/L) cited in the European Commission (2002) review. In the absence of further documentation on the longer-term NOAECs for imazamox, however, the NOAECs for imazamox cited in the European Commission (2002) review are not used quantitatively in the current risk assessment. As discussed further in the risk characterization, the acute NOAECs for fish are far below the level of concern, and the use of the very similar longer-term NOAECs from the European Commission (2002) review would have no impact on the risk characterization.

4.3.3.2. Amphibians (Aquatic-Phase)

As noted in Section 4.1.3.2, no information is available on the toxicity of imazamox to aquatic-phase amphibians. Consequently, no dose-response assessment is given for this group. Following the approach taken in U.S. EPA/OPP (2008a,b), risks to aquatic-phase amphibians are characterized based on risks to fish.

4.3.3.3. Aquatic Invertebrates

The available toxicity data on aquatic invertebrates (Section 4.1.3.3) are virtually identical to the toxicity data on fish. Consequently, the dose-response assessment for aquatic invertebrates closely parallels the dose-response assessment for fish.

Two well-documented bioassays are available in aquatic invertebrates, both of which fail to demonstrate any adverse effects—i.e., a NOAEC of 115 mg a.e./L in *Daphnia magna* (Yurk and Wisk 1994c) and an NOAEC of 89.3 mg a.e./L in mysid shrimp (Olivieri et al. 1998b). As with the NOAECs in fish, the differences between the NOAEC in daphnids and the NOAEC in mysids reflects the differences in the maximum concentrations of imazamox used in the two studies. These differences do not imply any detectable differences in the sensitivity of daphnids and mysids to imazamox. Consequently, the higher NOAEC of 115 mg a.e./L is used to characterize risk for tolerant species of aquatic invertebrates. No toxicity value is proposed for sensitive species of aquatic invertebrates, because sensitive species of aquatic invertebrates have not been identified.

Further paralleling the dose-response assessment for fish, the European Commission (2002) review cites a chronic NOAEC of 137 mg/L in *Daphnia magna* but provides no details of and no citation to the study. By analogy to imazapyr, a chronic NOAEC of 137 mg/L seems credible. As summarized in SERA (2004a), a well-documented chronic toxicity study with imazapyr in *Daphnia magna* yields a chronic NOAEC of 97.1 mg/L. As with imazamox, adverse effect levels for imazapyr have not been defined.

While the chronic NOAEC of 137 mg/L in *Daphnia magna* cited in the review by the European Commission (2002) may reflect a properly conducted study, this NOAEC is not used in the current risk assessment because of the lack of documented details of the study. As with fish, the failure to use this toxicity value does not add substantial uncertainty to the current risk assessment, because the acute toxicity data lead to NOAECs far below the level of concern.

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

As discussed in Section 4.1.3.4.1, data on the toxicity of imazamox to algae are marginal, consisting of a single study in four species of algae assayed at a single nominal concentration of about 0.038 mg a.e./L (Canez et al. 1995). At this concentration, no effects on growth were noted in one species of alga and growth was inhibited by from 3.6 to 11% in the three other species. This study offers few options in terms of the dose-response assessment. In the risk characterization (Section 4.4.3.4.1), the concentration of 0.038 mg a.e./L is compared with anticipated levels of exposure. Given the low rates of growth inhibition, the concentration of 0.038 mg a.e./L is used as an NOAEC for tolerant species. No toxicity value for sensitive species of algae is proposed. Limitations on this approach are discussed further in the risk characterization.

4.3.3.4.2. Aquatic Macrophytes

The toxicity data on aquatic macrophytes are substantially better than the data on algae. For macrophytes, a standard 14-day bioassay is available on *Lemna gibba* which defines both an NOAEC of 4.5 µg a.i./L and an EC_{50} of 11 µg a.e./L. This study is supported by the open literature publication of Cedergreen et al. (2005), which reports a 4-day EC_{50} of 54.5 µg a.e./L and a 7-day EC_{50} of 29 µg a.e./L in *Lemna minor*. Given the differences in exposure duration for the various EC_{50} values for the *Lemna* species, there is no basis for asserting that *Lemna gibba* is more sensitive than *Lemna minor*.

As noted in Section 4.3.3.4.2, no data are available on the toxicity of imazamox to genera of aquatic macrophytes other than *Lemna*. Thus, there is no objective basis for asserting that *Lemna* is a tolerant or sensitive genera. For the current risk assessment, the NOAEC 4.5 µg a.i./L, which corresponds to concentration of about 0.0043 mg a.e./L, is used as an NOAEC for tolerant species and uncertainties in the relative sensitivities of other groups of aquatic macrophytes are discussed further in the risk characterization (Section 4.4.3.4.2). The corresponding EC_{50} of 11 µg a.e., about 0.001 mg a.e./L, can be used to interpret the consequences of exposures that exceed the NOAEC.

4. RISK CHARACTERIZATION

4.4.1. Overview

In some respects, the risk characterization for imazamox is simple and intuitive. Imazamox is an effective herbicide for the control of both terrestrial and aquatic vegetation. Under some conditions, the terrestrial application of imazamox could damage nontarget terrestrial vegetation. Effective aquatic applications of imazamox will most certainly damage aquatic macrophytes and may damage some species of algae. While adverse effect on plants may be anticipated, there is no basis for asserting that applications of imazamox will harm terrestrial or aquatic animals. The risk characterization for imazamox, however, must be qualified both in the likelihood of adverse effects in nontarget terrestrial plants as well as data limitations in the risk characterization for terrestrial and aquatic animals and plants.

While imazamox is an effective terrestrial herbicide, the exposure scenarios developed for terrestrial plants in the current risk assessment lead to a very wide range of HQs, some of which are far below the level of concern and others substantially above the level of concern. This apparent ambiguity relates to the attempt made in the exposure assessments to encompass a wide range of potential exposures associated with different weather patterns and other site-specific variables. Thus, for applications of imazamox to areas in which potential effects on nontarget plants are a substantial concern, refinements to the exposure scenarios for nontarget plants might be justified.

The risk characterization for both aquatic and terrestrial animals must be qualified in terms of the differences in the toxicity data for different groups of organisms. These types of reservations are common to many pesticides which are typically tested in only a limited number of species and under conditions that may not well represent populations of free-ranging nontarget organisms. For mammals and birds, however, the reservations are modest. Imazamox has been subject to a standard and relatively extensive series of acute, subacute, and chronic studies in mammals. There is little doubt that imazamox is nontoxic to mammals and no anticipated exposures of mammals to imazamox raise concern. The data on birds are less extensive but include both acute toxicity and reproduction studies that fail to identify any potential hazards to birds. For other groups of organisms including amphibians, terrestrial invertebrates, fish and aquatic invertebrates, the toxicity data are very limited or, in the case of amphibians and reptiles, nonexistent. While the available studies on these groups of organisms fail to suggest any hazards, confidence in the risk characterization is less than that in the risk characterization for mammals and birds.

While the risk characterization for imazamox focuses on the potential for direct toxic effects, the potential for secondary effects is acknowledged. Terrestrial or aquatic applications of any effective herbicide, including imazamox, are likely to alter vegetation within the treatment area. This alteration is likely to have secondary effects on terrestrial or aquatic animals including, changes in food availability and habitat quality. These secondary effects, the magnitude of which is likely to vary over time, may be beneficial to some species and detrimental to others. These concerns are applicable to any effective method for vegetation management.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

The risk characterization for mammals and birds is summarized in Worksheet G02 of the EXCEL workbooks that accompany this risk assessment, Attachment 1 for terrestrial applications and Attachment 2 for aquatic applications. Both workbooks are based on the maximum anticipated use rates, an application rate of 0.5 lb a.e./acre for terrestrial applications and a target concentration of 0.5 mg/L for aquatic applications.

There is no basis for asserting that adverse effects are plausible in mammals. For terrestrial applications, the highest HQ is 0.1, the upper bound of the HQ for a small mammal consuming contaminated insects. This HQ is below the level of concern (HQ=1) by a factor of 10. For aquatic applications, the highest HQ is 0.01, the upper bound of the HQ for small mammal consuming contaminated water following an accidental spill. This HQ is below the level of concern by a factor of 100.

The only elaboration associated with these HQs is that they probably overestimate risk. As discussed in the dose-response assessment for mammals, the NOAEL for mammals is taken as 300 mg/kg bw/day, the NOAEL used to derive the RfD for imazamox in the human health risk assessment. Other NOAELs from chronic toxicity studies suggest that no adverse effects are likely to occur in mammals at doses of up to 1300 mg/kg bw/day. While the use of the lower NOAEL of 300 mg/kg bw/day may be viewed as conservative, this has no impact on the risk characterization.

4.4.2.2. Birds

The risk characterization for birds is also summarized in the Worksheet G02 of the EXCEL workbooks that accompany this risk assessment. As with mammals, there is no basis for asserting that the use of imazamox will lead to toxic effects in birds. For terrestrial exposures, the maximum HQ is 0.06, below the level of concern by a factor of about 17. This HQ is associated with the longer-term consumption of contaminated vegetation by a large bird that feeds exclusively on vegetation treated with imazamox. For aquatic applications, the highest HQ is 0.003, below the level of concern by a factor of over 300, and this HQ is associated with the consumption of contaminated water following an accidental spill.

As with the HQs for mammals, the only reservation with the HQs for birds is that they probably overestimate risk. As detailed in the dose-response assessment for birds, toxic exposure levels of imazamox have not been defined for birds.

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 imazamox 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 imazamox.

4.4.2.4. Terrestrial Invertebrates

Risks to terrestrial invertebrates are characterized only for terrestrial applications of imazamox. As summarized in Attachment 1, Worksheet G08a, the upper bounds of the HQs range from 0.07 to 1.1. The upper bound HQ of 1.1 is associated with the consumption of contaminated short grasses. Based the analysis by Fletcher et al. (1997), as detailed in Table 10, pesticide concentrations on short grasses are expected to be substantially higher than pesticide concentrations in other food sources.

Generally, an HQ of 1.1 would not be regarded as a substantial concern, and for imazamox, concern with an HQ of 1.1 is essentially negligible. As with all other groups of terrestrial and aquatic animals, imazamox toxicity has not been established for terrestrial invertebrates.

4.4.2.5. Terrestrial Plants

Risks to terrestrial plants are characterized only for terrestrial applications of imazamox (Attachment 1). A quantitative summary of the risk characterization for terrestrial plants is presented in Worksheets G04 for runoff, Worksheets G05 for drift, and Worksheet G06 for off-site contamination due to wind erosion. In Attachment 1, Worksheet G05 has been manually modified to reflect the use of four sets of values for drift: aerial application, ground high-boom broadcast application, ground low-boom broadcast application, and ground backpack application. 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, all HQs are based on either NOAECs or estimates of the EC_{10} which is used as a surrogate for the NOAEC for sensitive species of plants following foliar applications. All HQs are based on the maximum labeled application rate of 0.5 lb a.e./acre.

The highest HQs are associated with direct spray. For convenience, the HQs for direct spray and drift based on all four application methods discussed above are summarized in Table 15. Imazamox is an effective herbicide. If a plant is directly sprayed with imazamox at an application rate of 0.5 lb a.e./acre, it is likely that even tolerant species of plants will be damaged (HQ=10). Because imazamox has not been used or at least not used extensively in past Forest Service programs (Section 2.5), the range of application rates to be used by the Forest Service is unclear. Nonetheless, it seems unlikely that imazamox would be used at application rates as low as 0.05 lb a.e./acre. Thus, it seems reasonable to assert that the direct spray of a tolerant species of nontarget vegetation could and probably would cause damage. For sensitive species of plants, the HQ associated with direct spray is 2500 at an application rate of 0.5 lb a.e./acre. Because of the very high HQ for sensitive species of plants, considerations of variations in the application rate are irrelevant. If sensitive species of plants are directly sprayed with imazamox, they will die.

Based on the estimates of drift using AgDRIFT, potential risks to sensitive and tolerant species of plants differ substantially. For sensitive species of plants, drift associated with aerial or ground broadcast applications result in HQs that exceed the level of concern (HQ=1) at distances of up to 900 feet downwind of the application site. For backpack applications, the HQs for sensitive species of plants exceed the level of concern at distances of up to 300 feet downwind of the application site. For tolerant species of plants, the HQs are much lower. The only HQs that exceed the level of concern are those associated with drift at 25 feet downwind of the application site for aerial applications (HQ=2) and high boom ground applications (HQ=1). All other HQs are below the level of concern.

The HQs for drift, however, are associated with substantial uncertainty. As noted in Section 4.2.4.2 and explained further in the documentation for WorksheetMaker (SERA 2009), the drift estimates given in Worksheet G05 should be viewed as only crude approximations that do not consider the numerous site-specific variables that can affect pesticide drift. This consideration is particularly important for backpack applications. The drift estimates for backpack applications, which are based on a modified set of assumptions for low-boom ground applications, are likely to overestimate drift associated with carefully conducted backpack applications under conditions that do not favor drift. If risks to nontarget vegetation are a substantial concern in any site-specific application of imazamox, refinements to the drift estimates used in Worksheet G05 or generated using WorksheetMaker should be considered.

Risks to nontarget vegetation associated with runoff and sediment losses to a field that is adjacent to the treated site are estimated in Worksheet G04 (Attachment 1). For tolerant species of plants, the HQs are 0.4 (0.004 to 4). For sensitive species of plants, the HQs are 6 (0.06 to 59). As discussed in Section 4.2.4.3, the estimate of offsite transport of imazamox is based on Gleams-Driver modeling of three different soil textures (clay, loam, and sand) at nine different locations with varying weather patterns. 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 levels of exposures which may not be applicable to many site-specific applications made in Forest Service programs.

The HQs for the erosion of soil by wind are given in Worksheet G06. The HQs for both sensitive and tolerant species of plants are below the level of concern with upper bound HQs of 0.3 for sensitive species of plants and 0.001 for tolerant species of plants. As discussed in Section 4.2.4.5, the estimates of soil loss associated with wind erosion are not as severe as those associated with soil losses from a fallow field, etc.; nonetheless, the loss estimates are probably adequate for most forestry applications which will not involve the treatment of fallow fields.

4.4.2.6. Terrestrial Microorganisms

The potential impact of applications of imazamox on soil microorganisms cannot be characterized quantitatively. As discussed in Section 4.3.2.6, the only information on the effect of imazamox on microbial activity in soil is a brief note in the report by the European Commission (2002) that an application rate of about 0.13 lb a.e./acre has no impact on nitrogen metabolism or carbon mineralization in soil. As with similar sparse summaries from the European Commission (2002) report, this information is of little use in characterizing risks to soil microorganisms from applications of imazamox at rates of up to 0.5 lb a.e./acre.

4.4.3. Aquatic Organisms

4.4.3.1. Fish

The quantitative risk characterization for fish as well as other aquatic organisms is given in Worksheet G03 in the EXCEL workbooks for both terrestrial applications (Attachment 1) and aquatic applications (Attachment 2) of imazamox. As discussed in the dose-response assessment for fish (Section 4.3.3.1) only a single NOAEC of 115 mg a.e./L is used for risk characterization, and this NOAEC is assumed to apply to acute exposures of tolerant fish species. The limited toxicity data do not identify species of fish that are sensitive to imazamox. As with other groups of nontarget animals, the toxicity of imazamox to fish has not been established. While the toxicity data for fish are not extensive, the results of available studies are consistent with those for all other groups of animals indicating that imazamox is essentially nontoxic.

While limited, the available toxicity data on fish suggest that imazamox concentrations in surface water are unlikely to have an adverse effect on fish. For terrestrial applications of imazamox, the upper bound HQ for an accidental spill is 0.08, below the level of concern by a factor of about 12. Based on peak expected concentrations of imazamox in surface water, the upper bound of the HQ is 0.0008, below the level of concern by a factor of 1250.

For aquatic applications, the HQs are higher but still below the level of concern. The upper bound HQ for an accidental spill is 0.2 and the upper bound HQ based on the maximum target concentration of 0.5 mg a.e./L is 0.004, below the level of concern by a factor of 250.

The lack of an adequately documented chronic toxicity value for fish precludes the development of a chronic HQ for fish. Nonetheless, given the very low HQs associated with expected peak concentrations of imazamox in surface water as well as the general lack of any dose-duration relationship for imazamox in terrestrial animals, there is no basis for substantial concern about longer-term adverse effects in fish.

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 because no toxicity data on imazamox are available for this group of organisms. 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 imazamox.

4.4.3.3. Aquatic Invertebrates

As summarized in Table 14 and discussed in Section 4.3, the dose-response assessment for aquatic invertebrates is both qualitatively and quantitatively identical to that for fish. The only toxicity value used to characterize risk is an acute NOAEC of 115 mg a.e./L, which is assumed to apply to tolerant species of aquatic invertebrates. As is the case with fish, however, it is not clear that there are aquatic invertebrate species that are sensitive to imazamox. Because the NOAEC for aquatic invertebrates is identical to the NOAEC for fish, the HQs for aquatic invertebrates are numerically identical to the HQs for fish (Section 4.4.3.1).

4.4.3.4. Aquatic Plants

4.4.3.4.1. Algae

As noted in both the hazard identification (Section 4.1.3.4.1) and dose-response assessment (4.3.3.4.1), the toxicity data for algae are marginal—i.e., a concentration of .038 mg a.e./L may be nontoxic to moderately toxic to various species of algae.

Because of these limitations in the toxicity data, the risk characterization for algae is somewhat constrained for some exposure scenarios following terrestrial applications. Based on expected peak concentrations of imazamox in surface water following a terrestrial application, the HQs bracket the level of concern with a central estimate of 0.1 and a range of 0.0005 to 3. Thus, the risk characterization for terrestrial applications is essentially ambiguous. In some cases, it is possible that expected concentrations of imazamox in surface water could cause adverse effects on algae. The severity of the effects, however, cannot be elaborated. In other cases, terrestrial applications of imazamox might not cause any adverse effects in algae. Based on longer-term expected concentrations of imazamox in surface water, the upper bound HQ is only 1.4. While effects on some species of algae cannot be ruled out, it is not clear that these effects would be substantial or even detectable.

For aquatic applications of imazamox, however, the risk characterization is far less ambiguous. Based on the target concentration of 0.5 mg a.e./L—i.e., the expected concentration at the maximum target application rate—the HQ for algae is 13. While no data are available on the impact of concentrations in excess of 0.038 mg a.e./L, the available toxicity studies indicate that this concentration may cause slight to moderate growth inhibition in some species. Consequently, it seems reasonable to speculate that concentrations of 0.5 mg a.e./L could cause adverse effects in at least some species of algae.

For the accidental spill of imazamox into a small body of water, the HQs are substantial for both terrestrial applications (HQs ranging from 4 to about 240) and aquatic applications (HQs ranging from about 80 to 540). Notwithstanding limitations in the toxicity data on algae, it seems reasonable to suggest that spills of imazamox into a relatively small body of water could have an adverse effect and perhaps a very severe adverse effect on algae. This is not an unusual risk characterization for an effective herbicide. In the case of any specific spill, the potential for adverse effects in algae would depend on the amount of imazamox spilled and the size of the body of water into which the spill occurs.

4.4.3.4.2. Macrophytes

While the toxicity data for macrophytes are not extensive, it is clear that imazamox is more toxic to aquatic macrophytes than to algae. Unlike the case with algae, dose-response relationships are well defined in species of *Lemna*. All HQs are based on a NOAEC of 0.0043 mg a.e./L with an associated EC_{50} for growth inhibition of 0.001 mg a.e./L. Thus, an HQ of about 2.3 would be associated with a 50% inhibition in growth [0.001 mg a.e./L ÷ 0.0043 mg a.e./L ≈ 2.33].

For both terrestrial and aquatic applications of imazamox, the upper HQs substantially exceed an HQ of 2. For terrestrial applications, the HQs are 1.3 (0.005 to 22). As with algae, these HQs lead to an ambiguous risk characterization. Under conditions that favor the offsite transport of imazamox to surface water, there is likely to be adverse effects in aquatic macrophytes. Under

conditions that do not favor the offsite transport of imazamox, risks to aquatic macrophytes could be modest to negligible. While the concentrations of imazamox used in this risk assessment are based explicitly on Gleams-Driver modeling (Section 3.2.3.4.6), estimated concentrations of imazamox in surface water due to either direct spray or drift could be hazardous (Table 8). Thus, for specific imazamox applications that pose risks to nontarget aquatic macrophytes, consideration should be given to site-specific Gleams-Driver modeling that incorporates reasonable drift estimates based on the planned application method and anticipated application conditions.

Risks to aquatic macrophytes associated with aquatic applications of imazamox are not ambiguous. Imazamox is an effective herbicide for the control of unwanted aquatic macrophytes. If aquatic applications of imazamox are made at effective application rates, damage to aquatic macrophytes is a virtual certainty.

Similarly, risks associated with accidental spills of imazamox into a relatively small body of water lead to HQs of 528 (35 to 2113) for terrestrial applications and 2113 (697 to 4753) for aquatic applications. As with the risk characterization for algae, actual risks to aquatic macrophytes will vary with the conditions of the spill—i.e., the amount spilled and the size of the body of water. Nonetheless, given that aquatic macrophytes are particularly sensitive to imazamox, any significant spill of the herbicide into surface water is likely to pose an extreme hazard to resident populations of aquatic macrophytes. This risk characterization applies to the spill of virtually any effective aquatic herbicide.

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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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Internet	**References obtained from various sites on the Internet.**
SET00	**Papers from preliminary scoping.**
SET01-TOXL	**Preliminary TOXLINE literature search.**
SET02	**Papers added in secondary screen.**
MRID-DER01	**DERs of studies submitted to U.S. EPA/OPP in support of the registration of imazamox and provided by BASF, the registrant for imazamox.**
MRID-EPA	**Studies submitted to U.S. EPA/OPP in support of the registration of imazamox for which DERs are not available. Summaries are taken from EPA documents at specified in each citation below.**
Sec	**Summary of citation from a secondary source.**
Std	**Standard references used in most Forest Service risk assessments.**

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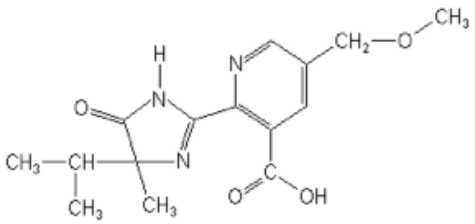
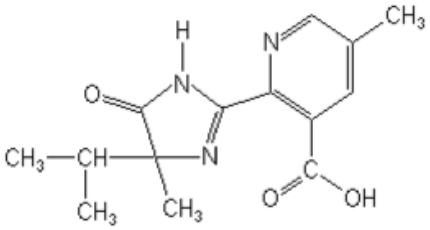
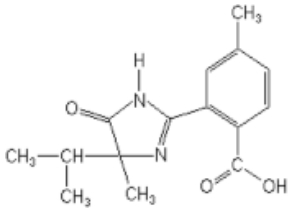
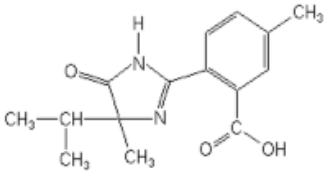


Imazamox

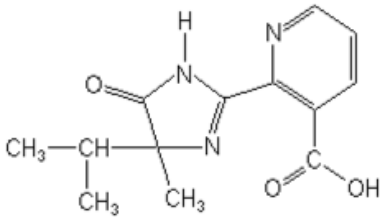


Imazapic

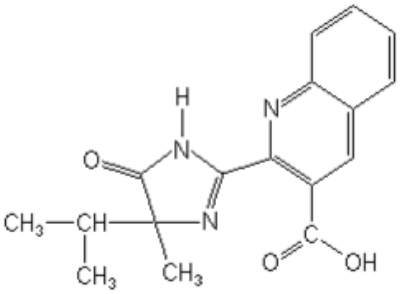




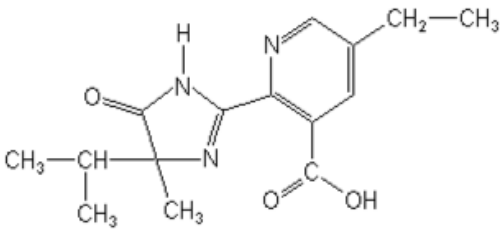
Imazamethabenz



Imazapyr



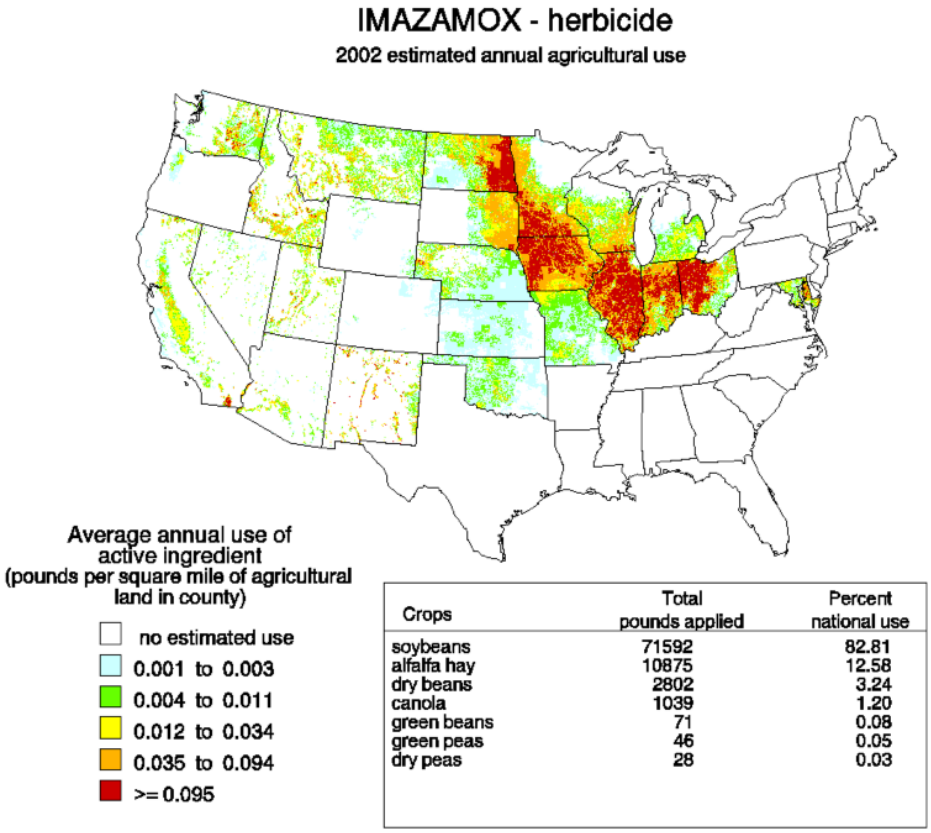
Imazaquin



Imazethapyr

Figure 1:Imazamox and Other Imidazolinone Herbicides

Structures reproduced with permission (courtesy of Alan Wood) from the Compendium of Pesticide Common Names (http://www.alanwood.net/pesticides/)
See discussion in Section 2.2.



Crops	Total pounds applied	Percent national use
soybeans	71592	82.81
alfalfa hay	10875	12.58
dry beans	2802	3.24
canola	1039	1.20
green beans	71	0.08
green peas	46	0.05
dry peas	28	0.03

Figure 2: Agricultural Uses of Imazamox

Source: USGS 2003a

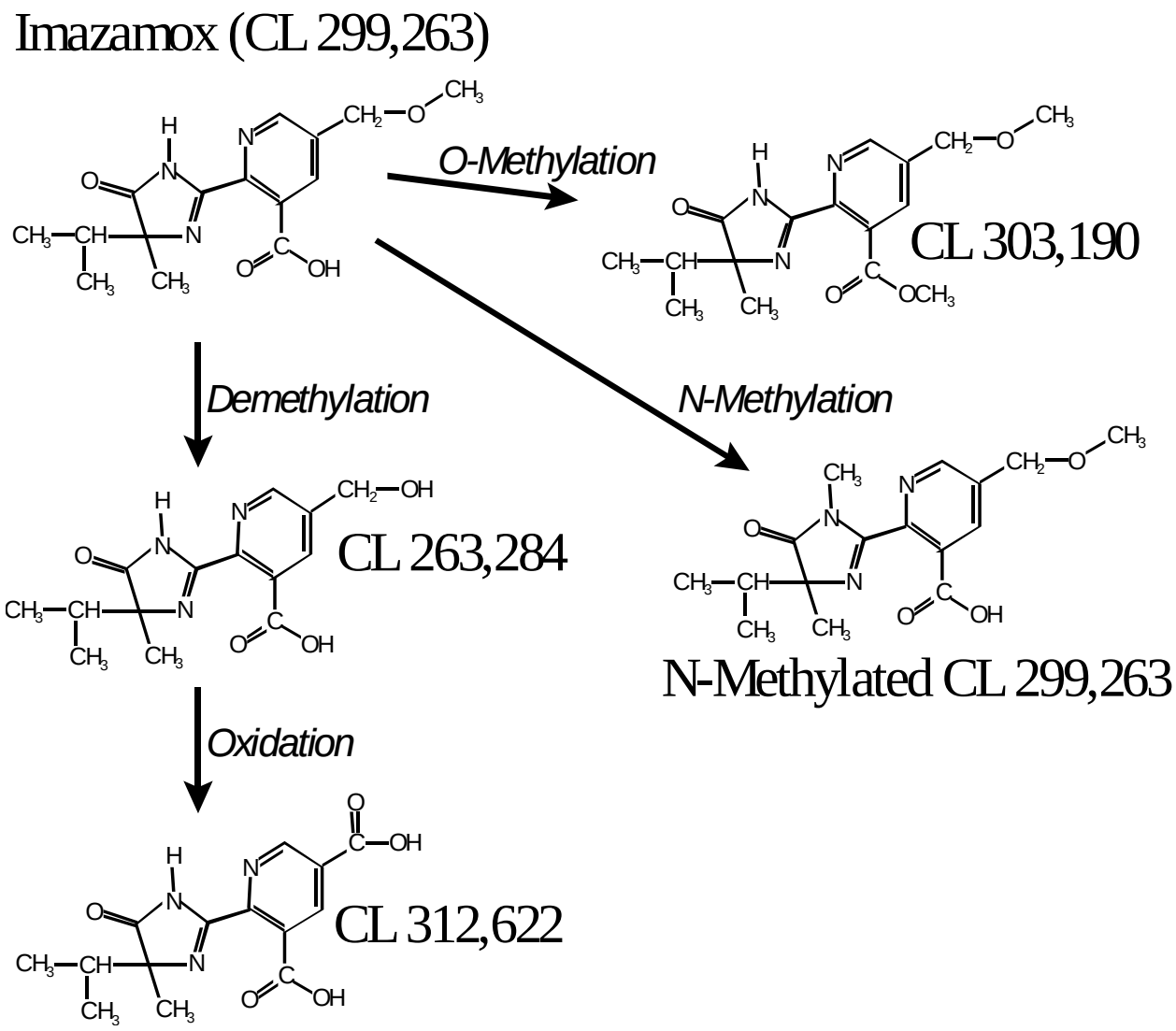


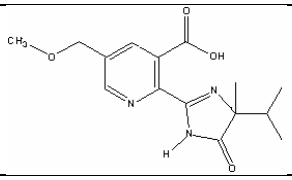
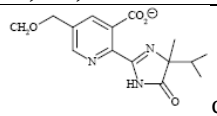
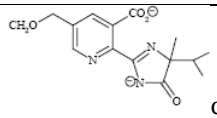
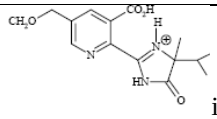
Figure 3: Metabolism of Imazamox in Rats

Source: Adapted from Chiu 1995a.
See Section 3.1.3.1 for discussion.

Table 1: EPA Guideline Studies for Imazamox

Number	Title	Number	Title
61-1	Chemical Identity	163-1	Soil Leaching/adsorption/desorption
61-2	Description of Beginning Materials and Manufacturing Process	164-1	Terrestrial field dissipation
61-3	Discussion of Formation of Impurities	165-1	Confined rotational crop
62-1	Preliminary Analysis	165-4	Bioaccumulation in fish
62-2	Certification of limits	171-4B	Residue Analytical Methods
62-3	Analytical Method	171-4C	Magnitude of the Residue [by commodity]
63-0	Physical/Chemical Characteristics	171-4A2	Nature of the Residue in Plants
63-17	Storage stability	171-4A3	Nature of the Residue in Livestock
71-1	**Avian Single Dose Oral Toxicity**	830.1550	Product Identity and composition
71-2	**Avian Dietary Toxicity**	830.1600	Description of materials used to produce the product
71-4	**Avian Reproduction**	830.1620	Description of production process
72-1	**Acute Toxicity to Freshwater Fish**	830.1650	Description of formulation process
72-2	**Acute Toxicity to Freshwater Invertebrates**	830.1670	Discussion of formation of impurities
72-3	**Acute Toxicity to Estuarine/Marine Organisms**	830.1750	Certified limits
81-1	**Acute oral toxicity in rats**	830.1800	Enforcement analytical method
81-2	**Acute dermal toxicity in rabbits or rats**	830.6302	Color
81-3	**Acute inhalation toxicity in rats**	830.6303	Physical state
81-4	**Primary eye irritation in rabbits**	830.6304	Odor
81-5	**Primary dermal irritation**	830.6314	Oxidizing or reducing action
81-6	**Dermal sensitization**	830.6315	Flammability
82-1	**Subchronic Oral Toxicity: 90-Day Study**	830.6316	Explodability
82-2	**21-day dermal-rabbit/rat**	830.6317	Storage stability of product
83-1	**Chronic Toxicity**	830.6320	Corrosion characteristics
83-2	**Oncogenicity**	830.7000	pH of water solutions or suspensions
83-3	**Teratogenicity**	830.7100	Viscosity
83-4	**2-Generation Reproduction**	830.7300	Density/relative density
84-2	**Interaction with Gonadal DNA**	835.4100	Aerobic soil metabolism
85-1	**General metabolism**	**870.1100**	**Acute oral toxicity**
122-2	**Aquatic plant growth**	**870.1200**	**Acute dermal toxicity**
123-1	**Seed germination/seedling emergence and vegetative vigor**	**870.1300**	**Acute inhalation toxicity**
141-1	**Honey bee acute contact**	**870.2400**	**Acute eye irritation**
161-1	Hydrolysis	**870.2500**	**Acute dermal irritation**
161-2	Photodegradation-water	**870.2600**	**Skin sensitization**
161-3	Photodegradation-soil	**870.5100**	**Bacterial reverse mutation test**
162-1	Aerobic soil metabolism	**870.5375**	***In vitro* mammalian chromosome aberration test**
162-2	Anaerobic soil metabolism	**870.3050**	**Repeated dose 28-day oral toxicity in rodents**
162-3	Anaerobic aquatic metabolism	N/A	Non-Guideline Study

Guidelines relevant to human health effects and ecological effects are given in bold typeface.
See Section 1 for discussion.

Table 2: Chemical and Physical Properties of Imazamox		
Property	**Value**	**Reference**
	Identifiers	
Common name:	Imazamox	
IUPAC Name	(RS)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-5-methoxymethylnicotinic acid	Tomlin 2004
CAS Name	(±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-(methoxymethyl)-3-pyridinecarboxylic acid	Tomlin 2004
CAS No.	114311-32-9 [acid] 247057-22-3 [ammonium salt]	U.S. EPA/OPP 1997a Clearcast MSDS
U.S. EPA PC Code	129171	U.S. EPA/OPP 2001c
Development Codes	AC 299,263; CL 299,263 (both Cyanamid); BAS 720 H (BASF)	Tomlin 2004
Smiles Notation	COCc1cnc(C2=NC(C)(C(C)C)C(=O)N2)c(c1)C(=O)O	Tomlin 2004
Structure		European Commission 2002
	Chemical Properties	
Henry's Law Const.	<9.76 x 10^{-7} Pa m^3 mol^{-1} (calc.)	Tomlin 2004
Hydrolysis	Stable [pH 5 to 9]	Tomlin 2004
Kow	5.37 [Log Kow = 0.73 [pH 5 and 6, corrected]	Tomlin 2004
	5.36 [pH 5 and 6 at 25ºC]	U.S. EPA/OPP 1997a
Melting Point	166.0-166.7 ºC	Tomlin 2004
Molecular formula	$C_{15}H_{19}N_3O_4$	Tomlin 2004
Molecular weight	305.34 g/mole [acid] 322.4 g/mole [ammonium salt]	EPI Suite 2008 Clearcast MSDS
a.i. to a.e. conversion	0.947 [305.34 g/mole ÷ 322.4 g/mole]	N/A
pH	5.36 [1% aqueous suspension (w:v) at 24.5ºC]	U.S. EPA/OPP 1997a
pK_a	2.3, 3.3, 10.8	Tomlin 2004
	 carboxylate anion	European Commission 2002
	 carboxylate and imi amide anions	European Commission 2002
	 imi nitrogen protonation	European Commission 2002
Specific gravity	1.39 (20 °C)	Tomlin 2004
Vapor pressure	<1.3 x 10^{-2} mPa (25 °C)	Tomlin 2004
Water solubility	4160 mg/L (20 °C).	Tomlin 2004
	4410 mg/L	U.S. EPA/OPP 1997a
	4413 mg/L	U.S. EPA/OPP 1997b
	> 626 g/l, 25 °C, pH 7	European Commission 2002

continued on next page

Table 2: Chemical and Physical Properties of Imazamox

<table>
<tr><th>Property</th><th>Value</th><th>Reference</th></tr>
<tr><td></td><td>Environmental Properties</td><td></td></tr>
<tr><td>Aqueous photolysis</td><td>DT_{50}: 6.7 hours at pH 7</td><td>European Commission 2002</td></tr>
<tr><td>Aqueous photolysis</td><td>Half-life of 6.8 hours at pH 5, 7, and 9</td><td>U.S. EPA/OPP 2008a</td></tr>
<tr><td>Bioconcentration Factor</td><td>0.11 to 0.13 L/kg on Days 14 to 28 in inedible tissue. BCF for edible tissues was below the limit of quantification.</td><td>Johnson 1995</td></tr>
<tr><td>Foliar half-life</td><td>No data. EFED uses a default half-life of 35 days.</td><td>U.S. EPA/OPP (2008a, p. 14)</td></tr>
<tr><td></td><td>Foliar half-lives of 1.2 to 12 days are reported for imazapic and half-lives of 26 to 30 days are reported for imazapyr.</td><td>SERA 2004a,b</td></tr>
<tr><td>Hydrolysis</td><td>Stable at pH 5, 7, and 9</td><td>Mangels 1994a, MRID 431932-40.</td></tr>
<tr><td>K_d</td><td>0.882</td><td>U.S. EPA/OPP 2008a citing Mangels 1994b, MRID 43193242</td></tr>
<tr><td>K_d</td><td>≈0 to 2263 [Various clays, generally increasing Kd with lower pH. See Table 2 of paper.]</td><td>Celis et al. 1999</td></tr>
<tr><td>K_d/Koc</td><td>
<table>
<tr><th>Soil Texture</th><th>pH</th><th>%OC</th><th>K_d</th><th>Koc*</th></tr>
<tr><td>Sandy loam</td><td>7.2</td><td>2.48</td><td>0.26</td><td>10.5</td></tr>
<tr><td>Silty clay</td><td>6.9</td><td>1.36</td><td>0.42</td><td>30.9</td></tr>
<tr><td>Sandy loam</td><td>5.8</td><td>0.95</td><td>0.33</td><td>34.7</td></tr>
<tr><td>Clay</td><td>6.5</td><td>2.24</td><td>0.30</td><td>13.4</td></tr>
<tr><td>Silt loam</td><td>6.2</td><td>1.4</td><td>0.19</td><td>13.6</td></tr>
<tr><td>Sandy loam</td><td>6.1</td><td>1.1</td><td>0.28</td><td>25.5</td></tr>
<tr><td>Loam</td><td>5.7</td><td>1.1</td><td>0.26</td><td>23.6</td></tr>
<tr><td>Average:</td><td></td><td></td><td>0.29</td><td>21.7</td></tr>
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*Koc = Kd ÷ prop. OC</td><td>Sakaliene et al. 2007</td></tr>
<tr><td>K_d/Koc</td><td>
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<tr><th>Soil Texture</th><th>K_d</th><th>%OC</th><th>Koc*</th></tr>
<tr><td>Arkansas loamy sand</td><td>0.05</td><td>0.29</td><td>17.2</td></tr>
<tr><td>Arkansas clay loam</td><td>2.71</td><td>1.88</td><td>144.1</td></tr>
<tr><td>Indiana silt loam</td><td>1.43</td><td>1.05</td><td>136.2</td></tr>
<tr><td>New Jersey silt loam</td><td>0.30</td><td>0.85</td><td>35.3</td></tr>
<tr><td>North Dakota silty clay loam</td><td>0.13</td><td>2.59</td><td>5.0</td></tr>
<tr><td>Wisconsin loam</td><td>0.24</td><td>1.37</td><td>17.5</td></tr>
<tr><td>Average</td><td>0.81</td><td></td><td>59.2</td></tr>
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*Koc = Kd ÷ prop. OC</td><td>Mangels 1994b, MRID 43193242</td></tr>
<tr><td>K_d/Koc</td><td>
<table>
<tr><th>Soil Texture</th><th>K_d</th><th>%OC</th><th>Koc*</th></tr>
<tr><td>Arkansas loamy sand</td><td>0.78</td><td>0.28</td><td>278.6</td></tr>
<tr><td>Arkansas clay loam</td><td>1.3</td><td>1.88</td><td>69.1</td></tr>
<tr><td>Indiana silt loam</td><td>2.19</td><td>1.05</td><td>208.6</td></tr>
<tr><td>New Jersey silt loam</td><td>0.79</td><td>0.85</td><td>92.9</td></tr>
<tr><td>North Dakota silty clay loam</td><td>0.71</td><td>2.59</td><td>27.4</td></tr>
<tr><td>Wisconsin loam</td><td>0.81</td><td>1.37</td><td>59.1</td></tr>
<tr><td>Average</td><td>1.09</td><td></td><td>122.6</td></tr>
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*Koc = Kd ÷ prop. OC</td><td>Kuhn 1995, MRID 43876227</td></tr>
<tr><td>Koc</td><td>58.7 (5 – 144) U.S. soils
96 (2 – 374) French soils
29.4 (5-65) Italian and UK soils
73 (4-145) Italian and German soils
67 (2 -374) Overall</td><td>European Commission 2002</td></tr>
</table>

Table 2: Chemical and Physical Properties of Imazamox

Property	Value	Reference
Soil degradation, laboratory	Type / OC (%) / pH / Temp. / DT_{50} (days) Sandy loam / 1.5 / 6.8 / 25ºC / 45* Sandy loam / 1.7 / / 25ºC / 40* Silt loam / 0.8 / 5.8 / 20ºC / 207 Silt loam / 0.8 / 6.5 / 20ºC / 44 Silty clay loam / 1.1 / 8.1 / 20ºC / 12 *Adjusted to 20ºC.	European Commission 2002
Aerobic soil half-life	30 days, 1 unidentified metabolite	Ta 1994, MRID 43193241
Aerobic soil half-life	28 days [cited as 27 days in U.S.EPA/OPP 2008a]	Ta 1995a, MRID 43876224
Anaerobic soil half-life	Stable	Ta 1995b, MRID 43876225
Anaerobic aquatic metabolism	Stable	MRID 43876231 in U.S. EPA/OPP 2008a
Terrestrial Field dissipation half-life	25.9 (21.1 to 34.7) days	Cobucci et al. 1998
	15 to 130 days	Kleiner 1995, MRID 43876230
Sediment DT_{50}	21 days, 1st order 203 days, 1st order 129 days, 1st order 428 days, 1st order	European Commission 2002
Sediment Half-life	761 days at 25°C, Extrapolated 1st order	Cady 1995, MRID 43876226

Table 3:Imazamox Formulations

Formulation	Composition	Application Information
Beyond [1] BASF EPA No.: 241-437 EPA Label: Sep 23, 2008	Imazamox ammonium salt, 12.1% Other: 87.9% [No information available.] 1 lb a.e./gallon	Agricultural products: Up to 8 oz/acre [0.0625 lb a.e./acre]. No specific forestry applications listed but forestry applications are noted on label.
Clearcast [1] BASF EPA No.: 241-437 EPA Label: Sep 23, 2008	Imazamox ammonium salt, 12.1% a.i. (corresponds to 11.5% a.e.) Other: 87.9% 1 lb a.e./gallon	**Aquatic:** Maximum concentration: 500 ppb (173 fl oz/acre foot). Multiple applications are permitted. Maximum and interval not specified. Foliar broadcast: 0.5 lb a.e./acre by surface or aerial (fixed-wing or helicopter). Can use surface or subsurface applications. Use nonionic surfactant (0.25% v/v) or methylated seed oils or vegetable oil concentrate. **Terrestrial** Maximum application rate: 0.5 lb a.e./acre. Use nonionic surfactant (0.25% v/v) or methylated seed oils or vegetable oil concentrate. Forestry applications involving broadcast application, hack and squirt, cut stump, and basal bark. Ground or aerial applications (fixed wing and helicopter) are permitted.
Clearmax BASF EPA No.: 7969-238 May 15, 2006	Imazamox ammonium salt and 2-ethylhexyl ester of 4-chloro-2-methylphenoxy)acetic acid	No forestry applications. For use only on Clearfield Wheat
Raptor DG BASF EPA No.: 241-380 EPA label: Aug 18,2000	Imazamox ammonium salt, 70% (w/w) granular.	No forestry applications. For use only on soybeans.
Raptor [1] BASF EPA No.: 241-379 EPA Label: Mar 30,2009	Imazamox ammonium salt, 12.1% Other: 87.9% [No information available.] 1 lb a.e./gallon	Agricultural products: Up to 8 oz/acre [0.0625 lb a.e./acre]. No specific forestry applications listed but forestry applications are noted on label.
Raptor (technical) BASF EPA No.: 241-378 EPA label: Sep 15,2005	Imazamox acid, 97.4%	For reformulation only. No forestry applications.

[1] Formulation information on MSDSs are identical for Beyond, Clearcast, and Raptor.

Note: Imazamox is not listed in Knisel and Davis (2000) or in USDA/ARS (2008).

Table 4: 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 5: General Site Conditions used in Gleams-Driver Simulations

Field Characteristics	Description		
Type of site	Mixed pine-hardwood		
Treated and total field areas	10 acres		
Field width	660 feet		
Slope	0.1		
Depth of root zone	60 inches		
Cover factor	0.15		
Type of clay	Mixed		
Surface cover	No surface depressions		
Pond Characteristics	**Description**		
Surface area	1 acre		
Drainage area:	10 acres		
Initial Depth	2 meters		
Minimum Depth	1 meter		
Maximum Depth	3 meters		
Sediment Depth	2 centimeters		
Stream Characteristics	**Description**		
Width	2 meters		
Flow Velocity	6900 meters/day		
Flow Rate	710,000 liters/day		
Soil Specific Factors [a]	**Clay**	**Loam**	**Sand**
Runoff potential	High	Moderate	Low
Surface type	Road	Woods	Meadow
Surface condition	Hard surface	Fair	Dirt

[a] Detailed input values for the soil types are given in SERA (2007b, Tables 2 and 3) .

Table 6: Locations Used for Gleams-Driver Silmulations

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 7: Chemical-specific parameters used in GLEAMS modeling

Parameter	Clay	Loam	Sand	Note/Reference
Halftimes (days)				
Aquatic Sediment	761			Note 1
Foliar	35			Note 2
Soil	81			Note 3
Water	365			Note 4
Soil $K_{o/c}$, mL/g	67 (2 to 374)			Note 5
Sediment K_d, mL/g	0.5 (0.05 to 3)			Note 6
Water Solubility, mg/L	4413			Note 7
Foliar wash-off fraction	0.9			Note 8
Fraction applied to foliage	0.5			Note 9

Note 1	Anaerobic aquatic metabolic half-life taken from U.S. EPA/OPP 2008b, Table 5, p. 14 for PRZM/EXAMS input. This is from Cady 1995.
Note 2	No data are available. Use the U.S. EPA/OPP/EFED default half-life of 35 days.
Note 3	Aerobic soil half-life of 27 days x 3 following U.S. EPA/OPP 2008b, Table 5, p. 13 for PRZM/EXAMS input.
Note 4	Hydrolysis half-life used in PRZM/EXAMS modeling by U.S. EPA/OPP 2008b. Do not use photolysis half-life because photolytic breakdown products will be treated as parent compound.
Note 5	The $K_{o/c}$ values for imazamox are highly variable and do not correlate well with standard soil characteristics – e.g., OC, pH, or cation exchange capacity. For the Gleams-Driver modeling, Koc is taken as a triangular distribution with a mode of 67 and a range of 2 to 374 based on the values given in European Commission 2002.
Note 6	As with $K_{o/c}$ values, the Kd values do not correlate with soil properties and a triangular distribution is used in the Gleams-Driver modeling combining the data from Sakaliene et al. (2007) and Mangels (1994b), detailed in Table 2, rounding the values to one significant decimal place.
Note 7	Used in PRZM/EXAMS modeling by U.S. EPA/OPP 2008b and taken from U.S. EPA/OPP 1997b.
Note 8	No data are available for imazamox. Use the 0.9 value for imazapyr amine from Knissel and Davis (2000).
Note 9	This is the standard default value for broadcast applications of liquid formulations used in all Forest Service risk assessments.

Note: In the database released with Gleams-Driver, only the central estimates are entered for Koc and Kd. The triangular distributions for Kd and Koc were implemented using the Full Run facility in Gleams-Driver.

Table 8: Summary of Modeled Concentrations in Surface Water

Scenario	Concentrations (ppb or µg/L)	
	Peak	Long-Term Average
MODELING FOR THIS RISK ASSESSMENT (1 lb a.i./acre)		
Direct Spray and Spray Drift		
Pond, Direct Spray (Section 3.2.3.4.2) [a]	56.0	N/A
Pond, drift at 25 feet (Section 3.2.3.4.2) [a]	12.5	N/A
Stream, Direct Spray (Section 3.2.3.4.2) [a]	45.7	N/A
Stream, drift at 25 feet (Section 3.2.3.4.2) [a]	10.2	N/A
Gleams-Driver		
Broadcast Foliar		
Pond [b], Section 3.2.3.4.4	10.5 (0 to 190)	5.1 (0 to 104)
Stream [c], Section 3.2.3.4.4	10.1 (0 to 106)	0.1 (0 to 3.9)
PRZM-EXAMS		
Standard farm pond, Section [d] 3.2.3.4.4	2.96 (2.8 to 4.8)	0.48 (0.36 to 0.66)
Other Modeling		
U.S. EPA		
GENEEC [e]	N/A	1

[a] Section 3.2.3.4.2 discusses expected concentrations in terms of the nominal application rate of 1 lb a.i./acre. The values for direct spray and drift are taken from Worksheet 10a (direct spray and drift as 25 feet for a pond) and Worksheet 10b (direct spray and drift as 25 feet for a stream) adjusted to WRC values based on the application rate of 0.75 lbs/acre.

[b] Appendix 8, Table A8-7 (peak) and Table A8-8 (longer-term).

[c] Appendix 8, Table A8-5 (peak) and Table A8-6 (longer-term).

[d] U.S. EPA/OPP (2008b), pp. 33-34. Model run at an application rate of 0.56 kg/ha (≈0.5 lb/acre). The modeled concentrations in this table are multiplied by a factor of 2 (i.e., an application rate of 1 lb a.e./acre) so that the concentrations are comparable to the Gleams-Driver modeling.

[e] U.S. EPA/OPP (1997a), GENEEC modeling. Application rate not clear.

Table 9: Concentrations of imazamox in surface water used in this risk assessment

	Water contamination rate in mg/L per lb/acre applied [a]	
Foliar Broadcast	**Peak**	**Longer-term**
Central	0.011	0.0051
Lower	0.00004	0.000002
Upper	0.19	0.104

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

See Section 3.2.3.4.6 for discussion.

Table 10: Estimated residues in food items per lb a.i. applied

Food Item	Concentration in Food Item (ppm per lb a.i./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. (1997).
[b] Central values × (Central Value ÷ Upper Value).

Table 11: Summary of Risk Characterization for Workers

	Hazard Quotients[1]		
	Central	**Lower**	**Upper**
General Exposures			
Backpack	2E-03	8E-05	1E-02
Ground Broadcast	4E-03	1E-04	3E-02
Aerial	2E-03	4E-05	1E-02
Aquatic	2E-03	9E-04	4E-03
Accidental/Incidental Exposures			
Terrestrial Applications			
Contaminated Gloves, 1 min.	1E-04	3E-05	4E-04
Contaminated Gloves, 1 hour	8E-03	2E-03	3E-02
Spill on Hands, 1 hour	6E-04	8E-05	3E-03
Spill on lower legs, 1 hour	2E-03	2E-04	7E-03
Aquatic Applications			
Contaminated Gloves, 1 min.	3E-03	2E-03	4E-03
Contaminated Gloves, 1 hour	0.2	1E-01	0.3
Spill on Hands, 1 hour	1E-02	5E-03	3E-02
Spill on lower legs, 1 hour	3E-02	1E-02	7E-02

[1] HQs for terrestrial applications taken from Attachment 1, Worksheet E02. HQs for aquatic applications taken from Attachment 1, Worksheet E02.

See Section 3.4.2 for discussion.

Table 12: Risk Characterization for the General Public, Terrestrial Applications

Scenario	Receptor	Hazard Quotients[1]		
		Central	Lower	Upper
Accidental Acute Exposures (dose in mg/kg/event)				
Direct Spray of Child, whole body	Child	6E-03	8E-04	3E-02
Direct Spray of Woman, feet and lower legs	Adult Female	6E-04	9E-05	3E-03
Water consumption (spill)	Child	6E-02	2E-03	0.3
Fish consumption (spill)	Adult Male	2E-04	1E-05	7E-04
Fish consumption (spill)	Subsistence Populations	8E-04	6E-05	3E-03
Non-Accidental Acute Exposures (dose in mg/kg/event)				
Vegetation Contact, shorts and T-shirt	Adult Female	3E-04	1E-04	8E-04
Contaminated Fruit	Adult Female	2E-03	9E-04	3E-02
Contaminated Vegetation	Adult Female	3E-02	2E-03	0.2
Swimming, one hour	Adult Female	4E-08	8E-11	1E-06
Water consumption	Child	1E-04	3E-07	4E-03
Fish consumption	Adult Male	4E-07	2E-09	7E-06
Fish consumption	Subsistence Populations	2E-06	7E-09	3E-05
Chronic/Longer Term Exposures (dose in mg/kg/day)				
Contaminated Fruit	Adult Female	6E-04	3E-04	1E-02
Contaminated Vegetation	Adult Female	8E-03	6E-04	7E-02
Water consumption	Adult Male	2E-05	7E-09	6E-04
Fish consumption	Adult Male	1E-08	5E-12	2E-07
Fish consumption	Subsistence Populations	1E-07	4E-11	2E-06

[1] The HQs are taken from Attachment 1, Worksheet E04.

See Section 3.4.3 for discussion.

Table 13: Risk Characterization for the General Public, Aquatic Applications

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	0.2	5E-02	0.8
Fish consumption (spill)	Adult Male	7E-04	2E-04	2E-03
Fish consumption (spill)	Subsistence Populations	3E-03	1E-03	7E-03
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	4E-06	2E-06	7E-06
Water consumption	Child	1E-02	8E-03	2E-02
Fish consumption	Adult Male	4E-05	4E-05	4E-05
Fish consumption	Subsistence Populations	2E-04	2E-04	2E-04
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	3E-03	2E-03	4E-03
Fish consumption	Adult Male	2E-06	2E-06	2E-06
Fish consumption	Subsistence Populations	1E-05	1E-05	1E-05

[1]The HQs are taken from Attachment 2, Worksheet E04.

See Section 3.4.3 for discussion.

Table 14: Summary of toxicity values used in ecological risk assessment

Group/Duration Organism	Endpoint	Toxicity Value (a.e.)	Reference
Terrestrial Animals			
Acute			
Mammals	Use longer-term NOAEL	300 mg/kg bw	Section 4.3.2.1.
Birds	Acute dietary NOAEL	1700 mg/kg bw	Section 4.3.2.2
Insect (oral)	Use contact NOAEC	250 mg/kg bw	Section 4.3.2.4.1
Honey Bee (contact)	Contact NOAEC	250 mg/kg bw	Section 4.3.2.4.2
Longer-term			
Mammals	Longer-term NOAEL	300 mg/kg bw/day	Section 4.3.2.1
Bird	Reproduction NOAEL	190 mg/kg bw	Section 4.3.2.2.
Terrestrial Plants			
Soil Sensitive	NOAEC cabbage	0.0008	Section 4.3.2.5
Tolerant	NOAEC lettuce	0.012	
Foliar Sensitive	EC_{10}, pigweed	0.0002	Section 4.3.2.5
Tolerant	NOAEC in soybeans	0.048	
Aquatic Animals			
Acute			
Amphibians Sensitive	No data	N/A	Section 4.3.3.2
Tolerant	No data	N/A	
Fish Sensitive	Species not identified.	N/A	Section 4.3.3.1
Tolerant	NOAEC	115 mg/L	
Invertebrates Sensitive	Species not identified.	N/A	Section 4.3.3.3
Tolerant	NOAEC	115 mg/L	Section 4.3.3.3
Longer-term			
Amphibians Sensitive	No data available	N/A	Section 4.3.3.2
Tolerant	No data available	N/A	
Fish Sensitive	Data poorly documented	N/A	Section 4.3.3.1
Tolerant	Data poorly documented	N/A	Section 4.3.3.1
Invertebrates Sensitive	Data poorly documented	N/A	Section 4.3.3.3
Tolerant	Data poorly documented	N/A	Section 4.3.3.3
Aquatic Plants			
Algae Sensitive	Species not identified.	N/A	Section 4.3.3.4
Tolerant	NOAEC	0.038 mg/L	Section 4.3.3.4
Macrophytes Sensitive	Species not identified.	N/A	Section 4.3.3.4
Tolerant	NOAEC	0.0043 mg/L	Section 4.3.3.4

Table 15: 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
	Sensitive Species			
0	**2,500**	**2,500**	**2,500**	**2,500**
25	**558**	**260**	**88**	**21**
50	**428**	**125**	**44**	**11**
100	**245**	**62**	**24**	**6**
300	**78**	**19**	**9**	**2**
500	**48**	**10**	**5**	**1.4**
900	**31**	**4**	**3**	0.8
	Tolerant Species			
0	**10**	**10**	**10**	**10**
25	**2**	**1.1**	0.4	0.1
50	**1.8**	0.5	0.2	5.E-02
100	**1.0**	0.3	0.1	3.E-02
300	0.3	8.E-02	4.E-02	1.E-02
500	0.2	4.E-02	2.E-02	6.E-03
900	0.1	2.E-02	1.E-02	3.E-03

Adapted from Attachment 1, Worksheet G05.
See Section 4.4.2.5 for discussion.

Appendix 1: List of Studies on Imazamox Submitted to the U.S. EPA/OPP

EPA OPP HQ-FOI # 0787-10
EPA OPP Freedom of Information Act Request
Imazamox (Pc code 129171)
Guideline Bibliography
N=206
Sorted by Guideline Number and then MRID Number

Guideline: 61-1 Chemical Identity

MRID: 43193201
Patel, J. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide Technical: Lab Project Number: CHDV-34-1: CHDV-34-2. Unpublished study prepared by American Cyanamid Co. 115 p.

MRID: 43193204
Schaaf, M. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 12 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876205
Patel, J. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Technical: (Addendum): Lab Project Number: CHDV 34 1.1. Unpublished study prepared by American Cyanamid Co. 56 p.

MRID: 43876233
Kovacs, G. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 70DG Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 10 p.

MRID: 43876234
Li, W.; Liu, D. (1995) Certification of Limits and Validation of Liquid Chromatographic Method, M-2439, for the Determination of the Active Ingredient (CL 299,263) in CL 299,263 70DG Herbicide Granular Formulation: Lab Project Number: F-1335: PRT00222: 94FAI-0554-13. Unpublished study prepared by XenoBiotic Labs, Inc. 43 p.

Guideline: 61-2 Description of Beginning Materials and Manufacturing Process

MRID: 43193201
Patel, J. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide Technical: Lab Project Number: CHDV-34-1: CHDV-34-2. Unpublished study prepared by American Cyanamid Co. 115 p.

MRID: 43193204
Schaaf, M. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 12 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876205

Patel, J. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Technical: (Addendum): Lab Project Number: CHDV 34 1.1. Unpublished study prepared by American Cyanamid Co. 56 p.

MRID: 43876233
Kovacs, G. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 70DG Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 10 p.

Guideline: 61-3 Discussion of Formation of Impurities

MRID: 43193201
Patel, J. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide Technical: Lab Project Number: CHDV-34-1: CHDV-34-2. Unpublished study prepared by American Cyanamid Co. 115 p.

MRID: 43193204
Schaaf, M. (1994) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 12 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876205
Patel, J. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Technical: (Addendum): Lab Project Number: CHDV 34 1.1. Unpublished study prepared by American Cyanamid Co. 56 p.

MRID: 43876233
Kovacs, G. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 70DG Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 10 p.

MRID: 44630401
Stellar, W. (1998) Discussion of the Formation of Impurities of Raptor DG Herbicide. Unpublished study prepared by American Cyanamid Company. 7 p. {OPPTS 830.1670}

Guideline: 62-1 Preliminary Analysis

MRID: 43193202
Czajkowska, T.; Humphries, K.; Hrabovsky, I. (1994) Preliminary Analysis, Certification of Limits, and Analytical Methods with Validation Data for AC 299,263 Herbicide Technical: Lab Project Number: APBR 322: APBR 309: APBR 311. Unpublished study prepared by American Cyanamid Co. 439 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876206
Philburn, K.; Humphries, K. (1995) Preliminary Analysis, Certification of Limits, and Analytical Methods With Validation Data for AC 299,263 Herbicide Technical: Addendum: Lab Project Number: APBR 471: APBR 468: CY-98. Unpublished study prepared by American Cyanamid Co. 288 p.

Guideline: 62-2 Certification of limits

MRID: 43193202
Czajkowska, T.; Humphries, K.; Hrabovsky, I. (1994) Preliminary Analysis, Certification of Limits, and Analytical Methods with Validation Data for AC 299,263 Herbicide Technical: Lab Project Number: APBR 322: APBR 309: APBR 311. Unpublished study prepared by American Cyanamid Co. 439 p.

MRID: 43193205
Banick, W. (1994) Certification of Limits and Analytical Method to Verify Certified Limits of AC 299,263 Herbicide End-Use Formulation: Lab Project Number: C-4105. Unpublished study prepared by American Cyanamid Co. 44 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876205
Patel, J. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 Technical: (Addendum): Lab Project Number: CHDV 34 1.1. Unpublished study prepared by American Cyanamid Co. 56 p.

MRID: 43876206
Philburn, K.; Humphries, K. (1995) Preliminary Analysis, Certification of Limits, and Analytical Methods With Validation Data for AC 299,263 Herbicide Technical: Addendum: Lab Project Number: APBR 471: APBR 468: CY-98. Unpublished study prepared by American Cyanamid Co. 288 p.

MRID: 43876233
Kovacs, G. (1995) Product Identity, Description of Beginning Materials and Manufacturing Process, and Theoretical Discussion of Impurities for AC 299,263 70DG Herbicide End-Use Formulation. Unpublished study prepared by American Cyanamid Co. 10 p.

MRID: 43876234
Li, W.; Liu, D. (1995) Certification of Limits and Validation of Liquid Chromatographic Method, M-2439, for the Determination of the Active Ingredient (CL 299,263) in CL 299,263 70DG Herbicide Granular Formulation: Lab Project Number: F-1335: PRT00222: 94FAI-0554-13. Unpublished study prepared by XenoBiotic Labs, Inc. 43 p.

Guideline: 62-3 Analytical Method

MRID: 43193202
Czajkowska, T.; Humphries, K.; Hrabovsky, I. (1994) Preliminary Analysis, Certification of Limits, and Analytical Methods with Validation Data for AC 299,263 Herbicide Technical: Lab Project Number: APBR 322: APBR 309: APBR 311. Unpublished study prepared by American Cyanamid Co. 439 p.

MRID: 43193205
Banick, W. (1994) Certification of Limits and Analytical Method to Verify Certified Limits of AC 299,263 Herbicide End-Use Formulation: Lab Project Number: C-4105. Unpublished study prepared by American Cyanamid Co. 44 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876206
Philburn, K.; Humphries, K. (1995) Preliminary Analysis, Certification of Limits, and Analytical Methods With Validation Data for AC 299,263 Herbicide Technical: Addendum: Lab Project Number: APBR 471: APBR 468: CY-98. Unpublished study prepared by American Cyanamid Co. 288 p.

MRID: 43876234
Li, W.; Liu, D. (1995) Certification of Limits and Validation of Liquid Chromatographic Method, M-2439, for the Determination of the Active Ingredient (CL 299,263) in CL 299,263 70DG Herbicide Granular Formulation: Lab Project Number: F-1335: PRT00222: 94FAI-0554-13. Unpublished study prepared by XenoBiotic Labs, Inc. 43 p.

Guideline: 63-0 Reports of Multiple phys/chem Characteristics

MRID: 43193203
Patel, J.; Ta, C.; Melcer, M. et al. (1994) Physical and Chemical Characteristics of AC 299,263 Herbicide Technical: Lab Project Number: P-80: ENV 93-025: ENV 94-012. Unpublished study prepared by American Cyanamid Co. and Hazleton Wisconsin, Inc. 356 p.

MRID: 43193206
Schaaf, M. (1994) Physical and Chemical Characteristics for AC 299,263 Herbicide End-Use Formulation: Lab Project Number: F-1272. Unpublished study prepared by American Cyanamid Co. 23 p.

MRID: 43876203
Little, D. (1995) Response to Residue Chemistry Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 106 p.

MRID: 43876207
Patel, J. (1995) Physical and Chemical Characteristics of AC 299,263 Herbicide Technical: Addendum: Lab Project Number: P-147: P-149: P-154. Unpublished study prepared by American Cyanamid Co. 69 p.

MRID: 43876235
Kovacs, G.; Lampert, W.; Sairin, D. (1995) AC 299,263 70 DG: Physical and Chemical Characteristics: Lab Project Number: F-1304. Unpublished study prepared by Cytec Industries. 17 p.

Guideline: 63-17 Storage stability

MRID: 43193203
Patel, J.; Ta, C.; Melcer, M. et al. (1994) Physical and Chemical Characteristics of AC 299,263 Herbicide Technical: Lab Project Number: P-80: ENV 93-025: ENV 94-012. Unpublished study prepared by American Cyanamid Co. and Hazleton Wisconsin, Inc. 356 p.

MRID: 43876207
Patel, J. (1995) Physical and Chemical Characteristics of AC 299,263 Herbicide Technical: Addendum: Lab Project Number: P-147: P-149: P-154. Unpublished study prepared by American Cyanamid Co. 69 p.

Guideline: 71-1 Avian Single Dose Oral Toxicity

MRID: 43193226
Campbell, S.; Beavers, J.; Sullivan, J. (1994) 14-Day Acute Toxicity Test with AC 299,263 Technical in Mallard Duck (Anas platyrhynchos): Lab Project Number: 130-158: 954-93-102. Unpublished study prepared by Wildlife International Ltd. 54 p.

MRID: 43193227
Campbell, S.; Beavers, J.; Sullivan, J. (1994) 14-Day Acute Toxicity Test with AC 299,263 Technical in Northern Bobwhite (Colinus virginianus): Lab Project Number: 130-157: 954-93-101. Unpublished study prepared by Wildlife International Ltd. 56 p.

Guideline: 71-2 Avian Dietary Toxicity

MRID: 43193228
Campbell, S.; Beavers, J.; Sullivan, J. (1994) 8-Day Acute Dietary Test with AC 299,263 Technical in Northern Bobwhite (Colinus virginianus): Lab Project Number: 130-160: 954-93-103. Unpublished study prepared by Wildlife International Ltd. 75 p.

MRID: 43193229
Campbell, S.; Beavers, J.; Sullivan, J. (1994) 8-Day Acute Dietary Test with AC 299,263 Technical in Mallard Duck (Anas platrhynchos): Lab Project Number: 130-161: 954-93-104. Unpublished study prepared by Wildlife International Ltd. 75 p.

Guideline: 71-4 Avian Reproduction

MRID: 43876208
Beavers, J.; Sullivan, J.; Gagne, J. (1995) Pilot Dietary Toxicity Study with AC 299,263 Technical in Northern Bobwhite (Colinus virginianus): Lab Project Number: 954-93-204: 130-162: TAN 94-009. Unpublished study prepared by American Cyanamid Co. and Wildlife International, Ltd. 74 p.

MRID: 43876209
Gagne, J.; Sullivan, J.; Travis, D.; et al. (1995) Reproduction Study with AC 299,263 Technical in the Northern Bobwhite (Colinus virginianus): Lab Project Number: 130-168: 954-93-216: TAN 93-011. Unpublished study prepared by American Cyanamid Co. and Wildlife International, Ltd. 274 p.

MRID: 43876210
Beavers, J.; Grimes, J.; Jaber, M.; et al. (1995) Pilot Dietary Toxicity Study with AC 299,263 Technical in Mallard Duck (Anas platyrhynchos): Lab Project Number: AC 954-93-205: WIL 130-163: 576.01. Unpublished study prepared by American Cyanamid Co. and Wildlife International, Ltd. 73 p.

MRID: 43876211
Gagne, J.; Sullivan, J.; Travis, D.; et al. (1995) Reproduction Study with AC 299,263 Technical in the Mallard Ducks (Anas platyrhynchos): Lab Project Number: 130-169: 954-93-217: TAN 93-011. Unpublished study prepared by American Cyanamid Co. and Wildlife International, Ltd. 269 p.

Guideline: 72-1 Acute Toxicity to Freshwater Fish

MRID: 43193230
Yurk, J.; Wisk, J. (1994) Acute Toxicity of AC 299,263 to the Bluegill Sunfish (Lepomis macrochirus) Under Flow-Through Test Conditions: Lab Project Number: 3933010-0400-3140: 954-93-105. Unpublished study prepared by Environmental Science & Engineering, Inc. 62 p.

MRID: 43193231
Yurk, J.; Wisk, J. (1994) Acute Toxicity of AC 299,263 to the Rainbow Trout (Oncorhynchus mykiss) Under Flow-Through Test Conditions: Lab Project Number: 3933010-0200-3140: 954-93-106. Unpublished study prepared by Environmental Science & Engineering, Inc. 63 p.

Guideline: 72-2 Acute Toxicity to Freshwater Invertebrates

MRID: 43193232
Yurk, J.; Wisk, J. (1994) Acute Toxicity of AC 299,263 to Daphnia magna Under Flow-Through Test Conditions: Lab Project Number: 3933010-0300-3140: 954-93-107. Unpublished study prepared by Environmental Science & Engineering, Inc. 66 p.

Guideline: 72-3 Acute Toxicity to Estuarine/Marine Organisms

MRID: 44565201

Olivieri, C.; Christensen, G.; Magazu, J. (1998) Acute Toxicity of AC 299263 (Imazamox) Technical to the Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Test Conditions: Lab Project Number: ECO 97-218. Unpublished study prepared by T.R. Wilbury Labs, Inc. 116 p. {OPPTS 850.1075}

MRID: 44565202
Olivieri, C.; Christensen, G.; Magazu, J. (1998) Acute Toxicity of AC 299263 (Imazamox) Technical to the Mysid (Mysiopsis bahia) Under Flow-Through Test Conditions: Lab Project Number: ECO 97-219. Unpublished study prepared by T.R. Wilbury Labs, Inc. 111 p. {OPPTS 850.1035}

Guideline: 81-1 Acute oral toxicity in rats

MRID: 43193207
Fischer, J. (1993) Oral LD50 Study in Albino Rats with AC 299,263 Technical: Lab Project Number: T-0522. Unpublished study prepared by American Cyanamid Co. 11 p.

MRID: 43193213
Bradley, D. (1994) Oral LD50 Study in Albino Rats with AC 299,263 1 As Formulation: Lab Project Number: T-0661: A94-13. Unpublished study prepared by American Cyanamid Co. 15 p.

MRID: 43876212
Lowe, C.; Bradley, D. (1995) Oral LD50 Study in Albino Rats with AC 312,622 and CL 354,825: (Soil Metabolites) (of AC 299,263): Lab Project Number: A95-92: A95-221: T-0794. Unpublished study prepared by American Cyanamid Co. 46 p.

MRID: 43876236
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Guideline: 81-2 Acute dermal toxicity in rabbits or rats

MRID: 43193208
Fischer, J. (1994) Dermal LD50 Study in Albino Rabbits with AC 299,263 Technical: Lab Project Number: T-0531. Unpublished study prepared by American Cyanamid Co. 12 p.

MRID: 43193214
Bradley, D. (1994) Dermal LD50 Study in Albino Rats with AC 299,263 1 As Formulation: Lab Project Number: T-0660: A94-12. Unpublished study prepared by American Cyanamid Co. 15 p.

MRID: 43876237
Bradley, D. (1995) Dermal LD50 Study in Albino Rats with AC 299,263 70 DG Formulation: Lab Project Number: A94-279: T-0740: P94-1240. Unpublished study prepared by American Cyanamid Co. 17 p.

Guideline: 81-3 Acute inhalation toxicity in rats

MRID: 43193209
Hoffman, G. (1994) Acute Inhalation Toxicity Study with AC 299,263 in Rats: Lab Project Number: 971-92-103: 92-8391. Unpublished study prepared by American Cyanamid Co. 131 p.

MRID: 43193215
Hoffman, G. (1994) Acute Inhalation Toxicity Study with AC 299,263 1 As In Rats: Lab Project Number: 93-5150. Unpublished study prepared by Pharmaco LSR Inc. 136 p.

MRID: 43876238

Hoffman, G. (1995) Acute Inhalation Toxicity Study with AC 299,263 70 DG in Rats: Lab Project Number: 94-5193: TAN 94-050: 971-94-109. Unpublished study prepared by Pharmaco LSR Inc. 109 p.

Guideline: 81-4 Primary eye irritation in rabbits

MRID: 43193210
Fischer, J. (1992) Eye Irritation Study in Albino Rabbits with AC 299,263 Technical: Lab Project Number: T-0520. Unpublished study prepared by American Cyanamid Co. 12 p.

MRID: 43193216
Boczon, L. (1994) Eye Irritation Study in Albino Rabbits with AC 299,263 1AS Formulation: Lab Project Number: T-0644: A 94-11. Unpublished study prepared by American Cyanamid Co. 16 p.

MRID: 43876239
Boczon, L. (1995) Eye Irritation Study in Albino Rabbits with AC 299,263 70 DG Formulation: Lab Project Number: A94-285.01: T-0727. Unpublished study prepared by American Cyanamid Co. 18 p.

Guideline: 81-5 Primary dermal irritation

MRID: 43193211
Fischer, J. (1992) Skin Irritation Study in Albino Rabbits with AC 299,263 Technical: Lab Project Number: T-0519. Unpublished study prepared by American Cyanamid Co. 11 p.

MRID: 43193217
Boczon, L. (1994) Skin Irritation Study in Albino Rabbits with AC 299,263 1AS Formulation: Lab Project Number: T-0645: A 94-10. Unpublished study prepared by American Cyanamid Co. 16 p.

MRID: 43876240
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Guideline: 81-6 Dermal sensitization

MRID: 43193212
Glaza, S. (1992) Dermal Sensitization Study with AC 299,263 in Guinea Pigs: Lab Project Number: HWI 20600489. Unpublished study prepared by Hazleton Laboratories America, Inc. 44 p.

MRID: 43193218
Boczon, L. (1994) Dermal Sensitization Study in Albino Guinea Pigs with CL 299,263 1AS Formulation Using the Buehler Closed Patch Method: Lab Project Number: T-0650: A94-14. Unpublished study prepared by American Cyanamid Co. 27 p.

MRID: 43876241
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Guideline: 82-1 Subchronic Oral Toxicity: 90-Day Study

MRID: 43193219
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MRID: 43193220

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Guideline: 82-2 21-day dermal-rabbit/rat

MRID: 43876213
Blaszcak, D. (1995) A 28-Day Dermal Toxicity Study with AC 299,263 in Rats: Lab Project Number: 93-2235. Unpublished study prepared by Pharmaco LSR Inc. 240 p.

Guideline: 83-1 Chronic Toxicity

MRID: 43876214
Kelly, C. (1995) One-Year Dietary Toxicity Study with AC 299,263 in Purebred Beagle Dogs: Lab Project Number: 93-3154. Unpublished study prepared by Pharmaco LSR Inc. 752 p.

MRID: 43891001
Fischer, J.; Hess, F. (1995) Chronic Dietary Toxicity and Oncogenicity Study with AC 299,263 in the Albino Rat: Lab Project Number: T-0496: AX95-1. Unpublished study prepared by American Cyanamid Co. and Experimental Pathology Labs, Inc. 1657 p.

Guideline: 83-2 Oncogenicity

MRID: 43876215
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MRID: 43891001
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Guideline: 83-3 Teratogenicity -- 2 Species

MRID: 43193221
Foss, J. (1994) An Oral Developmental Toxicity (Embryo-Fetal Toxicity/Teratogenicity) Study with AC 299,263 in Rats: Lab Project Number: 101-020. Unpublished study prepared by Argus Research Laboratories, Inc. 206 p.

MRID: 43876216
Hoberman, A. (1995) An Oral Developmental Toxicity (Embryo-Fetal Toxicity/Teratogenicity) Definitive Study with AC 299,263 in Rabbits: Lab Project Number: 971-93-107: 101-021: ARGUS 101-021. Unpublished study prepared by Argus Research Labs, Inc. 285 p.

Guideline: 83-4 2-generation repro.-rat

MRID: 43876217
Schroeder, R. (1995) A Two-Generation Reproduction Study with AC 299,263 in Rats: Lab Project Number: 92-4043. Unpublished study prepared by Pharmaco LSR Inc. 1417 p.

MRID: 44008001
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Guideline: 84-2 Interaction with Gonadal DNA

MRID: 43193222
Mulligan, E. (1994) Evaluation of CL 299,263 in A Bacterial/Microsome Mutagenicity Assay: Lab Project Number: 92-02-001. Unpublished study prepared by American Cyanamid Co. 29 p.

MRID: 43193223
Sharma, R. (1993) Evaluation of CL 299,263 in The Mammalian Cell CHO/HGPRT Mutagenicity Assay: Lab Project Number: 92-05-001. Unpublished study prepared by Genetic Toxicology Laboratory, American Cyanamid Co. 71 p.

MRID: 43193224
Sharma, R. (1993) Evaluation of CL 299,263 in the in vivo Micronucleus Assay in Mouse Bone Marrow Cells: Lab Project Number: 92-18-001. Unpublished study prepared by Genetic Toxicology Laboratory, American Cyanamid Co. 58 p.

MRID: 43193225
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MRID: 46581702
Engelhardt, G.; Leibold, E. (2004) Salmonella typhimurium/ Escherichia coli Reverse Mutation Assay (Standard Plate Test and Preincubation Test) with CL 354825. Project Number: 2004/1026635, 40M0219/044050. Unpublished study prepared by BASF Aktiengesellschaft. 58 p.

MRID: 46581703
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Guideline: 85-1 General metabolism

MRID: 43876218
Chiu, T. (1995) CL 299,263: Metabolism of (carbon 14)-CL 299,263 in Rats: Lab Project Number: MET 95-009: M92A263OH1: SC920234. Unpublished study prepared by American Cyanamid Co. and Battelle Columbus Div. 338 p.

Guideline: 122-2 Aquatic plant growth

MRID: 43876219
Canez, V.; Hoberg, J.; Christensen, G. (1995) Effect of AC 299,263 on the Growth of Anabaena flos-aquae, Selenastrum capricornutum, Skeletonema costatum, Navicula pelliculosa, and Lemna gibba: Lab Project Number: 954-93-226: 954-93-230: 954-93-228. Unpublished study prepared by American Cyanamid Co. and Springborn Labs, Inc. 649 p.

Guideline: 123-1 Seed germination/seedling emergence and vegitative vigor
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MRID: 43876220
Cone, C.; Chetram, R.; Lucash, K.; et al. (1995) Nontarget Plant Seed Germination and Seedling Emergence Phytotoxicity Study Using AC 299,263 and Validation of an Analytical Method for the Determination of AC 299,263 Residue in Water: Lab Project Number: 954-93-108: 954-93-109: 954-93-218. Unpublished study prepared by American Cyanamid Co. and Pan-Agricultural Labs, Inc. 361 p.

MRID: 43876221
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Guideline: 141-1 Honey bee acute contact

MRID: 43193233
Parrish, J.; Yeager, B.; Canez, V. et al. (1994) An Acute Contact Toxicity Study with AC 299,263 in the Honey Bee (Apis mellifera L.): Lab Project Number: ECO 93-115: 954-93-115. Unpublished study prepared by BIO/WEST, Inc. 61 p.

Guideline: 161-1 Hydrolysis

MRID: 43193240
Mangels, G. (1994) AC 299,263: Hydrolysis: Lab Project Number: ENV 93-028. Unpublished study prepared by American Cyanamid Co. 28 p.

Guideline: 161-2 Photodegradation-water

MRID: 43876222
An, D.; Ta, C. (1995) Aqueous Photolysis of AC 299,263: (Includes Report Amendment): Lab Project Number: ENV 95-022: ENV 95-022.01. Unpublished study prepared by American Cyanamid Co. 111 p.

Guideline: 161-3 Photodegradation-soil

MRID: 43876223
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Guideline: 162-1 Aerobic soil metabolism

MRID: 43193241
Ta, C. (1994) AC 299,263: Aerobic Soil Metabolism: Lab Project Number: ENV 94-013. Unpublished study prepared by American Cyanamid Co. 89 p.

MRID: 43876201
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MRID: 43876224
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MRID: 46089101
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Guideline: 162-2 Anaerobic soil metabolism

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Guideline: 162-3 Anaerobic aquatic metab.

MRID: 43876226

Cady, C. (1995) Biotransformation of (carbon 14)-AC 299,263 Under Anaerobic Aquatic Conditions: Lab Project Number: ENV 95-025: 41244: ABC 41244. Unpublished study prepared by ABC Labs, Inc. 86 p.

Guideline: 163-1 Leach/adsorp/desorption

MRID: 43193242
Mangels, G. (1994) AC 299,263: Adsorption/Desorption: Lab Project Number: ENV 93-030. Unpublished study prepared by American Cyanamid Co. 47 p.

MRID: 43876201
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MRID: 43876227
Kuhn, P. (1995) CL 312,622 and CL 354,825: Adsorption/Desorption on Soils: Lab Project Number: ENV 95-019: ENV 95-042. Unpublished study prepared by American Cyanamid Co. 132 p.

Guideline: 164-1 Terrestrial field dissipation

MRID: 43876228
Khunachak, A.; Higham, J.; Connelly, J. (1995) CL 299,263: Freezer Storage Stability of CL 299,263 and the Related Compound, CL 312,622 in Soil and CL 354,825: Freezer Storage Stability of CL 354,825 Residues in Soil (Interim Report): Lab Project Number: RES 95-115: RES 95-182: XP93PT02. Unpublished study prepared by Centre Analytical Labs, Inc. 109 p.

MRID: 43876229
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MRID: 43876230
Kleiner, A. (1995) CL 299,263: Soil Dissipation Studies (1992, 1993): Lab Project Number: RES 94-155: RES 94-156: RES 95-175. Unpublished study prepared by Centre Analytical Labs, Inc.; Research Options, Inc. and Analytical Bio-Chemistry Labs, Inc. 1472 p.

Guideline: 165-1 Confined rotational crop

MRID: 43193243
Gatterdam, P. (1994) CL 299,263: Confined Accumulation Study of Carbon-14 labeled CL 299,263 Using Radishes, Corn, Lettuce, and Wheat as Rotational Crops: Lab Project Number: MET 94-007. Unpublished study prepared by American Cyanamid Co. and American Agricultural Services, Inc. 319 p.

Guideline: 165-4 Bioaccumulation in fish

MRID: 43876231
Johnson, D. (1995) CL 299,263: Uptake, Depuration, Bioconcentration, and Metabolism of (carbon 14)-CL 299,263 in Bluegill Sunfish (Lepomis macrochirus) Under Flow-Through Test Conditions: Lab Project Number: MET 95-012: M93F263M01: P93-893. Unpublished study prepared by American Cyanamid Co.; ABC Labs, Inc. and XenoBiotic Labs, Inc. 170 p.

Guideline: 171-4B Residue Analytical Methods

MRID: 43193237
Witkonton, S.; Stout, S.; daCunha, A. (1994) Validation of Methods for the Determination of CL 299,263 Residues in Soybean Seed: Lab Project Number: RES 93-013: RES 93-033: RES 93-153. Unpublished study prepared by American Cyanamid Co. and ABC Laboratories, Inc. 125 p.

MRID: 43193238
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MRID: 44994110
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MRID: 44994111
Gross, J.; Sweeney, R. (1998) CL 299263: Independent Laboratory Validation of CE Method M 3076 for the Determination of Residues of CL 299263 in Canola Seed: Lab Project Number: 97-069: XP97PT04. Unpublished study prepared by ABC Labs., Inc. 53 p. {OPPTS 860.1340}

MRID: 44994112
Koroma, J.; Nejad, H.; Xu, B. et al. (1999) Imazamox (AC 299263/CL 299263): Independent Laboratory Validation, Extractability and Accountability of Method M 3098 for the Determination of Residues of Imazamox and CL 263284 in Wheat Forage Grain, Hay, and Straw and the Independent Laboratory Validation of Method M 3252 for the Determination of Residues of Imazamox and CL 263284 in Wheat Grain and its Processed Fractions: Lab Project Number: 98-100: 99-037.01: 99-130. Unpublished study prepared by Centre Analytical Labs., Inc. 242 p. {OPPTS 860.1340}

Guideline: 171-4C Magnitude of the Residue [by commodity]

MRID: 43193239
York, C.;Witkonton, S. (1994) CL 299,263 (1 AS): Residues of CL 299,263 in Soybean Seed (Postemergence; 1992 and 1993) and CL 299,263: Interim 12-Month Freezer Storage Stability of CL 299,263 Residues in Soybean Seed: Lab Project Number: RES 93-122: RES 93-124: RES 93-143. Unpublished study prepared by American Cyanamid Co. 450 p.

MRID: 43876232
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MRID: 44994102
Rodriguez, D. (1999) Imazamox (AC 299263/CL 299263): CL 299263 and CL 263284 in Residues in Imidazolinone Tolerant Spring Wheat RACs and Processed Commodities After Postemergence Treatment with Imazamox AC 299263 (1AS) Herbicide in North Dakota: Lab Project Number: RES 99094: XP98ND04: RAN-99-001. Unpublished study prepared by American Cyanamid Co. and Agvise Research, Inc. 246 p. {OPPTS 860.1520}

MRID: 44994113
Fletcher, J. (1999) CL 299263 (Imazamox): Freezer Storage Stability of CL 299263, CL 263284, CL 189215, and CL 312622 Residues in Alfalfa Seed, Forage, and Hay: Lab Project Number: 99-098: XP99PT01. Unpublished study prepared by American Cyanamid Co. 71 p. {OPPTS 860.1380}

MRID: 44994114
Koroma, J. (1999) CL 299263 (Imazamox): Freezer Storage Stability of CL 299263 Residues in Canola Seed: Lab Project Number: 99-074: XP98PT03. Unpublished study prepared by American Cyanamid Co. 34 p. {OPPTS 860.1380}

MRID: 44994115
Duan, B.; Singh, S. (1999) Freezer Storage Stabilities of CL 299263 and CL 263284 in Wheat Forage, Hay, Straw, and Grain: Lab Project Number: 99-131: XP97PT10. Unpublished study prepared by American Cyanamid Co. and Centre Analytical Labs., Inc. 134 p. {OPPTS 860.1380}

MRID: 44994116
Hallman, D.; Higham, J.; Kenny, S. et al. (1999) Residues in Alfalfa Seed, Forage, Hay, and Straw, After Treatment with Imazamox (AC 299263) (1 AS&70DG) Herbicide: Lab Project Number: 98-233: 98-234: 98-237. Unpublished study prepared by American Cyanamid Co. and Centre Analytical Labs., Inc. 1979 p. {OPPTS 860.1500}

MRID: 44994117
McDonnell, R. (1998) Residues in Canola After Post-Emergence Application of (Imazamox) AC 299263 (1 AS & 70DG) Herbicide: Lab Project Number: 98-021: 98-022: 98-017. Unpublished study prepared by American Cyanamid Co. and ABC Labs., Inc. 382 p. {OPPTS 860.1500}

MRID: 44994118
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MRID: 44994119
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Guideline: 171-4A2 Nature of the Residue in Plants

MRID: 43193234
Mallipudi, N. (1994) CL 299,263: Metabolism of carbon 14 labeled CL 299,263 in Soybean Under Field Conditions: Lab Project Number: MET 94-003. Unpublished study prepared by American Cyanamid Co. and American Agricultural Services, Inc. 251 p.

MRID: 44994104
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MRID: 44994105
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MRID: 44994106
Chiu, T. (1995) CL 299263: Metabolism of Carbon-14 Labeled CL 299263 in Peas Under Field Conditions: Lab Project Number: 95-011: M93P263NC1. Unpublished study prepared by American Cyanamid Co. 207 p. {OPPTS 860.1300}

MRID: 44994107
Johnson, D. (1996) CL 299263: Metabolism of Carbon-14 Labeled CL 299263 in Wheat Under Field Conditions: Lab Project Number: 96-004: M93P263PT1. Unpublished study prepared by American Cyanamid Co. 225 p. {OPPTS 860.1300}

Guideline: 171-4A3 Nature of the Residue in Livestock

MRID: 43193235

Johnson, D. (1994) CL 299,263: Metabolic Fate of carbon 14 labeled CL 299,263 in the Milk and Edible Tissues of the Lactating Goat: Lab Project Number: MET 94-001. Unpublished study prepared by American Cyanamid Co. 173 p.

MRID: 43193236
Johnson, D. (1994) CL 299,263: Metabolic Fate of carbon 14 labeled CL 299,263 in Tissues and Eggs of the Laying Hen: Lab Project Number: MET 93-025. Unpublished study prepared by American Cyanamid Co. 109 p.

MRID: 43876204
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MRID: 44994108
Tsalta, C. (1999) CL 312622: Metabolism of(carbon-14)-CL 312622 in the Goat: Lab Project Number: 99-006: M98A622PT2. Unpublished study prepared by American Cyanamid Co. and Global Agricultural Research Center. 217 p. {OPPTS 860.1300}

MRID: 44994109
Afzal, J. (1999) CL 312622: Metabolic Fate of (carbon-14)-CL 312622 in Tissues and Eggs of the Laying Hen: Lab Project Number: 99-004: M98A622PT1: L-2555. Unpublished study prepared by American Cyanamid Co. and Global Agricultural Research Center. 158 p. {OPPTS 860.1300}

Guideline: 830.1550 Product Identity and composition

MRID: 46592401
Jones, R. (2005) BAS 777 03 H: Group A - Product Identity, Composition, and Analysis. Project Number: FR0502, 2005/5000096, AFR0017/04. Unpublished study prepared by BASF Corporation. 87 p.

MRID: 47640401
Landis, W.; Galloway, P. (2008) Clearcast 2.7G Herbicide: Product Identity and Disclosure of Ingredients, Including Manufacturing Process, Discussion of Formation of Impurities and Certified Limits. Unpublished study prepared by Landis International, Inc. 19 p.

Guideline: 830.1600 Description of materials used to produce the product
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MRID: 46592401
Jones, R. (2005) BAS 777 03 H: Group A - Product Identity, Composition, and Analysis. Project Number: FR0502, 2005/5000096, AFR0017/04. Unpublished study prepared by BASF Corporation. 87 p.

MRID: 47640401
Landis, W.; Galloway, P. (2008) Clearcast 2.7G Herbicide: Product Identity and Disclosure of Ingredients, Including Manufacturing Process, Discussion of Formation of Impurities and Certified Limits. Unpublished study prepared by Landis International, Inc. 19 p.

Guideline: 830.1620 Description of production process

MRID: 47640401
Landis, W.; Galloway, P. (2008) Clearcast 2.7G Herbicide: Product Identity and Disclosure of Ingredients, Including Manufacturing Process, Discussion of Formation of Impurities and Certified Limits. Unpublished study prepared by Landis International, Inc. 19 p.

Guideline: 830.1650 Description of formulation process

MRID: 46592401

Jones, R. (2005) BAS 777 03 H: Group A - Product Identity, Composition, and Analysis. Project Number: FR0502, 2005/5000096, AFR0017/04. Unpublished study prepared by BASF Corporation. 87 p.

MRID: 47640401
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Guideline: 830.1670 Discussion of formation of impurities

MRID: 46592401
Jones, R. (2005) BAS 777 03 H: Group A - Product Identity, Composition, and Analysis. Project Number: FR0502, 2005/5000096, AFR0017/04. Unpublished study prepared by BASF Corporation. 87 p.

MRID: 47640401
Landis, W.; Galloway, P. (2008) Clearcast 2.7G Herbicide: Product Identity and Disclosure of Ingredients, Including Manufacturing Process, Discussion of Formation of Impurities and Certified Limits. Unpublished study prepared by Landis International, Inc. 19 p.

Guideline: 830.1750 Certified limits

MRID: 46592401
Jones, R. (2005) BAS 777 03 H: Group A - Product Identity, Composition, and Analysis. Project Number: FR0502, 2005/5000096, AFR0017/04. Unpublished study prepared by BASF Corporation. 87 p.

MRID: 47640401
Landis, W.; Galloway, P. (2008) Clearcast 2.7G Herbicide: Product Identity and Disclosure of Ingredients, Including Manufacturing Process, Discussion of Formation of Impurities and Certified Limits. Unpublished study prepared by Landis International, Inc. 19 p.

Guideline: 830.1800 Enforcement analytical method

MRID: 46592401
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MRID: 46592402
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MRID: 46592403
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Guideline: 830.6303 Physical state

MRID: 46592403

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Guideline: 830.6304 Odor

MRID: 47640402
Kaminsky, M. (2008) Product Chemistry: Clearcast 2.7G: Final Report. Project Number: 12078/08. Unpublished study prepared by Stillmeadow, Inc. 12 p.

Guideline: 830.6314 Oxidizing or reducing action

MRID: 46592404
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Guideline: 830.6315 Flammability

MRID: 46592403
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MRID: 47640402
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Guideline: 830.7100 Viscosity

MRID: 46592403
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Guideline: 830.7300 Density/relative density

MRID: 46592402
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MRID: 47640402
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Guideline: 835.4100 Aerobic soil metabolism

MRID: 46089101
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Guideline: 870.1100 Acute oral toxicity

MRID: 46603701
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MRID: 46603707
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MRID: 47640403
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Guideline: 870.1200 Acute dermal toxicity

MRID: 46603702

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MRID: 47640404
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Guideline: 870.1300 Acute inhalation toxicity

MRID: 46603703
Ma-Hock, L.; Leibold, E. (2004) BAS 777 01 H - Acute Inhalation Toxicity Study in Wistar Rats: 4-Hour Liquid Aerosol Exposure. Project Number: 13I0283/047005, 2004/1021176. Unpublished study prepared by BASF Aktiengesellschaft. 35 p.

MRID: 46603707
Doi, A. (2005) Bridging of Acute Data for BAS 777 01 H to BAS 777 03 H (Imazamox/MCPA-2EH Formulation). Project Number: 2005/5000109. Unpublished study prepared by BASF Corporation. 21 p.

MRID: 47640405
Carter, L. (2008) Acute Inhalation Toxicity Study in Rats: Clearcast 2.7G: Final Report. Project Number: 12062/08. Unpublished study prepared by Stillmeadow, Inc. 7 p.

Guideline: 870.2400 Acute eye irritation

MRID: 46603704
Remmele, M.; Leibold, E. (2005) BAS 777 01 H - Acute Eye Irritation in Rabbits. Project Number: 11H0211/052018, 2005/1012913. Unpublished study prepared by BASF Aktiengesellschaft. 22 p.

MRID: 46603707
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Guideline: 870.2500 Acute dermal irritation

MRID: 46603705
Remmele, M.; Leibold, E. (2004) BAS 777 01 H - Acute Dermal Irritation / Corrosion in Rabbits. Project Number: 18H0283/042094, 2004/1021215. Unpublished study prepared by BASF Aktiengesellschaft. 21 p.

MRID: 46603707
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MRID: 47640407

Kuhn, J. (2008) Acute Dermal Irritation Study in Rabbits: Clearcast 2.7G: Final Report. Project Number: 12064/08. Unpublished study prepared by Stillmeadow, Inc. 12 p.

Guideline: 870.2600 Skin sensitization

MRID: 46603706
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MRID: 46603707
Doi, A. (2005) Bridging of Acute Data for BAS 777 01 H to BAS 777 03 H (Imazamox/MCPA-2EH Formulation). Project Number: 2005/5000109. Unpublished study prepared by BASF Corporation. 21 p.

MRID: 47640408
Kuhn, J. (2008) Skin Sensitization Study in Guinea Pigs: Clearcast 2.7G: Final Report. Project Number: 12065/08. Unpublished study prepared by Stillmeadow, Inc. 17 p.

Guideline: 870.5100 Bacterial reverse mutation test

MRID: 46581702
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Guideline: 870.5375 In vitro mammalian chromosome aberration test

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MRID: 46581703
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MRID: 46581701
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MRID: 43193200
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MRID: 43876200
Citation: American Cyanamid Co. (1995) Submission of Product Chemistry, Toxicology, Environmental Fate, Metabolism, Hazard to Non-Target Organisms, and Residue Data in Support of the Application for Registration of AC 299,263 Technical and End-Use Formulations and Tolerance Petition for AC 299,263 in/on Soybean Seed. Transmittal of 41 Studies.

MRID: 43876202
Citation: Gagne, J.; Little, D. (1995) Response to Ecological Effects Branch Review of the EUP Request and Temporary Tolerance Petition: (AC 299,263). Unpublished study prepared by American Cyanamid Co. 119 p.

MRID: 43891000

Citation: American Cyanamid Co. (1995) Submission of Toxicology Data in Support of the Applications for Registration and Tolerance Petition for AC 299,263 Technical and End-Use Products. Transmittal of 1 Study.

MRID: 44008000
Citation: American Cyanamid Co. (1996) Submission of Toxicology Data in Support of the Application for Registration and Petition for Tolerance for Raptor (AC 299,263) Herbicide Technical. Transmittal of 1 Study.

MRID: 44565200
Citation: American Cyanamid Company (1998) Submission of Toxicity Data in Support of the Registration of Raptor Herbicide Technical, Raptor Herbicide, and Raptor DG Herbicide. Transmittal of 2 Studies.

MRID: 44630400
Citation: American Cyanamid Company (1998) Submission of Product Chemistry Data in Support of the Registration of Raptor DG Herbicide. Transmittal of 1 Study.

MRID: 44994100
Citation: American Cyanamid Company (1999) Submission of Environmental Fate, Residue Chemistry, Risk Assessment and Exposure Data in Support of the Registration of Raptor and Raptor DG Herbicides and the Petition for Tolerance of Imazamox in/on Alfalfa, Canola, Wheat, and Legume Vegetables. Transmittal of 19 Studies.

MRID: 44994101
Citation: Galley, M.; Rice, P.; Wisk, J. et al. (1999) Imazamox (AC299263): Registration Amendment Application (Volume1) and Tolerance Petition (Volume2) for Use on Alfalfa, Canola, Edible Legumes and Wheat: Lab Project Number: CY 273. Unpublished study prepared by American Cyanamid Co. 1 p.

MRID: 44994103
Citation: Kidwell, J.; Watters, J. (1999) Chronic Dietary Exposure and Risk Assessment: Imazamox: Lab Project Number: 99-01. Unpublished study prepared by Novigen Sciences, Inc. 21 p.

MRID: 46089100
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MRID: 46592400
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MRID: 47111600
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MRID: 47111601
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MRID: 47640400
Citation: BASF Corporation (2009) Submission of Product Chemistry and Toxicity Data in Support of the Application for Registration of Clearcast 2.7G Herbicide. Transmittal of 8 Studies.

MRID: 47876300
Citation: BASF Corporation (2009) Submission of Product Chemistry Data in Support of the Application for Registration of Clearcast 2.7G. Transmittal of 1 Study.

Appendix 2: Toxicity to Mammals

Table A2-1: Acute Oral Toxicity

Species	Exposure	Response	Reference
Rats, Sprague-Dawley, males and females, 7–8 weeks, 193-218 g (M) & 160 -180 g (F) at initiation, 5/sex/dose group	Single oral dose of 5000 mg/kg neat nicotinic acid, AC 299,263 1 AS Formulation (11.83%)	No mortality; no clinical signs of toxicity; all rats gained weight throughout the study, no treatment-related gross pathology. LD_{50} >5000 mg formulation/kg (limit dose). Equivalent to ≈590 mg a.i./kg bw or ≈560 mg a.e./kg bw. Toxicity Category : IV Core Classification: Acceptable	Bradley 1994a MRID 43193213
Rats, Sprague-Dawley, males and females, 8 weeks, 156-196 g at initiation, 5/sex/dose group	AC 299,263 technical (98.2%) as a 50% [w/v] solution in corn oil at 5000 mg/kg to both sexes; 14-day observation period	No mortality; no clinical signs of toxicity observed in males; females exhibited decreased activity during the first 2 hours after treatment; no treatment-related gross pathology observed at sacrifice. LD_{50} >5000 mg a.e./kg (limit dose). Toxicity Category : IV Core Classification: Acceptable	Fischer 1993 MRID 43193207

Table A2-1: Acute Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Rats, Crl:CD (SD)BR, males (218-328 g) and females (178-204 g), 8-10 weeks old, 5/sex/dose group	**Soil Metabolite**: CL 354,825 (90% purity). Vehicle: high purity water. Single gavage doses of 750, 1500, or 3000 mg/kg **Working Note: Discuss in both Sections 3.1.4 and 3.1.15.1. Note that U.S. EPA/OPP 2008a,b cites this study and these toxicity values as imazamox. This appears to be an error based on the DER.**	LD_{50} = 2313 mg/kg (males) (95% CI = 1863-2873 mg/kg) LD_{50} = 2121 mg/kg (females) (95% CI = 639-7047 mg/kg) LD_{50} = 2274 mg/kg (combined) (95% CI = 1694-3051 mg/kg) Signs of toxicity in animals that died: decreased activity, tremors, ataxia, prostration. Other observations included discolored urine, chromodacryorrhea (blood in tears), dehydration. Signs of toxicity in surviving animals: Decreased activity, excessive urination, droopy eyelid. No apparent adverse effects in any surviving animal by Day 3 after dosing. Working Note: Many of the above effects could be associated with the presence of large amounts of the test substance in the GI tract. The DER notes that: *"…test material – filled intestinal tract (5/9), test material-filled stomach (2/9)"*. NOAEL: Males, 1,500 mg/kg bw Females: 750 mg/kg bw	Lowe and Bradley 1995a MRID 43876212

Table A2-2: Acute and Subchronic Dermal Toxicity			
Species	**Exposure**	**Response**	**Reference**
ACUTE			
Rats, CrI:CD(SD)B, males and females, 8-10 weeks, 270-288 g (M) & 203-247 g (F) at initiation, 5/sex/dose group	Nicotinic acid, AC 299,263 1 AS Formulation (11.83% a.i.). 4000 mg/kg (***2x limit dose***) applied to shaved, intact skin of each rat's back (site encompassed ≈10% of total body surface) for 24 hours. 14-day observation period followed treatment.	No mortality; slight erythema on day 3, which resolved on day 11; clinical signs of toxicity included brown material around nose, chromodacryorrhea, and blood around nose; no systemic toxicity; all rats gained weight throughout course of the study; no gross pathological changes observed at necropsy. LD_{50} >4000 mg/kg (2x limit dose). Toxicity Category: III. Core Classification: Acceptable	Bradley 1994b MRID 43193214
Rabbits, New Zealand white, males and females, 10-16 weeks, 2.0-3.1 kg at initiation, 5/sex/dose group	AC 299,263 technical (98.2%) moistened with tap water, applied to shaved, intact skin at 4000 mg/kg (***2x limit dose***) for 24 hours. Residual test material removed by wiping test site with cloth wrap, followed by 14-day observation period. All rabbits sacrificed and complete necropsy performed.	No mortality; no observed dermal irritation; no systemic toxicity, no signs of clinical toxicity, all rabbits gained weight during 14-day observation period; no gross pathological changes observed at necropsy. LD_{50} >4000 mg/kg (2x limit dose). Toxicity Category: III. Core Classification: Acceptable `Working Note: In places, the DER refers to the animals as rats. This appears to be a cut-and-paste error.`	Fischer 1994 MRID 43193208
SUBCHRONIC			
Rats, Sprague-Dawley CD, adults, 5/sex/dose; males were 7 weeks old and weighed 218-262 g; females were 8 weeks old and weighed 190-223 g.	0, 250, 500, or 1000 mg/kg AC 299, 263 (98.2% a.i.) applied to shaved skin of rats for 6 hours/day, 5 days/week, for 4 weeks. Vehicle = 0.9% saline During testing, approximately 10-15% of the body surface was exposed.	NOEL = 1000 mg/kg No treatment-related effects observed at any dose level; no signs of erythema, edema, or other dermal irritation. No mortality; no clinical signs of toxicity; no observed effects on body weight, body weight gain, or food consumption, relative to controls; no observed changes in ophthalmology, hematology, clinical blood chemistry, organ weights, or organ morphology, relative to controls. No observations of neoplastic tissue.	Blaszcak 1995 MRID 43876213

Table A2-3: Acute Inhalation Studies

Species	Exposure	Response	Reference
Rats, Sprague-Dawley, males (231-246 g) and females (210-277 g), 7-8 weeks at initiation, 5/sex/dose group	Aerosol concentrations of AC 299,263 technical (98.2% pure) for 4 hours. Nominal concentration: 31 mg/L Mean analytical concentration: 6.3 mg/L Targeted atmospheric concentration: 5 mg/L or maximum attainable level. MMAD of particles = 4.8µM	No treatment related mortalities throughout the 14-day study period. Treatment-related clinical signs observed during the 2-hour post-exposure observation period included: lacrimation; mucoidal/ dried nasal discharge; dried red/brown material on facial area; salivation; labored breathing (females only); dry/moist rates; yellow ano-genital staining; and matted contaminated coats. All rats appeared normal by the second week, gained weight, and showed no gross pathological, alterations at termination. LC_{50} >6.3 mg/L for both sexes. Toxicity Category: IV Core classification: Acceptable. `Working note: Executive summary indicates that purity of test material was 98.5%; materials and methods section indicates that purity was 98.2%, apparently due to typographical error.`	Hoffman 1994a MRID 43193209
Rats, Sprague-Dawley, males (272-298 g) and females (215-236 g), 7-8 weeks at initiation, 5/sex/dose group	Nose only exposure to aerosol concentrations of AC 299,263 1 AS formulation (11.83% a.i.) for 4 hours. Nominal concentration: 12 mg/L Mean analytical concentration: 5.0 mg/L (range of 4.4-5.2 mg/L) MMAD of particles = 1.3µM	No treatment related mortalities throughout the 14-day study period. No treatment-related clinical signs of toxicity; no effects on body weight and no gross pathological changes. LC_{50} >5 mg/L for both sexes. Toxicity Category: IV Core classification: Acceptable.	Hoffman 1994b MRID 43193215

Table A2-4: Skin Irritation Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbits, New Zealand white, 6 young adult males, weight not specified	AC 299,263 1 AS Formulation (11.83% a.i.). 0.5 mL applied to shaved intact skin of dorsal middle via gauze patches for 4-hour semi-occluded exposure period. Test sites cleaned with tap water to remove residual test material. Treated sites evaluated at approximately 1, 24, 48, and 72 hours according to Draize scoring system.	At 1 hour: slight erythema in 1/6 rabbits. Primary Irritation Index (PEI) = 0.2 All signs of irritation resolved by 24-hour observation period (PEI = 0.0) Toxicity Category: IV Core Classification: Acceptable.	Boczon 1994b MRID 43193217
Rabbits, New Zealand white, 6 young adult males, weight not specified	AC 299,263 technical (98.2% a.i.). 0.5 mL applied to shaved intact skin via gauze patches for 4-hour semi-occluded exposure period. Test sites cleaned with tap water to remove residual test material. Treated sites evaluated at approximately 1, 24, 48, and 72 hours according to Draize scoring system.	At 24-hours: *barely perceptible erythema* observed in two rabbits (PEI = 0.3); no dermal irritation observed at any other observation period. Toxicity Category : IV Core Classification: Acceptable.	Fischer 1992b MRID 43193211

Table A2-5: Skin Sensitization Studies

Species	Exposure	Response	Reference
Guinea pigs, Hartley, 10 males, 340-392 g	Nicotinic acid, AC 299,263 1 AS Formulation (11.83% a.i.). Induction phase: 0.4 mL test material applied to shaved left upper flank for 6-hour exposure period, after which treated sites were washed with tap water. Positive controls treated with 0.1% (w/v) DNCB in 50% ethanol. Process was repeated on the same day each week up until sites received a total of three dose applications. Challenge phase: On day 15, test group received challenge dose of 0.4 mL of neat (100%) test material on naïve site (anterior right flank); controls received 0.05% (w/v) DNCB in acetone; previously untreated (naïve) guinea pigs received challenge application of 0.4 mL neat test material. All sites were evaluated for sensitization responses (according to Draize method) at 23 and 48 hours after induction and challenge doses.	No dermal responses observed in test animals after either induction or challenge applications. No irritation observed in naïve guinea pigs after the challenge phase. Control group showed slight to moderate erythema at induction and at challenge. CORE CLASSIFICATION: Acceptable Working Note: In places, the DER refers to the animals as rabbits. This appears to be a cut-and-paste error.	Boczon 1994c MRID 43193218
Guinea pigs, Hazleton, 10 males, 364-508 g	AC 299,263, technical (98.2% pure). Induction phase: 0.2 g test material moistened with deionized water applied to shaved anterior left flank for 6-hour exposure period, after which treated sites were washed with deionized water. Positive controls treated with 0.3% DNCB in 80% ethanol in deionized water. Process was repeated on the same day each week up until sites received a total of three dose applications. Challenge phase: On day 15, test group received challenge dose of 0.2 g of test material on naïve site (anterior right flank); controls received 0.1% (w/v) DNCB in acetone; previously untreated (naïve) guinea pigs received challenge application of 0.2g test material in same manner as test group. All sites were evaluated for sensitization responses (according to Draize method) at 23 and 48 hours after induction and challenge doses.	No dermal responses observed in test animals after either induction or challenge applications. No irritation observed in naïve guinea pigs after the challenge phase. Guinea pigs in positive control group showed moderate to strong dermal reactions to the challenge dose. CORE CLASSIFICATION: Acceptable	Glaza 1992 MRID 43193212

Table A2-6: Eye Irritation Studies

Species	Exposure	Response	Reference
Rabbit, New Zealand White, six males, 10-13 weeks old, weight not reported	Instillation of 0.1 g of neat "AC 299,263 1 AS Formulation" (11.83% a.i.) in the conjunctival sac of the left eye of each rabbit; right eye served as control. Exposure duration = 24 hours, after which treated eyes were rinsed with tap water and examined for irritation. Eyes examined at 1, 24 and 72 hours post treatment; eye irritation scored using Draize scale.	Primary Eye Irritation Index was 0.2 at 1 hour post treatment (i.e., slight conjunctival redness was observed in the treated eye of one rabbit). No irritation was observed in any treated eyes at 24 hours post treatment. AC 299, 263 was shown to be non-irritating to the rabbit eye. Toxicity category: IV	Boczon 1994 MRID 43193216
Rabbit, New Zealand White, six females, 10-16 weeks old, weight not reported	Instillation of 0.1 g neat AC 299,263 technical (98.2% pure) into conjunctival sac of the left eye; right eyes served as controls. Treated eyes were rinsed with tap water 24-hours after exposure.	Primary Eye Irritation Index was 8.7 at 1 hour, 6.3 at 24 hours, 4.0 at 48 hours, 1.3 at 72 hours, and 1.0 on day 4 after treatment. All irritation was resolved by day 7. At **1 hour**: slight (4/6) to moderate (2/6) chemosis and moderate (6/6) ocular discharge and slight redness of the conjunctivae (6/6). At **24 hours**: scattered and diffuse areas of corneal opacity (4/6) and mild iritis (1/6). All rabbits had slight to moderate redness of the conjunctivae, 4/6 had slight chemosis and mild to moderate ocular discharge. At **48 hours**: slight (416) to moderate (2/6) conjunctival redness, slight chemosis (2/6) and slight ocular discharge (2/6). Corneal opacities and iritis had resolved in all rabbits. At **72 hours**: all signs of irritation had resolved in 2/6 rabbits With the remaining 4 still showing a slight conjunctival redness. At **4 days**." irritation had resolved in another animal with the remaining 3 animals still showing a slight redness of the conjunctivae. At **7 days**: irritation had resolved in the remaining 3 animals. Toxicity Category III	Fischer 1992a MRID 43193210

Table A2-7: Developmental Toxicity Studies

Species	Exposure	Response	Reference
Rabbits, New Zealand white, females, 5.5.-6.5 months (at mating), 2.80-4.28 kg (at mating), 20/dose group	Once daily gavage doses of AC 299,263 technical (97.1% a.i.) at 0, 300, 600, or 900 mg/kg/day (limit dose) from days 7 through 19 of gestation. Vehicle = 0.5% carboxymethyl-cellulose (CMC)	No treatment-related effects on mortality, clinical signs of toxicity, or cesarean parameters at any dose level. Maternal toxicity: At 600 mg/kg/day: reduced (15-20%) food consumption. At 900 mg/kg/day: reduced (14-22%) food consumption and reduced body weight gains (19% during treatment and 21% post treatment). NOEL = 300 mg/kg/day LOEL = 600 mg/kg/day Developmental toxicity: no treatment related effects. NOEL = 900 mg/kg/day This study is classified as **acceptable**. NB: U.S. EPA/OPP (2001b, pp. 3-4) indicates that the LOAEL was reclassified as a NOAEL in 2001. See Section 3.1.9.1 for discussion. This study is the basis of RfD. See Section 3.3 for discussion.	Hoberman 1995 MRID 43876216
Rats, CD, Charles River, females (164-239 g), 65 days old, 25/group	Gavage doses of AC 299,263 (98.2%) at 0, 100, 500 or 1000 mg/kg/day (limit dose) during days 6 through 15 of gestation. Vehicle = carboxymethyl-cellulose (CMC)	No mortality, abortions, or premature deliveries occurred during the study; no treatment-related clinical signs of toxicity observed. Mean body weights: decreases observed in dams at 1000 mg/kg/day (97% of control weight); however the decreases were not statistically significant. Food consumption was decreased at this dose (about 98% of controls). Mean body weight gain: a statistically significant decreases in body weight gain only at the 1000 mg/kg bw/day dose group and only for Days 6-12 (77% of control weight gain). Developmental toxicity: No biologically or statistically significant effects on pregnancy rate, number of corpora lutea, number of implantations, litter sizes, live fetuses per litter, early and late resorptions, number and percent of litters with resorptions, fetal sex ratio, or mean fetal body weights. Maternal effects: **NOEL** = 500 mg/kg/day, based on weight effects. **LOEL** = 1000 mg/kg/day Developmental toxicity: **NOEL** >1000 mg/kg/day **LOEL** not established. This study is classified as **acceptable**.	Foss 1994 MRID 43193221

Table A2-8: Reproductive Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Rats, Sprague-Dawley, (P) 6 weeks, (F_1) 3 weeks; (P) males 159-208 g, females 120-165 g; (F_1) males 86-265 g, females 80-192g; 30/sex/dose.	AC 299,263 technical (98.2% a.i.) in diet (no vehicle). Exposure (P) rats: beginning at 6 weeks of age for 10 weeks prior to mating to produce F_1 pups. Exposure (F_1) pups: beginning at 28 days of age for 11 weeks prior to mating. Nominal dietary concentrations: 0, 1000, 10,000, or 20,000 ppm. Test substance intake (mean mg/kg bw/day): (P) males: 76, 770, or 1554 (P) females: 88, 892, or 1826 (F_1) males: 73, 748, or 1469 (F_1) females: 85, 867, 1705	No treatment-related clinical findings or increases in mortality were noted in the P or F_1 adults at any dose level. No treatment related effects observed with respect to systemic or reproductive toxicity at any of the administered dose levels, including the 20,000 ppm limit dose. NOEL = 20,000 ppm (limit dose) (1469 mg/kg/day in males; 1705 mg/kg/day in females). LOEL not observed.	Schroeder 1995 MRID 43876217

Table A2-9: Subchronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Dogs, beagle, males (8-11 kg) and females (7.8-9.2 kg), 5 months old at initiation, 4/sex/dose group	Dietary concentrations of AC 299,263, technical (97.1% purity) for 13 weeks. Nominal concentrations: 0, 1000, 10,000, or 40, 000 ppm. Corresponding mg/kg/day dose (males): 0, 34, 329, or 1333 Corresponding mg/kg/day dose (females): 0, 36, 381, 1403	No mortalities, abnormal clinical signs of toxicity or ophthalmological observations and no adverse effects on body weight, body weight gain or food consumption in either sex at any dose level. No treatment-related effects were observed in hematology, clinical chemistry or urinalyses parameters in either sex at any dose level. Organ weights, and gross and histopathology showed no treatment-related effects at any dose level. NOEL = 40,000 ppm (1,300 mg/kg/day for males and 1,400 mg/kg/day for females). LOEL not established.	Kelly 1994 MRID 43193220
Rats, CD, Charles River, males (137-170 g) and females (122-151 g), ≈5 weeks old, 10/sex/dose group	AC 299,263, technical (98.2%) in *ad libitum* diet for 90 days. Dose levels: 0, 1000, 10,000, or 20,000 ppm (based on 28-day feeding study that demonstrated a NOEL of >20,000 ppm) Mean nominal compound consumption doses : **81, 833, or 1661 mg/kg/day**	No mortality; no treatment-related abnormal clinical signs or ophthalmological findings; no effects on hematology, clinical chemistry, urinalyses, absolute organ weight, or organ weights relative to body weights; no treatment related gross or microscopic pathology observations, and mean body weights, body weight gains, and food consumption were comparable among all treatment groups and equal to or greater than control group. NOEL = 20,000 ppm (1661 mg/kg/day); highest dose tested. LOEL not established. Study classified as **Core Guideline**	Fischer 1992c MRID 43193219

Table A2-10: Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Dogs, purebred beagle, males (8.5-11.3 kg) and females (7.6-9..72 kg), 6 months old at initiation, 5/sex/dose group	Dietary concentrations of AC 299,263, technical (97.1% purity) for 1 year. Dietary concentrations: 0, 1000, 10,000, or 40,000 ppm. Nominal dose: 0, 25, 250, or 1000 mg/kg/day Mean test substance intake (males): 0, 29, 283, 1174 mg/kg/day Mean test substance intake (females): 0, 30, 282, 1156 mg/kg/day	No mortality; no treatment-related differences observed for appearance, body weights, food consumption, ophthalmology, hematology, blood chemistry, urinalysis, organ weights, and gross and microscopic pathology. NOEL = 40,000 ppm (≈1165 mg/kg/day)	Kelly 1995a MRID 43876214
Mice, albino, males (25.3-31.2 g) and females (20.5-24.24 g), 43 days old, 55/sex/dose group	Dietary concentrations of AC 299,263, technical (97.1% purity) for 78 weeks. Dietary concentrations: 0, 500, 3500, or 7000 ppm Nominal dose: 0, 75, 525, or 1050 mg/kg/day Mean (and range) test substance intake (males): 73 (64-94), 535 (440-686), or 1053 (908-1349) mg/kg/day Mean (and range) test substance intake (females): 96 (79-119), 664 (528-838), or 1348 (1132-1727) mg/kg/day	No treatment-related differences in clinical signs of toxicity, mortality, mean body weights, mean body weight gains, feed consumption, or feed efficiency observed between control and treatment groups. No statistically significant differences in hematology parameters, absolute organ weights, or relative organ/body weights for mice in the treated and control groups. No treatment-related gross postmortem or histological differences in the treated and control groups. NOEL = 7000 ppm (1053 mg/kg/day for males and 1348 mg/kg/day for females). LOEL not established. According to HED Risk Characterization: *study is acceptable and 7000 ppm is considered a limit dose*.	Kelly 1995b MRID 43876215

Table A2-10: Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Rats, males and females	Imazamox technical (a.i. not specified) in diet for 24 months. Nominal concentrations: 0, 1000, 10,000, or 20, 000 ppm Nominal concentrations equivalent to: 0, 52, 528, or 1068 mg/kg/day (males) 0, 63, 626, or 1284 mg/kg/day (females).	No treatment-related effects on mortality, body weights, body weight gains, food consumption, or feed efficiency. No overt clinical signs of toxicity or ophthalmological changes observed throughout the study, and no effects observed on hematological, blood chemistry or urological parameters. Observed increase in absolute and relative kidney weights in males at 10,000 ppm was not corroborated by macroscopic or histopathological kidney changes and was also not considered dose related. There were no treatment-related neoplastic lesions detected in any treated groups. According to HED Risk Characterization, *A chronic LOEL was not observed, however, the dose level of 20,000 ppm in the diet is considered an adequate upper limit for chronic and carcinogenicity studies. The chronic NOEL is equivalent to 1,068 mg/kg/day males and 1,284 mg/kg/day in females (20,000 ppm), HDT.*	Summarized in U.S. EPA/ OPP 1997 MRID 43891001

Appendix 3: Toxicity to Birds

Table A3-1: Acute Oral/Gavage Toxicity to Birds

Species	Exposure	Response	Reference
Bobwhite *(Colinus virginianus)*, 20.5 weeks at initiation, 10/dose group	AC 299,263 Technical (98.2% purity) Mean measured doses: 1010, 1200, 1397, 1676, or 1846 mg/kg Vehicle = corn oil Observation period = 14 days	No mortality observed at highest dose. Single-dose LD_{50} >1846 mg/kg a.i. (highest dose tested based on measured doses) NOEL = 1846 mg/kg a.i. Study classification: Core	Campbell et al. 1994b MRID 43193227
Mallard duck	Imazamox (98.2% a.i.)	LD_{50} >1950 mg a.i./kg	MRID 43193226 (cited in U.S. EPA/OPP 2008a)

Table A3-2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference
Bobwhite quail *(Colinus virginianus)*, 10 days at initiation, 12/dose group	Dietary concentrations of AC 299,263 Technical (97.1% purity). Duration: 5 days with treated feed and 3 days with clean feed. Nominal concentrations: 0, 100, 270, 729, 1968, or 5314 ppm a.i. Mean measured concentrations: 0, 103, 276, 746, 2041, or 5572 ppm a.i. Vehicle = corn oil and acetone (acetone evaporated form the feed during mixing).	Mortality (4/12) at 2041 ppm a.i. not treatment-related; no treatment-related signs of toxicity. LC_{50} >5572 ppm a.i. NOEL = 5572 ppm a.i. Study classification: Core Working Note: The highest dietary concentration corresponds to an estimated dose of about 1700 mg/kg bw/day. See Section 4.1.2.2 for details.	Campbell et al. 1994c MRID 43193228
Mallard duck *(Anas platyrhynchos)*, 10 days at initiation, 12/dose group	Dietary concentrations of AC 299,263 Technical (97.1% purity). Duration: 5 days with treated feed and 3 days with clean feed. Nominal concentrations: 0, 100, 270, 729, 1968, or 5314 ppm a.i. Mean measured concentrations: 0, 103, 276, 746, 2041, or 5572 ppm a.i. Vehicle = corn oil and acetone (acetone evaporated form the feed during mixing).	No mortality in any treated group; 1 death occurred in control group on day 7. No reported signs of toxicity. LC_{50} >5572 ppm a.i. NOEL = 5572 ppm a.i. Study classification: Core Working Note: In places, the DER refers to the animals as bobwhites. This appears to be a cut-and-paste error. Working Note: The highest dietary concentration corresponds to an estimated dose of about 2300 mg/kg bw/day. See Section 4.1.2.2 for details.	Campbell 1994d MRID 43193229

Table A3-3: Reproductive Toxicity Studies in Birds

Species	Exposure	Response	Reference
Northern Bobwhite *(Colinus virginianus)*, males and females, 24 weeks old, 16/sex/dose group	AC 299,263 technical (97.1% a.i.) dietary concentrations of 500, 1000, or 2000 ppm for 10 weeks. Vehicle = 6.9% acetone and 1.9% corn oil in premixes (equivalent to 0.3% acetone and 0.07% corn oil in test diets). Working Note: Based on mean food consumption and final body weights (the only adult weights in the DER (p. 9), the birds consumed food at about 9.4% of their bw per day.	No treatment-related mortality; no overt signs of toxicity, no treatment-related effects on reproduction, body weight or food consumption at any concentration tested. NOEC = 2000 ppm [≈ 190 mg/kg bw/day] LOEC >2000 ppm Incidental effects included three mortalities unrelated to treatment and a slight but statistically significant decrease in food consumption in the 1000 ppm group during weeks 1-3 and in the 2000 ppm group during week1, with no apparent affects on body weight during the study. DER appears to quote from the study as follows: **"Therefore, any differences in feed consumption were not indicative of an adverse effect upon the health of the birds, and were not considered in the establishment of the no-observable-effect concentration (NOEC)."** Working Note: A very slight decrease in food consumption at two higher exposures. Not statistically significant.	Gagne et al. 1995a MRID 43876209
Mallard *(Anas platyrhynchos)*, males and females, 18 weeks old, 16/sex/dose group	AC 299,263 technical (97.1 a.i.) dietary concentrations of 500, 1000, or 2000 ppm for 10 weeks. Vehicle = 6.9% acetone and 1.9% corn oil in premixes (equivalent to 0.3% acetone and 0.07% corn oil in test diets). Working Note: Based on mean food consumption and final body weights (the only adult weights in the DER (p. 9), the birds consumed food at about 11% of their bw per day.	No treatment-related mortality; no overt signs of toxicity, no treatment-related effects on reproduction, body weight or food consumption at any concentration tested. NOEC = 2000 ppm [≈ 220 mg/kg bw/day] LOEC >2000 ppm Incidental effects included two mortalities (one male found dead on week 2 in the 1000 ppm group and one female on week 8 in the 2000 ppm group), and a statistically significant difference in male body weight at 2000 ppm (week 2) attributed to a lightly lighter initial body weight for that dose group. Also, there was a statistically significant increase in food consumption during week 6 and a statistically significant decrease during week 7, which were not considered to be related to treatment. An EPA reviewer indicates that the nominal concentrations were *"based upon the mallard pilot reproduction study (American Cyanamid Study Number 954-93-205) and expected use rates on the product label.*" The maximum residue level was not reported, and the reviewer assumed that it is expected to be less than the highest labeled use rate.	Gagne et al. 1995b MRID 43876211

Appendix 4: Toxicity to Terrestrial Plants

Table A4-1: Vegetative Vigor Bioassays

Species	Exposure	Response		Reference
Monocots: Corn, onion, ryegrass, oat; 5 plants/rep; 1-3 true leaf stage; 14-30 days post-planting	**Vegetative Vigor** AC 299, 263 (purity 97.1%) with Triton surfactant. Application rates: 0.00075, 0.0015, 0.0030, 0.0060, 0.012, 0.024, and 0.048 lb a.i/acre with the exception of corn which was tested only up to 0.012 lb a.i./acre. Replicates: 4 Duration: 21 days	**Species/Most Sensitive Parameter**	**Results (lbs a.i./acre)**	Chetram and Canex 1995 MRID 43876221
		Study Results		
		corn/plant height	EC_{25} = 0.0021 NOAEC = 0.0015	
		oat/dry weight ***most sensitive species***	EC_{25} = 0.0016 NOAEC = 0.0015	
		onion/dry weight	EC_{25} = 0.012 NOAEC = 0.0060	
		ryegrass/dry weight	EC_{25} = 0.0052 NOAEC = 0.0030	
		General signs of toxicity included stunting of plants; chlorosis, necrosis, desiccation, and deformity of leaves; and plant death		
		Results of EPA Probit Analysis		
		corn/plant height	EC_{25} = 0.0025 NOAEC = 0.0008	
		oat/dry weight ***most sensitive species***	EC_{25} = 0.0012 NOAEC = 0.0008	
		onion/dry weight	EC_{25} = 0.012 NOAEC = 0.0060	
		ryegrass/dry weight	EC_{25} = 0.0057 NOAEC = 0.0030	

Appendix 4: Toxicity to Terrestrial Vegetation *(continued)*

Table A4-1: Vegetative Vigor Bioassays

Species	Exposure	Response	Reference
Dicots: Cabbage, cucumber, lettuce radish, soybean, tomato; 5 plants/rep; 1-3 true leaf stage; 14-30 days post-planting	**Vegetative Vigor** AC 299, 263 (purity 97.1%) w/Triton surfactant applied with single nozzle spray booth delivering 50 gallons/acre. Application rates: 0.00075, 0.0015, 0.0030, 0.0060, 0.012, 0.024, and 0.048 lb a.i/acre. Replicates: 4 Duration: 21 days	**Species/Most Sensitive Parameter** / **Results (lbs a.i./acre)** **Study Results** cabbage/dry weight: EC_{25} = 0.0031 NOAEC = 0.0015 cucumber/dry weight: EC_{25} = 0.0022 NOAEC = 0.00075 lettuce/dry weight: EC_{25} >0.048 NOAEC = 0.012 radish/dry weight: EC_{25} = 0.0020 NOAEC = 0.0015 soybean/all similar: EC_{25} >0.048 NOAEC = 0.048 Tomato/dry weight ***most sensitive species***: EC_{25} = 0.0010 NOAEC = 0.00075 *General signs of toxicity included stunting of plants; chlorosis, necrosis, desiccation, and deformity of leaves; and plant death* **Results of EPA Probit Analysis** cabbage/dry weight: EC_{25} = 0.0032 NOAEC = 0.0015 cucumber/dry weight: EC_{25} = 0.0022 NOAEC = 0.0008 lettuce/dry weight: EC_{25} = 0.049 NOAEC = 0.012 radish/dry weight: EC_{25} = 0.0025 NOAEC = 0.0015 soybean/dry weight: EC_{25} >0.048 NOAEC = 0.048 Tomato/dry weight ***most sensitive species***: EC_{25} = 0.0008 NOAEC = 0.00075	Chetram and Canex 1995 MRID 43876221

Table A4-2: Seedling Emergence Bioassays

Species	Exposure	Response		Reference
Monocots: Corn, onion, ryegrass, oat; 10 seeds/rep; planted day of application	AC 299, 263 (purity 97.1%). Application rates: 0.00075, 0.0015, 0.0030, 0.0060, 0.012, 0.024, and 0.048 lb a.i/acre. Replicates: 4 Duration: 21 days	**Species/Most Sensitive Parameter**	**Results (lbs a.i./acre)**	Chetram et al. 1995 MRID 43876220
		Study Results		
		corn/dry weight	EC_{25} = 0.014 NOAEC = 0.012	
		oat/dry weight ***most sensitive species***	EC_{25} = 0.0026 NOAEC = 0.0015	
		onion/dry weight	EC_{25} = 0.0095 NOAEC = 0.0060	
		ryegrass/dry weight	EC_{25} = 0.0062 NOAEC = 0.0030	
		General signs of toxicity included stunting of plants; leaf chlorosis, leaf necrosis, and plant death		
		Results of EPA Probit Analysis		
		corn/dry weight	EC_{25} = 0.013 NOAEC = 0.012	
		oat/dry weight ***most sensitive species***	EC_{25} = 0.0020 NOAEC = 0.001	
		onion/dry weight	EC_{25} = 0.0112 NOAEC = 0.0060	
		ryegrass/dry weight	EC_{25} = 0.0051 NOAEC = 0.0030	

Table A4-2: Seedling Emergence Bioassays

Species	Exposure	Response		Reference
Dicots: Cabbage, cucumber, lettuce radish, soybean, tomato; 10 seeds/rep; planted day of application	**Seedling Emergence**: AC 299, 263 (purity 97.1%). . Application rates: 0.00075, 0.0015, 0.0030, 0.0060, 0.012, 0.024, and 0.048 lb a.i/acre. Replicates: 4 (3 replicates for lettuce). Duration: 21 days	**Species/Most Sensitive Parameter**	**Results (lbs a.i./acre)**	Chetram et al. 1995 MRID 43876220
		Study Results		
		cabbage/dry weight	EC_{25} = 0.0018 NOAEC = 0.00075	
		cucumber/ plant height	EC_{25} = 0.0065 NOAEC = 0.0015	
		lettuce/dry weight	EC_{25} >0.028 NOAEC = 0.024	
		radish/dry weight	EC_{25} = 0.0024 NOAEC = 0.0015	
		soybean/ phytotoxicity	EC_{25} >ND* NOAEC = 0.0015	
		Tomato/dry weight ***most sensitive species***	EC_{25} = 0.0041 NOAEC = 0.0015	
		*ND = not determined		
		General signs of toxicity included stunting of plants; leaf chlorosis, leaf necrosis, increased anthocyanin pigmentation (cabbage), and plant death		
		Results of EPA Probit Analysis		
		cabbage/dry weight ***most sensitive species***	EC_{25} = 0.0018 NOAEC = 0.0008	
		cucumber/ plant height	EC_{25} = 0.0073 NOAEC = 0.0015	
		lettuce/dry weight	EC_{25} = 0.029 NOAEC = 0.012	
		radish/dry weight	EC_{25} = 0.0026 NOAEC = 0.0015	
		soybean/ phytotoxicity	EC_{25} >0.048 NOAEC = 0.0015	
		Tomato/dry weight	EC_{25} = 0.0075 NOAEC = 0.0015	

Table A4-3: Field, Field Simulation, and Efficacy Studies

Species	Exposure	Response	Reference
Parasitic witchweeds (*Striga* spp.), dicot	Three post-emergent application of 71 g a.e./ha (≈0.063 lb a.e./acre) as Raptor formulation to corn.	Delayed emergence of witchweeds by only 1 week but did not reduce the number of emergent weeds. Working Note: Imazamox did not appear to be effective.	Abyo et al. 1998
Jointed goatgrass (*Aegilops cylindrica*, monocot) in herbicide-resistant wheat	Imazamox (formulation not specified) at 27 to 71 g a.i./ha (≈25.6 to 67.2 g a.e./ha or 0.023 to 0.50 lb a.e./acre)	Good control of weeds at 36 g a.i./ha (34 g a.e./ha or about 0.03 lb a.e./acre). Overall increases in wheat yield of 19 to 41%. Generally clear dose-response relationships (see Tables 5 and 6 in paper).	Ball et al. 1999
Mixed grass and broadleaf weeds in peas (*Pisum sativum*), dicot.	Post-emergent applications of imazamox (formulation not specified) at 7 to 36 g a.i./ha (≈6.6 to 34 g a.e./ha or 0.0059 to 0.030 lb a.e./acre).	Effective (90%) control of weeds with no damage to peas. Adjuvants (Agral 90, Merge, or Sun-It II) increased efficacy. Working Note: The lowest application appears to be the lowest reported effective dose. The shoot biomass of redroot pigweed was reduced by about 90% at 7 g a.i./ha. See Figure 2, p. 66, of paper.	Blackshaw 1998
Cordgrass, *Spartina densiflora*, monocot	Field simulation (potted plants). Swiss formulation of imazamox (Pulsar, 40 g a.i./L) at application rates of 20-68 g a.i./ha (≈19 to 64 g a.e./ha or ≈0.017 to 0.057 lb a.e./acre).	No effect. Lack of efficacy attributed to rapid metabolism of imazamox by cordgrass.	Mateos-Naranjo et al. 2009
Cuscuta campestris, dicot, above ground parasitic plant	Imazamox (Raptor) at 10 to 80 g a.e./ha (0.0090 to 0.071 lb a.e./acre) applied to canola with Activator 90 surfactant.	Complete mortality of target species when attached to herbicide resistant host (see Table 3, p. 814 of paper).	Nadler-Hassar et al. 2009
Several species of weeds (i.e., foxtail, pigweed, ragweed, lambquarters, and velvetleaf) in cultivated soybeans	Imazamox (formulation not specified) at 35 and 45 g a.i./ha (33 to 43 g a.e./ha or 0.030 to 0.038 lb a.e./acre) with 1% methylated seed oil	Little indication of transient damage to soybeans – less damage at DAT 14 than DAT 7. Good control of weeds by DAT 28 – i.e., 78 to 99% (Table 3 of paper for details). Excellent (99%) control of pigweed up to DAT 56 (Table 4 of paper). Efficacy also indicated by substantial increases in soybean yields (Table 5 of paper).	Nelson and Renner 1998
Tomato, cabbage, and potatoes grown in rotation with soybeans treated with imazamox.	Imazamox (formulation not specified) at 35 g a.i./ha (33 g a.e./ha or 0.030 lb a.e./acre). Effects of soil residues with crops grown in rotation.	Little sign of visual injury and no significant reductions in crop yields (Table 2 of publication).	O'Sullivan et al. 1998

Table A4-3: Field, Field Simulation, and Efficacy Studies

Species	Exposure	Response	Reference
Purple nutsedge (*Cyperus rotundus*) and sicklepod (*Senna obtusifolia*)	Greenhouse applications of imazamox (formulation not specified) at 21 or 42 g a.i./ha (20 or 40 g a.e./ha or 0.018 or 0.035 lb a.e./acre).	Dose-related reductions in shoot weights at 3 weeks after application with clear dose-response relationship (Table 1 of paper). In separate assays, no enhancement of the toxicity of glyphosate to target species.	Rao and Reddy 1999
Quackgrass (*Elytrigia repens*) and Canada thistle (*Cirsium arvense*)	Greenhouse applications of imazamox (ammonium salt but formulation not specified) at 70 g a.i./ha (66 g a.e./ha or 0.059 lb a.e./acre) with 1% v/v methylated seed oil,	Adequate control of target vegetation at 4 weeks after treatment based on visual inspection (Table 2 of paper). Decrease in height in sensitive but not in tolerant strains of corn (Figure 1 in paper).	Sprague et al 1999
Velvetleaf (*Abutilon theophrasti*) and Ivyleaf morning-glory (*Pomoea hederacea*)	Greenhouse applications of imazamox (not otherwise specified) at 9 to 35 g/ha (a.i. vs a.e. not specified)	Dose-related inhibition of weed growth at 7 and 21 days after treatment (see Table 1 of paper). Dose-response relationship is not very steep but visual damage is apparent at lowest dose.	Unland et al. 1999

Appendix 5: Toxicity to Fish

Table A5-1: Acute Toxicity to Fish

Species	Exposure	Response	Reference
Bluegill sunfish (L*epomis macrochirus*), juvenile, 0.33-0.58 g, 23-29 mm, 10/concentration	AC 229,263 technical (97.1% a.i.) under flow-through conditions for 96 hours. Nominal concentrations: 15.6, 25.9, 43.2, 72.0, or 120 mg a.i./L and dilution water control. Mean measured concentrations: 17.1, 26.1, 40.6, 69.9, or 119 mg a.i./L (represents 92-108% of nominal concentrations.	No sublethal effects observed. LC_{50} >119 mg a.i./L NOEC = 119 mg a.i./L or 113 mg a.e./L	Yurk and Wisk 1994a MRID 43193230
Rainbow trout *(Onchorhynchus mykiss)*, juvenile, 0.64-0.82 g, 31-42 mm, 10/concentration	AC 229,263 technical (97.1% a.i.) under flow-through conditions for 96 hours. Nominal concentrations: 15.6, 25.9, 43.2, 72.0, or 120 mg a.i./L and dilution water control. Mean measured concentrations: 16.7, 25.7, 40.6, 69.2, or 122 mg a.i./L (92-106% of nominal).	No sublethal effects observed. LC_{50} >122 mg a.i./L NOEC = 122 mg a.i./L or 115 mg a.e./L	Yurk and Wisk 1994b MRID 43193231
Sheepshead minnow (*Cyprinodon variegates*), mean weight 0.28 g, lengths not reported.	AC 299,263 (Imazamox) technical (97.1%) for 96 hours under flow-through conditions. Mean measured concentrations (SD): 12.6 (0.57), 20.9 (0.85), 34.1 (1.30), 56.2 (2.07), 94.2 (3.12) mg a.i./L	No sublethal effects observed. LC_{50} >94.2 ppm a.i. NOEL = 94.2 ppm a.i. or 89.2 mg a.e./L	Olivieri et al. 1998a MRID 44565201

Table A5-2: Bioconcentration in Fish

Species	Exposure	Response	Reference
Bluegill sunfish (L*epomis macrochirus*), mean weight 5.47 ± 1.03 g; mean length 56 ± 2.3 mm; 120 fish/ aquarium	C^{14}-CL 299,263 under flow-through conditions for 28 days. Test aquarium contained ≈70 L of aerated dilution water with radiolabelled test solution.	Whole fish: less than minimum quantifiable limit at all sampling intervals. Edible tissues: less than minimum quantifiable limit at all sampling intervals. Mean Measured Water Concentration: 0.48 mg/L. Inedible tissues (mg/kg): 0.063 on day 14 0.054 on day 21 0.066 on day 28 BCF in inedible tissues (mg/kg): 0.13 on day 14 0.11 on day 21 0.14 on day 28 BCFs for edible tissue could not be quantified. Total radioactive residues in water, whole fish, edible and inedible tissues decreased to non-detectable levels within 1 day of depuration period. Study classified as acceptable.	Johnson 1995 MRID 43876231

Table A5-3: Longer-term Toxicity to Fish

Species	Exposure	Response	Reference
Rainbow trout *(Onchorhynchus mykiss)*	Imazamox, NOS, 28 days	NOEC: 122 mg/L	European Commission 2002
Rainbow trout *(Onchorhynchus mykiss)*	Imazamox, NOS, 96 days	NOEC: 11.8 mg/L	European Commission 2002

Note: European Commission (2002) provides only a very brief summary of these longer-term studies in fish. Longer-term studies in fish are not noted in the listing of studies submitted to U.S. EPA/OPP (Appendix 1 of the current Forest Service risk assessment) and longer-term studies in fish are not cited in ecological risk assessments by U.S. EPA/OPP (2008a,b).

Appendix 6: Toxicity to Aquatic Invertebrates

Table A6-1: Acute Toxicity to Aquatic Invertebrates

Species	Exposure	Response	Reference
Daphnia magna, between 0 and 22.5 hours old at initiation 10/concentration.	AC 229,263 technical (97.1% a.i.) under flow-through conditions for 96 hours. Nominal concentrations: 16.1, 26.8, 44.6, 74.4, or 124 mg a.i./L. Mean measured concentrations: 16.7, 29.7, 49.0, 81.0, or 122 mg a.i./L (98-111% of nominal).	Mortality included one (5%) daphnid at 49.0 mg/L and one (5%) at 81.0 mg/L. Both concentrations refer to measured values. No sublethal effects observed. LC_{50} >122 mg a.i./L(measured) NOEC = 122 mg a.i./L or 115 mg a.e./L (measured)	Yurk and Wisk 1994c MRID 43193232
Mysid (*Mysidopsis bahia*), <24 hours old.	AC 299,263 (Imazamox) technical (97.1%) for 96 hours under flow-through conditions. Mean measured concentrations (SD): 11.7 (0.50), 19.2 (0.84), 33.2 (0.98), 56.0 (0.99), 94.3 (1.53) mg a.i./L	No sublethal effects observed. LC_{50} >94.3 ppm a.i.(measured) NOEL = 94.3 ppm a.i. or 89.3 mg a.e./L	Olivieri et al. 1998b MRID 44565202

Table A6-2: Longer-term Toxicity to Aquatic Invertebrates

Species	Exposure	Response	Reference
Daphnia magna	Imazamox, NOS, 21 days	NOEC: 137 mg/L (a.i. or a.e. units are not specified)	European Commission 2002

Note: European Commission (2002) provides only a very brief summary of the longer-term study in daphnids. Longer-term studies in aquatic invertebrates are not noted in the listing of studies submitted to U.S. EPA/OPP (Appendix 1 of the current Forest Service risk assessment) and longer-term studies in aquatic invertebrates are not cited in ecological risk assessments by U.S. EPA/OPP (2008a,b).

Appendix 7: Toxicity to Aquatic Plants

Table A7-1: Toxicity to Algae

Species	Exposure	Response		Reference
Anabaena flos-aquae, *Selenastrum capricornutum*, *Skeletonema costatum*, *Navicula pelliculosa*; 10,000 cells/mL *A. flosaquae*, and *S. costatum*; 3000 cells/mL for S. *capricornutum* and N. *pelliculosa.*	AC 299,263 (purity 97.1%), nominal concentration of 40 ppb (0.040 mg a.i./L, equivalent to 0.038 mg a.e./L). Duration: 120 hours	<50% inhibition of growth (i.e., 0–11%) in all test species.		Canez et al. 1995 MRID 43876219 Very similar values for the same four species are cited in European Commission 2002.
		Freshwater diatom ***Navicula pelliculosa***	EC_{50} >40 ppb 0% reduction	
		Green algae ***Selenastrum capricornutum***	EC_{50} >40 ppb 8.3% reduction	
		Marine diatom ***Skeletonema costatum***	EC_{50} >40 ppb 11% reduction	
		Bluegreen algae ***Anabaena flos-aquae***	EC_{50} >40 ppb 3.6% reduction	

Note: 40 ppb a.i. = 0.04 mg a.i./L x 0.947 a.e./a.i. = 0.038 mg a.e./L

MACROPHYTES

Table A7-2: Toxicity to Macrophytes

Species	Exposure	Response	Reference
Duckweed *Lemna gibba*	Imazamox (97.1% a.i.) Exposure period: 14 days (U.S. EPA/OPP 2008a, p. 16)	EC_{50} = 11 ppb a.i. or about 10.4 ppb a.e. NOEC = 4.5 ppb a.i. or 4.3 ppb a.e. `Working Note: The DER for this study is available but the DER does not summarize the duckweed data. The data given in this entry is taken from U.S. EPA/ OPP 2008a, p. 16).`	Canez 1995 MRID 43876219
Duckweed *Lemna minor*	Imazamox as Bolero, a European formulation (40 g/L) from BASF. 3-hour pulse exposure	Assay 1 [1]: EC_{50}: 1080 nM (329 µg a.e./L) EC_{10}: 305 nM (93 µg a.e./L) Assay 2 [1]: EC_{50}: 1341 nM (409 µg a.e./L) EC_{10}: 305 nM (93 µg a.e./L)	Cedergreen et al. 2005
Duckweed *Lemna minor*	Imazamox as Bolero, a European formulation (40 g/L) from BASF. 4 and 7 day exposures a specified in the column to the right.	Assay 1: 4 day exposure [1]: EC_{50}: 179 nM (54.6 µg a.e./L) EC_{10}: 30 nM (9.5 µg a.e./L) Assay 2: 7 day exposure [1]: EC_{50}: 96 nM (29 µg a.e./L) EC_{10}: 34 nM (10 µg a.e./L)	Cedergreen et al. 2005

[1] Note on conversions from nM to µg/L (ppb): nM x 305 ng/nM ÷ 1000 ng/µg = µg/L. The µg/L conversions are in units of a.e.

Appendix 8: Gleams-Driver Simulations

Table A8-1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.00254 (0 - 0.0288)	0 (0 - 0.0043)	0 (0 - 0)
Dry and Temperate Location	0.00137 (0 - 0.0066)	0 (0 - 0.00078)	0 (0 - 0)
Dry and Cold Location	0.00061 (1.88E-06 - 0.0082)	0 (0 - 0.000066)	0 (0 - 0)
Average Rainfall and Warm Location	0.037 (0.0102 - 0.104)	0.0038 (0.00029 - 0.0248)	0 (0 - 4.90E-06)
Average Rainfall and Temperate Location	0.0314 (0.0106 - 0.11)	0.004 (0.000042 - 0.0287)	0 (0 - 3.01E-05)
Average Rainfall and Cool Location	0.0166 (0.0043 - 0.06)	0.00098 (2.68E-05 - 0.0114)	0 (0 - 5.30E-09)
Wet and Warm Location	0.0219 (0.0068 - 0.088)	0.00234 (0.000036 - 0.0128)	6.20E-09 (0 - 5.10E-06)
Wet and Temperate Location	0.0177 (0.0064 - 0.044)	0.00131 (9.70E-06 - 0.0092)	0 (0 - 1.24E-07)
Wet and Cool Location	0.095 (0.035 - 0.153)	0.0169 (0.00246 - 0.037)	0 (0 - 1.45E-06)
		Average of Central Values:	0.00939
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.153
		Summary of Values:	0.0094 (0 - 0.153)

Table A8-2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.212 (0.208 - 0.216)	0.195 (0.19 - 0.199)	0.193 (0.187 - 0.198)
Dry and Temperate Location	0.211 (0.207 - 0.214)	0.193 (0.19 - 0.197)	0.192 (0.187 - 0.196)
Dry and Cold Location	0.203 (0.201 - 0.208)	0.187 (0.185 - 0.193)	0.186 (0.184 - 0.189)
Average Rainfall and Warm Location	0.202 (0.191 - 0.205)	0.186 (0.178 - 0.189)	0.178 (0.175 - 0.186)
Average Rainfall and Temperate Location	0.201 (0.191 - 0.204)	0.185 (0.176 - 0.187)	0.179 (0.175 - 0.185)
Average Rainfall and Cool Location	0.201 (0.191 - 0.203)	0.184 (0.176 - 0.186)	0.177 (0.175 - 0.184)
Wet and Warm Location	0.193 (0.19 - 0.199)	0.177 (0.175 - 0.182)	0.175 (0.175 - 0.176)
Wet and Temperate Location	0.194 (0.19 - 0.2)	0.177 (0.175 - 0.182)	0.175 (0.175 - 0.176)
Wet and Cool Location	0.185 (0.167 - 0.194)	0.175 (0.171 - 0.182)	0.175 (0.154 - 0.176)
		Average of Central Values:	0.1886
		25th Percentile of Lower Bounds:	0.175
		Maximum Value:	0.216
		Summary of Values:	0.189 (0.175 - 0.216)

Table A8-3: Concentration in Top 60 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.042 (0.042 - 0.043)	0.039 (0.038 - 0.04)	0.039 (0.038 - 0.04)
Dry and Temperate Location	0.042 (0.041 - 0.043)	0.039 (0.038 - 0.039)	0.038 (0.038 - 0.039)
Dry and Cold Location	0.041 (0.04 - 0.042)	0.037 (0.037 - 0.039)	0.037 (0.037 - 0.038)
Average Rainfall and Warm Location	0.041 (0.038 - 0.041)	0.037 (0.037 - 0.038)	0.037 (0.036 - 0.037)
Average Rainfall and Temperate Location	0.04 (0.039 - 0.041)	0.037 (0.037 - 0.038)	0.037 (0.036 - 0.037)
Average Rainfall and Cool Location	0.04 (0.039 - 0.041)	0.037 (0.037 - 0.037)	0.037 (0.037 - 0.037)
Wet and Warm Location	0.04 (0.039 - 0.04)	0.037 (0.035 - 0.037)	0.036 (0.035 - 0.037)
Wet and Temperate Location	0.04 (0.04 - 0.041)	0.037 (0.035 - 0.037)	0.036 (0.035 - 0.037)
Wet and Cool Location	0.038 (0.035 - 0.04)	0.037 (0.036 - 0.037)	0.037 (0.035 - 0.037)
		Average of Central Values:	0.0383
		25th Percentile of Lower Bounds:	0.036
		Maximum Value:	0.043
		Summary of Values:	0.038 (0.036 - 0.043)

Table A8-4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	18 (12 - 30)	18 (8 - 30)	18 (8 - 60)
Dry and Temperate Location	18 (8 - 36)	18 (8 - 36)	24 (8 - 60)
Dry and Cold Location	18 (12 - 30)	18 (12 - 36)	24 (18 - 48)
Average Rainfall and Warm Location	36 (24 - 60)	42 (30 - 60)	60 (48 - 60)
Average Rainfall and Temperate Location	30 (24 - 60)	36 (24 - 60)	60 (36 - 60)
Average Rainfall and Cool Location	30 (24 - 60)	36 (30 - 60)	60 (36 - 60)
Wet and Warm Location	48 (30 - 60)	60 (36 - 60)	60 (60 - 60)
Wet and Temperate Location	48 (30 - 60)	60 (42 - 60)	60 (60 - 60)
Wet and Cool Location	48 (30 - 60)	60 (42 - 60)	60 (60 - 60)
		Average of Central Values:	39.6
		25th Percentile of Lower Bounds:	12
		Maximum Value:	60
		Summary of Values:	39.6 (12 - 60)

Table A8-5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	9	0	0
	(0 - 42)	(0 - 8.9)	(0 - 0.001)
Dry and Temperate	3.7	0	0
Location	(0 - 13.4)	(0 - 1.63)	(0 - 0.015)
Dry and Cold Location	1.84	0	0
	(0.01 - 34)	(0 - 0.19)	(0 - 0.000012)
Average Rainfall and	42	5.2	0.1
Warm Location	(16.2 - 104)	(0.3 - 28.1)	(0.000005 - 22)
Average Rainfall and	37	4.5	0.006
Temperate Location	(11.6 - 106)	(0.15 - 24.2)	(0 - 13.4)
Average Rainfall and Cool	25.4	1.51	0.0027
Location	(8.4 - 73)	(0.07 - 10.5)	(0 - 4.7)
Wet and Warm Location	27.8	3.4	2.18
	(8.8 - 77)	(0.29 - 14.5)	(0.025 - 41)
Wet and Temperate	24.2	2.62	2.76
Location	(9.3 - 67)	(0.3 - 11.7)	(0.0031 - 27.3)
Wet and Cool Location	61	12.8	4.9
	(31.1 - 97)	(5.1 - 25.3)	(0.06 - 59)
		Average of Central Values:	10.1
		25th Percentile of Lower Bounds:	0
		Maximum Value:	106
		Summary of Values:	10.1 (0 - 106)

Table A8-6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.029	0	0
	(0 - 0.2)	(0 - 0.03)	(0 - 0.000005)
Dry and Temperate	0.016	0	0
Location	(0 - 0.07)	(0 - 0.008)	(0 - 0.00005)
Dry and Cold Location	0.008	0	0
	(0.000028 - 0.1)	(0 - 0.0005)	(0 - 4.0E-08)
Average Rainfall and	0.27	0.024	0.0014
Warm Location	(0.12 - 0.5)	(0.0023 - 0.1)	(1.4E-08 - 0.7)
Average Rainfall and	0.23	0.023	0.000019
Temperate Location	(0.1 - 0.5)	(0.0009 - 0.1)	(0 - 0.5)
Average Rainfall and Cool	0.15	0.007	0.000026
Location	(0.06 - 0.4)	(0.00028 - 0.05)	(0 - 0.28)
Wet and Warm Location	0.19	0.028	0.27
	(0.08 - 0.5)	(0.0028 - 0.9)	(0.0004 - 2.18)
Wet and Temperate	0.17	0.02	0.28
Location	(0.07 - 0.3)	(0.0017 - 1.13)	(0.00005 - 1.46)
Wet and Cool Location	0.5	0.09	0.4
	(0.3 - 0.7)	(0.04 - 0.6)	(0.0027 - 3.9)
		Average of Central Values:	0.1002
		25th Percentile of Lower Bounds:	0
		Maximum Value:	3.9
		Summary of Values:	0.1 (0 - 3.9)

Table A8-7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	2.82	0	0
	(0 - 39)	(0 - 5.6)	(0 - 0.0016)
Dry and Temperate	1.63	0	0
Location	(0 - 9.1)	(0 - 1)	(0 - 0.009)
Dry and Cold Location	0.8	0	0
	(0.0021 - 9.2)	(0 - 0.07)	(0 - 0.000006)
Average Rainfall and	51	4.7	0.26
Warm Location	(12.2 - 137)	(0.4 - 27.4)	(0.000007 - 100)
Average Rainfall and	42	5.5	0.008
Temperate Location	(16.2 - 166)	(0.18 - 32)	(0 - 56)
Average Rainfall and Cool	24.2	1.16	0.005
Location	(6.3 - 85)	(0.04 - 12.5)	(0 - 30.8)
Wet and Warm Location	23.1	4.9	17.4
	(9.9 - 73)	(0.3 - 34)	(0.04 - 151)
Wet and Temperate	20.7	2.96	18.9
Location	(7.2 - 54)	(0.24 - 37)	(0.004 - 51)
Wet and Cool Location	26.4	5.9	28.9
	(12 - 48)	(1.77 - 43)	(0.18 - 190)
		Average of Central Values:	10.5
		25th Percentile of Lower Bounds:	0
		Maximum Value:	190
		Summary of Values:	10.5 (0 - 190)

Table A8-8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	1.25 (0 - 14.3)	0 (0 - 2.38)	0 (0 - 0.0004)
Dry and Temperate Location	1.01 (0 - 4.7)	0 (0 - 0.5)	0 (0 - 0.007)
Dry and Cold Location	0.4 (0.001 - 4.7)	0 (0 - 0.04)	0 (0 - 2.8E-06)
Average Rainfall and Warm Location	32 (9.5 - 78)	2.6 (0.29 - 18.7)	0.14 (1.3E-06 - 85)
Average Rainfall and Temperate Location	29.6 (9 - 104)	3.3 (0.11 - 22.4)	0.0022 (0 - 45)
Average Rainfall and Cool Location	14.8 (4.4 - 52)	0.6 (0.026 - 5.8)	0.0018 (0 - 16.6)
Wet and Warm Location	7.7 (3.5 - 25.4)	1.64 (0.14 - 18.8)	7.5 (0.011 - 71)
Wet and Temperate Location	6.3 (1.83 - 17.2)	0.9 (0.04 - 18.1)	8.9 (0.0023 - 28.7)
Wet and Cool Location	10.2 (2.85 - 25.5)	1.78 (0.3 - 12.2)	7.2 (0.04 - 95)
		Average of Central Values:	5.1
		25th Percentile of Lower Bounds:	0
		Maximum Value:	104
		Summary of Values:	5.1 (0 - 104)