Imazapyr
(Arsenal, Chopper, and Stalker Formulations)
Final Report

Prepared for:

USDA, Forest Service

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AC	applicators concentrate
a.e.	acid equivalents
a.i.	active ingredient
AEL	adverse-effect level
ACGIH	American Conference of Governmental Industrial Hygienists
ALS	acetolactate synthesase
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
F	female
F_1	first filial generation
g	gram
HQ	hazard quotient
k_a	absorption coefficient
K_d	soil-water distribution coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	soil-water distribution coefficient based on organic carbon
$K_{o/w}$	octanol-water partition coefficient
Kp	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
m	meter
M	male
MCS	multiple chemical sensitivity
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
MW	molecular weight

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

MOE	margin of exposure
MOS	margin of safety
MSDS	material safety data sheet
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
ppm	parts per million
RBC	red blood cells
RfD	reference dose
ROW	rights-of-way
UF	uncertainty factor
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
WHO	World Health Organization
µ	micron
>	greater than
≥	greater than or equal to
<	less than
≤	less than or equal to
=	equal to
≃	approximately equal to
~	approximately

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	1.8C°+32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	0.556F°-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 ($µg/cm^2$)	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

Program Description

The USDA Forest Service uses imazapyr in its vegetation management programs. The Forest Service generally uses aqueous formulations of imazapyr (Arsenal or Arsenal AC) although emulsifiable concentrates (Chopper and Stalker) may be used in some rights-of-way applications. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using imazapyr in current and future Forest Service programs. The Forest Service uses Arsenal AC almost exclusively in site preparation and conifer release. Minor uses for Arsenal AC include hardwood release, hardwood control, rights-of-way management, and wildlife site improvement. Arsenal is used in facilities and rights-of-way maintenance as well as wildlife openings.

Imazapyr is classified as a broad-spectrum/non-selective herbicide used primarily in the control of a number of broadleaf weeds, grasses, and brush. Different plant species may differ in their sensitivity to imazapyr by factors of 10 or greater and some plant species can develop resistance to imazapyr. The most common methods of ground application for Arsenal or Chopper formulations involve backpack (selective foliar) and boom spray (broadcast foliar) operations. In selective foliar applications, the herbicide sprayer or container is carried by backpack and the herbicide is applied to selected target vegetation.

For this risk assessment, application rates used to construct the various exposure scenarios range from 0.08 lb a.e./acre to 2.5 lb a.e./acre with a typical rate taken as 0.15 lb a.e./acre. The typical application rate is about the average application rate that the Forest Service used in 1997, when imazapyr was applied as the sole herbicide. Although this rate is less than the lower end of the labelled application rates, 0.25 lb a.e./acre, the rate of 0.15 lb a.e./acre is typical for most current Forest Service programs. Similarly, the lower range of the application rate reflects the lowest application used by the Forest Service in any application. The upper range of the application rate, 2.5 lbs/acre, is the maximum labeled rate for any imazapyr formulation. This rate is over fifteen times higher than any application used by the Forest Service and is included in this risk assessment only to illustrate the consequences of using imazapyr at the highest labeled application rate.

Human Health Risk Assessment

The risk characterization for potential human health effects associated with the use of imazapyr in Forest Service programs is relatively unambiguous. Based on the estimated levels of exposure and the RfD derived by the U.S. EPA's Office of Pesticide Programs, exposures that can be anticipated both in the typical use of imazapyr or in a number of accidental exposure scenarios do not lead to dose levels that exceed the RfD. In other words, all of the anticipated exposures - most of which involve highly conservative or protective assumptions - are below the RfD by at least a factor of 2. The use of the RfD - which is designed to be protective of chronic or lifetime exposures - is itself a very conservative component of this risk characterization because the duration of any plausible and substantial exposures is far less than lifetime.

Imazapyr can cause irritation to the eyes and skin. Based on the available information, eye and/or skin irritation are the only overt effects that can be associated with the mishandling of imazapyr. These effects can be minimized or avoided by prudent hygiene practices during the handling of imazapyr.

The only reservation attached to this assessment of imazapyr is that associated with any risk assessment in which no plausible hazards can be identified: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated***. No chemical, including imazapyr, has been studied for all possible effects and the use of data from laboratory animals to estimate hazard or the lack of hazard to humans is an uncertain process. Prudence dictates that normal and reasonable care should be taken in the handling of this or any other chemical. Notwithstanding these reservations, the use of imazapyr does not pose any identifiable hazard to workers or the general public in Forest Service programs.

Ecological Risk Assessment

For both aquatic and terrestrial animals, the weight of evidence suggests that no adverse effects are plausible using typical or even very conservative worst-case exposure assumptions. As with the human health risk assessment, this characterization of risk must be qualified. Imazapyr has been tested in only a limited number of animal species and under conditions that may not well-represent populations of free-ranging non-target animals. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects associated with the toxicity of imazapyr can be anticipated in terrestrial or aquatic animals from the use of this compound in Forest Service programs.

Imazapyr is an effective herbicide and adverse effects on some non-target plant species, either terrestrial or aquatic, are likely under certain application conditions and circumstances. Some sensitive plant species could be adversely affected by off-site drift over a relatively narrow band - about 100 feet. More tolerant species are not likely to be affected by off-site drift. This risk characterization is conservative in that the drift estimates are based only on aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no impact on off-site plant species.

Residual soil contamination with imazapyr could be a longer-term problem in some areas. In areas with annual rainfall rates of 10 inches/year or more, imazapyr will be removed from the soil by runoff or percolation. Runoff is likely to be the dominant mechanism in clay soils and percolation the dominant mechanism in sandy soils. Intermediate soil types such as loam, while not specifically modeled in this risk assessment, will likely evidence a mix of runoff and percolation depending on specific soil and site characteristics. In more sandy soils and at the typical application rate of 0.15 lb a.e./acre, imazapyr concentrations in soil could drop below a concentration of 0.02 ppm, the approximate EC_{95} for decreased growth in sensitive species and the approximate NOAEL for tolerant plant species, in a two to four week period in very moist climates - i.e., annual rainfall rates of 50 to 250 inches. Under more moderate rainfall conditions - i.e., 10 to 25 inches per year - the time required to reach concentrations of 0.02 ppm could range

from one to over three months. In predominantly clay soils, variations in rainfall have less effect on decreases in the concentration of imazapyr. To reach a level of 0.02 ppm in clay would require about 30 to 60 days, depending on the amount of rainfall.

Adverse effects on aquatic plants are plausible. At the typical application rate of 0.15 lb a.e./acre, the anticipated water concentration of 0.06 mg/L is about a factor of 5 above the EC_{25} for growth inhibition of 0.013 (0.009-0.019) mg/L in *Lemna gibba*. Thus, in this species and any other aquatic plant species with similar sensitivities, the application of imazapyr could cause a detectable reduction in plant growth. This, in turn, could have an impact on aquatic animal communities. Based on the results of the GLEAMS modeling, levels in excess of 0.013 mg/L could be expected in areas with predominantly clay soil and relatively high rainfall rates for about 2 weeks to two months. In areas with very sandy soil and rainfall rates of 50 inches/year or more, imazapyr concentrations in pond water could be expected to exceed 0.013 mg/L for more prolonged periods - i.e., about 100 days.

This general characterization of risk for aquatic plants could vary substantially depending on site-specific considerations. If imazapyr is applied near ponds, small lakes, or other bodies of water that have low rates of turnover, contamination of the water with imazapyr due either to runoff or percolation could impact aquatic vegetation for a period of time that could be sufficient to cause secondary effects on aquatic animals. Such effects would most likely be noted in areas with greater than average to heavy rainfall - i.e., >25 inches per year. For bodies of water that are more distant from the application site or have a relatively high flow rate - i.e., streams or rivers - phytotoxic concentrations of imazapyr are likely to be transient and have little impact on any plant species.

This characterization of risk for both terrestrial and aquatic plants is heavily influenced by estimates of persistence in soil and transport to water. These estimates should be considered only as crude approximations of environmentally plausible rates. A variety of site-specific factors could substantially impact these assessments, particularly application rate, microbial activity, soil binding of imazapyr, depth of the water table, proximity to open water, and rates of flow in and volumes of groundwater, streams, ponds, or lakes, and specific patterns of rainfall. These site-specific considerations could lead to substantial variations from the modeled values upward or downward. In other words, the exposure assessments modeled in this risk assessment are reasonably consistent with monitoring data. Nonetheless, given the number of factors that can impact the transport and degradation of imazapyr, these assessments are not universally and perhaps not even generally applicable. There are adequate data in the open literature to conduct site-specific exposure assessments that could lead to far more defensible estimates of exposure.

1. INTRODUCTION

The USDA Forest Service uses the herbicide, imazapyr, in its vegetation management programs. The Forest Service generally uses aqueous formulations of imazapyr (Arsenal or Arsenal AC) although emulsifiable concentrates (Chopper and Stalker) may be used in some rights-of-way applications. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using imazapyr in current and future Forest Service programs.

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 imazapyr and its commercial formulation, an assessment of potential exposure to the product, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These are the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

Although this is a technical support document and addresses some specialized technical areas, 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 1998). Furthermore, the technical terms are defined in the glossary to this risk assessment. Some of the more complicated terms and concepts are defined, as necessary, in the text.

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. Brief reviews regarding the human health or ecological effects of imazapyr have been published and were used in the preparation of this risk assessment (Cox 1996; Gagne et al. 1991; Peoples 1984). Almost all of the mammalian toxicology studies and most of the ecotoxicology studies, however, are unpublished reports submitted to the U.S. EPA as part of the registration process for this compound.

Because of the lack of a detailed, recent review concerning imazapyr and the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA files was conducted. Full text copies of relevant studies were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies were reviewed, discussed in sections 3 and 4 as necessary, and synopses of the most relevant studies are provided in the appendices 1 through 4 of this document. An additional appendix (appendix 5) summarizes some of the details of the environmental fate and modeling of the transport of imazapyr that may be of limited interest to some readers.

In the interest of economy, an updated chemical background statement has not been prepared with the current risk assessment. The information presented in the appendices and the detailed discussions in sections 2, 3, and 4 of the risk assessment are intended to be detailed enough to support an independent review of the risk analyses; however, they are not intended to be as detailed as the information generally presented in Chemical Background documents.

For the most part, the risk assessment methods used in this document are similar to those used in risk assessments previously conducted for the Forest Service as well as risk assessments conducted by other government agencies. Details regarding the specific methods used to prepare the human health risk assessment are provided in SERA (1998), while detailed explanations of specific methods used in estimating occupational exposure are provided in Rubin et al. (1998). Similar documentation for methods used in assessing dermal absorption are provided in Durkin et al. (1998).

Risk assessments are usually expressed with numbers; however, the numbers are far from exact. *Variability* and *uncertainty* may be dominant factors in any risk assessment, and these factors should be expressed. Within the context of a risk assessment, the terms *variability* and *uncertainty* signify different conditions.

Variability reflects the knowledge of how things may change. Variability may take several forms. For this risk assessment, three types of variability are distinguished: *statistical*, *situational*, and *arbitrary*. *Statistical variability* reflects, at least, apparently random patterns in data. For example, various types of estimates used in this risk assessment involve relationships of certain physical properties to certain biological properties. In such cases, best or maximum likelihood estimates can be calculated as well as upper and lower confidence intervals that reflect the statistical variability in the relationships. *Situational variability* describes variations depending on known circumstances. For example, the application rate or the applied concentration of a herbicide will vary according to local conditions and goals. As discussed in the following section, the limits on this variability are known and there is some information to indicate what the variations are. In other words, *situational variability* is not random. *Arbitrary variability*, as the name implies, represents an attempt to describe changes that cannot be characterized statistically or by a given set of conditions that cannot be well defined. This type of variability dominates some spill scenarios involving either a spill of a chemical on to the surface of the skin or a spill of a chemical into water. In either case, exposure depends on the amount of chemical spilled and the area of skin or volume of water that is contaminated.

Variability reflects a knowledge or at least an explicit assumption about how things may change, while *uncertainty* reflects a lack of knowledge. For example, the focus of the human health dose-response assessment is an estimation of an “acceptable” or “no adverse effect“ dose that will not be associated with adverse human health effects. For imazapyr and for most other chemicals, however, this estimation regarding human health must be based on data from experimental animal studies, which cover only a limited number of effects. Generally, judgment, not analytical methods, is the basis for the methods used to make the assessment. Although the judgments may

reflect a consensus (i.e., be used by many groups in a reasonably consistent manner), the resulting estimations of risk cannot be proven analytically. In other words, the estimates regarding risk involve uncertainty. The primary functional distinction between variability and uncertainty is that variability is expressed quantitatively, while uncertainty is generally expressed qualitatively.

In considering different forms of variability, almost no risk estimate presented in this document is given as a single number. Usually, risk is expressed as a central estimate and a range, which is sometimes very 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 the calculations are relatively simple, and the very simple calculations are included in the body of the document. Some of the calculations, however, are cumbersome. For those calculations, a set of worksheets is included as an attachment to the risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on non-target organisms.

2. PROGRAM DESCRIPTION

2.1. OVERVIEW

Imazapyr is classified as a broad-spectrum/non-selective herbicide used primarily in the control of a number of broadleaf weeds, grasses, and brush. As noted in section 4.1.2.4, however, different plant species may differ in their sensitivity to imazapyr by factors of 10 or greater and some plant species can develop resistance to imazapyr. The Forest Service may use four commercial formulations of imazapyr: Arsenal, Arsenal AC (applicators concentrate), Chopper, and Stalker, all of which are produced by American Cyanamid. The Arsenal, Chopper, and Stalker formulations contain imazapyr at 2 lb a.e./gallon. Arsenal AC is more concentrated (4 lbs a.e./gallon). Stalker contains imazapyr as the isopropylamine salt and the other formulations contain imazapyr as the isopropanolamine salt. The Arsenal formulations are aqueous solutions designed to be mixed with water and a surfactant. The Chopper and Stalker formulations are emulsifiable concentrates that can be mixed with diesel fuel, penetrating oils, or some other similar non-aqueous liquid and/or water.

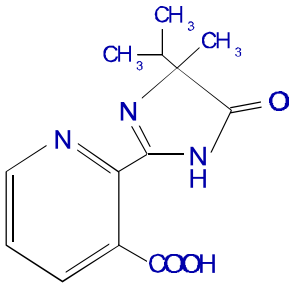
The Forest Service uses Arsenal AC almost exclusively in site preparation and conifer release. Minor uses for Arsenal AC include hardwood release, hardwood control, rights-of-way management, and wildlife site improvement. Arsenal is used in facilities and rights-of-way maintenance as well as wildlife openings. The Chopper may sometimes be used in rights-of-way maintenance and Stalker is generally used in cut stem or basal bark treatments.

Although imazapyr may be applied as the sole herbicide in some situations, it is more typically applied in combination with triclopyr in Forest Service programs. The most common methods of ground application for imazapyr formulations are cut-surface, backpack (selective foliar) and boom spray (broadcast foliar) operations. Although Arsenal and Arsenal AC are registered for aerial applications, the Forest Service does not typically use aerial applications. Nonetheless, aerial applications are included in this risk assessment.

The labeled application rates for imazapyr range from 0.25 to 2.5 lb a.e./acre. Typically, the Forest Service uses rates that are below the lower range of the recommended application rates. In 1997, application rates in Forest Service programs covered a narrow range: 0.08-0.2 lb a.e./acre with an average rate of about 0.15 lb a.e./acre. For this risk assessment, the typical rate of 0.15 lb a.e./acre with a lower range of 0.08 lb a.e./acre is used to reflect Forest Service practice. An upper range of 2.5 lb a.e./acre is used to assess the consequences of using the highest labeled rate should the Forest Service need to consider this option.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Imazapyr is the common name for 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylic acid:



Selected chemical and physical properties of imazapyr are summarized in Table 2-1. Additional information is presented in worksheet B03.

The Forest Service may use four commercial formulations of imazapyr: Arsenal, Arsenal AC (applicators concentrate), Chopper, and Stalker, all of which are produced by American Cyanamid. The Arsenal, Chopper, and Stalker formulations contain imazapyr 2 lb a.e./gallon. Arsenal AC is more concentrated (4 lbs a.e./gallon). Stalker contains imazapyr as the isopropylamine salt and the other formulations contain imazapyr as the isopropanolamine salt. Information on inerts in Arsenal formulations have been reviewed as part of this risk assessment (American Cyanamid. 1983a; Arendt and Comisky. 1995). This information is considered proprietary under FIFRA. Other than to state that no apparently hazardous materials have been identified, this information is not further detailed.

Arsenal is labeled for use only in non-crop areas to control a variety of grasses, broadleaf weeds, vines, and brush species. Recommended uses include the control of undesirable vegetation on rights-of-way, fence rows, storage areas, non-irrigation ditchbanks, wildlife openings, and the release of unimproved bermudagrass. Arsenal may not be used in crop areas and may not be directly applied to water. The uses for Arsenal AC are similar to those for Arsenal. Unlike Arsenal, however, Arsenal AC is labeled for forestry sites - i.e., land managed for timber production (C&P Press 1998). Chopper is also labeled for forestry uses including site preparation but is more typically used by the Forest Service in rights-of-way maintenance. Stalker is labeled for application as a spray to cut stumps or to the basal bark of brush and trees.

While imazapyr formulations can be used in pre-emergence applications, the most common and effective applications are post-emergent when the vegetation to be controlled is growing vigorously. As discussed further in section 4, imazapyr is absorbed from leaves, stems, and roots, and accumulates in meristematic tissue. Plant growth is inhibited shortly after treatment with discoloration initially evident on the newest leaves. In some plant species, obvious signs of damage may not be apparent for over two weeks. In postemergence applications, imazapyr requires the use of an adjuvant. Recommended adjuvants include silicone or nonionic surfactants as well as seed or vegetable oils.

2.3. APPLICATION METHODS

Detailed descriptions regarding the use of herbicides in silviculture and the various methods of herbicide application are available in the general literature [e.g., Cantrell and Hyland (1985)] and in earlier risk assessments conducted by the Forest Service (USDA 1989a,b,c). The following summary focuses on those aspects of application that are most relevant to the exposure assessments (sections 3.2 and 4.2).

The most common methods of ground application for Arsenal or Chopper formulations involve backpack (selective foliar) and boom spray (broadcast foliar) operations. In selective foliar applications, the herbicide sprayer or container is carried by backpack and the herbicide is applied to selected target vegetation. Application crews may treat up to shoulder high brush, which means that chemical contact with the arms, hands, or face is plausible. To reduce the likelihood of significant exposure, application crews are directed not to walk through treated vegetation. Usually, a worker treats approximately 0.5 acre/hour with a plausible range of 0.25-1.0 acre/hour.

Cut surface treatment methods may also be used by the Forest Service in applications of Stalker and Arsenal AC and could be used with other imazapyr formulations. These methods involve creating a cut surface on the tree by either cutting the tree down [cut stump treatment] or piercing the bark of a standing tree with a hatchet [hack and squirt] or an injector [injection]. The herbicide is then applied using a backpack sprayer [cut stump], squirt bottle [hack and squirt], or the injector itself [injection]. These treatments are used to eliminate large trees during site preparation, precommercial thinning, and release operations.

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

Arsenal is registered for aerial applications, fixed-wing or helicopter, and Arsenal AC is labeled for aerial applications, helicopter only (C&P Press 1998). In Forest Service programs, aerial applications for imazapyr are restricted to helicopter only. Arsenal is applied under pressure through specially designed spray nozzles and booms. The nozzles are designed to minimize turbulence and maintain a large droplet size, both of which contribute to a reduction in spray drift. In aerial applications, approximately 40-100 acres may be treated per hour.

Table 2-1: Identification and Physical/Chemical Properties of Imazapyr and the Monethanolamine salt of Imazapyr.		
Property	Value	Reference
Synonyms	Formulations: Arsenal, Arsenal AC, Chopper, Stalker, Truce	C&P Press 1998 Peoples 1984
CAS Number	081510-83-0 (isopropanolamine salt)	C&P Press 1998
EPA Registration Number	241-346	C&P Press 1998
MW $C_{13}H_{15}N_3O_3 \bullet C_3H_9N$	261 (acid) 320 (salt)	C&P Press 1998
Salt to acid conversion factor	0.816	[261÷320]
pK_a	1.9 and 3.6 1.81 and 3.64 1.9 (pyridine) and 3.6 (carboxylate)	American Cyanamide 1983b Chambarlain et al. 1995 Pusino et al. 1997
Water solubility	11,000 mg/L (acid) 13,100 mg/L(acid @ 25°C) 1%-1.5% (acid @ 25°C)	Knisel et al. 1992 Cortes. 1990 Peoples 1984
pH of formulation	6.6-7.2	C&P Press 1998
$K_{o/w}$ (acid) $K_{o/w}$ Log_{10} $K_{o/w}$ (neutral solution)	1.3 1.3 (0.7-1.6) 0.114	C&P Press 1998 Reichert and Stanley-Millner 1983 Chambarlain et al. 1995
Soil $t_{1/2}$ *Note: Persistence in soil is highly variable. See section 4.2.3.3 for discussion*	90 days 210 days (lab, aerobic) 138 days (field dissipation) 30 days 34-65 days 77-155 days	Knisel et al. 1992 American Cyanamid 1983b American Cyanamid 1983b Michael et al. 1996 Michael and Neary 1993 McDowell et al. 1996
Plant $t_{1/2}$	15-37 days (composite of different types of vegetation 30 days	Neary and Michael 1993 Knisel et al. 1992
Water $t_{1/2}$	28 days	American Cyanamid (1991)
$K_{o/c}$ (ml/g)	100 46	Knisel et al. 1992 Michael et al. 1996

2.4. MIXING AND APPLICATION RATES

The specific application rates used in a ground application vary according to local conditions and the nature of the target vegetation.

Arsenal - Application rates of 1-6 pints Arsenal/acre are recommended on the product label (C&P Press 1998). This is equivalent to ½ to 3 quarts Arsenal per acre or 0.125-0.75 gallons Arsenal per acre. Given that there is 2 lb a.e./gallon in Arsenal, these rates correspond to 0.25 to 1.5 lb a.e./acre. In rights-of-way application, the maximum recommended rate is 3 pints Arsenal/acre or 0.7 lbs a.e./acre. In low volume ground applications, Arsenal may be applied in 5 to 20 gallons of water per acre. High volume ground applications may involve up to 100 gallons of water per acre. In aerial applications, Arsenal should be applied in solutions that result in 5 to 30 gallons of water per acre (C&P Press 1998).

Arsenal AC - The product label for Arsenal AC recommends application rates of 10-40 oz/acre for site preparation, 4-20 oz/acre for conifer release, and 4-10 oz/acre for herbaceous weed control (C&P Press 1998). The overall range of 4-40 oz Arsenal AC/acre is equivalent to 0.0625-0.625 gallons Arsenal AC/acre. Given that there is 4 lb imazapyr a.e./gallon in Arsenal AC, these rates correspond to 0.25 to 2.5 lb a.e./acre. Arsenal AC is typically diluted with 5 to 100 gallons of water per acre in ground applications with high volume ground applications (75-100 gallons/acre) recommended for the control of kudzu. In aerial applications, Arsenal AC is diluted in 5 to 30 gallons of water per acre (C&P Press 1998).

Chopper - Chopper is an emulsifiable concentrate that may be mixed with water or diesel fuel and penetrating oils. In general, 48-80 ounces Chopper/acre are mixed with 25 or 50% (v/v) oil:water emulsion and applied in final spray volumes of 3-10 gallons per acre.

Stalker - Stalker is also an emulsifiable concentrate. Typically, Stalker is mixed with. In general, 8-12 ounces of Stalker are mixed with one gallon of water, diesel fuel or penetrating oils and applied as a spray to stumps, stubble, or basal bark.

For this risk assessment, the extent to which imazapyr formulations are diluted prior to application primarily influences dermal and direct spray scenarios, both of which are dependent on the 'field dilution' - i.e., the concentration of imazapyr in the applied spray. In all cases, the higher the concentration of imazapyr, the greater the risk. For this risk assessment, the lowest dilution will be taken at 5 gallons/acre. The highest dilution - i.e., that which results in the lowest risk - will be based on 20 gallons of water per acre. This is a conservative approach in that some applications of imazapyr formulations will involve more dilute solutions that consequently present a lesser risk. As detailed in sections 3 and 4, this conservative approach has relatively little impact on the characterization of risk.

The use of imazapyr by the Forest Service in 1997, the most recent year for which statistics are available, is summarized in Table 2-2. As indicated in this table, the Forest Service treated about 2000 acres with about 300 lbs of imazapyr as the only herbicide for an average application rate of

Table 2-2. Uses of imazapyr by the Forest Service in 1997 (USDA 1998).

Herbicide or Herbicide Mixture	Use	Acres Treated	Amount Used (lbs)	lbs/acre[1]
Imazapyr as sole herbicide	conifer release	1840	265	0.14
	hardwood release	198	16	0.08
	noxious weed control	56	9.25	0.2
	sole herbicide subtotal	2094	290.25	0.14
with fosamine ammonium	ROW management	10.9	70	
with triclopyr	conifer release	2458	1111.1	
	hardwood control	53.0	6.1	
	site preparation	5456	2427.8	
	mixture subtotal	7977.9		
Total (sole herbicide plus mixture subtotals)		10071.9		

[1] For imazapyr as the sole herbicide, this column is calculated at the total number of pounds used divided by the total number of acres treated - i.e., average application rate. For tank mixtures, the Forest Service statistics do not specify the amount or proportion of each herbicide in the mixture. Thus, average application rates for imazapyr with other herbicides are not calculated.

0.14 lbs/acre. About 90% [1840/2094=0.878] of acres treated with imazapyr only involved conifer release. By far the greatest use of imazapyr is in combination with triclopyr for site preparation and conifer release. These two uses account for about 80% [(2458+5456)/10,071.9 = 0.786] of the total acres treated with imazapyr in 1997. Thus, the primary use of imazapyr, either alone or in combination with triclopyr involves site preparation or conifer release, which account for about 97% of the acres treated with imazapyr by the Forest Service in 1997 [(1840+2458+5456)/10071.9 = 0.968].

For this risk assessment, application rates used to construct the various exposure scenarios range from 0.08 lb a.e./acre to 2.5 lb a.e./acre with a typical rate taken as 0.15 lb a.e./acre. The typical application rate is about the average application rate that the Forest Service used in 1997, when imazapyr was applied as the sole herbicide (see Table 2-2). Although this rate is less than the lower end of the labeled application rates, 0.25 lb a.e./acre, the rate of 0.15 lb a.e./acre is typical for most current Forest Service programs. As indicated in Table 2-2, this is about the average rate used on about 88% [1840 acres ÷ 2094 acres] of the acres treated by the Forest Service in 1997.

The lower limit of the application rate is taken as 0.08 lbs a.e./acre, the reported average application rate of imazapyr used by the Forest Service in 1997 for hardwood release.

The upper end of the range of application rates is taken as 2.5 lb imazapyr a.e./acre, the highest labeled application rate for any imazapyr formulation - i.e., Arsenal AC in site preparation for Loblolly pine and several other pine species. This rate is considered in this risk assessment simply to illustrate the consequences of using the highest rate but is far above the rate that the Forest Service is likely to use in any of its programs.

For ground applications, spray volumes of 20 gallons or more per acre are recommended. For this risk assessment, 20 gallons per acre is taken as the minimum spray volume. A spray volume of 40 gallons per acre is taken as an upper range. Based on these application rates and spray volumes, the typical field concentration - i.e., the concentration of imazapyr in solution after mixing and dilution - is taken as 0.6 mg/L with a range of 0.24 mg/L to 15 mg/L. These values are summarized in worksheet B02 and the calculations for these values are given in the detailed calculations that follow worksheet B01.

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview. Although no information is available on the toxicity of imazapyr to humans, the toxicity of imazapyr has been relatively well-characterized in mammals. All of this information is contained in unpublished studies that were submitted to the U.S. EPA as part of the registration process for imazapyr and were obtained and reviewed as part of this risk assessment.

Although the mode of action of imazapyr in humans or other mammals is unclear, this is at least partially a reflection of the apparently low and essentially undetectable acute and chronic systemic toxicity of this compound. The acute oral LD_{50} of unformulated imazapyr is greater than 5,000 mg/kg and the chronic dietary NOAEL for imazapyr is 10,000 ppm in dogs, rats, and mice. In the dog, this dietary concentration is equivalent to a daily dose of 250 mg/kg/day. In the other species, the equivalent daily doses are higher than 250 mg/kg/day. An adequate number of reproductive and developmental studies have been conducted and no adverse effects on reproductive capacity or normal development have been demonstrated. Tests of carcinogenic and mutagenic activity are consistently negative and the U.S. EPA has categorized the carcinogenic potential of imazapyr as *Class E: evidence of non-carcinogenicity*.

Two standard teratology studies report dose related increases in salivation in treated rats. While speculative and tenuous, this suggests that a possible neurologic involvement. In addition, Schwarcz et al. (1983) have noted that quinolinic acid, a photolytic breakdown product of imazapyr, causes neurotoxic effects at very low doses when injected directly into the brains of rats - i.e., intracerebral injection. There is no indication, however, that quinolinic acid is a mammalian metabolite of imazapyr. In addition, frank signs of neurotoxicity have not been noted in other studies on reproductive or developmental effects and neurotoxicity has not been noted in standard acute and chronic toxicity studies. Thus, the weight-of-evidence does not support the assertion that imazapyr is likely to have neurotoxic potential.

Increased food consumption during the conduct of chronic toxicity studies has been noted in male and female mice as well as female rats. It is unclear if this effect can be attributed to imazapyr and, if so, toxicologic significance of this effect is unclear.

There is no information suggesting that systemic toxic effects are plausible after dermal or inhalation exposures to imazapyr. Similarly, while the available data are limited, there is no basis for asserting that impurities or adjuvants in or metabolites of imazapyr are likely to impact the assessment of risk.

Imazapyr and imazapyr formulations can be mildly irritating to the eyes and skin. From a practical perspective, this is probably the effect that is most likely to be observed in the application of this compound if proper personal protection practices are not employed.

3.1.2. Acute Oral Toxicity. Little information is available on the acute toxicity of imazapyr to experimental mammals. As part of the pesticide registration process, an acute oral toxicity study is required. As summarized in appendix 1, single oral doses of 5000 mg/kg of a 2 lbs a.e./gallon formulation of imazapyr - corresponding to 25 mL formulation/kg body weight - was administered to groups of five male and female rats. Over the 14-day observation period, one male rat died. Abnormal findings in this rat included congestion of liver, kidney, and intestinal tract, as well as hemorrhagic lungs (Fischer 1983). All surviving rats showed no signs of toxicity. It is unclear if the death of the one male rat was associated with treatment. In a similar study using a mixture of imazapyr and a related herbicide, imazethapyr, at a total dose of 5000 mg/kg, no effects were noted (Lowe 1988). A review of unpublished studies of imazapyr sponsored by American Cyanamid (Peoples 1984) indicates that the oral LD_{50} of unformulated imazapyr - i.e., presumably technical grade imazapyr - is greater than 5000 mg/kg. No further information on the acute oral toxicity of imazapyr has been encountered in U.S. EPA's files on this compound or other reviews in the published literature (Cox 1996; Gagne et al. 1991).

3.1.3. Subchronic or Chronic Systemic Toxic Effects. Chronic toxicity studies on imazapyr have been conducted in three species: dogs (Shellenger 1987), mice (Auletta 1988), and rats (Daly 1988). These studies were submitted to the U.S. EPA in support of the registration of imazapyr, and none of the studies are published in the open peer-reviewed literature. In the preparation of this risk assessment, full copies of these studies were obtained from the U.S. EPA and reviewed (Appendix 1).

For the most part, these studies do not suggest any specific signs of frank toxicity at dietary concentrations of up to 10,000 ppm. In the rat feeding study (Daly 1988), a slight decrease in survivorship is apparent with increasing dose. Nonetheless, these changes are not statistically significant, using the Fischer exact test, at any of observation intervals - i.e., 6 months, 12 months, 18 months, and 24 months. The dietary NOAEL of 10,000 ppm from the one-year dog feeding study (Shellenger 1987) is used as the basis for the U.S. EPA's RfD, as discussed further in section 3.3.2. Based on individual food consumption data, the dietary level 10,000 ppm resulted in daily doses of about 1300 to 3149 mg/kg/day (Shellenger 1987).

The food consumption rates in the both the rat (Daly 1988) and mouse (Auletta 1988) studies are somewhat unusual. In both studies, there was a slight and in some cases statistically significant increase in food consumption. In many longer-term feeding studies, food consumption may decrease, either because of a toxic effect or simply because the food is not palatable to the test animals. While somewhat speculative, the increases in food consumption observed in rats and mice with imazapyr suggest that this substance may be palatable at least to these species. Alternatively, imazapyr has been implicated in the development thyroid tumors (section 3.1.5). While a detailed review of the carcinogenicity studies do not support the assertion that imazapyr is carcinogenic, changes in appetite could be associated with effects on the thyroid.

Two standard teratology studies in Charles River rats involving gavage administration (discussed further in the following section), reported dose related increases in salivation in treated dams

(Salamon et al. 1983a,b). Salivation can be a sign of a neurologic involvement (e.g., Anthony et al. 1996). This effect, however, was not reported in a dietary reproduction study involving Sprague-Dawley rats (Robinson 1987) and was not noted in any of the acute toxicity studies summarized in section 3.1.2 or in the chronic toxicity studies discussed above. Thus, while the results of Salamon et al. (1983a,b) are suggestive of a potential neurotoxic effect, this suggestion is not supported by the weight of the evidence.

3.1.4. Reproductive and Teratogenic Effects. As reviewed by Cox (1996), no studies on potential reproductive or teratogenic effects are available in the published literature. Nonetheless, several studies, summarized in appendix 1, on the reproductive effects of imazapyr in rats and rabbits have been conducted and submitted to the U.S. EPA in support of the registration of imazapyr. As with the chronic studies, full copies of these studies were obtained from the U.S. EPA and reviewed in the preparation of this risk assessment. These studies were also reviewed by the U.S. EPA (1997) in the derivation of the U.S. EPA/OPP RfD for imazapyr and were classified as acceptable and adequate. All of the studies are essentially negative. In other words, even at dose levels that cause signs of maternal toxicity, imazapyr does not cause adverse reproductive or developmental effects.

3.1.5. Carcinogenicity and Mutagenicity. The U.S. EPA (1997) has reviewed a number of assays for mutagenicity as well as chronic studies in mice (Auletta 1988) and rats (Daly 1988) that can be used to assess carcinogenic potential. Two gene mutation studies (*Salmonella typhimurium/Escherichia coli* and Chinese hamster ovary cell gene mutation) as well as one chromosomal aberration study (Chinese hamster ovary cells) were classified as acceptable and negative for potential mutagenic activity. An additional chromosomal aberration study (dominant lethal assay) was also negative but had been classified as inadequate because the complete spermatogenic cycle had not been evaluated. In a re-review of this study, however, the U.S. EPA (1997) has recommended that the study be upgraded to acceptable. Based on these studies, the U.S. EPA (1997) has categorized imazapyr as *CLASS E: evidence of non-carcinogenicity*.

As reviewed by Cox (1996), some of the observations from the chronic rat study (Daly 1988) raise concerns for potential carcinogenic activity. While this study was reviewed by the U.S. EPA (1997), it was further reviewed as part of this risk assessment.

As summarized in Table 3-1, microscopic pathology did reveal an increased incidence of C-cell carcinomas of the thyroid gland in male rats exposed to10,000 ppm for up to 2 years, compared with male rats in the middle dose, low dose (1000 ppm), and matched control (0 ppm) groups. Nonetheless, the incidences of C-cell carcinomas for all groups of male rats in the Daly (1988) study are within the range of the historical control data (13.7%) (Table 3-2), although the incidence in high dose male rats (7.69%) is almost twice the average incidence (4.10%) reported in the historical control data (Daly et al. 1988, 1991).

According to Daly (1988) and consistent with the interpretation of the U.S. EPA (1997), the increased incidence of C-cell carcinoma in the thyroid gland of high dose male rats is an incidental

Table 3-1: Incidence of proliferative lesions relative to matched controls (Daly 1988, 1991).

SEX	**MALES**			
Dietary Level (ppm)	0	1,000	5,000	10,000
Thyroid Gland (#examined)	65	65	63	65
C-cell hyperplasia	15 (23.10%)	8 (12.31%)	13 (20.63%)	6 (9.23%)
C-cell adenoma	2 (3.10%)	3 (4.62%)	9 (14.29%)	4 (6.15%)
C-cell carcinoma	1 (1.54%)	1 (1.54%)	1 (1.59%)	5 (7.69%)
C-cell adenoma and carcinoma	3 (4.62%)	4 (6.15%)	10 (15.87%)	9 (13.85%)
C-cell hyperplasia, adenoma and carcinoma combined	17 (26.15%)	12 (18.46%)	21 (33.33%)	15 (23.8%)

finding, based on the following observations: first, the combined incidences of C-cell adenoma and carcinoma in all male rats in the matched control study are within the range reported in the historical control data (17.14%); moreover, the incidences in the control (4.62%) and low dose (6.15%) groups are below the average incidence reported in the historical control data (9.13%); second, a comparison of the combined incidences of C-cell hyperplasia, adenoma, and carcinoma reveals higher than average incidences in the control (26.15%) and middle dose group (33.33%), compared with the historical data (25.71%), whereas the low dose (18.46%) and high dose (23.08%) groups fall within the range of the historical control data; and, finally, the overall incidences of C-cell proliferative lesions in the Daly (Daly 1988, Daly et al. 1991) study, in general, do not demonstrate a clear dose-response relationship or a clear progression from C-cell hyperplasia to adenoma to carcinoma (Table 3-1).

Support for this argument was provided by another pathologist hired by the sponsor of the study to review the data on 260 thyroid glands from male rats in the study. The consultant concludes that the difference in C-cell carcinomas between the treated and untreated rats is not statistically significant at $p<0.05$ and that the difference between the control and high dose male rats with respect to the incidence of C-cell carcinomas is of no biological significance because it is consistent with that reported in other studies conducted at the same laboratory as the Daly (1988) study and in studies published in the open literature. The apparent increase in the incidence of the C-cell carcinomas in the high dose males is viewed as a consequence of the "extremely low" incidence of C-cell carcinomas in the matched control group. Finally, in summarizing the

Table 3-2: Summary incidence of proliferative lesions/historical controls (Daly 1988) Thyroid gland - males (compiled from 14 studies conducted at Bio/dynamics, inc.)

No examined/lesion/percentage	Low	High	Mean Incidence of Historical Data
# examined	73	69	1413
C-cell hyperplasia	0	10	60
percentage	0	14.59	4.25
# examined	131	70	1413
C-cell adenoma	0	8	72
percentage	0	11.43	5.10
# examined	129	131	1413
C-cell carcinoma	0	18	58
percentage	0	13.74	4.10
# examined	54	70	1413
C-cell adenoma and carcinoma combined	0	12	129
percentage	0	17.14	9.13
# examined	54	70	1413
C-cell hyperplasia, adenoma and carcinoma combined	0	18	183
percentage	0	25.71	12.95

microscopic evaluation of the thyroid glands from rats exposed to 1000, 5000, or 10,000 ppm for up to 2 years, the consulting pathologist concluded that there is no evidence of treatment-related effects on the incidence or progression of proliferative lesions in the Daly (1988) study (i.e, no indication of a carcinogenic effect). Again, this is consistent with the interpretation by the U.S. EPA (1997) and is consistent with the available data from the study.

While it is impossible, by definition, to prove the negative, the available data appear to be of sufficient quality and detail to assert that no potential carcinogenic risk from exposure to imazapyr can be identified at this time.

3.1.6. Effects on the Skin and Eyes. Imazapyr and its formulations can be irritating to the eyes and skin. The published reviews on imazapyr (Cox 1996; Gagne et al. 1991; Peoples 1984) all appear to site the study on ocular and dermal toxicity (Fischer 1983) summarized in appendix 1. As with the previous section, this study was conducted and submitted to the U.S. EPA in support of the registration of imazapyr and a copy of the study was obtained from the U.S. EPA and reviewed in the preparation of this risk assessment. Other studies available from the U.S. EPA involve mixture of imazapyr and imazethapyr. These mixture studies, while summarized in appendix 1, are not further detailed in this risk assessment.

In a standard assay of skin irritation, an imazapyr formulation was classified as mildly irritating, causing redness in intact or abraded skin and edema (swelling) only in abraded skin. When the formulation was instilled directly into the eyes of rabbits, transient eye irritation was observed with complete recovery by day 7 after administration. The extent of irritation was substantially less in eyes that had been rinsed with water one hour after instillation of the imazapyr formulation (Fischer 1983).

3.1.7. Systemic Toxic Effects from Dermal Exposure. The available toxicity studies summarized in appendix 1 suggest that dermal exposure to 2000 mg/kg imazapyr was not associated with any signs of systemic toxicity in rabbits based on standard acute/single application bioassays with 14-day observation periods. It is not clear if the mottled and pale liver and congestion of the lungs, each observed in 1 of 9 rabbits after the dermal application of an imazapyr formulation, were incidental or treatment related. Effects on the lungs have been observed in rabbits after dermal application of a mixture of imazapyr and imazethapyr (Lowe 1988), but these effects were apparently due to a respiratory infection in the treated group rather than a direct effect of the imazapyr/imazethapyr mixture.

Although there are no data concerning the dermal absorption kinetics of imazapyr, dermal absorption is typically less rapid than absorption after oral exposure and dermal LD_{50}'s are typically higher than oral LD_{50}'s (e.g., Gaines 1969). Since the acute oral LD_{50} of imazapyr is more than 5000 mg/kg (Fischer 1983), the lack of apparent toxicity at dermal doses of up to 2000 mg/kg/day is to be expected and these studies add little to the assessment of risk for imazapyr after dermal contact.

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

As discussed in Durkin et al. (1995), dermal exposure scenarios involving immersion or prolonged contact with chemical solutions use Fick's first law and require an estimate of the permeability

coefficient, K_p, expressed in cm/hour. Because no kinetic data are available on the dermal absorption of imazapyr, the method for estimating a zero-order absorption rate (U.S. EPA 1992) is used in this risk assessment. Using this method, a dermal permeability coefficient for imazapyr is estimated at 0.000056 cm/hour with a 95% confidence interval of 0.000028-0.00011 cm/hour. These estimates are used in all exposure assessments that are based on Fick's first law. The calculations for these estimates are presented in worksheet B05.

For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the skin's surface, dermal absorption rates (proportion of the deposited dose per unit time) rather than dermal permeability rates are used in the exposure assessment. Using the methods detailed in Durkin et al. (1998), the estimated first-order dermal absorption coefficient is 0.0011 $hour^{-1}$ with 95% confidence intervals of 0.00044-0.0029 $hour^{-1}$. The calculations for these estimates are presented in worksheet B04.

3.1.8. Inhalation Exposure. Compared with oral exposure data, data regarding the inhalation toxicity of imazapyr are extremely limited. No toxic effects were observed during or after 4 hour exposures to either imazapyr or imazapyr an imazapyr formulations at aerosol concentrations of >5 mg/L (Peoples 1984).

Although inhalation of imazapyr is not a typical route of exposure, it may occur during brown-and-burn operations. The post-treatment burns in brown-and-burn operations are conducted 45–180 days after treatment with the herbicide. McMahon and Bush (1992) found no detectable levels of imazapyr in the breathing zone of workers during brown-and-burn operations in plots that had been treated with imazapyr at application rates of up to 3.5 L/ha [0.92 gal/ha or 1.84 lbs imazapyr a.e./ha or about 0.77 lb a.e./acre].

3.1.9. Impurities, Adjuvants, and Metabolites.

3.1.9.1. Impurities **--** No information has been encountered in the published or unpublished literature on impurities in imazapyr. Virtually no chemical synthesis yields a totally pure product. Technical grade imazapyr, as with other technical grade products, undoubtedly contains some impurities. To some extent, concern for impurities in technical grade imazapyr is reduced by the fact that the existing toxicity studies on imazapyr were conducted with the technical grade product. Thus, if toxic impurities are present in the technical grade product, they are likely to be encompassed by the available toxicity studies on the technical grade product.

3.1.9.2. Metabolites **--** The metabolism and kinetics of imazapyr has been studied in rats (Mallipudi et al. 1983a) and lactating goats (Zdybak 1992). In rats, ^{14}C-imazapyr labeled on the carboxy group, dissolved in ethanol/water, was administered to 15 Sprague Dawley males (225 g) by gavage at a dose of 4.4 mg/kg. Imazapyr was excreted in the urine and feces, 87.2% and 93.3% of the administered dose by days 1 and 2 respectively after dosing. Approximately 98% of the administered dose was recovered in the urine and feces after 8 days. No metabolites were identified (Mallipudi et al. 1983a) . A similar pattern was noted in lactating goats administered ^{14}C-imazapyr acid in gelatin capsules in amounts equivalent to dietary exposures of 0, 17.7, or

42.5 ppm for 7 days. Most of the radioactivity, 60-65% of the administered dose, was excreted in the urine.

The only other metabolism study on imazapyr was conducted on white leghorn chickens (Tsalta 1995). As with the mammalian studies, the only significant component in excreted residues was the parent compound - i.e., imazapyr.

These studies do not rule-out the formation of minor metabolites. Nonetheless, there is no basis for asserting that metabolites may be formed that would have any substantial impact on this risk assessment.

3.1.9.3. Adjuvants -- As noted in section 2, information on inerts in imazapyr formulations have been reviewed as part of this risk assessment. Specific notes are included in appendix 1 concerning those toxicity studies in which information on inerts is specified. This information, however, is considered proprietary under FIFRA. Other than to state that no apparently hazardous materials have been identified, this information cannot be detailed.

All of the technical formulations of imazapyr covered in this risk assessment involve the isopropyl or isopropanolamine salts of imazapyr. Little toxicity information is available on these compounds. Isopropanolamine is classified by the U.S. EPA (1998) as a List 3 inert. These are compounds that the U.S. EPA cannot classify as hazardous or non-hazardous based on the available information. Similarly, for some of the other inerts used in imazapyr formulations, the toxicity data are limited. This lack of information adds uncertainty to this risk assessment. The minimal testing requirements for compounds that have been used as inerts or adjuvants for many years is a general problem in many pesticide risk assessments. For new inerts, the U.S. EPA does require more extensive testing (Levine 1996). Notwithstanding this uncertainty, none of the inerts used in any of the imazapyr formulations have been classified by the U.S. EPA as hazardous (List 1 or List 2).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. Both workers and member of the general public are considered in this exposure assessment. No occupational exposure studies are available in the literature that involve the application of imazapyr. Consequently, worker exposure rates are estimated from an empirical relationship between absorbed dose per kilogram of body weight and the amount of chemical handled in worker exposure studies on nine different pesticides (Rubin et al. 1998). Separate exposure assessments are given for backpack and boom spray ground applications as well as for aerial applications. For all three groups, the central estimates of exposure are similar: 0.0020 mg/kg/day for backpack workers, 0.0034 mg/kg/day for boom spray applicators, and 0.0023 mg/kg/day for aerial applicators including pilots and mixer/loaders. The upper limits of exposure are higher for ground applications, 0.2 to 0.38 mg/kg/day, than for aerial applications (0.012 mg/kg/day). The lower estimates of exposure are less than 0.00006 mg/kg/day for all three groups. 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 sprayers). It seems that much of the variability can be attributed to the hygienic measures taken by individual workers (i.e., how careful the workers are to avoid unnecessary exposure).

For the general public, all of the chronic or longer term exposure scenarios lead to levels of exposure that are below those for workers. The highest dose associated with any of the longer term exposure scenarios for the general public involves the consumption of contaminated fruit with exposure estimates of 0.00079 (0.00036 to 0.15) mg/kg/day. The accidental exposure scenario involving the consumption of contaminated water results in a central estimate of exposure of up to 0.034 mg/kg/day with an upper range of 1.28 mg/kg/day. The other accidental exposure scenarios for the general public result in central estimates of dose from 0.0002 to 0.005 mg/kg/day with estimates of the upper ranges of exposure between 0.016 and 0.16 mg/kg/day. All of the accidental exposure scenarios involve relatively brief periods of exposure and most should be regarded as extreme, some to the extent of limited plausibility.

3.2.2. Workers. A summary of the exposure assessments for workers is presented in Table 3-3. Two types of exposure assessments are considered: general and accidental/incidental. The term *general* exposure assessment is used to designate those exposures that involve estimates of absorbed dose based on the handling of a specified amount of a chemical during specific types of applications. The accidental/incidental exposure scenarios involve specific types of events that could occur during any type of application. Details regarding all of these exposure assessments are presented in the imazapyr worksheets that accompany this risk assessment, as indicated in Table 3-3. In Table 3-3 and other similar tables presented below, numbers greater than or equal to 0.0001 are expressed in standard decimal notation. Smaller numbers are expressed in scientific notations, such as 7e-07 which is equivalent to 7×10^{-7} or 0.0000007. Details of the conversion of scientific to decimal notation are given on page ix of this report.

3.2.2.1. General Exposures **--** As outlined in the program description (see chapter 2), this risk assessment is concerned primarily with backpack and boom spray ground applications. Nonetheless, imazapyr formulations are labeled for aerial applications and the Forest Service may consider aerial applications in some program activities. Consequently, aerial applications are considered in this risk assessment.

Table 3-3: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.002	4e-05	0.2	WSC01a
Broadcast ground spray (Boom spray)	0.0034	5e-05	0.38	WSC01b
Aerial applications	0.0023	4e-05	0.012	WSC01c
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	7e-06	1.4e-06	0.000333	WSC02
Contaminated Gloves, 1 hour	0.0004	8.2e-05	0.01998	WSC02
Spill on hands, 1 hour	7e-05	1.0e-05	0.0042	WSC03
Spill on lower legs, 1 hour	0.00016	2.50e-05	0.0103	WSC03

No worker exposure studies with imazapyr were found in the literature. Consequently, the exposure estimates are based on empirical relationships between the amount of the chemical that is handled and absorbed dose (Rubin et al. 1998). The specific assumptions used in worker exposure assessments for backpack, boom spray, and aerial applications are detailed in worksheets C01a through C01c.

As described in Rubin et al. (1998), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. These exposure rates are based on worker exposure studies on nine different pesticides with molecular weights ranging from 221 to 416 and log K_{ow} values at pH 7 ranging from -0.75 to 6.50. The estimated exposure rates are based on estimated absorbed doses in workers as well as the amounts of the chemical handled by the workers (Rubin et al. 1998, Table 2). As summarized in Table 2-1 of this risk assessment on imazapyr, the molecular weight of imazapyr is 261 and the log K_{ow} in a neutral solution is 0.114. Thus, the molecular weight and K_{ow} of imazapyr is in the range of values used in the analysis by Rubin et al. (1998).

As further described in Rubin et al. (1998), 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 sprayers). It seems that much of the variability can be attributed to the hygienic measures taken by individual workers (i.e., how careful the workers are to avoid unnecessary exposure).

The estimated number of acres treated per hour is taken from previous USDA risk assessments (USDA 1989a,b,c). The number of hours worked per day is expressed as a range, the lower end of which, 6 hours per day, is based on an 8-hour work day with 1 hour at each end of the work day spent in activities that do not involve herbicide exposure. The upper end of the range, 8 hours per day, is based on an extended (10-hour) work day, allowing for 1 hour at each end of the work day to be spent in activities that do not involve herbicide exposure.

It is recognized that the use of 6 hours as the lower range of time spent per day applying herbicides is not a true lower limit. It is conceivable and perhaps common for workers to spend much less time in the actual application of a herbicide if they are engaged in other activities. Thus, using 6 hours can be regarded as conservative. In the absence of any published or otherwise documented work practice statistics to support the use of a lower limit, this conservative approach is used.

The range of acres treated per hour and hours worked per day is used to calculate a range for the number of acres treated per day. For this calculation as well as others in this section involving the multiplication of ranges, the lower end of the resulting range is the product of the lower end of one range and the lower end of the other range. Similarly, the upper end of the resulting range is the product of the upper end of one range and the upper end of the other range. This approach is taken to encompass as broadly as possible the range of potential exposures.

The central estimate of the acres treated per day is taken as the arithmetic average of the range. Because of the relatively narrow limits of the ranges for backpack, boom spray, and aerial applications, the use of the arithmetic mean rather than some other measure of central tendency such as the geometric mean has no marked effect on the risk assessment.

The range of application rates, 0.08 lb a.e./acre to 2.5 lb a.e./acre, and the typical application rate, 0.15 lb a.e./acre, are taken directly from the program description (see section 2.4). The central estimate of the amount handled per day is calculated as the product of the central estimate of the acres treated per day and the typical application rate. The ranges for the amounts handled per day are calculated as the product of the range of acres treated per day and the range of application rates. Similarly, the central estimate of the daily absorbed dose is calculated as the product of the central estimate of the exposure rate and the central estimate of the amount handled per day. The ranges of the daily absorbed dose are calculated as the product of the range of exposure rates and the range for the amounts handled per day.

3.2.2.2. Accidental/Incidental Exposures **--** Typical occupational exposures may involve multiple routes of exposure (i.e., oral, dermal, and inhalation); nonetheless, dermal exposure is generally the predominant route for herbicide applicators (van Hemmen 1992). Typical multi-route exposures are encompassed by the methods used in section 3.2.2.1 on general exposures. Accidental exposures, on the other hand, are most likely to involve splashing a solution of herbicides into the eyes or a variety of dermal exposure scenarios.

Imazapyr can cause irritant effects in the skin and eyes (see section 3.1.6). Quantitative methods for characterizing exposures or responses associated with incidents such as splashing a solution of a chemical into the skin or eyes have not been encountered. Consequently, accidental exposure scenarios of this type are considered qualitatively in the risk characterization (section 3.4).

There are various methods for estimating absorbed doses associated with accidental dermal exposure (U.S. EPA 1992, Durkin et al. 1995,1998) which can in turn be used to estimate the potential for systemic toxic effects. Two general types of exposure are modeled: those involving direct contact with a solution of the herbicide and those associated with accidental spills of the herbicide onto the surface of the skin. Any number of specific 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 surface of the skin and by varying the surface area of the skin that is contaminated.

For this risk assessment, 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. Details of these exposure estimates are presented in the worksheets appended to this risk assessment as specified in Table 3-3.

Exposure scenarios involving direct contact with solutions of the chemical are characterized by immersion of the hands for 1 minute and wearing contaminated gloves for 1 hour. Generally, it is not reasonable to assume or postulate that the hands or any other part of a worker will be immersed in a solution of a herbicide for any period of time. On the other hand, contamination of gloves or other clothing is quite plausible. For these exposure scenarios, the key element is the assumption that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in a solution. In either case, the concentration of the chemical in solution that is in contact with the surface of the skin and the resulting dermal absorption rate are essentially constant.

For both scenarios (the hand immersion and the contaminated glove), the assumption of zero-order absorption kinetics is appropriate. Following the general recommendations of U.S. EPA (1992), Fick's first law is used to estimate dermal exposure.

Exposure scenarios involving chemical spills on to the skin are characterized by a spill on to the lower legs as well as a spill on to the hands. In these scenarios, it is assumed that a solution of the chemical is spilled on to a given surface area of skin and that a certain amount of the chemical

adheres to the skin. The absorbed dose is then calculated as the product of the amount of the chemical on the surface of the skin (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 concentration of the chemical in the liquid), the first-order absorption rate, and the duration of exposure. For both scenarios, it is assumed that the contaminated skin is effectively cleaned after 1 hour. As with the exposure assessments based on Fick's first law, this product (mg of absorbed dose) is divided by body weight (kg) to yield an estimated dose in units of mg chemical/kg body weight. The specific equation used in these exposure assessments is taken from Durkin et al. (1998).

Confidence in these exposure assessments is diminished by the lack of experimental data on the dermal absorption of imazapyr. In addition, the exposure scenario in which contaminated gloves are worn for 1 hour is similar to the exposure scenario in which a chemical solution is spilled on to the skin surface of the hands and cleaned after 1 hour. As indicated in Table 3-3, the central estimates as well as the upper and lower ranges of exposure for the spill scenario is about a factor of 10 lower than the immersion/gloves scenario. This inconsistency between these two similar scenarios further diminishes confidence in these exposure assessments. Nonetheless, as detailed in section 3.4 (risk characterization), these dose estimates are all at least a factor of 100 below the level of concern. Thus, even very large errors in the estimates have little impact on the characterization of risk.

3.2.3. General Public.

3.2.3.1. General Considerations **--**Under normal conditions, members of the general public should not be exposed to substantial levels of imazapyr. Nonetheless, any number of exposure scenarios can be constructed for the general public, depending on various assumptions regarding application rates, dispersion, canopy interception, and human activity. Several highly conservative scenarios are developed for this risk assessment.

The two types of exposure scenarios developed for the general public include acute exposure and longer-term or chronic exposure. All of the acute exposure scenarios are primarily accidental. They assume that an individual is exposed to the compound either during or shortly after its application. Specific scenarios are developed for direct spray, dermal contact with contaminated vegetation, as well as the consumption of contaminated fruit, water, and fish. Most of these scenarios should be regarded as extreme, some to the point of limited plausibility. The longer-term or chronic exposure scenarios parallel the acute exposure scenarios for the consumption of contaminated fruit, water, and fish but are based on estimated levels of exposure for longer periods after application.

The exposure scenarios developed for the general public are summarized in Table 3-4. As with the worker exposure scenarios, details of the assumptions and calculations involved in these exposure assessments are given in the worksheets that accompany this risk assessment (worksheets D01-D09). The remainder of this section focuses on a qualitative description of the rationale for and quality of the data supporting each of the assessments.

Table 3-4: Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00246	0.000383	0.158	WSD01
Direct spray, lower legs	Woman	0.000247	0.0000385	0.0159	WSD02
Dermal, contaminated vegetation	Woman	0.00445	0.000870	0.2447	WSD03
Contaminated fruit, acute exposure	Woman	0.0016	0.00085	0.124	WSD04
Contaminated water, acute exposure	Child	0.034	0.0083	1.28	WSD06
Consumption of fish, general public	Man	0.001	0.00041	0.0256	WSD08
Consumption of fish, subsistence populations	Man	0.005	0.00198	0.125	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.00079	0.00036	0.075	WSD05
Consumption of water	Man	0.00035	1.76e-05	0.0369	WSD07
Consumption of fish, general public	Man	1.76e-06	1.26e-07	0.00243	WSD09
Consumption of fish, subsistence populations	Man	1.42e-05	1.02e-06	0.01183	WSD09

3.2.3.2. Direct Spray **--** Direct sprays involving ground applications are modeled in a manner similar to accidental spills for workers (see 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. As with the similar worker exposure scenarios, the first-order absorption kinetics are estimated from the empirical relationship of first-order absorption rate coefficients to molecular weight and octanol-water partition coefficients (Durkin et al. 1998), as defined in worksheet A07a.

For these exposure scenarios, it is assumed that during a ground application, a naked child is sprayed directly with imazapyr. These scenarios also assume that the child is completely covered (that is, 100% of the surface area of the body is exposed). These are extremely conservative exposure scenarios and are likely to represent upper limits of plausible exposure. An additional

set of scenarios are included involving a young woman who is accidentally sprayed over the feet and legs. For each of these scenarios, some assumptions are made regarding the surface area of the skin and body weight, as detailed in worksheet A04.

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 an individual comes in contact with sprayed vegetation or other contaminated surfaces at some period after the spray operation.

For these exposure scenarios, some estimates of dislodgeable residue and the rate of transfer from the contaminated vegetation to the surface of the skin must be available. No such data are directly available for imazapyr, and the estimation methods of Durkin et al. (1995) are used as defined in worksheet D03. Other estimates used in this exposure scenario involve 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 -- Water can be contaminated from runoff, as a result of percolation through contaminated soil into ground water, from a direct spill, or from unintentional contamination from aerial applications. As indicated in Table 2-2, imazapyr is highly soluble in water (about 13,000/mg/L) and has a very low octanol/water partition coefficient - i.e., it will tend to remain in water rather than partition to soil or be absorbed by fish. Imazapyr is also chemically stable in water over a pH range from 5 to 9 (Peoples 1984). At pH 9, the reported halftime of imazapyr in water is 325 days (American Cyanamid 1983b). Very little information is available on the microbial breakdown of imazapyr in water other than that imazapyr is poorly metabolized in water by *Streptomyces* species (Shelton et al. 1996).

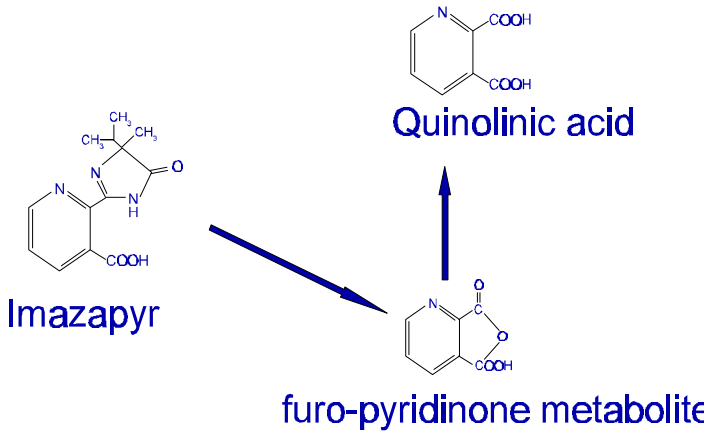


Figure 3-1: Major photolytic breakdown products of imazapyr (American Cyanamid, 1991).

The major mechanism for the breakdown imazapyr in water appears to be photolysis. Based on studies conducted in both pond water and sediments, there appear to be at least 25 photolytic breakdown products of imazapyr. The major breakdown products are quinolinic acid and a furo(3,4-b)pyridin-5(7H)-one-7-hydroxy compound (Figure 3-1). Quinolinic acid is a natural metabolite of the amino acid tryptophan and has been shown to cause damage to nerve tissue after intracerebral injection - i.e., direct injection into the brain (Schwarcz et al. 1983). Nonetheless, the oral LD_{50} of each of these compounds is >5000 mg/kg in male and

female rats. (American Cyanamid 1991). In addition, these breakdown products of imazapyr are not persistent in water (appendix 5).

Information on the identity and toxicity of other photolytic breakdown products of imazapyr has not been encountered. While this adds uncertainty to the risk assessment, there is no basis for asserting or suspecting that the photolytic breakdown products of imazapyr are sufficiently toxic or persistent to alter the characterization of risk for imazapyr.

For this risk assessment, the two types of estimates made for the concentration of imazapyr in ambient water are acute/accidental exposure and longer-term exposure. The accidental exposure scenario is based on a spill of a fixed amount of imazapyr into a body of water of a fixed size assuming instantaneous mixing. The longer-term exposure scenario is based on monitoring data that can be used to associate the application rate of imazapyr with imazapyr concentrations in ambient water.

3.2.3.4.1. ACUTE EXPOSURE **--** As detailed in worksheet D06, the acute exposure scenario assumes that a young child (2- to 3-years old) consumes 1 L of contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation of imazapyr is considered.

This is an extremely conservative scenario dominated by arbitrary variability. The actual concentrations in the water would depend heavily on 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 that is consumed.

As indicated in Table 3-4, there is about a 150-fold difference in the upper and lower limits of the exposure assessment - i.e., 0.0083 mg/kg/day to 1.28 mg/kg/day. As detailed in worksheet D06, this wide range is attributable primarily to the differences in field concentrations (a factor of about 60) which is in turn attributable to the range in application rates (a factor of about 30 as detailed in worksheet D05). Differences in the estimated amounts of water that might be consumed (a factor of only about 2.5) have relatively little impact on the exposure estimate.

Since the Forest Service is not likely to use an application rate that approaches 2.5 lb. a.e./acre, the estimated dose of 1.28 mg/kg/day is higher than any level that might be seen in Forest Service sponsored programs.

3.2.3.4.2. LONGER-TERM EXPOSURE -- The scenario for chronic exposure to imazapyr from contaminated water is detailed in worksheet D07. This scenario assumes that an adult (70 kg male) consumes contaminated ambient water for a lifetime.

Monitoring data from the review by Neary and Michael (1996) are the most relevant for estimating longer-term levels in ambient water after the application of imazapyr. Additional details are taken from Michael and Neary (1993). Neary and Michael (1996) summarize data on four applications of imazapyr, two conducted in Alabama (Michael and Neary (1993) and two conducted in Washington state (Rashin and Graber 1993).

In the Michael and Neary (1993) study, a liquid formulation of imazapyr was applied at a rate of 2.2 kg a.i./ha, which is equivalent to 1.96 lbs a.i./acre. While Michael and Neary (1993) do not specify the formulation, they indicate that it was a formulation produced by American Cyanamid. Thus, it will be assumed that an Arsenal formulation of the isopropylamine salt of imazapyr was applied. Consequently, correcting for differences in molecular weight (Table 2-1), an application rate of 1.96 lbs a.i./acre corresponds to 1.59 lbs a.e./acre [1.96 lbs a.i. × (MW acid 261÷MW 320 salt)].

The broadcast aerial applications were made in two similar watersheds in Alabama (designated as Sites 12 and 13 in Michael and Neary (1993). At one site (13), a buffer zone was maintained along streams. The maximum surface water concentration in the site with the buffer zone was 130 µg/L, whereas the maximum surface water concentration in the site without the buffer zone (site 12) was 680 µg/L (Michael and Neary 1993, Table 3, p.407). The maximum levels of imazapyr occurred as a pulse immediately after a 30 mm rainfall and decreased to trace or non-detectable levels within 9 hours. Subsequent rainfalls of (>10 mm) resulted in maximum imazapyr concentrations of 6 µg/L which decreased to non-detectable or trace levels within 1.5 hours.

The study by Rashin and Graber (1993) involved the aerial application of imazapyr at 0.1 a.i. kg/ha or 0.0892 lb a.i./acre to two watersheds in Washington state. Again correcting for molecular weight, this application rate corresponds to 0.082 lb a.e./acre [0.0892 lbs a.i. × (MW acid 261÷MW 320 salt)]. At both sites, buffer zones were used around surface water and the maximum concentrations detected in surface water was 1 µg/L at both sites. It is not clear from the review by Neary and Michael (1996) if this concentration was an actual maximum observed measurement or simply represented the limit of detection. For this risk assessment, the conservative assumption will be made that these were observed values.

For this risk assessment, the maximum concentration reported by Michael and Neary (1993) at the site with the buffer zone, 130 µg/L, is used as the basis for the central estimate of imazapyr in surface water. The upper limit of the estimated amount in surface water is taken from the site in which no buffer zone was used. The lower limit on the concentration of imazapyr in surface water is taken from the study by Rashin and Graber (1993). In the exposure assessment, these values are normalized for application rate - i.e., the concentration in water anticipated at an application rate of 1 lb a.e./acre. The central estimate is 0.082 mg/L÷lb a.e./acre with a range of 0.011 to 0.43 mg/L÷lb a.e./acre (worksheet B07).

For comparison, imazapyr concentrations in ambient water can be estimated using the GLEAMS model (Knisel et al. 1992). Details of the application of this model to estimating imazapyr runoff

and percolation are provided in Appendix 5. The basic exposure scenario assumes that imazapyr is applied along a ten acre right-of-way that is 50 feet wide and 8712 feet long. It is also assumed that a body of water runs along the length of the right-of-way and that the slope toward the water is 10 percent. Two types of soils are modeled: clay (high runoff potential) and sand (low runoff potential). Annual rainfall rates ranging from 5 to 250 inches are used to reflect the variability of regional rainfall rates based on statistics from the U.S. National Weather Service (1998) for 152 cities in 45 states covering the period from 1961 to 1990. Average annual rainfall ranged from a low of 0.3 inches (lower range for Yuma, Arizona) to 172.2 inches (upper range for Yakutat, Alaska) with a average annual rainfall of 27.69 inches. For both clay and sand, the specific model parameters are selected to yield central estimates of pesticide runoff and percolation.

As detailed in Appendix 5 (section A5.2), runoff or percolation of imazapyr into ground or surface water from clay or sand is not likely in relatively arid areas - i.e., annual rainfall of less than 10 inches. Because of the general rather than site-specific nature of the GLEAMS modeling, however, some loss could occur in arid areas during unusually severe rainfalls, at least at sites with high runoff or leaching potential. For clay soils in areas of extremely high rainfall - i.e., approaching 200 to 250 inches per year - annual runoff could range up to about 30% of the applied amount but no percolation into ground water would be expected. In sandy soil, on the other hand, no runoff is estimated under any modeled conditions. Percolation below 3 feet over a one year period, however, could reach up to 80% of the applied amount in sandy soil at annual precipitation rates of 200 to 250 inches.

Estimates of the concentrations of imazapyr in a 1 meter deep pond, detailed in appendix 5, section A5.3, are based on the typical application rate of 0.15 lb a.e./acre, a measured halftime of about 28 days for imazapyr and its photolytic breakdown products in pond water (American Cyanamid 1991), and the assumptions that imazapyr in both runoff and percolation are transported directly to the pond. At an annual rainfall of 100 inches, about a factor of 3 above the national average, peak concentrations in pond water are about 0.017 mg/L for runoff from clay and 0.06 mg/L for percolation through sand. Normalized for an application rate of 1 lb a.e./acre - i.e., dividing by 0.15 lb a.e./acre - these correspond to rates of about 0.1 to 0.4 mg a.e./L per lb a.e./acre. This range of modeled values encompass the central to upper range of the estimates based on monitoring data - i.e., 0.082 (0.011 to 0.43) mg/L per lb a.e./acre as discussed above and detailed in worksheet B07. At an annual rainfall rate of 25 inches, somewhat below the national average, peak concentrations in pond water range from about 0.005 mg/L (runoff from clay) to 0.055 mg/L (percolation through sand), which normalize to about 0.03 to 0.36 mg/L per lb a.e./acre, very close to the estimates based on the monitoring data. The concordance between the monitoring data and modeled estimates enhances confidence in the exposure assessment.

Although the estimates of exposure based on monitoring data are used for the longer-term exposure scenario for humans, it is implausible to suggest that these concentrations would be maintained for prolonged periods of time. For the characterization of potential human health effects (section 3.4), the issue of persistence makes no difference because the peak exposure levels are far below those of toxicological concern. A fuller use of the modeled estimates and

monitoring studies, however, is required for the assessment of toxicological effects on aquatic vegetation, as discussed in section 4.2.3.

3.2.3.5. Oral Exposure from Contaminated Fish **--** Chemicals that are highly soluble in fat or fatty substances tend to be concentrated or partitioned from water into the tissues of animals or plants in the water. 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]. Details regarding the relationship of bioconcentration to standard pharmacokinetic principles are provided in Calabrese and Baldwin (1993).

As part of the registration process, experimental bioconcentration factors are required and one such study has been submitted to U.S. EPA (McAllister et al. 1985). McAllister et al. (1985) exposed bluegill sunfish to 14C-labeled imazapyr for 28 days and found no indication of bioconcentration. The measured bioconcentration factor was less than 0.5. In other words, the concentration of imazapyr in the fish was less than the concentration of imazapyr in the water. As summarized in worksheet B03, this is close to a calculated BCF of about 1.5 for fish muscle based the octanol/water partition coefficient of imazapyr. For exposure assessments based on the consumption of contaminated fish, a BCF of 1 is used (i.e., the concentration in the fish will be equal to the concentration in the water). This is mid-range between the measured value from McAllister et al. (1985) and the calculated BCF from worksheet B03. As summarized in the risk characterization (section 3.4), these relatively minor variations in BCFs have no impact on this risk assessment.

For both the acute and longer-term exposure scenarios involving the consumption of contaminated fish, the water concentrations of imazapyr used are identical to the concentrations used in the contaminated water scenarios (see section 3.2.3.4). The acute exposure scenario is based on the assumption that an adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. No dissipation or degradation is considered. Because of the available and well-documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations (U.S. EPA 1996), separate exposure estimates are made for these two groups, as illustrated in worksheet D08. The chronic exposure scenario is constructed in a similar way, as detailed in worksheet D09, except that estimates of imazapyr concentrations in ambient water are based on the monitoring data from Neary and Michael (1996).

3.2.3.6. Oral Exposure from Contaminated Vegetation **--** None of the Forest Service applications of imazapyr will involve the treatment of crops. Thus, under normal circumstances and in most types of applications conducted as part of Forest Service programs, the consumption of vegetation contaminated with imazapyr is unlikely. Nonetheless, any number of scenarios could be developed involving either accidental spraying of crops or the spraying of edible wild

vegetation such as berries. Again, in most instances and particularly for longer-term scenarios, treated vegetation would probably show signs of damage from exposure to imazapyr (section 4.3.2.4), thereby reducing the likelihood of consumption that would lead to significant levels of human exposure.

Notwithstanding that assertion, it is conceivable that individuals could consume contaminated vegetation. One of the more plausible scenarios involves the consumption of contaminated berries after treatment of a right-of-way or some other area in which wild berries grow. The two accidental exposure scenarios developed for this exposure assessment include one scenario for acute exposure (worksheet D04) and one scenario for longer-term exposure (worksheet D05). In both scenarios, the concentration of imazapyr on contaminated vegetation is estimated using the empirical relationships between application rate and concentration on vegetation developed by Hoerger and Kenaga (1972). These relationships are defined in worksheet A05a. For the acute exposure scenario, the estimated residue level is taken as the product of the application rate and the residue rate given in worksheet A05a.

For the longer-term exposure scenario, a duration of 90 days is used - i.e., a fruit bearing plant is treated on day 0 and consumed by an individual over a 90-day post-treatment period. For this exposure scenario, an estimate is needed of the residues on the day of treatment as well as the rate of decrease in the residues over time. For this exposure assessment, estimates of halftimes in vegetation are taken from Michael and Neary (1993), who report a range of halftimes from 15 to 37 days. This range is used as the upper and lower limit and the arithmetic mean, 26 days, is taken as the central estimate.

For the acute exposure scenario, it is assumed that a woman consumes 1 lb (0.4536 kg) of contaminated fruit. Based on statistics summarized in U.S. EPA (1996) and presented in worksheet D04, this consumption rate is approximately the mid-range between the mean and upper 95% confidence interval for the total vegetable intake for a 64 kg woman. The range of exposures presented in Table 3-4 is based on the range of concentrations on vegetation from Hoerger and Kenaga (1972) and the range of application rates for imazapyr. The longer-term exposure scenario is constructed in a similar way, except that the estimated exposures include the range of vegetable consumption (U.S. EPA 1996) as well as the range of concentrations on vegetation, the range of application rates for imazapyr, and the range of the halftimes on vegetation.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The dose-response assessment for imazapyr is relatively straightforward and the toxicity data base is reasonably complete and unambiguous. The U.S. EPA has derived an RfD of 2.5 mg/kg/day using a dog NOAEL of 250 mg/kg/day and an uncertainty factor of 100. The NOAEL selected by the U.S. EPA appears to be the most appropriate and is supported by additional NOAELs in rats and mice as well as a number of studies on potential reproduction and developmental effects.

3.3.2. Existing Guidelines. The U.S. EPA has not derived an agency-wide RfD for imazapyr. Nonetheless, the Office of Pesticide Programs of the U.S. EPA has derived an RfD of 2.5 mg/kg/day (U.S. EPA 1997). The RfD is based on a study in which groups of male and female dogs were administered imazapyr in the diet for one year at concentrations of 0, 1000, 5000, or 10,000 ppm (Shellenger 1987). As discussed in section 3.1.3, no adverse effects attributable to treatment were noted in any treatment group. The highest dietary concentration corresponded to reported daily doses of 262.88 and 269.80 in male and female dogs, respectively. These doses were rounded to 250 mg/kg/day. In deriving the RfD, the U.S. EPA (1997) used an uncertainty factor of 100 (10 for species-to-species extrapolation and 10 for sensitive subgroups in the human population) [250 mg/kg/day ÷ 100 = 2.5 mg/kg/day]. Because the available data on reproductive toxicity and teratogenicity do not indicate that young animals are more sensitive than adults to imazapyr, no additional uncertainty factor for infants or children was applied.

No other criteria for imazapyr have been found on INTERNET sites of any of the organizations responsible for setting environmental or occupational exposure recommendations, criteria or standards - i.e., WHO, OSHA, NIOSH, or ACGIH. No published recommendations from these agencies or organizations were encountered in the literature search, which included databases covering the Federal Register.

As discussed in section 3.1.3 and detailed in Appendix 1, the dog study (Shellenger 1987) is supported by chronic oral toxicity studies in both rats (Daly 1988) and mice (Auletta 1988) as well as several studies designed to detect adverse effects on reproduction and development (section 3.1.4). Because these studies fail to demonstrate any clear dose-response or dose-severity relationships, these data cannot be used to develop a more elaborate dose-response or dose-severity assessment. However, as detailed in section 3.2, none of the exposure scenarios for imazapyr result in doses that substantially exceed the RfD. Consequently, an elaboration of dose-response or dose-severity relationships is unnecessary.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. The risk characterization for potential human health effects associated with the use of imazapyr in Forest Service programs is relatively unambiguous. Based on the estimated levels of exposure and the RfD derived by the U.S. EPA's Office of Pesticide Programs, exposures that can be anticipated both in the typical use of imazapyr or in a number of accidental exposure scenarios do not lead to dose levels that exceed the RfD. All of the anticipated exposures - most of which involve highly protective assumptions - are below the RfD by a least a factor of 2. The use of the RfD - which is designed to be protective of chronic or lifetime exposures - is itself a very conservative component of this risk characterization because the duration of any plausible and substantial exposures is far less than lifetime.

Imazapyr can cause irritation to the eyes and skin. Based on the available information, eye and/or skin irritation are the only overt effects that can be associated with the mishandling of imazapyr. These effects can be minimized or avoided by prudent hygiene practices during the handling of imazapyr.

Table 3-5: Summary of risk characterization for workers [1]

RfD	2.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.001	0.00001	0.08	WSC01a
Broadcast ground spray (Boom spray)	0.001	0.00002	0.15	WSC01b
Aerial applications	0.0009	0.00001	0.005	WSC01c
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	3e-06	5e-07	0.00013	WSC02
Contaminated Gloves, 1 hour	0.0002	3.27e-05	0.01	WSC02
Spill on hands, 1 hour	0.00003	4e-06	0.002	WSC03
Spill on lower legs, 1 hour	0.0001	0.00001	0.004	WSC03

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Table 3-3 for summary of exposure assessment.

The only reservation attached to this assessment of imazapyr is that associated with any risk assessment in which no plausible hazards can be identified: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated***. No chemical, including imazapyr, has been studied for all possible effects and the use of data from laboratory animals to estimate hazard or the lack of hazard to humans is an uncertain process. Prudence dictates that normal and reasonable care should be taken in the handling of this or any other chemical. Notwithstanding these reservations, the use of imazapyr does not pose any identifiable hazard to workers or the general public in Forest Service programs.

3.4.2. Workers. A quantitative summary of the risk characterization for workers is presented in Table 3-5. The quantitative risk characterization is expressed as the hazard quotient, which is the ratio of the estimated exposure doses from Table 3-3 to the RfD of 2.5 mg/kg/day, as derived in

section 3.3.2. As in previous tables, numbers greater than or equal to 0.000001 are expressed in standard decimal notation and smaller numbers are expressed in scientific notations - e.g., 7e-07 equivalent to 7×10^{-7} or 0.0000007. Details of the conversion of scientific to decimal notation are given on page ix of this report.

Given the very low hazard quotients for both general occupational exposures as well as accidental exposures, the risk characterization for workers is unambiguous. None of the exposure scenarios approach a level of concern.

While the accidental exposure scenarios are not the most severe one might imagine (e.g., complete immersion of the worker or contamination of the entire body surface for a prolonged period of time) they are representative of reasonable accidental exposures. Given that the highest hazard quotient for any of the accidental exposures is a factor of 100 below the level of concern (i.e., a hazard quotient of 0.01 as the upper limit for wearing contaminated gloves for 1 hour), far more severe and less plausible scenarios would be required to suggest a potential for systemic toxic effects.

As discussed in section 3.2, however, confidence in this assessment is diminished by the lack of information regarding the dermal absorption kinetics of imazapyr in humans. Nonetheless, the statistical uncertainties in the estimated dermal absorption rates, both zero-order and first-order, are incorporated into the exposure assessment and risk characterization. Again, these estimates would have to be in error by a factor of over 100 in order for the basic characterization of risk to change. In addition, the hazard quotients for these acute occupational exposure are based on a chronic RfD. This adds an additional level of conservatism and, given the very low hazard quotients for these scenarios, reinforces the conclusion that there is no basis for asserting that systemic toxic effects are plausible.

The hazard quotients for general occupational exposure scenarios are somewhat higher than those for the accidental exposure scenarios. Nonetheless, the upper limit of the hazard quotients for backpack, boom spray, and aerial applications are below the level of concern - i.e., a hazard index of 1. As discussed in section 3.2 and detailed in worksheets C01a through C01c, these upper limits of exposure are constructed using the highest anticipated application rate, the highest anticipated number of acres treated per day, and the upper limit of the occupational exposure rate. If any of these conservative assumptions are modified (e.g., the compound is applied at the typical rather than the maximum application rate) the hazard quotients would drop substantially. For example, the upper end of the range for the hazard quotient involving broadcast application is 0.15. This is based on an application of 2.5 lb a.e./acre. At the typical application rate of 0.15 lb a.e./acre, the hazard quotient would be 0.009 [0.15 × 0.15 lb a.e./acre ÷2.5 a.e./acre], a factor of about 17 below the level of concern.

The simple verbal interpretation of this quantitative characterization of risk is that even under the most conservative set of exposure assumptions, workers would not be exposed to levels of

Table 3-6: Summary of risk characterization for the general public [1] .

Provisional RfD		2.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.001	0.0002	0.1	WSD01
Direct spray, lower legs	Woman	0.0001	0.00002	0.01	WSD02
Dermal, contaminated vegetation	Woman	0.002	0.0003	0.1	WSD03
Contaminated fruit, acute exposure	Woman	0.001	0.0003	0.05	WSD04
Contaminated water, acute exposure	Child	0.01	0.003	0.5	WSD06
Consumption of fish, general public	Man	0.0004	0.0002	0.01	WSD08
Consumption of fish, subsistence populations	Man	0.002	0.0008	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0003	0.00014	0.03	WSD05
Consumption of water	Man	0.0001	7.00e-06	0.01	WSD07
Consumption of fish, general public	Man	7.00e-07	5.00e-08	0.001	WSD09
Consumption of fish, subsistence populations	Man	0.00001	4.00e-07	0.005	WSD09

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Table 3-4 for summary of exposure assessments.

imazapyr that are regarded as unacceptable. Under typical application conditions, levels of exposure will be far below levels of concern.

As discussed in section 3.1.6, imazapyr can cause irritation and damage to the skin and eyes. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling imazapyr. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of imazapyr.

3.4.3. General Public. The quantitative hazard characterization for the general public is summarized in Table 3-6. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the RfD of 2.5 mg/kg/day.

None of the acute or longer-term exposure scenarios approach a level of concern. Although there are several uncertainties in the exposure assessments for the general public, as discussed in section 3.2, the upper limits for hazard quotients are sufficiently far below a level of concern that the risk characterization is relatively unambiguous: based on the available information and under the foreseeable conditions of application, there is no route of exposure or scenario suggesting that the general public will be at any substantial risk from longer-term exposure to imazapyr.

All of the specific assumptions used to develop the acute exposure scenarios involve arbitrary variability to at least some extent and these scenarios use exposure assumptions that have a simple linear relationship to the resulting hazard quotient. For example, the direct spray of a young child assumes that the compound is effectively removed after 1 hour. If the assumption were made that the compound was not removed for 10 hours, the level of exposure would reach the RfD. The main purpose of these scenarios, however, is to identify the types of exposures that are of greatest concern and may warrant the greatest steps to mitigate. For imazapyr, such scenarios involve the consumption of contaminated water after an accidental spill and dermal contact from an accidental spray or contact with contaminated vegetation. For longer-term exposure, the consumption of contaminated vegetation leads to the highest hazard quotient. Nonetheless, the highest chronic hazard quotient is below the level of concern by a factor of 10.

3.4.4. Sensitive Subgroups. There is no information to suggest that specific groups or individuals may be especially sensitive to the systemic effects of imazapyr. As discussed in sections 3.3.2, the U.S. EPA (1997) has judged that infants and children are not likely to be more sensitive to imazapyr than adults. Given the number of studies available on reproductive and developmental effects and the unremarkable findings from these studies, this judgement appears appropriate.

Nonetheless, some individuals may suffer from multiple chemical sensitivity (e.g., ATSDR 1995). Such individuals may respond adversely to extremely low levels of chemicals and in a manner that is atypical of the general population. There are no data or case reports, however, on idiosyncratic responses to imazapyr.

3.4.5. Connected Actions. As indicated in section 2, imazapyr is often applied in combination with triclopyr and is occasionally applied in combination with fosamine ammonium. No data have been encountered in the literature that permit a characterization of the joint action of imazapyr - i.e., synergism, antagonism, or additivity - with these compounds. The limited information encountered in the U.S. EPA files on mixtures of imazapyr with imazethapyr (Lowe 1988 as summarized in appendix 1) does not indicate any substantial interaction.

3.4.6. Cumulative Effects. This risk assessment specifically considers the effect of repeated exposures in that the chronic RfD is used as an index of acceptable exposure for both acute and longer-term scenarios. Consequently, repeated exposure to levels below the toxic threshold - i.e., all of the exposure scenarios described in this risk assessment - should not be associated with cumulative toxic effects.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. As with the human health risk assessment, a limitation in the identification of potential hazards to terrestrial or aquatic animals is that the great majority of the toxicity studies have failed to demonstrate any significant or substantial association between imazapyr exposure and toxicity. In addition, few wildlife species have been assayed relative to the large number of non-target animal species that might be exposed to imazapyr. Within these admittedly substantial reservations, imazapyr appears to be relatively non-toxic to terrestrial or aquatic animals. In other words, no hazards associated with the direct toxic action of imazapyr can be identified for either terrestrial or aquatic animals.

The toxicity of imazapyr to terrestrial plants is relatively well characterized. As with several sulfonylurea, imidazolinone, and triazolopyrimidine herbicides, imazapyr inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. Although post-emergence application is more effective than pre-emergence application, toxicity can be induced either through foliar or root absorption. Imazapyr is not metabolized extensively in plants but is transported rapidly from treated leaves to root systems and may be exuded into the soil from the roots of treated plants.

A number of standard bioassays are available on the toxicity of imazapyr to aquatic plants. The most sensitive species appears to be the aquatic macrophyte *Lemna gibba*, with a reported EC_{25} of 0.013 (0.009-0.019) mg/L. Some aquatic algae appear to be substantially less sensitive, with EC_{50} values on the order of about 0.2 mg/L. In tolerant species, concentrations of up to 100 mg/L may cause either no effect or be associated with a stimulation rather than inhibition of growth. The reasons for these large differences in sensitivity within aquatic plant species is not apparent.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals– The toxicity studies used to assess the potential hazards of imazapyr to humans (appendix 1) can also be applied to the risk assessment for mammalian wildlife. Perhaps the most substantial limitation in the identification of potential hazards relates to the lack of information on dose levels that are harmful to mammals. As discussed in section 3.1 and further detailed in appendix 1, virtually all of the studies on imazapyr are negative - i.e., no effects clearly attributable to the compound have been identified. Thus, while the toxicity of imazapyr to plants is understood relatively well (section 4.1.2.4), it is not clear what, if any, specific toxicity imazapyr may cause in mammalian wildlife. While this may be considered an uncertainty or a lack of knowledge, it has a relatively minor impact on this risk assessment because the available toxicity studies are relatively complete - chronic studies in three mammalian species and several reproduction studies in two mammalian species - and indicate that imazapyr is not likely to be associated with adverse effect at relatively high dose levels.

Only one field study relevant to assessing potential effects of imazapyr on terrestrial mammals has been encountered. Brooks et al. (1995) examined the impact of imazapyr, as well as picloram, triclopyr, and hexazinone, all used in site preparation, on small mammal and avian communities. The study area was located in Georgia and consisted of a 157-ha tract of residual hardwoods. Imazapyr (Arsenal) was applied at 4.1 kg a.e./ha. After herbicide treatment and a prescribed burn, loblolly pine were planted. Data on small mammals was collected by trapping and data on birds involved visual surveys. Observations were made at pre-treatment and three times per year at 1, 2, and 3 years after treatment. No substantial differences were noted among the different herbicides. With all herbicides, the number of small animals trapped after treatment was diminished compared to pre-treatment levels. Because no non-herbicide treated sites - i.e., control sites - were used in this study, observed changes in populations of small mammals or birds cannot be clearly associated with herbicide treatment.

4.1.2.2. Birds– While toxicity studies on birds (appendix 2) are less extensive than those on mammals, both ducks and quail have been assayed in 5 day acute toxicity studies and 18 week reproduction studies. As with the mammalian studies, no adverse effects have been noted. In the acute studies (Fletcher 1983a,b), no mortality was observed at imazapyr concentrations of up to 5000 ppm in the diet. These acute exposures were equivalent to average daily doses of 674 mg/kg in quail (Fletcher 1983a) and 1149 mg/kg in ducks (Fletcher 1983b). Similarly, in the 18-week dietary studies, no effects on reproductive endpoints - i.e., egg production, hatchability, survival of hatchlings - were observed at dietary concentrations of up to 2000 ppm. These 18-week exposures were equivalent to average daily doses of 200 mg/kg in both quail and ducks (Fletcher et al. 1995a,b).

4.1.2.3. Terrestrial Invertebrates– No information of the toxicity of imazapyr to terrestrial invertebrates was located in a search of EPA's files. The only information on the toxicity of imazapyr to a terrestrial invertebrate is given in the review by Peoples (1984) that indicates a dermal LD_{50} in the honey bee of >100 µg/bee, equivalent to >0.1 mg/bee. Taking an average weight of 0.093 g/bee or 0.000093 kg/bee (USDA/APHIS 1993) and making the very conservative assumption of 100% absorption, this would correspond to an LD_{50} greater than 1000 mg/kg bw [0.1 mg imazapyr/bee ÷ 0.000093 kg bw/bee = 1075 mg/kg]. This order of toxicity is comparable to the LD_{50} values reported in experimental mammals (appendix 1) and birds (appendix 2). This suggests that the toxicity of imazapyr to terrestrial invertebrates may be similar to the toxicity of this compound to terrestrial vertebrates. On the other hand, there are a very large number of terrestrial invertebrates in any diverse environment. Typically, as with imazapyr, information is available on only a single terrestrial invertebrate species, the honey bee. Thus, the ability to characterized potential effects in other species is limited.

4.1.2.4. Terrestrial Plants (Macrophytes)– The toxicity of imazapyr to terrestrial plants is relatively well characterized (appendix 3). As with several sulfonylurea, imidazolinone, and triazolopyrimidine herbicides, imazapyr inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant

growth (Boutsalis and Powles 1995). Post-emergence application is more effective than pre-emergence application and time to complete kill may require several weeks (Peoples 1984).

Several types of weed species have developed resistance to imazapyr. In some plant species, resistance is based on a modified form of ALS that is associated with a single nuclear gene (Boutsalis and Powles 1995). Resistant strains of common chickweed, perennial ryegrass, and Russian thistle have also been associated with a less sensitive ALS (Saari et al. 1992). Based on a comparison of different levels of resistance to various herbicides, including imazapyr, Burnet et al. (1994) have suggested that there is likely to be more than one mechanism involved in the development of resistance to imazapyr and other similarly acting herbicides.

After foliar application, imazapyr as well as other structurally similar herbicides (e.g., picloram, clopyralid, and other imidazolinone herbicides) are transported via the phloem and thus are able to control deeply rooted weeds. The efficacy of imazapyr appears to be particularly strongly related to its transport in phloem, which is more rapid than would be expected from simple structure-activity correlations (Chamberlain et al. 1995). Although a number of herbicides inhibit ALS, the kinetics of inhibition and thus the mechanisms are not necessarily identical. For example, imazapyr acts as an uncompetitive inhibitor of ALS in *Arabidopsis thaliana* whereas chlorsulphuron acts as a non-competitive inhibitor (Chang and Duggleby 1997).

Rapid transport from treated leaves to root systems has also been noted by Nissen et al. (1995) using liquid growth cultures of leafy spurge (*Euphordia esula*) after foliar treatments with ^{14}C-imazapyr. By day 8 after application, 14% of the applied imazapyr remained in the leaf tissue but 17% was transported to the root system. In terms of total absorption, 62.5% of the applied radioactivity was absorbed by day 2 and 80.0% by day 8. Under the assumption of simple first-order absorption, the absorption rate, k_a, should be constant over time and can be calculated as the natural logarithm of the proportion of the unabsorbed dose divided by the duration of exposure - i.e.,

$$k_a = \ln(1 - Prop.absorbed)/t.$$

The k_a valuess calculated for day 2 and day 8 are 0.49 day^{-1} [ln(1-0.625)/2] and 0.20 day^{-1} [ln(1-0.8)/8], respectively. Thus, at least in this species, the rate of absorption may not be constant with time and first order absorption kinetics may not apply. Alternatively, these differences may simply reflect random variation in the responses of the plants or the measurements taken during the study. The data reported by Nissen et al. (1995) do not include a sufficient number of time points to evaluate either possibility.

Imazapyr does not appear to be readily or extensively metabolized by plants although imazapyr metabolites from leafy spurge were detected but not identified after 8 days in the study by Nissen et al. (1995). These authors noted two groups of metabolites, one eluting earlier and one eluting later than imazapyr. Nissen et al. (1995) suggest that the earlier eluting (more polar metabolites)

were 2-carbamoylnicotinic acid and 2,3-pyridinedicarboxylic acid. The later eluting metabolite was thought to be a ring closure product, imidazopyrrolopyridine.

The phytotoxicity of imazapyr can be reduced by some compounds such as naphthalic anhydride and BAS 145138 (Davies et al. 1995). Combined exposure, as soil treatments below the recommended application rates, to both diuron and imazapyr has been shown to increase the sensitivity of water oak (*Quercus nigra*) to infections from the fungus *Tubakia dryina* (Zhang and Walker 1995). This effect was not seen in plants treated with diuron or imazapyr separately. This effect was associated with an inhibition of stem elongation but the mechanism for the apparent interaction is unclear.

Some herbicides may be absorbed by plant foliage, translocated to the roots of plants, and subsequently exuded from the roots to the surrounding soil, posing a risk to neighboring plants. This process, referred to as allelopathy, has been demonstrated for picloram, 2,4-D, and 2,4,5-T (Reid and Hurtt 1970; Webb and Newton 1972). These herbicides, like imazapyr, are weak acids with pK_a values between 1.9 and 2.8 (Willis and McDowell 1987) and are poorly soluble in non-polar liquids (Bromilow et al. 1990). Although reports of allelopathic effects for imazapyr have not been reported in field studies, Nissen et al. (1995) found that about 3% of absorbed imazapyr may be exuded from the root system of leafy spurge into a liquid culture medium by day 8 after treatment. This report combined with the fact that herbicides with similar physical and chemical properties generally translocate similarly in plants (Bromilow et al. 1990) suggests that imazapyr has the potential to induce allelopathic effects. Nonetheless, given the relatively rapid movement of imazapyr in soil (appendix 5), the potential for allelopathic effects may not have a practical or substantial impact on potential risk to non-target plants.

4.1.2.5. Terrestrial Microorganisms– Relatively little information is available on the toxicity of imazapyr to terrestrial microorganisms. In pure culture laboratory assays, imazapyr inhibited the growth of two strains of plant-associated bacteria, *Bacillus subtilis* and *Bacillus circulans*, both isolated from wheat. LC_{50} valuess ranged from about 10 to 100 µM (see Forlani et al., 1995, Fig 1, p 248). Three other species of *Bacillus* as well as several additional soil bacteria were not affected at concentrations up to 1000 µM (Forlani et al. 1995). Thus, effects on bacteria appear to be highly species specific with variations in sensitivity of up to a factor of 100. Consequently, imazapyr does appear to have the potential to shift bacterial soil populations that contain sensitive species of bacteria. In addition, imazapyr has been shown to inhibit rates of cellulose decomposition and carboxymethyl cellulase activity in peat soil with 59% organic carbon (Ismail and Wong 1994). These investigators speculate that *'the reduction in cellulose degradation is likely to be only a temporary effect'* (Ismail and Wong 1994, p. 122) and that the activity of imazapyr on terrestrial microorganisms may decline as the herbicide is adsorbed to soil and thus unavailable to microorganisms. This may be a reasonable speculation for peat. As detailed in appendix 5, imazapyr is likely to bind relatively strongly to peat. On the other hand, as also detailed in appendix 5, imazapyr may persist in soil for a prolonged period of time, particularly in relatively arid regions, and will not bind tightly to alkaline soils with low organic matter. Thus, in at least some areas, a potential for longer term effects on soil microorganisms seems plausible. As

with effects on both terrestrial and aquatic plants, the plausibility and magnitude of any such effects are likely to be highly site-specific.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish– Standard toxicity bioassays to assess the effects of imazapyr on fish and other aquatic species are summarized in appendix 4. For fish, standard 96-hour acute toxicity bioassays indicate that the LC_{50} is greater than 100 mg/L. The longer term toxicity of imazapyr has also been tested in an early life-stage bioassay using rainbow trout at concentrations of 0, 6.59, 12.1, 24.0, 43.1, or 92.4 mg/L for 62 days. At the highest concentration, a "nearly significant effect on hatching" was observed (Manning 1989a). The investigator judged that this effect was not toxicologically significant. A review of the data tables provided in the study does not contradict this assessment. Nonetheless, the classification of 92.4 mg/L as a NOAEL is questionable. For this risk assessment, the next lower dose, 43.1 mg/L, will be taken as the NOAEL. As discussed in section 4.4, any of these concentrations are far in excess of concentrations that are plausible in the environment. Thus, any uncertainty concerning the classification of the 92.4 mg/L concentration has no impact on the risk characterization.

4.1.3.2. Amphibians– Neither the published literature nor the U.S. EPA files include data regarding the toxicity of imazapyr to amphibian species.

4.1.3.3. Aquatic Invertebrates– Two standard aquatic toxicity studies are available on the common test species, *Daphnia magna*. As with fish, the 48-hour LC_{50} is greater than 100 mg/L (Kintner and Forbis 1983). In addition, a 21-day chronic study noted no effects on reproduction or growth at concentrations of up to 97.1 mg/L (Manning 1989b).

4.1.3.4. Aquatic Plants– A number of standard bioassays are available on the toxicity of imazapyr to aquatic plants. The most sensitive species appears to be the aquatic macrophyte *Lemna gibba*, with a reported EC_{25} of 0.013 (0.009-0.019) mg/L (Hughes 1987). As detailed in appendix 4, aquatic algae appear to be substantially less sensitive. The most sensitive species of algae appears to be *Chlorella emersonii*, with an EC_{50} of about 0.2 mg/L (Landstein et al. 1993). The growth of other species of algae is stimulated rather than inhibited by imazapyr at concentrations of up to 100 mg/l (Hughes 1987).

As with terrestrial plants, some species of aquatic plants may develop resistance to imazapyr. Bioassays conducted on *Chlorella emersonii* indicate that resistant strains may be less sensitive to imazapyr by a factor of about 10 (Landstein et al. 1993).

4.1.3.5. Other Aquatic Microorganisms– There are no published or unpublished data regarding the toxicity of imazapyr to aquatic bacteria or fungi.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview. Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or

indirect contact with contaminated vegetation. In acute exposure scenarios, the highest exposures for small terrestrial vertebrates will occur after a direct spray and could reach up to about 4 mg/kg under typical exposure conditions and up to about 60 mg/kg under more extreme conditions. Other routes of exposure such as the consumption of contaminated water or contaminated vegetation will generally lead to much lower levels of exposure. In chronic exposures, estimated daily doses for a small vertebrate are generally below 1 mg/kg/day although daily doses of up to about 20 mg/kg/day are possible in the consumption of contaminated vegetation. Based on general relationships of body size to body volume, larger vertebrates will be exposed to lower doses and smaller animals, such as insects, to much higher doses than small vertebrates under comparable exposure conditions. Because of the apparently low toxicity of imazapyr to animals, the rather substantial variations in the different exposure assessments have little impact on the assessment of risk to terrestrial animals.

The primary hazards to non-target terrestrial plants are associated with unintended direct deposition or spray drift as well as persistence in or migration through soil. Unintended direct spray will result in an exposure level equivalent to the application rate. At least some plants that are sprayed directly with imazapyr at or near the recommended range of application rates will be damaged. Based on monitoring studies involving low-flight agricultural applications of various pesticides and employing various types of nozzles under a wide range of meteorological conditions, the central estimates of off-site drift for single swath applications, expressed as a proportion of the nominal application rate, are approximately 0.03 at 100 feet, 0.002 at 500 feet, 0.0006 at 1000 feet, and 0.0002 at 2500 feet. Estimates of off-site deposition can also be based on Stoke's Law. Using this method and assuming a wind velocity of no more than 5 miles/hour perpendicular to the line of application, 100 µ particles falling from 3 feet above the surface could drift as far as 23 feet. A raindrop or 400 µ particle applied at 6 feet above the surface could drift about 3 feet.

There are major areas of uncertainty and variability in assessing potential levels of exposure in soil. The binding of imazapyr to soil is very complex because of the different charge configurations that imazapyr may have at different pH's. In general, imazapyr adsorption to a variety of different soil types will increase as the pH decreases - i.e., the soil becomes more acidic. Additional site specific factors such as iron oxides, organic carbon, and soil moisture can substantially impact the binding of imazapyr to soil and this in turn will substantially impact the transport of imazapyr in soil. The persistence of imazapyr in soil is highly variable and reported soil halftimes range from about 5 days to 17 months, depending on factors such as temperature, pH, aeration, organic matter, and soil depth. The most influential factor in the persistence of imazapyr in soil, however, appears to be microbial activity. For the exposure assessment, a central estimate of 70 days is used but a range of about 30 days to 150 days is plausible.

In order to encompass a wide range of field conditions, GLEAMS simulations were conducted for both clay and sand at annual rainfall rates from 5 to 250 inches and the typical application rate of 0.15 lb a.e./acre. In sand or clay under arid conditions - i.e., annual rainfall of about 10 inches or

less - there is no percolation or runoff and the rate of decrease of imazapyr concentrations in soil is attributable solely to presumed microbial breakdown.

Taking an imazapyr concentration of 0.005 ppm in soil as a reference level that could impact sensitive species and using a typical application rate of 0.15 lb a.e./acre, residual toxicity in arid soil could be anticipated for around 200 days. In clay soils, runoff is the only significant mode of imazapyr dissipation in soil. At annual rainfall rates of up to 250 inches in clay soils, imazapyr concentrations of 0.005 ppm or greater in soil could be seen for over 150 days. Sandy soils are more sensitive to rainfall rates than clay soils because of the greater proportion of imazapyr that can percolate through the soil column. At relatively low rainfall rates - i.e., 25 inches per year - imazapyr concentrations of 0.005 ppm or more could be maintained for about 100 days. At annual rainfall rates of 50 to 250 inches per year, concentrations of 0.005 ppm or more would be sustained for only about 10 to 40 days.

Exposures to aquatic species are impacted by the same factors that influence terrestrial plants except the directions of the impact are reversed. In other words, in very arid environments - i.e., the greatest persistence in soil - substantial contamination of water is unlikely. In areas with increasing levels of rainfall, toxicologically significant exposures to aquatic plants are more likely to occur. Taking a concentration of about 0.01 mg imazapyr per liter of water as a level that is likely to impact sensitive species of aquatic plants, as detailed in the dose-response assessment for aquatic plants, the application of imazapyr at 0.15 lb a.e./acre in areas with annual rainfall rates of 25 inches or less is unlikely to lead to significant water contamination. In areas with sandy soil, annual rainfall rates of 50 inches or more could be associated with phytotoxic concentrations of imazapyr in water for periods in excess of 100 days. Losses from clay soil will likely be less than those from sandy soil. In predominantly clay soils, annual rainfall rates of 50 inches would plausibly lead to detectable but subtoxic concentrations. Applications in areas with annual rainfall rates of 100 inches or more could result in phytotoxic concentrations in water for periods of 50 to 100 days.

These estimates of persistence in soil and transport to water should be considered only as crude approximations of plausible levels of exposure. A variety of site-specific factors could substantially impact these assessments, particularly application rate, microbial activity, soil binding of imazapyr, depth of the water table, proximity to open water, and rates of flow in and volumes of groundwater, streams, ponds, or lakes, and specific patterns of rainfall. These site-specific considerations could lead to substantial variations from the modeled values upward or downward. In other words, the exposure assessments modeled using GLEAMS are reasonably consistent with monitoring data. Nonetheless, given the number of factors that can impact the transport and degradation of imazapyr, these assessments are not universally applicable. There are adequate data in the open literature to conduct site-specific exposure assessments that could lead to far more defensible estimates of exposure in specific application programs.

4.2.2. Terrestrial Animals. Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation.

In this exposure assessment, estimates of oral exposure are expressed in the same units as the available toxicity data (i.e., oral LD_{50} and similar values). As in the human health risk assessment, these units are usually expressed as mg of agent per kg of body weight and abbreviated as mg/kg body weight. For dermal exposure, the units of measure usually are expressed in mg of agent per cm^2 of surface area of the organism and abbreviated as mg/cm^2. In estimating dose, however, a distinction is made between the exposure dose and the absorbed dose. The *exposure dose* is the amount of material on the organism (i.e., the product of the residue level in mg/cm^2 and the amount of surface area exposed), which can be expressed either as mg/organism or mg/kg body weight. The *absorbed dose* is the proportion of the exposure dose that is actually taken in or absorbed by the animal.

For the exposure assessments discussed below, general allometric relationships are used to model exposure. In the biological sciences, allometry is the study of the relationship of body size or mass to various anatomical, physiological, or pharmacological parameters (e.g., Boxenbaum and D'Souza 1990). Allometric relationships take the general form:

$$y = aW^x$$

where W is the weight of the animal, y is the variable to be estimated, and the model parameters are **a** and **x**.

For most allometric relationships used in this exposure assessment, **x** ranges from approximately 0.65 to 0.75. These relationships dictate that, for a fixed level of exposure (e.g., levels of a chemical in food or water), small animals will receive a higher dose, in terms of mg/kg body weight, than large animals will receive.

For many compounds, allometric relationships for interspecies sensitivity to toxicants indicate that for exposure levels expressed as mg toxicant per kg body weight (mg/kg body weight), large animals, compared with small animals, are more sensitive. For imazapyr, the available information is not adequate to quantify species differences in sensitivity to imazapyr. As with the dose-response relationship, generic estimates of exposure are given for a small mammal. A body weight of 20 g is used for a small animal, which approximates the body weight of small mammals such as mice, voles, shrews, and bats. All body weight values are taken from U.S. EPA (1989), unless otherwise specified.

The exposure assessments for terrestrial animals are summarized in Table 4-1. As with the human health exposure assessment, the computational details for each exposure assessment presented in this section are provided in the attached worksheets (worksheets F01 through F07).

Table 4-1: Summary of Exposure Scenarios for terrestrial animals

Scenario	Dose (mg/kg/day)			Worksheet
	Typical	Lower	Upper	
Acute/Accidental Exposures				
Direct spray, small mammal, first-order absorption	0.098	0.02049	4.1	WSF01
Direct spray, small animal, 100% absorption	3.7	1.95	61	WSF02
Direct spray, bee, 100% absorption	24	13	407	WSF03
Consumption of contaminated vegetation, acute exposure	0.79	0.42	46.9	WSF04
Consumption of contaminated water, acute exposure	0.113	0.046	2.84	WSF06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.23	0.053	19.9	WSF05
Consumption of contaminated water, chronic exposure	0.0031	0.00022	0.269	WSF07

4.2.2.1. Direct Spray **–** In the broadcast application of any herbicide, wildlife species may be sprayed directly. This scenario is 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 extent of dermal contact depends on the application rate, the surface area of the organism, and the rate of absorption.

For this risk assessment, three groups of direct spray exposure assessments are conducted. The first, which is defined in worksheet F01, involves a 20 g mammal that is sprayed directly over one half of the body surface as the chemical is being applied. The range of application rates as well as the typical application rate is used to define the amount deposited on the organism. The absorbed dose over the first day (i.e., a 24-hour period) is estimated using the assumption of first-order dermal absorption. In the absence of any data regarding dermal absorption in a small mammal,

the estimated absorption rate for humans is used (see section 3.1.7). An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal. The estimates of absorbed doses in this scenario may bracket plausible levels of exposure for small mammals based on uncertainties in the dermal absorption rate of imazapyr.

Other, perhaps more substantial, uncertainties affect the estimates for absorbed dose. For example, the estimate based on first-order dermal absorption does not consider fugitive losses from the surface of the animal and may overestimate the absorbed dose. Conversely, some animals, particularly birds and mammals, groom frequently, and grooming may contribute to the total absorbed dose by direct ingestion of the compound residing on fur or feathers. Furthermore, other vertebrates, particularly amphibians, may have skin that is far more permeable than the skin of most mammals (Moore 1964).

Quantitative methods for considering the effects of grooming or increased dermal permeability are not available. As a conservative upper limit, the second exposure scenario, detailed in worksheet F02, is developed in which complete absorption over day 1 of exposure is assumed.

Because of the relationship of body size to surface area, very small organisms, like bees and other terrestrial insects, might be exposed to much greater amounts of imazapyr per unit body weight, compared with small mammals. Consequently, a third exposure assessment is developed using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993) and the equation above for body surface area proposed by Boxenbaum and D'Souza (1990). Because there is no information regarding the dermal absorption rate of imazapyr by bees or other invertebrates, this exposure scenario, detailed in worksheet F03, also assumes complete absorption over the first day of exposure.

4.2.2.2. Indirect Contact – As in the human health risk assessment (see section 3.2.3.3), the only approach for estimating the potential significance of indirect dermal contact is to assume a relationship between the application rate and dislodgeable foliar residue. The study by Harris and Solomon (1992) (worksheet A04) is used to estimate that the dislodgeable residue will be approximately 10 times less than the nominal application rate.

Unlike the human health risk assessment in which transfer rates for humans are available, there are no transfer rates available for wildlife species. As discussed in Durkin et al. (1995), the transfer rates for humans are based on brief (e.g., 0.5- to 1-hour) exposures that measure the transfer from contaminated soil to uncontaminated skin. Wildlife, compared with humans, are likely to spend longer periods of time in contact with contaminated vegetation.

It is reasonable to assume that for prolonged exposures an equilibrium may be reached between levels on the skin, rates of absorption, and levels on contaminated vegetation, although there are no data regarding the kinetics of such a process. The bioconcentration data on imazapyr (section 3.2.3.5) as well as its high water solubility and low octanol/water partition coefficient suggest that

imazapyr is not likely to partition from the surface of contaminated vegetation to the surface of skin, feathers, or fur. Thus, a plausible partition coefficient is unity (i.e., the concentration of the chemical on the surface of the animal will be equal to the dislodgeable residue on the vegetation).

Under these assumptions, the absorbed dose resulting from contact with contaminated vegetation will be one-tenth that associated with comparable direct spray scenarios. As discussed in the risk characterization for ecological effects (section 4.4), the direct spray scenarios result in exposure levels far below those of toxicological concern. Consequently, details of the indirect exposure scenarios for contaminated vegetation are not further elaborated in this document.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey – For this component of the exposure assessment, the estimated amounts of residue on food are based on the relationship between application rate and residue rates on leaves and leafy vegetables. For the lower and central estimates of absorbed dose, the 'typical' value given in worksheet A05a is used because Hoerger and Kenaga (1972) do not provide estimates of the lower range of expected residues.

Allometric relationships and species specific data (U.S. EPA 1989) suggest that the amount of food consumed per day by a small mammal (i.e., an animal weighing approximately 20 g) is equal to about 15% of the mammal's total body weight. All of the estimates of ingested dose are based on the assumption that 100% of the diet is contaminated. Under the assumption that only 10% of the diet is contaminated, the dose estimates decrease by a factor of 10. Details regarding the calculations for these acute exposure scenarios are given in worksheet F04.

As discussed in section 4.4, the exposure estimates discussed above are of minimal concern for acute exposure. For estimating the effects of longer-term exposures, time-weighted average concentrations are used based on the same set of assumptions that were used in the human health risk assessment. Like the acute exposure scenario, this exposure scenario assumes that 100% of the diet is contaminated. Details regarding the calculations for these chronic exposure scenarios are given in worksheet F05.

4.2.2.4. Ingestion of Contaminated Water **--** Estimated concentrations of imazapyr in water are identical to those used in the human health risk assessment (worksheet B07). As detailed in section 3.2.3.4.2, these estimates are probably very conservative - i.e., they tend to overestimate exposure and subsequent risk. The only major differences from the human health risk assessment involve the weight of the animal and the amount of water consumed. There are well-established relationships between body weight and water consumption across a wide range of mammalian species [e.g., U.S. EPA (1989)]. Mice, weighing about 0.02 kg, consume approximately 0.005 L of water/day (i.e., 0.25 L/kg body weight/day). These values are used in the exposure assessment for the small (20g) mammal. Unlike the human health risk assessment, estimates of the variability of water consumption are not available. Thus, for the acute scenario, the only factors affecting the variability of the ingested dose estimates include the field dilution rates (i.e., the concentration of the chemical in the solution that is spilled) and the amount of solution that is spilled. As in the acute exposure scenario for the human health risk assessment, the amount of the spilled solution is

taken as 200 gallons. In the chronic exposure scenario, the factors that affect the variability are the water contamination rate (section 3.2.3.4.2) and the application rate. Details regarding these calculations are summarized in worksheet F06 (acute exposure) and worksheet F07 (chronic exposure).

4.2.3. Terrestrial Plants. In general, the primary hazard to non-target terrestrial plants associated with the application of most herbicides is unintended direct deposition or spray drift, particularly in aerial applications (e.g., Bird 1995). In addition, migration through or erosion of soil may result in off-site soil contamination.

4.2.3.1. Direct Spray – Unintended direct spray will result in an exposure level equivalent to the application rate. At least some plants that are sprayed directly with imazapyr at or near the recommended range of application rates will be damaged (section 4.3.2.4).

4.2.3.2. Off-Site Drift – Data regarding the drift of imazapyr during ground or aerial applications were not found in the literature. Because off-site drift is more or less a physical process that depends on droplet size and meteorological conditions rather than the specific properties of the herbicide, estimates of off-site drift can be made based on data for other compounds. The potential for spray drift was investigated in numerous field studies reviewed recently by Bird (1995), as summarized in worksheet A06. The monitoring studies involved low-flight agricultural applications of pesticides and employed various types of nozzles under a wide range of meteorological conditions. The central estimates of off-site drift for single swath applications, expressed as a proportion of the nominal application rate, were approximately 0.03 at 100 feet, 0.002 at 500 feet, 0.0006 at 1000 feet, and 0.0002 at 2500 feet (Bird 1995, Figure 2, p. 204). Although multiple swath applications lead to higher rates of off-site deposition, they are less suitable for estimating drift from ground spray applications of imazapyr.

Another approach to estimating drift involves the use of Stoke's law, which describes the viscous drag on a moving sphere. According to Stoke's law:

$$v = \frac{D^2 \cdot g}{18n}$$

or

$$v = 2.87 \cdot 10^5 \cdot D^2$$

where v is the velocity of fall (cm sec^{-1}), D is the diameter of the sphere (cm), g is the force of gravity (980 cm sec^{-2}), and n is the viscosity of air ($1.9 \cdot 10^{-4}$ g sec^{-1} cm^{-1} at 20°C) (Goldstein et al. 1974).

In typical backpack ground sprays, droplet sizes are greater than 100 µ, and the distance from the spray nozzle to the ground is 3 feet or less. In mechanical sprays, raindrop nozzles might be used. These nozzles generate droplets that are usually greater than 400 µ, and the maximum distance above the ground is about 6 feet. In both cases, the sprays are directed downward.

Thus, the amount of time required for a 100 µ droplet to fall 3 feet (91.4 cm) is approximately 3.2 seconds,

$$91.4 \div (2.87 \cdot 10^5(0.01)^2).$$

The comparable time for a 400 µ droplet to fall 6 feet (182.8 cm) is approximately 0.4 seconds,

$$182.8 \div (2.87 \cdot 10^5(0.04)^2).$$

For most applications, the wind velocity will be no more than 5 miles/hour, which is equivalent to approximately 7.5 feet/second (1 mile/hour = 1.467 feet/second). Assuming a wind direction perpendicular to the line of application, 100 µ particles falling from 3 feet above the surface could drift as far as 23 feet (3 seconds · 7.5 feet/second). A raindrop or 400 µ particle applied at 6 feet above the surface could drift about 3 feet (0.4 seconds · 7.5 feet/second).

For backpack applications, wind speeds of up to 15 miles/hour are allowed in Forest Service programs. At this wind speed, a 100 µ droplet can drift as far as 68 feet (3 seconds · 15 · 1.5 feet/second). Smaller droplets will of course drift further, and the proportion of these particles in the spray as well as the wind speed will affect the proportion of the applied herbicide that drifts off-site.

4.2.3.3. Soil Contamination – Other mechanisms of transport for herbicides, in addition to aerial transport, involve movement in the soil either by run-off or percolation. Both of these processes will be governed by the binding of imazapyr to soil and the persistence of imazapyr in soil.

For assessing the effects of imazapyr soil residues on non-target plants, estimates of imazapyr concentrations in soil are required. A concentration in soil can be crudely approximated based on the application rate. A unit application rate of 1 lb a.e./acre is equivalent to about 11.21 µg/cm^2. Using a root zone depth of 12 inches or about 30 cm and assuming that imazapyr is relatively rapidly transported into this soil layer, the resulting soil concentration would be about 0.37 µg/cm^3 [11.21 µg/cm^2 ÷ 30 cm]. Taking a soil bulk density of 1.5 g/cm^3 (Knisel et al. 1992, p. 56), this in turn corresponds to about 0.25 µg/g or 0.25 ppm. - i.e., this is the maximum concentration that would be expected at an application rate of 1 lb a.e./acre in the top 30 cm of soil. This calculation assumes that mixing in the top 30 cm of soil is rapid. This assumption is reasonably well supported by both laboratory and field studies (Mallipudi et al. 1983b; Mallipudi et al. 1985; McDowell et al. 1997; Rahman et al. 1993; Vizantinopoulos and Lolos 1994).

The above simple calculation can be compared to both modeled concentrations as well as field data. As detailed below, the GLEAMS model was used to estimate levels of imazapyr in soil, as well as other parameters. At an application rate of 0.15 lb a.e./acre, initial concentrations in the top 1 cm of soil - the depth of incorporation used in the GLEAMS model - corresponded to about 0.6 ppm for both clay and sand, assuming 50% foliar interception. This concentration, averaged over the top one foot (30.5 cm) of soil and correcting for foliar interception is about 0.04 ppm

[0.6 ppm × 1 cm ÷ (30.5 cm × 0.5) = 0.03934 ppm]. Normalized for an application rate of 1 lb a.e./acre, this corresponds to about 0.26 ppm [0.04 ppm ÷ 0.15 lb a.e./acre = 0.13 ppm per 1 lb a.e./acre], virtually identical to the calculated value based on soil volume.

In a field study conducted by Vizantinopoulos and Lolos (1994), imazapyr was applied to clay loam soil at an application rate of 1 kg a.i./ha. Using a salt to acid conversion factor of 0.816 (Table 2-1) the rate of 1 kg a.i./ha is equivalent to 0.816 kg a.e./ha or 0.728 lb a.e./acre. By day 3 after application, the concentrations in the 0-10, 10-20, and 20-30 cm soil layers were about 0.24 ppm, 0.12 ppm, and 0.06 ppm, respectively, for an overall average of 0.14 ppm. Based on the above calculation of 0.25 ppm per lb a.e. applied /acre, the expected concentration would be about 0.17 ppm:

0.25 ppm. per lb a.e./acre × 0.728 lb a.e./acre = 0.182 ppm,

very close to the observed value of 0.14 ppm.

Because of this reasonable concordance between the calculated, modeled, and observed concentrations, the expected concentrations in soil will be estimated from the unit rate of 0.25 ppm per lb a.e./acre. Thus, at the typical application rate of 0.15 lb a.e./acre, the expected concentration of imazapyr in the top 30 cm of soil is calculated at about 0.04 ppm:

0.15 lb a.e./acre × 0.25 ppm per lb a.e./acre = 0.0375 ppm.

Similarly, the concentrations in soil at the lower and upper ranges of the application rates are calculated as 0.02 ppm:

0.08 lb a.e./acre × 0.25 ppm per lb a.e./acre = 0.02 ppm.

and 0.6 ppm:

2.5 lb a.e./acre × 0.25 ppm per lb a.e./acre = 0.625 ppm,

respectively. As illustrated in the GLEAMS modeling, initial concentrations could be less than this amount because of foliar interception. Nonetheless, any significant amount of rainfall would lead to increases in soil concentrations that approximate the amounts calculated above.

All of the above concentrations may reasonably approximate the concentration of imazapyr in soil immediately after application. For this risk assessment, however, a central concern is the duration over which imazapyr concentrations in soil may be phytotoxic.

As detailed in appendix 5, the GLEAMS model was applied to estimate concentrations of imazapyr in the top one foot of soil for clay and sand under a wide range of annual precipitation rates. There are major areas of uncertainty in modeling the fate of imazapyr in soil in terms of

both soil binding and soil halftime (appendix 5). As discussed in appendix 5 and illustrated in Figure A5-1, the binding of imazapyr to soil is very complex because of the different charge configurations that imazapyr may have at different pH's. In general, imazapyr adsorption to a variety of different soil types will increase as the pH decreases - i.e., the soil becomes more acidic. Additional site specific factors such as iron oxides, organic carbon, and soil moisture can substantially impact the soil binding and this in turn will substantially impact the transport of imazapyr in soil.

As also detailed in appendix 5, the persistence of imazapyr in soil is highly variable and reported soil halftimes range from about 5 days to 17 months depending on factors such as temperature, pH, aeration, organic matter, and soil depth.

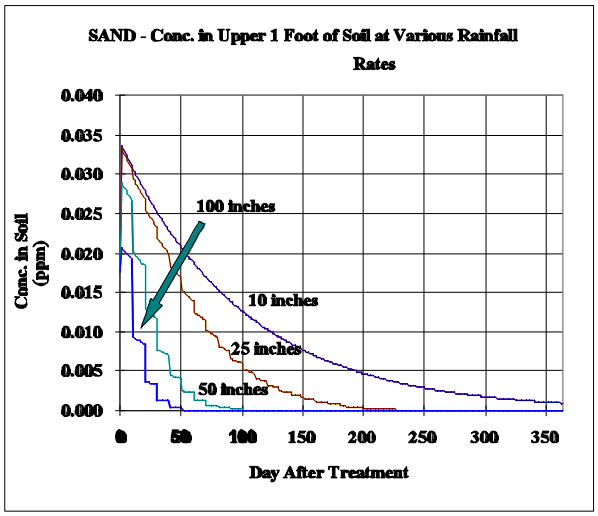


Figure 4-1: Soil concentrations of imazapyr applied at a rate of 0.15 lb a.e./acre in the top 1 foot of sandy soil at various annual precipitation rates.

The most influential factor in the persistence of imazapyr in soil, however, appears to be microbial activity. In other words, imazapyr is chemically stable in soil and microbial breakdown along with dispersive processes such as percolation and runoff will be the primary mechanisms in the decrease in imazapyr in soil over time. In general, soil halftimes of 30 to about 150 days are probably reasonable. In the GLEAMS modeling, a central estimate of 70 days was used.

In sandy soil under arid conditions - i.e., annual rainfall of 5 inches or less - there is no percolation or runoff and the rate of decrease is attributable solely to presumed microbial breakdown. For example, in Figure 4-1 the time to a 50% decrease in soil concentrations is about 70 days at rainfall rates of 10 inches per year. This rate of decrease is identical to the soil halftime used in the GLEAMS modeling. At higher precipitation rates, percolation becomes increasing significant and is clearly the dominant factor at rainfall rates of 50 inches/year or more. Note that the stepped appearance of the time plots for higher rainfall rates simply reflects the *every tenth day* rainfall pattern used in the GLEAMS modeling.

In clay soil (Figure 4-2), the modeling results under arid conditions are essentially identical to those of sand. In an arid environment (annual precipitation of 5 inches per year or less), runoff from clay soil will be negligible and the rate of degradation in soil will depend primarily on microbial activity. Thus, in Figure 4-2, the line for a 5-inch annual rainfall is virtually identical to the corresponding line for sandy soil (Figure 4-1) and reflects the soil halftime of 70 days used in the modeling. The every tenth day rainfall pattern used in the GLEAMS modeling is less apparent

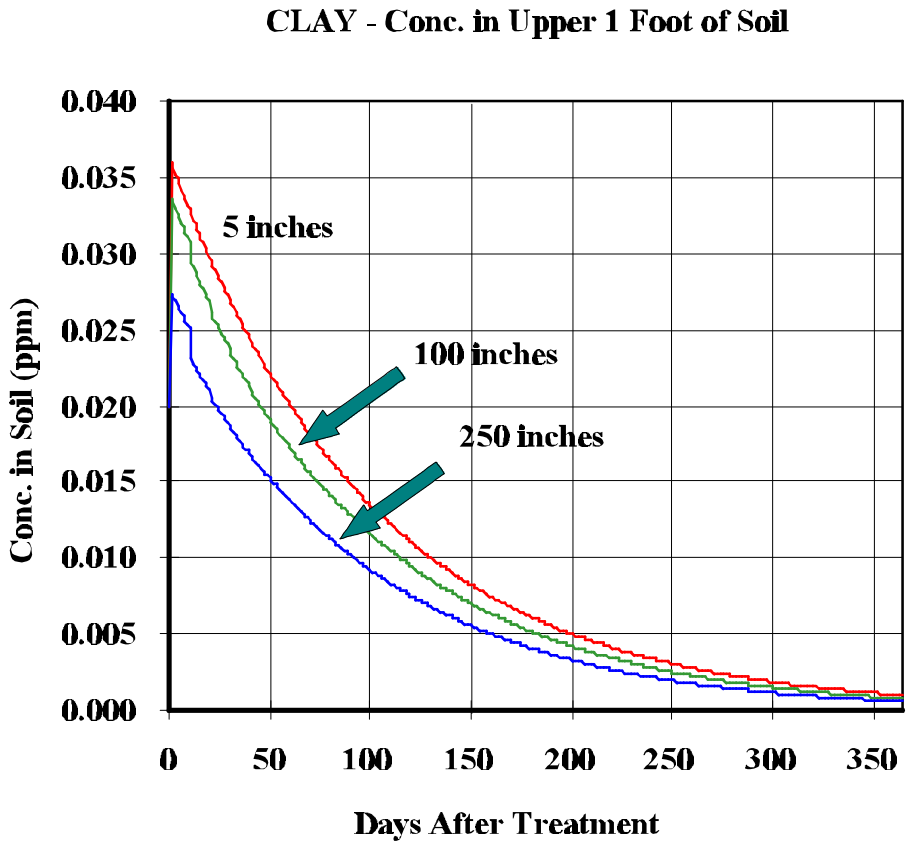


Figure 4-2: Soil concentrations of imazapyr applied at a rate of 0.15 lb a.e./acre in the top 1 foot of clay soil at various annual precipitation rates.

for clay (Figure 4-2) than sand (Figure 4-1) primarily because the amount of runoff from clay is less than the amount of percolation in sand.

In an extremely arid environment in which the microbial activity of the soil is very low, soil halftimes of much greater than 70 days - i.e., that used in the GLEAMS modeling - are plausible. In some cases, the 'sterile' soil halftime of 17 months or about 500 days (American Cyanamid 1983b) could be approximated.

4.2.4. Aquatic Organisms. For aquatic organisms, the estimated amount of imazapyr in ambient water and in water bodies associated with an accidental spill (see section 3.2.3.4.1) may be used as a conservative estimate of exposure.

For longer term exposures, the estimated rate of contamination of ambient water based on the available monitoring data is 0.082 (0.011 to 0.43) mg a.e./L at an application rate of 1 lb a.e./acre. As indicated in section 3.2.3.4.2, these estimates are reasonably consistent with peak concentrations of imazapyr based on the application of the GLEAMS model (appendix 5). However, just as the monitoring studies report that the peak levels rapidly fall below the limit of detection in streams (Michael and Neary 1993; Michael et al. 1996), the GLEAMS modeling also indicates a marked decrease in the concentrations of imazapyr depending on the rainfall rates (Figures 4-3 and 4-4).

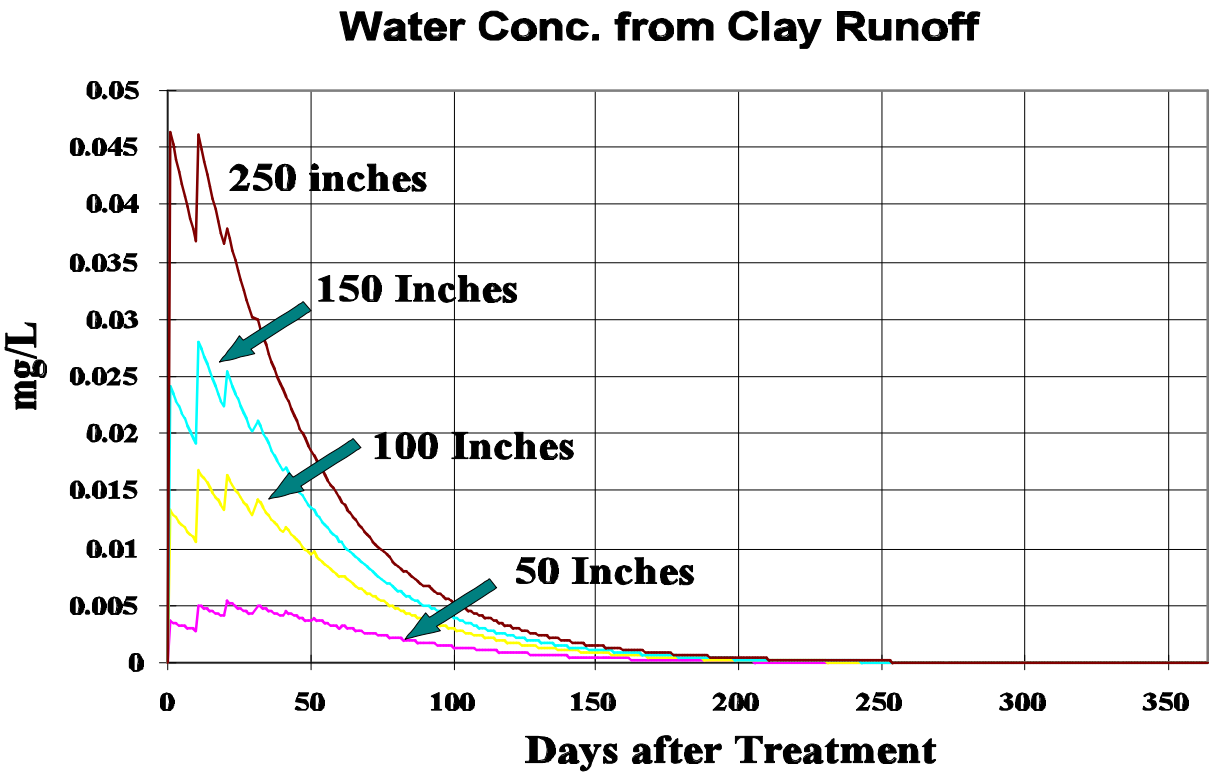


Figure 4-3: Imazapyr concentrations in a small pond as a result of runoff from clay at an application rate of 0.15 lb a.e./acre and various annual rainfall rates.

As illustrated in Figures 4-3 and 4-4, peak water concentrations will vary substantially with rainfall rates. Below annual rainfall rates of 10 inches per year, no runoff from clay or percolation through sand is anticipated. At annual rainfall rates of 50 to 250 inches per year, peak water concentrations associated with runoff from clay vary from about 0.005 mg/L to 0.045 mg/L (Figure 4-3). Over the same range of rainfall rates, higher concentrations of imazapyr are anticipated from percolation, at least if it is assumed that the percolate will quickly and directly mix with ambient standing water (Figure 4-4). As a result of percolation through sand, peak levels of about 0.03 to 0.09 mg/L are projected at annual rainfall rates ranging from 50 to 250 inches.

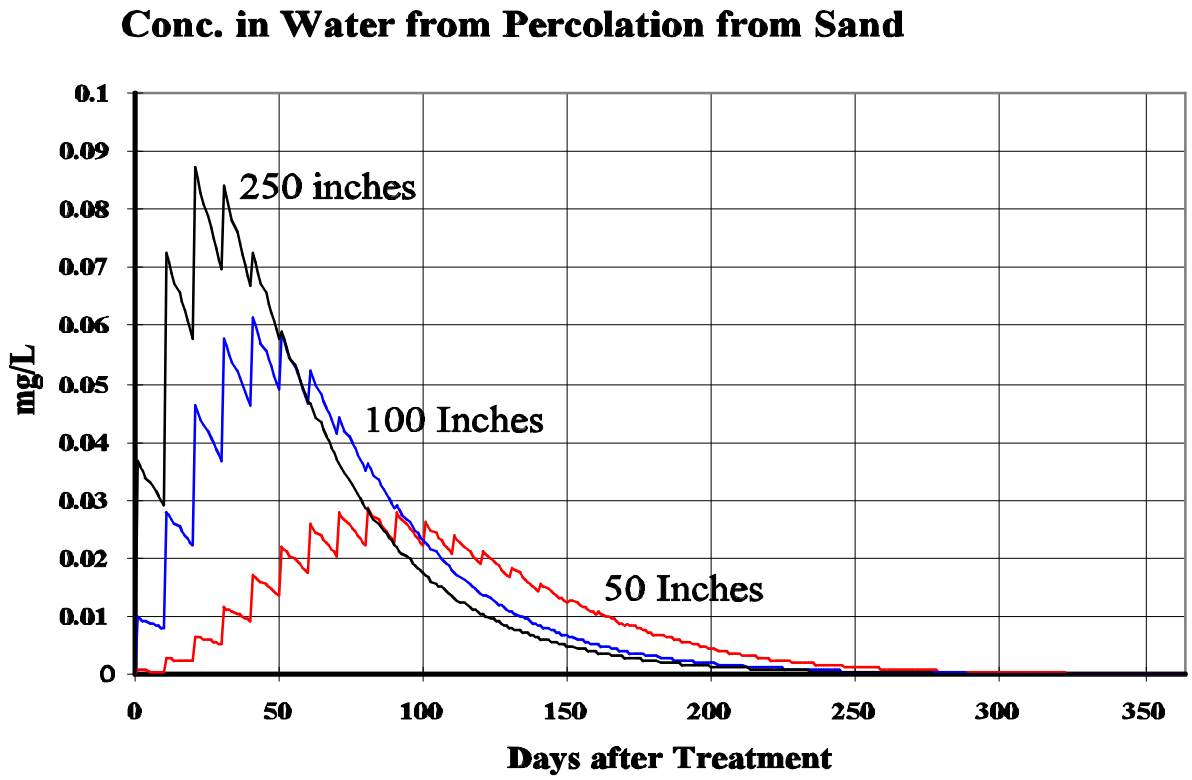


Figure 4-4: Imazapyr concentrations in a small pond as a result of percolation from sand at an application rate of 0.15 lb a.e./acre and various annual rainfall rates.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview. For terrestrial mammals, the dose-response assessment is based on the same data as the human health risk assessment (i.e., a NOAEL of 250 mg/kg/day from a 1-year dietary study using dogs). None of the mammalian exposure scenarios, acute or longer-term, result in exposure estimates that exceed this NOAEL. The very limited data on toxicity to birds do not suggest that birds are any more sensitive to imazapyr than mammals. The data on birds, however, are not as extensive or of the same detail as the data on experimental mammals. The available data on terrestrial invertebrates are much less complete than the data on mammals. Nonetheless, there is no indication that imazapyr is highly toxic to any animal species.

The toxicity of imazapyr to terrestrial and aquatic plants can be characterized relatively well and with little ambiguity (Table 4-2). For accidental sprays or drift, functional application rates of about 0.02 lbs a.e./acre are likely to cause overt signs of toxicity, specifically decreased growth, in even relatively tolerant terrestrial plants. In some sensitive terrestrial plants, effects could be apparent at functional application rates as low as about 0.001 lbs a.e./acre. Substantial mortality is expected at application rates of about 0.25 lb a.e./acre in relatively tolerant plants and at about 0.008 lb a.e./acre in plants that are relatively sensitive to imazapyr. In terms of residual soil contamination, EC_{50} values for growth of about 0.005 mg a.e./kg soil are estimated for sensitive

Table 4-2: Toxicity values used in risk assessment of terrestrial and aquatic plants

End-point	Level of tolerance	Value	Source
Terrestrial Plants, Direct Deposition in units of lb a.e./acre			
Decreased growth, approximate threshold	Sensitive species	0.001	Figure 4-5
	Tolerant species	0.02	Figure 4-6
Mortality	Sensitive species	0.008	American Cyanamid 1980
	Tolerant species	0.25	
Terrestrial Plants, Residual soil toxicity in units of ppm in soil.			
Approximate ED_{50} for Decreased growth	Sensitive species	0.005	Figure 4-8
	Tolerant species	0.1	
Mortality/Approximate ED_{95} for Decreased growth	Sensitive species	0.02	
	Tolerant species	0.5	
Aquatic Plants, Concentrations in water in units of mg/L			
Approximate ED_{25} or ED_{50} for growth	Most sensitive	0.01	[1]Hughes 1987
	Sensitive	0.2	[2]Landstein et al 1993
	Tolerant species	10	[3] Hughes 1987

[1] ED_{25} for *Lemna sp*. rounded to 1 significant digit.
[2] ED_{50} for Some species of *Chlorella*. Resistant species of *Chlorella* may have 10 fold higher EC_{50} values.
[3] Some more tolerant species may have EC_{50} values or NOAELs up to 100 mg/L.

plant species and 0.1 mg a.e./kg soil for relatively tolerant plant species. Substantial levels of mortality are expected at concentrations of 0.5 ppm in tolerant species and 0.02 ppm in sensitive species. Although the available dose-response data on terrestrial plants is sufficient for an elaboration of dose-response relationships, such data are available on relatively few species. If data were available on a larger number of species, it is reasonable to assume that the range of effective doses would increase. In other words, some untested species would be more sensitive and others more tolerant than the species that have been tested.

A substantially greater range of sensitivities is apparent in aquatic plants (Table 4-2). The most sensitive species appears to be the aquatic macrophyte *Lemna gibba*, with a reported EC_{25} for growth of 0.013 (0.009-0.019) mg/L. Other species of aquatic plants, particularly the unicellular algae, may be much less sensitive, with EC_{50} of about 0.2 mg/L to 2 mg/L for *Chlorella*. Some

aquatic plants are relatively tolerant to imazapyr, with NOAELs on the order of 100 mg/L, similar to fish and aquatic invertebrates.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals– As summarized in the dose-response assessment for the human health risk assessment (see section 3.3.3), the U.S. EPA (1997) has derived an RfD of 2.5 mg/kg/day. This estimate is based on a one-year dog NOAEL of 250 mg/kg/day and an uncertainty factor of 100 and is supported by higher chronic/lifetime NOAELs in rats and mice. All chronic exposures are substantially below the chronic NOAEL for dogs and, except for the upper limit of exposure from the consumption of contaminated vegetation, all of the potential longer-term exposures are below the human RfD by a least a factor of 10 (see Table 4-1). Consequently, there is little need to elaborate upon the dose response assessment for terrestrial mammals and the chronic dog NOAEL of 250 mg/kg/day is used to assess the consequences of all exposures (section 4-4).

4.3.2.2. Birds – As noted in section 4.1.2.2, the18-week dietary NOAEL for birds based on reproductive endpoints - i.e., egg production, hatchability, survival of hatchlings - is 200 mg/kg/day. While the bird NOAEL is somewhat lower than the chronic NOAEL for dogs (250 mg/kg/day), this does not imply that birds are more sensitive than mammals. Quite simply, 200 mg/kg/day is the highest subchronic (18 week) dose tested in birds, just as 250 mg/kg/day is the highest chronic dose tested. Thus, for exposure scenarios involving the ingestion of imazapyr from either contaminated vegetation or water, the dose-response relationships for mammals may serve as reasonable estimates for avian species. Notwithstanding this approach and as discussed in section 4.1.2.2, the available data on birds are not as extensive or of the same quality as the data on experimental mammals. This limitation adds somewhat to the uncertainty in the dose/response assessment. Nonetheless, as detailed in section 4.4, the plausible levels of exposure are far below 200 mg/kg/day and thus the uncertainty in the dose-response assessment has little impact on the characterization of risk (section 4.4).

4.3.2.3. Terrestrial Invertebrates– There is practically no information regarding the toxicity of imazapyr to terrestrial invertebrates. As discussed in section 4.1.2.3, all that is known is that the acute LD_{50} in the honey bee is greater than 1000 mg/kg bw. This apparently low toxicity is consistent with the data on mammals. However, no quantitative consideration can be given to other potential subchronic or non-lethal effects and no information is available on other invertebrate species. This limitation also adds substantial uncertainty to the risk assessment, which is discussed in more detail in the risk characterization (section 4.4).

4.3.2.4. Terrestrial Plants (Macrophytes)-- Toxicity studies are available on imazapyr in which exposure is characterized either as an application rate (i.e., American Cyanamid 1988) or a concentration in soil (e.g., Rahman et al. 1993; Vizantinopoulos and Lolos 1994). The study by American Cyanamid (1980), in which exposure is characterized as an application rate, was conducted as part of the registration requirements for herbicides and can be used directly to assess the potential effects from unintentional spraying or off-site drift. The studies in which imazapyr exposure is characterized as a concentration in soil (Rahman et al. 1993; Vizantinopoulos and

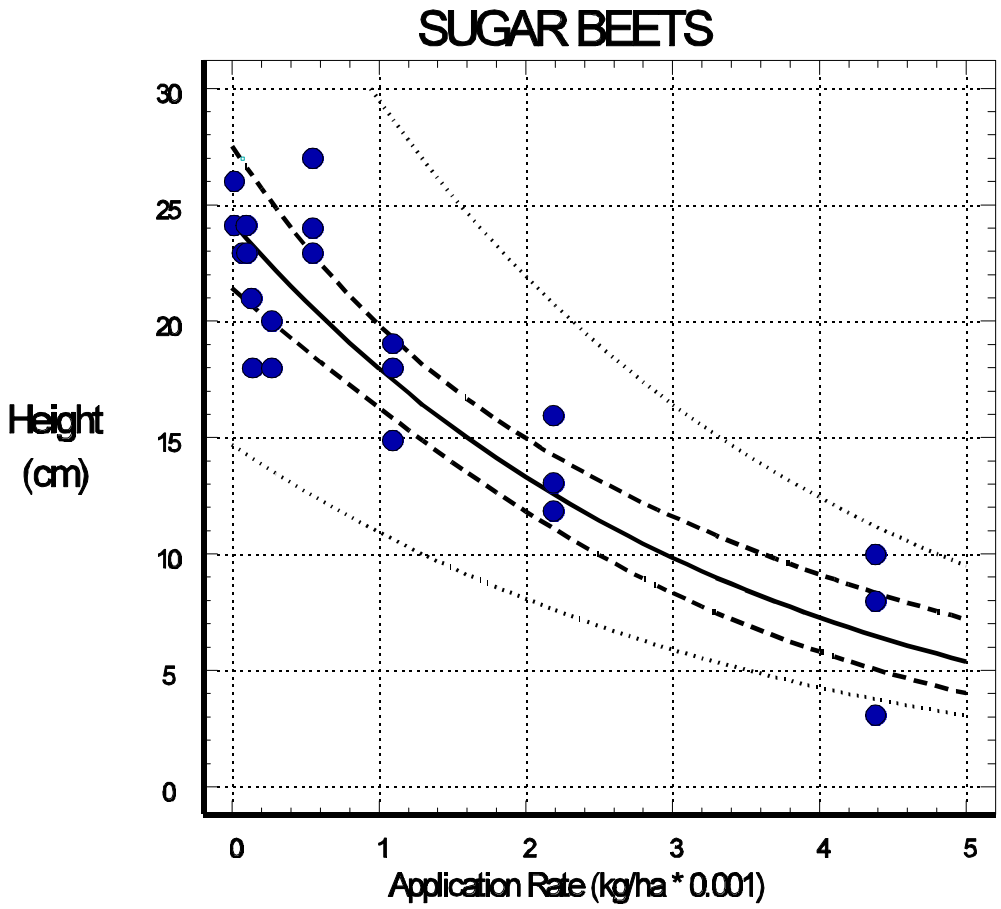


Figure 4-5: Responses of sugar beets to postemergent applications of imazapyr (data from American Cyanamid 1980).

Lolos 1994) were conducted essentially as classical bioassays. In other words, the response of plants at various concentrations of imazapyr in soil was determined so that plant responses rather than direct chemical analysis could be used to assess the movement and concentrations of imazapyr in soil. Thus, these types of studies are appropriate for assessing the effects of residual imazapyr concentrations in soil.

A detailed summary of the study by American Cyanamid (1980) is given in appendix 3. As indicated in this appendix, this type of study is referred to as a Tier II assay and is actually a series of bioassays on seed germination, seed emergence, and effects on postemergent plant growth and viability. In the study by American Cyanamid (1980), imazapyr was tested in all three types of assays at application rates ranging from 0.000068 kg/ha to1.12 kg/ha, corresponding to about 0.00006 to 1.0 lb a.e./acre. As indicated in appendix 3, the greatest toxicity was observed in postemergence assays, with reported EC_{50} values of 0.00219-0.0175 kg/ha in a number of different species (green peas, soybeans, onions, corn, wheat, oats, sugarbeets, sunflowers, tomatoes and cucumbers). Lesser toxicity was observed in pre-emergence assays, with no

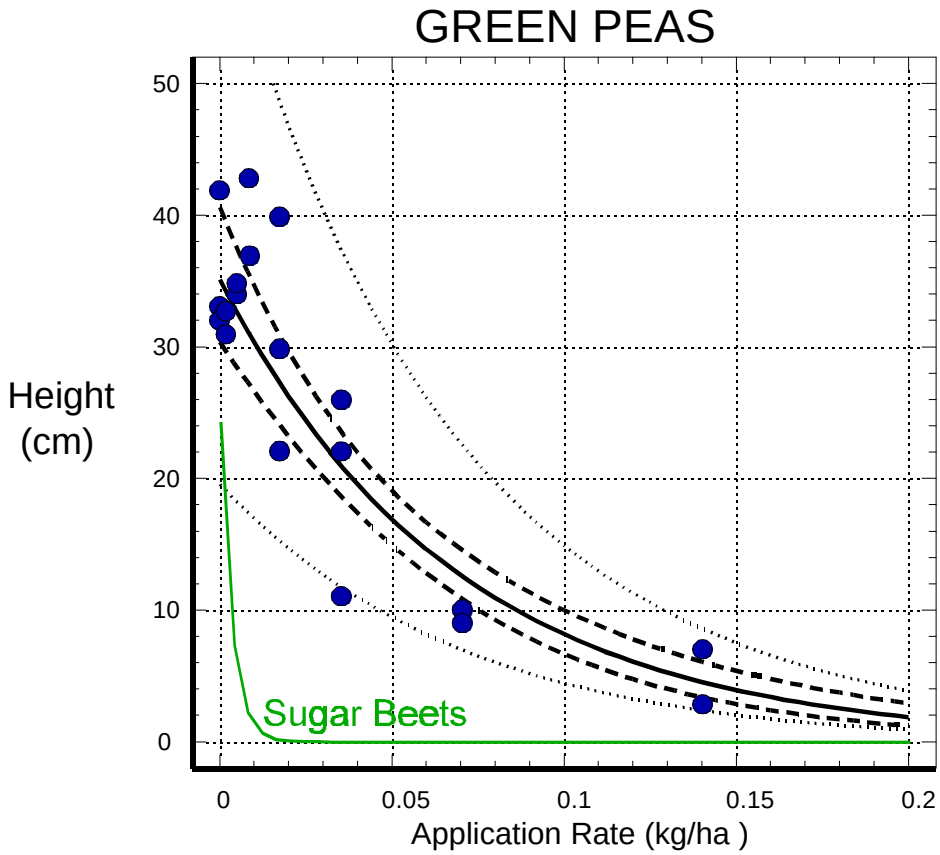


Figure 4-6: Responses of green peas to postemergent applications of imazapyr (data from American Cyanamid 1980) [Comparison line for sugar beets adapted from the data illustrated in Figure 4-6].

significant effects observed in several species. The least toxicity was observed in seed germination assays (American Cyanamid 1980).

For this risk assessment, the most sensitive life stage, that is post-emergent plants, will be used for the risk characterization. In order to bracket a plausible range of sensitivity based on the available data, the least and most sensitive species - i.e., green peas and sugar beets, respectively - were analyzed quantitatively. The raw data for these assessments as well as summaries of some of the statistical analyses are given at the end of appendix 3. American Cyanamid (1980) provides three response variables, height, weight, and a subjective measure of visual damage. In addition, American Cyanamid (1980) provides a statistical analysis of these data based on a linear-linear model - i.e., regression analyses of height or weight against application rate. Visual inspection of the dose/response patterns, however, suggest that the exponential model,

$$R = e^{\alpha + \beta x}$$

generally gives a better fit to the data, where x is the application rate, R is the response, and α and β are model parameters. Also in general, data on plant height yielded better fit to the exponential model than plant weight. Thus, for the analysis presented below, only the response based on plant height using the exponential model is detailed. Other measures of response do not add substantially to or alter this basic dose/response assessment.

The results for the most sensitive species tested by American Cyanamid (1980), sugar beets, is illustrated in Figure 4-5. As summarized in appendix 3, these data fit the exponential model:

$$\text{Height} = e^{\,3.18 - 300\ X(\text{kg a.e./acre})}$$

with a squared correlation coefficient of 0.78 and a p-value of <0.0001. [All statistical analysis were conducted in Statgraphics (Manugistics1995).] The best estimate of the control response - i.e., an application rate or X of 0 - is thus 24 cm ($e^{3.18}$). Although this dose response model is non-threshold, visual inspection of the dose/response relationship (Figure 4-5) does not suggest any significant inhibition at application rates of 0.0005 kg a.e./ha or less. About 20% inhibition, however, is apparent at about 0.001 kg/ha and about 80% inhibition is apparent at an application rate of 0.005 kg/ha. At application rates of 0.00875 kg/ha, or about 0.008 lb a.e./acre, and above, all sugar beets died.

The results for green peas, the least sensitive species tested by American Cyanamid (1980), are illustrated in Figure 4-6. As also summarized in appendix 3, these data fit the exponential model:

$$\text{Height} = e^{\,3.29 - 24\ X(\text{kg a.e./acre})}$$

with a squared correlation coefficient of 0.84 and a p-value of <0.0001. In other words, green peas are less sensitive to imazapyr than sugar beets by a factor of about 12 (300 ÷ 24 = 12.5). For visual comparison, Figure 4-6 also gives the maximum likelihood estimate of the response of sugar beets, taken and re-scaled from Figure 4-5. Although scatter in the data is apparent, particularly at application rates of less than 0.05 kg a.e./ha, a potential threshold/NOAEL for imazapyr for effects on green peas is less clear than for sugar beets. In any event, application rates as low as 0.03 kg a.e./ha are clearly associated with a decrease in the height of green peas. At 0.28 kg/ha and above, all green beans died. An apparent threshold of about 0.02 kg a.e./ha is used in this risk assessment to characterize potential risks to relatively tolerant plant species.

Thus, in terms of accidental sprays or drift, functional application rates of 0.05 kg a.e./ha or about 0.04 lbs a.e./acre are likely to cause overt signs of toxicity, specifically decreased growth, in even relatively tolerant plant species. In some sensitive species, effects could be apparent at functional application rates as low as 0.001 kg a.e./ha or about 0.0009 lbs a.e./acre. Substantial mortality is expected at application rates of 0.28 kg/ha (about 0.25 lb a.e./acre) in relatively tolerant plants and at 0.00875 kg/ha (about 0.008 lb a.e./acre) in plants that are relatively sensitive to imazapyr.

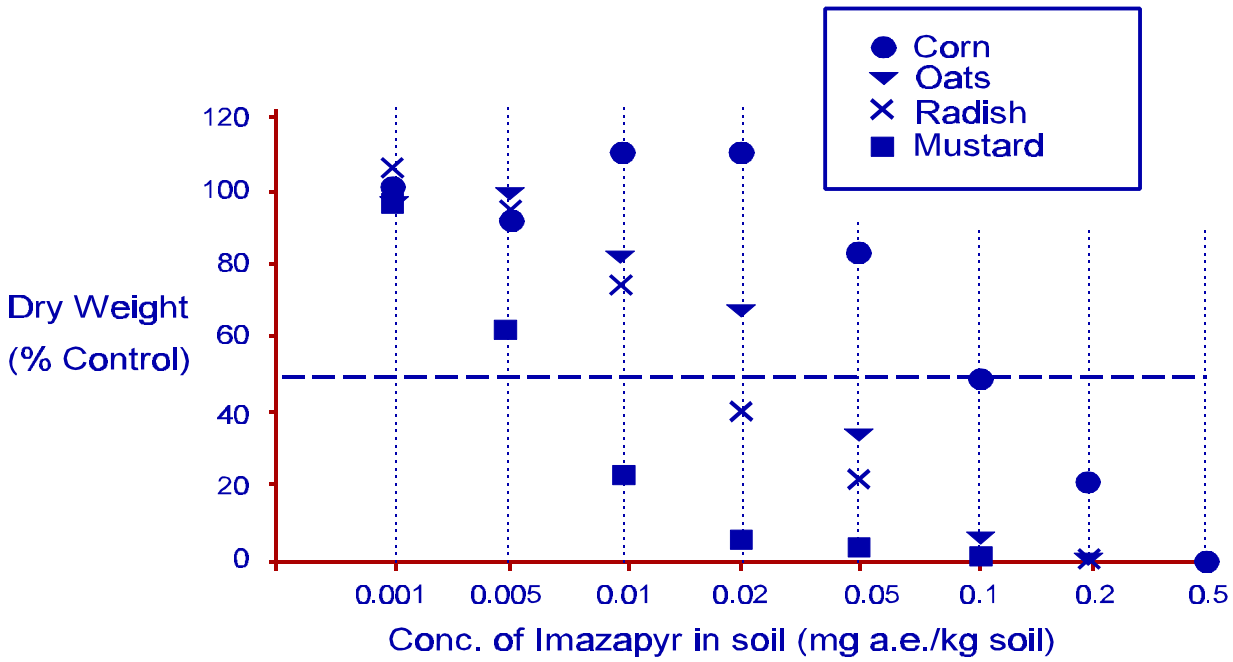


Figure 4-7: Growth in four plant species as a function of imazapyr concentration in the sandy loam soil (redrawn from Rahman et al. 1993).

While the American Cyanamid (1980) study can be used directly to assess the potential consequences of direct spray or drift, there is also a concern for the latent toxicity of imazapyr in soil. As detailed in section 4.2.3.3, imazapyr can be extremely persistent in soil, particularly under conditions of low rainfall and low microbial activity. Two studies (Rahman et al. 1993; Vizantinopoulos and Lolos 1994) could be used to characterize the dose/response relationships for toxicity to plants in terms of concentrations of imazapyr in soil. Vizantinopoulos and Lolos (1994) assayed the effects of varying concentrations of imazapyr in soil on the growth of wheat (*Triticum vulgare*) in clay and clay loam soils (see Figure 1, p. 406 in Vizantinopoulos and Lolos 1994). Rahman et al. (1993) assayed the effects of varying concentrations of imazapyr in soil on the growth of four plant species in sandy loam soil: white mustard (*Sinapis alba*), radish, oats, and corn (*Zea mays*). For this risk assessment, the study by Rahman et al. (1993) is used because of the greater number of species tested and because the results noted by Vizantinopoulos and Lolos (1994) for wheat are encompassed by the responses in the different species tested by Rahman et al. (1993).

The influence on varying concentrations of imazapyr in soil and the growth of the four species tested by Rahman et al. (1993) are illustrated in Figure 4-7. In this series of assays, seeds were

planted in pots containing sandy loam soil with pre-mixed levels of imazapyr. The plants were thinned to eight plants after emergence, and grown for 28 days. The plants were all irrigated to maintain 80% to100% field capacity.

A separate series of studies were conducted in clay loam soil. Although Rahman et al. (1993) do not give details of the series of bioassays with clay loam soil, they indicate that *the level of biological activity was slightly higher* in the clay loam soil [pH 5.2] than in sandy loam soil [pH 5.8] (p. 117, above Figure 1 in Rahman et al. 1993). As indicated in section 4.2.3.3, the adsorption of imazapyr to a variety of different soil types increases as the pH decreases. While speculative, this suggests that the presumably higher binding of imazapyr to the clay loam soil [lower pH and higher binding] did not significantly impact the bioavailability of imazapyr or that the apparently lower activity in the sandy loam soil [higher pH and lower binding] could be attributable to increased percolation through the soil because of the irrigation.

In any event, the data from Figure 4-7 clearly indicate that white mustard is the most sensitive species, with an EC_{50} of about 0.006 mg a.e./kg soil and that corn is the least sensitive species, with an EC_{50} of about 0.1 mg a.e./kg soil. The range of sensitivities is about 17 [0.1÷0.006 = 16.6], relatively close to the range of sensitivities noted in the post-emergence applications conducted by American Cyanamid (1980).

4.3.2.5. Terrestrial Microorganisms– No data have been encountered that permit the quantitative assessment of the effects of imazapyr in soil on soil microorganisms. As summarized in section 4.1.2.5, liquid culture solutions of imazapyr were toxic to various soil bacteria, with LC_{50}s ranging from about 10 to 1000 µM (see Forlani et al., 1995, Fig 1, p 248). These concentrations correspond to about 2.61 to 261 mg/L (ppm) [1 µM = 1 µM/L, MW of acid = 261 g/mole]. This concentration is substantially above the soil concentrations associated with severe effects in plants. Thus, it seems reasonable to assert that while effects in microbial populations due to the toxicity of imazapyr cannot be ruled out, changes in microbial populations under field conditions would most likely be secondary to toxic effects in plants with subsequent changes in soil chemistry and nutrients.

4.3.3. Aquatic Organisms.

4.3.3.1. Animals–As indicated in sections 4.1.3.1 through 4.1.3.3, fish and aquatic invertebrates appear to have a similar sensitivity to imazapyr. The only reported exposure that induced any potentially toxic effect is the 92.4 mg/L exposure to trout fry (Manning 1989a). As discussed in section 4.1.3.1, the authors classified this as a NOAEL although a “nearly significant effect on hatching” was observed (Manning 1989a). For this risk assessment, the next lower concentration from this study, 43.1 mg/L is taken as a NOAEL. Given the relatively low levels of exposure in aquatic organisms, even in the event of an accidental spill, there is no further need to elaborate on the dose/response assessment for aquatic animals.

4.3.3.2. Aquatic Plants– As would be expected of a herbicide, some aquatic plants are much more sensitive to imazapyr than aquatic animals. The most sensitive species appears to be the

aquatic macrophyte *Lemna gibba*, with a reported EC_{25} for growth of 0.013 (0.009-0.019) mg/L (Hughes 1987) and these estimated levels for growth inhibition will be used for the characterization of risk to sensitive aquatic plants. Other species of aquatic plants, particularly the unicellular algae, may be much less sensitive, with EC_{50} values of about 0.2 mg/L to 2 mg/L for *Chlorella* (Landstein et al. 1993). Some aquatic plants are relatively tolerant to imazapyr, with NOAELs on the order of 10 to 100 mg/L, similar to aquatic animals (Hughes 1987). Further details of these studies are presented in appendix 4.

4.3.3.3. Aquatic Microorganisms– There is no information that would permit a quantitative dose-response assessment for aquatic microorganisms.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. For both aquatic and terrestrial animals, the weight of evidence suggests that no adverse effects are plausible using typical or even very conservative worst-case exposure assumptions. As with the human health risk assessment, this characterization of risk must be qualified. Imazapyr has been tested in only a limited number of animal species and under conditions that may not well-represent populations of free-ranging non-target animals. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects associated with the toxicity of imazapyr can be anticipated in terrestrial or aquatic animals from the use of this compound in Forest Service programs.

Imazapyr is an effective herbicide and adverse effects on some non-target plant species, either terrestrial or aquatic, are likely under certain application conditions and circumstances. Some sensitive plant species could be adversely affected by off-site drift over a relatively narrow band - about 100 feet. More tolerant species are not likely to be affected by off-site drift. This risk characterization is conservative in that the drift estimates are based only on aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no impact on off-site plant species.

Residual soil contamination with imazapyr could be a longer-term problem in some areas. In areas with annual rainfall rates of 10 inches/year or more, imazapyr will be removed from the soil by runoff or percolation. Runoff is likely to be the dominant mechanism in clay soils and percolation the dominant mechanism in sandy soils. Intermediate soil types such as loam, while not specifically modeled in this risk assessment, will likely evidence a mix of runoff and percolation depending on specific soil and site characteristics. In more sandy soils and at the typical application rate of 0.15 lb a.e./acre, imazapyr concentrations in soil could drop below a concentration of 0.02 ppm, the approximate LC_{95} for decreased growth in sensitive species, in a two to four week period in very moist climates - i.e., annual rainfall rates of 50 to 250 inches. Under more moderate rainfall conditions - i.e., 10 to 25 inches per year - the time required to reach concentrations of 0.02 ppm could range from one to over three months. In predominantly clay soils, variations in rainfall have less effect on decreases in the concentration of imazapyr. To reach a level of 0.02 ppm in clay would require about 30 to 60 days, depending on the amount of rainfall.

At higher application rates, much longer periods of time would be required to reach a imazapyr concentration in soil that would be non-toxic. For example, an application rate is 1.5 lb a.e./acre is 10 times higher than the typical rate and in clay soils at any plausible rainfall rate, the time required to reach a concentration of 0.02 ppm would be approximately one year. As illustrated in Figures 4-1 and 4-2, concentrations of imazapyr in soil could remain above 0.006 ppm, the approximate EC_{50} for growth inhibition in sensitive species, for prolonged periods of time.

Adverse effects on aquatic plants are plausible. At the typical application rate of 0.15 lb a.e./acre, the anticipated water concentration of 0.06 mg/L is about a factor of 5 above the EC_{50} for growth of 0.013 (0.009-0.019) mg/L in *Lemna gibba*. Thus, in this species and any other aquatic plant species with similar sensitivities, the application of imazapyr could cause detectable and probably substantial reduction in aquatic plant growth. This, in turn, could have an impact on aquatic animal communities. Based on the results of the GLEAMS modeling, levels in excess of 0.013 mg/L could be expected in areas with predominantly clay soil and relatively high rainfall rates for about 2 weeks to two months. In areas with very sandy soil and rainfall rates of 50 inches/year or more, imazapyr concentrations in pond water could be expected to exceed 0.013 mg/L for more prolonged periods - i.e., about 100 days.

4.4.2. Terrestrial Organisms.

4.4.2.1. Terrestrial Animals–The quantitative risk characterization for terrestrial animals is summarized in Table 4-3. Except for the direct spray scenario for the bee, all of the quantitative risk characterizations apply to a 20 g mammal. In Table 4-3, the hazard quotient for each scenario, except that for the honey bee, is calculated as the exposure estimate presented in Table 4-1 divided by the chronic NOAEL for dogs of 250 mg/kg/day, discussed in section 4.3.2.1. In some respects, this approach may be regarded as extremely conservative, particularly in the application of the chronic NOAEL to acute exposure scenarios. For the honey bee, the hazard quotient is based on reported LD_{50} of >1000 mg/kg (Gagne et al. 1991).

As specified in Table 4-3, both the central estimates as well as the upper range of the hazard quotients associated with the longer-term exposure scenarios are below the level of concern by factors of 500 to 2,000,000.

For acute exposures of small mammals, none of the central values for the hazard quotient reach a level of concern although the scenarios for direct spray and the acute consumption of contaminated vegetation are only a factor of 5 below the level of concern. The highest hazard quotient, the upper limit for direct spray of the bee is a factor of 2.5 below the level of concern. All of these hazard quotients are sufficiently below the level of concern that multi-route exposures also do not trigger concern. In other words, even if a small mammal were directly sprayed and then consumed contaminated vegetation and contaminated water, the resulting hazard quotient, 0.4 [0.2+0.2+0.003], would be below the level of concern.

The simple verbal interpretation of this quantitative risk characterization is similar to that of the human health risk assessment: the weight of evidence suggests that no adverse effects in terrestrial

animals are plausible using typical or even very conservative worst case exposure assumptions. As with the human health risk assessment, this characterization of risk must be qualified. Imazapyr has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging non-target animals. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects can be anticipated in terrestrial animals from the use of this compound in Forest Service programs.

4.4.2.2. **Terrestrial Plants–**Imazapyr is an effective herbicide and adverse effects on some non-target plant species are likely under certain application conditions and circumstances. As discussed in section 4.2.3, three types of exposures are considered in this assessment for non-target plants species: direct spray, drift, and erosion.

As is the case with any herbicide, the likelihood of damage to non-target plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential non-target species. At the typical application rate of 0.15 lb a.e./acre, direct spray is likely to seriously injure or kill non-target as well as target plant species. The low range of application rates anticipated in this risk assessment, 0.08 lb a.e./acre, is not that far below the typical rate and it seems plausible, based on the dose/response patterns illustrated in Figure 4-7, that many target and non-target plant species would evidence signs of toxicity. No data are directly available on the effects of higher application rates on non-target species but it seems obvious that the upper range of labeled application rates, 2.5 lb a.e./acre, will kill most plant species.

Based on estimates using Stoke's Law (see section 4.2.3.2), it is plausible that droplets ranging in size from 100 µ to 400 µ might drift about 3-23 feet at a wind speed of 5 miles per hour and 9-69 feet at a wind speed of 15 miles per hour. Although this drift might cause damage to some sensitive species, the impact would be limited and damage to non-target species probably could be minimized or avoided during the application process.

The empirical measures of drift summarized by Bird (1995) and discussed in section 4.2.3.2 suggest that 0.03 of the nominal application rate could drift 100 feet off-site. At an application rate of 0.15 lb a.e./acre, this would correspond to an effective off-site application of 0.0045 lb a.e./acre. This rate is about a factor of 10 above the NOAEL for post-emergent foliar spray of sensitive species, 0.0005 kg a.e./ha (Figure 4-5) [equivalent to 0.000446 lb a.e./acre] and in the range where substantial growth inhibition and some mortality would be expected. No effects, however, would probably be apparent in more tolerant plant species (Figure 4-6). At 1000 feet off-site, the data summarized by Bird (1995) can be used to estimate an effective rate of 0.00009 lb a.e./acre [0.0006 ×0.15 lb a.e./acre], which is below the post-emergence NOAEL for sensitive species by a factor of about 50 [0.0005 lb a.e./acre ÷ 0.00009 lb a.e./acre].

The simple verbal interpretation for this quantitative risk characterization is that some sensitive plant species could be adversely affected by off-site drift distances of about 100 feet but less than

Table 4-3: Summary of quantitative risk characterization for terrestrial animals[1]

Scenario	Hazard Quotient[2]		
	Typical	Lower	Upper
Acute/Accidental Exposures			
Direct spray, small mammal, first-order absorption	0.0004	0.00008	0.02
Direct spray, small animal, 100% absorption	0.01	0.008	0.2
Direct spray, bee, 100% absorption[3]	0.02	0.01	0.4
Consumption of contaminated vegetation, acute exposure	0.003	0.002	0.2
Consumption of contaminated water, acute exposure	0.0005	0.0002	0.003
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.0002	5.00e-07	0.002
Consumption of contaminated water, chronic exposure	0.00001	9e-07	0.001
Toxicity value for mammal [2]		250	mg/kg/day
Toxicity value for bee [3]		1000	mg/kg

[1] See Worksheet G01 for details of exposure assessment.
[2] Except for the honey bee, the hazard quotient is calculated as the estimated exposure divided by the chronic dogs NOAEL of 250 mg/kg/day and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on LD_{50} of >1000 mg/kg (Gagne et al. 1991) .

1000 feet. More tolerant species are not likely to be affected by off-site drift. This risk characterization is conservative in that the drift estimates from Bird (1995) are based only on aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no impact on off-site plant species.

Residual soil contamination with imazapyr could be a longer-term problem in some areas. As summarized in section 4.2.3.3, the expected concentrations of imazapyr in soil at an application rate of 1 lb a.e./acre is about 0.25 ppm. Thus, at the typical application rate of 0.15 lb a.e./acre, the expected concentration of imazapyr in the top 30 cm of soil shortly after treatment is about

0.04 ppm. This is reasonably consistent with the results of the GLEAMS modeling - i.e., about 0.035 ppm (Figures 4.2 and 4-3).

Based on the dose/response data from Rahman et al. (1993), illustrated in Figure 4-7, this concentration in soil would be associated with substantial growth inhibition in the four plant species for which data are available. At the upper range of the labeled application rate, 2.5 lbs a.e./acre, the resulting initial soil concentrations would be on the order of 0.6 ppm:

$$2.5 \text{ lbs a.e./ acre} \times 0.25 \text{ ppm. per lb a.e./acre} = 0.625 \text{ ppm.}$$

At this level, marked growth inhibition and/or mortality in non-target plant species would be expected.

A central issue for the characterization of risk is how long these effects might last. As summarized in section 4.2.3.3, reported halftimes in soil under field conditions range from about 30 days to 155 days, corresponding to dissipation or degradation rate coefficients of 0.0045 to 0.23 $days^{-1}$ [$k=\log_e(2) \div t_{1/2}$]. In any first order dissipation model, the fraction, *f*, remaining after time *t* is:

$$f = e^{-kt}.$$

By rearrangement, the time required to reach a certain fraction is:

$$t = \log_e(f) \div -k.$$

As illustrated in Figure 4-6, the approximate concentration of imazapyr in soil associated with a NOAEL for the most sensitive plant species is about 0.001 ppm and the NOAEL for the most tolerant plant species is about 0.02 ppm. Thus, taking the range of degradation rate coefficients of 0.0014 to 0.23 $days^{-1}$, time required to go from a concentration of 0.04 ppm - i.e., after the application of 0.15 lb a.e./acre - to 0.001 ppm would be:

$$t = \log_e(0.001 \text{ ppm} \div 0.04 \text{ ppm}) \div - 0.0045 \text{ to } 0.23 \text{ days}^{-1} = 16 \text{ to } 820 \text{ days,}$$

with the upper limit of the range corresponding to about 2.25 years. Thus, at the typical application rate, some residual effects on plant species could be expected for up about 2 years if microbial degradation were the only significant mechanism in the reduction of imazapyr in the soil.

As illustrated in Figures 4-1 and 4-2, however, microbial degradation will be the controlling factor only in very arid environments. At annual rainfall rates of 10 inches/year or more, imazapyr will be removed from the soil by runoff or percolation. Runoff is likely to be the dominant mechanism in clay soils and percolation the dominant mechanism in sandy soils. Intermediate soil types such as loam, while not specifically modeled in this risk assessment, will likely evidence a mix of runoff and percolation depending on specific soil and site characteristics. In more sandy soils (Figure

4-1) and at the typical application rate of 0.15 lb a.e./acre, imazapyr concentrations in soil could drop below the NOAEL of 0.02 ppm for tolerant species in a two to four week period in very moist climates - i.e., annual rainfall rates of 50 to 250 inches. Under more moderate rainfall conditions - i.e., 10 to 25 inches per year - the time required to reach concentrations of 0.02 ppm could range from one to over three months. In predominantly clay soils, variations in rainfall have less effect on decreases in the concentration of imazapyr. To reach NOAEL level of 0.02 ppm in clay would require about 30 to 60 days, depending on the amount of rainfall.

At higher application rates, much longer periods of time would be required to reach an imazapyr concentration in soil. For example, an application rate of 1.5 lb a.e./acre is 10 times higher than the typical rate used to generate Figures 4-1 and 4-2. Thus, in using these figures, a level of 0.02 ppm would be read as 0.002 ppm. In clay soils at any plausible rainfall rates, the time required to reach this level would be approximately one year. To reach soil concentrations below the NOAEL of 0.001 ppm for sensitive species could require a much longer period of time (Figures 4-1 and 4-2). Thus, if the Forest Service were to consider the use of substantially higher application rates, impacts on non-target vegetation could be prolonged.

As stressed in appendix 5, this characterization of risk is general rather than site-specific. The persistence and movement of imazapyr in soil is highly complex and substantially different estimates of persistence and transport could be made if different site-specific factors were considered. Thus, these estimates of exposure should be considered only as crude approximations of environmentally plausible levels.

4.4.3. Aquatic Organisms. For aquatic animals, the estimated concentrations of imazapyr in ambient water are identical to those used in the human health risk assessment. As a result of an accidental spill (worksheet D06) the highest estimated concentration of imazapyr in water is about 11 mg a.e./L. Under typical applications conditions, the estimated rate of contamination of ambient water is 0.082 (0.011 to 0.43) mg a.e./L at an application rate of 1 lb a.e./acre (worksheet B07). Thus, since the highest application rate considered in this risk assessment is 2.5 lb a.e./acre, the maximum estimated water concentration in ambient water would be about 1 mg/L [2.5 lb a.e./acre × 0.43 mg a.e./L÷1 lb a.e./acre = 1.075 mg a.e./L]. At the typical application rate of 0.15 lb a.e./acre, the estimated concentration of imazapyr in water is about 0.06 mg/L [0.15 lb a.e./acre × 0.43 mg a.e./L÷1 lb a.e./acre = 0.0645 mg a.e./L].

4.4.3.1. Aquatic Animals -- In terms of a direct toxic effect, the characterization of risk for aquatic animals is unambiguous. Based on both acute and chronic toxicity studies, the lowest dose that might be associated with an adverse effect is 92.4 mg a.e./L (a 62 day exposure to trout fry from Manning 1989a). The next lower concentration from this study, 43.1 mg a.e./L is a NOAEL for aquatic animals. Thus, it seems plausible that no toxic effects would be anticipated in aquatic animals either as the result of the accidental spills scenario or the highest application rate. The accidental spill scenario, as with any of the exposure scenarios that are subject to arbitrary variability, could be made more severe by increasing the amount of the spill or decreasing the size of the body of water. Plausibility of a more severe scenario, however, is questionable. A much

more realistic concern, however, would be secondary effects on aquatic animal populations because of toxic effects on aquatic plant species, as detailed in the following section.

4.4.3.2. Aquatic Plants -- Adverse effects on aquatic plants are plausible. At the typical application rate of 0.15 lb a.e./acre, the anticipated water concentration of 0.06 mg/L is about a factor of 5 above the EC_{25} for growth inhibition of 0.013 (0.009-0.019) mg/L in *Lemna gibba* (Hughes 1987). Thus, in this species and any other aquatic plant species with similar sensitivities, the application of imazapyr could cause detectable and probably substantial reduction in plant grow. This, in turn, could have an impact on aquatic animal communities. Based on the results of the GLEAMS modeling (Figure 4-3), levels in excess of 0.013 mg/L could be expected in areas with predominantly clay soil and relatively high rainfall rates for about 2 weeks (at rainfall rates of 100 inches/year) to two months (at rainfall rates of 250 inches/year). In areas with very sandy soil (Figure 4-4) and rainfall rates of 50 inches/year or more, imazapyr concentrations in pond water could be expected to exceed 0.013 mg/L for more prolonged periods - i.e., about 100 days.

Nonetheless, not all aquatic plant species would be impacted as greatly as *Lemna gibba* or species with similar sensitivities. Based on the available toxicity studies, unicellular algae may be much less sensitive, with EC_{50} values of about 0.2 mg/L to 2 mg/L for *Chlorella* (Landstein et al. 1993). Species at the lower but not the upper end of this range would be impacted, although for briefer periods of time than the most sensitive species.

As detailed in appendix 3, other aquatic plants are even less sensitive to imazapyr, with NOAELs on the order of 100 mg/L, similar to aquatic animals. No effects would be anticipated in these species under any conditions.

At the highest labelled application rate of 2.5 lb a.e./acre, the anticipated peak water concentration of 1 mg/L is about a factor of 77 above the EC_{50} for growth in *Lemna gibba*. Thus, in this species and any other aquatic plant species with similar sensitivities, the application of imazapyr would likely to cause obvious and substantial reduction in plant growth as well as mortality. In addition, some unicellular algae (i.e., EC_{50} values in the range of 0.2 mg/L to 2 mg/L) would evidence decreased growth. Again, some other aquatic plants that have sensitivities to imazapyr that are similar to aquatic animals would not evidence any adverse effects.

In the case of an accidental spill, concentrations on the order of 10 mg/L would likely cause detectable and substantial mortality in both unicellular algae and macrophytes. The duration of the effects would, of course, depend on rates of both dispersion and degradation, either biological or by photolysis. Taking the halftime of about 28 days in pond water (American Cyanamid 1991) corresponding to a degradation rate of 0.025 day^{-1}, the time required to reach 0.013 ppm would be 265 days:

$$t = \log_e(0.013 \text{ mg/L} \div 10 \text{ mg/L}) \div - 0.025 \text{ days}^{-1} = 265 \text{ days}.$$

Thus, an accidental spill of the magnitude used in this risk assessment could cause substantial adverse effects on aquatic plants for a prolonged period of time. As with most accidental scenarios used in this risk assessment, this characterization is dominated by arbitrary variability. Spills of lesser amounts or spills into bodies of water that are very large or have high turnover rates would cause less of an impact.

This general characterization of risk for aquatic plants could vary substantially depending on site-specific considerations. If imazapyr is applied near ponds, small lakes, or other bodies of water that have low rates of turnover, contamination of the water with imazapyr due either to runoff or percolation could impact aquatic vegetation for a period of time that could be sufficient to cause secondary effects on aquatic animals. Such effects would most likely be noted in areas with greater than average rainfall - i.e., >25 inches per year. For bodies of water that are more distant from the application site or have a relatively high flow rate - i.e., streams or rivers - phytotoxic concentrations of imazapyr are likely to be transient and have little impact on any plant species.

While confidence in this risk characterization is enhanced by the apparent concordance of the anticipated concentrations on imazapyr in water based on monitoring and modeling, this concordance should not be interpreted to suggest a general applicability of the exposure estimates. As detailed in appendix 5, the fate and transport of imazapyr in soil is highly complex and will be highly site-specific. Furthermore, while the modeled values are somewhat lower than the values based on monitoring, the modeled values may over-estimate exposure for many applications. For clay, the modeled values assume that all runoff is directly to a standing body of water with no consideration of buffer zones. For sand, it is assumed that all of the imazapyr percolating through the top three feet of soil reaches ground water and is transported directly to the standing body of water. Both of these assumptions are likely to over-estimate, perhaps grossly so, plausible levels of exposure at many sites.

Another factor that must be considered in assessing the probability of damage to aquatic plant species involves differences in species sensitivity. Data are available on relatively few species of aquatic plants and these data suggest that differences in sensitivity may range over a factor of about 1000: 0.013 mg/L to about 100 mg/L. It seems reasonable to suppose that if more data were available on a larger number of species this apparent difference in sensitivity would increase.

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6. GLOSSARY

Absorption -- The process by which the agent is able to pass through the body membranes and enter the bloodstream. The main routes by which toxic agents are absorbed are the gastrointestinal tract, lungs, and skin.

Acute exposure -- A single exposure or multiple exposure occurring within a short time (24 hours or less).

Additive effect -- A situation in which the combined effects of two chemicals is equal to the sum of the effect of each chemical given alone. The effect most commonly observed when two chemicals are given together is an additive effect.

Adjuvant(s) -- Formulation factors used to enhance the pharmacological or toxic agent effect of the active ingredient.

Adsorption -- The tendency of one chemical to adhere to another material.

Adverse-effect level (AEL) -- Signs of toxicity that must be detected by invasive methods, external monitoring devices, or prolonged systematic observations. Symptoms that are not accompanied by grossly observable signs of toxicity. In contrast to Frank-effect level.

Alkaline phosphatase – An enzyme that occurs in various normal and malignant tissues. The activity of the enzyme in blood is useful in diagnosing many illnesses.

Allelopathy – translocation of a herbicide to the roots of plants and subsequent loss from the roots to the surrounding soil, possibly posing a risk to neighboring vegetation.

Allometric -- pertaining to allometry, the study and measure of growth. In toxicology, the study of the relationship of body size to various physiological, pharmacological, pharmacokinetic, or toxicodynamic processes among species.

Amphibian – A cold-blooded vertebrate capable of operating on land and in water.

Arid – A terrestrial region lacking moisture, or a climate in which the rainfall is not sufficient to support the growth of trees or woody plants.

Assay -- A kind of test (noun); to test (verb).

Bioconcentration factor (BCF) -- The concentration of a compound in an aquatic orgainism divided by the concentration in the ambient water of the organism.

Biologically sensitive -- A term used to identify a group of individuals who, because of their developmental stage or some other biological condition, are more susceptible than the general population to a chemical or biological agent in the environment.

Broadleaf weed -- A nonwoody dicotyledonous plant with wide bladed leaves designated as a pest species in gardens, farms, or forests.

Cancer potency parameter -- A model-dependent measure of cancer potency $(mg/kg/day)^{-1}$ over lifetime exposure. [Often expressed as a q_1^* which is the upper 95% confidence limit of the first dose coefficient (q_1) from the multistage model.]

Carcinogen -- A chemical capable of inducing cancer.

Carcinoma -- A malignant tumor.

Carrier -- In commercial formulations of insecticides or control agents, a substance added to the formulation to make it easier to handle or apply.

Chlorosis -- yellowing or blanching of the leaves of plants. Restricted to causes other than light deficiency.

Chronic exposure -- Long-term exposure studies often used to determine the carcinogenic potential of chemicals. These studies are usually performed in rats, mice, or dogs and extend over the average lifetime of the species (for a rat, exposure is 2 years).

Conifer -- An order of the Gymnospermae, comprising a wide range of trees, mostly evergreens that bear cones and have needle-shaped or scalelike leaves; timber commercially identified as softwood.

Connected actions -- Exposure to other chemical and biological agents in addition to exposure to the control agent during program activities to control vegetation.

Contaminants -- For chemicals, impurities present in a commercial grade chemical. For biological agents, other agents that may be present in a commercial product.

Controls -- In toxicology or epidemiology studies, a population that is not exposed to the potentially toxic agent under study.

Creatine – An organic acid composed of nitrogen. It supplies the energy required for muscle contraction.

Creatinine – The end product of the metabolism of creatine. It is found in muscle and blood and is excreted in the urine.

Cumulative exposures -- Exposures that may last for several days to several months or exposures resulting from program activities that are repeated more than once during a year or for several consecutive years.

Dams – A term used to designate females of some species such as rats.

Degraded -- Broken down or destroyed.

Dermal -- Pertaining to the skin.

Dislodgeable residues – The residue of a chemical or biological agent on foliage as a result of aerial or ground spray applications, which can be removed readily from the foliage by washing, rubbing or having some other form of direct contact with the treated vegetation.

Dose-response assessment -- A description of the relationship between the dose of a chemical and the incidence of occurrence or intensity of an effect. In general, this relationship is plotted by statistical methods. Separate plots are made for experimental data obtained on different species or strains within a species.

Drift -- That portion of a sprayed chemical that is moved by wind off a target site.

EC_{50} -- A concentration that causes 50% inhibition or reduction. As used in this document, this values refers to a 50% inhibition of growth.

EC_{100} -- A concentration that causes complete inhibition or reduction. As used in this document, this values refers to a complete inhibition of growth.

Electrochemical process -- A newer manufacturing process for clopyralid. Details of the method are proprietary.

Empirical -- Refers to an observed, but not necessarily fully understood, relationship in contrast to a hypothesized or theoretical relationship.

Enzymes -- A biological catalyst; a protein, produced by an organism itself, that enables the splitting (as in digestion) or fusion of other chemicals.

Epidemiology study -- A study of a human population or human populations. In toxicology, a study which examines the relationship of exposures to one or more potentially toxic agent to adverse health effects in human populations.

Exposure assessment -- The process of estimating the extent to which a population will come into contact with a chemical or biological agent.

Extrapolation -- The use of a model to make estimates outside of the observable range.

Fetal anomaly – An abnormal condition in a fetus, which is usually the result of a congenital defect.

Formulation -- A commercial preparation of a chemical including any inerts or contaminants.

Frank effects -- Obvious signs of toxicity.

Frank-effect level (FEL) -- The dose or concentration of a chemical or biological agent that causes gross and immediately observable signs of toxicity.

Gavage -- The placement of a toxic agent directly into the stomach of an animal, using a gastric tube.

Genotoxic -- Causing direct damage to genetic material. Associated with carcinogenicity.

Geometric mean -- The measure of an average value often applied to numbers for which a log normal distribution is assumed.

Gestation -- The period between conception and birth; in humans, the period known as pregnancy.

Half-time or half-life -- For compounds that are eliminated by first-order kinetics, the time required for the concentration of the chemical to decrease by one-half.

Hazard quotient (HQ) -- The ratio of the estimated level of exposure to the RfD or some other index of acceptable exposure.

Hazard identification -- The process of identifying the array of potential effects that an agent may induce in an exposed human population.

Hematological -- Pertaining to the blood.

Hematology -- One or more measurements regarding the state or quality of the blood.

Henry's law constant -- An index of the tendency of a compound to volatilize from aqueous solutions.

Herbaceous -- A plant that does not develop persistent woody tissue above the ground (annual, biennial, or perennial, but whose aerial portion naturally dies back to the ground at the end of a growing season. They include such categories as grasses and grass-like vegetation.

Herbicide -- A chemical used to control, suppress, or kill plants, or to severely interrupt their normal growth processes.

Histopathology -- Signs of tissue damage that can be observed only by microscopic examination.

Hydrolysis -- Decomposition or alteration of a chemical substance by water.

Hydroxylation -- The addition of a hydrogen-oxygen or hydroxy (-OH) group to one of the rings. Hydroxylation increases the water solubility of aromatic compounds. Particularly when followed by conjugation with other water soluble compounds in the body, such as sugars or amino acids, hydroxylation greatly facilitates the elimination of the compound in the urine or bile.

Hymolytic anemia – A medical condition in which the number of red blood cells is decreased due to intravascular fragmentation or destruction.

In vivo -- Occurring in the living organism.

In vitro **--** Isolated from the living organism and artificially maintained, as in a test tube.

Inerts -- Adjuvants or additives in commercial formulations of glyphosate that are not readily active with the other components of the mixture.

Interpolation -- The use of mathematical models within the range of observations

Intraperitoneal -- Injection into the abdominal cavity.

Invertebrate -- An animal that does not have a spine (backbone).

Irritant effect -- A reversible effect, compared with a corrosive effect.

LC_{50} (lethal concentration$_{50}$) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LD_{50} (lethal dose$_{50}$) -- The dose of a chemical calculated to cause death in 50% of a defined experimental animal population over a specified observation period. The observation period is typically 14 days.

Lowest-observed-adverse-effect level (LOAEL) -- The lowest dose of a chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lymphatic – Pertaining to lymph, a lymph vessel, or a lymph node.

Lymph – A clear water fluid containing white blood cells. Lymph circulates throughout the lymphatic system, removing bacteria and certain proteins from body tissue. It also is responsible for transporting fat from the small intestine and suppling mature lymphocytes to the blood.

Macrophyte – Terrestrial plant

Malignant -- Cancerous.

Margin of safety (MOS) -- The ratio between an effect or no effect level in an animal and the estimated human dose.

Metabolite -- A compound formed as a result of the metabolism or biochemical change of another compound.

Metameter -- Literally, the unit of measure. Used in dose-response or exposure assessments to describe the most relevant way of expressing dose or exposure.

Microorganisms -- A generic term for all organisms consisting only of a single cell, such as bacteria, viruses, and fungi.

Microsomal -- Pertaining to portions of cell preparations commonly associated with the oxidative metabolism of chemicals.

Minimal risk level (MRL) -- A route-specific (oral or inhalation) and duration- specific estimate of an exposure level that is not likely to be associated with adverse effects in the general population, including sensitive subgroups.

Mitochondria -- Subcellular organelles involved in the conversion of food to stored chemical energy.

Most sensitive effect -- The adverse effect observed at the lowest dose level, given the available data. This is an important concept in risk assessment because, by definition, if the most sensitive effect is prevented, no other effects will develop. Thus, RfDs and other similar values are normally based on doses at which the most sensitive effect is not likely to develop.

Multiple chemical sensitivity -- A syndrome that affects individuals who are extremely sensitive to chemicals at extremely low levels of exposure.

Mutagenicity -- The ability to cause genetic damage (that is damage to DNA or RNA). A mutagen is substance that causes mutations. A mutation is change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Non-target -- Any plant or animal that a treatment inadvertently or unavoidably harms.

No-observed-adverse-effect level (NOAEL) -- The dose of a chemical at which no statistically or biologically significant increases in frequency or severity of adverse effects were observed

between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-observed-effect level (NOEL) -- The dose of a chemical at no treatment-related effects were observed.

Normal distribution -- One of several standard patterns used in statistics to describe the way in which variability occurs in a populations.

Octanol-water partition coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Ocular -- Pertaining to the eye.

Parenteral -- Any form of injection.

Partition -- In chemistry, the process by which a compound or mixture moves between two or more media.

Pathogen – A living organism that causes disease; for example, a fungus or bacteria.

Pathway -- In metabolism, a sequence of metabolic reactions.

Penta process -- The original manufacturing process for clopyralid. Details of the method are proprietary.

Perennial -- A plant species having a life span of more than 2 years.

Permeability – The property or condition of being permeable. In this risk assessment, dermal permeability refers to the degree to which a chemical or herbicide in contact with the skin is able to penetrate the skin.

pH -- The negative log of the hydrogen ion concentration. A high pH (>7) is alkaline or basic and a low pH (<7) is acidic.

pK_a -- The negative log of the hydrogen ion concentration or pH at which 50% of a weak acid is dissociated.

Pharmacokinetics -- The quantitative study of metabolism (i.e., the processes of absorption, distribution, biotransformation, elimination).

Prospective -- looking ahead. In epidemiology, referring to a study in which the populations for study are identified prior to exposure to a presumptive toxic agent, in contrast to a retrospective study.

Pup – The offspring or young of various animal species.

Release -- A work done to free desirable trees from competition with overstory trees, less desirable trees or grasses, and other forms of vegetative growth.

Reference dose (RfD) -- Oral dose (mg/kg/day) not likely to be associated with adverse effects over lifetime exposure, in the general population, including sensitive subgroups.

Relative weight -- The weight of an organ, such as the liver or kidney, divided by the total body weight of the animal.

Reproductive effects -- Adverse effects on the reproductive system that may result from exposure to a chemical or biological agent. The toxicity of the agents may be directed to the reproductive organs or the related endocrine system. The manifestations of these effects may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions dependent on the integrity of this system.

Resorption -- Removal by absorption. Often used in describing the unsuccessful development and subsequent removal of post-implantation embryos.

Retrospective -- looking behind. In epidemiology, referring to a study in which the populations for study are identified after exposure to a presumptive toxic agent, in contrast to a prospective study.

RfD -- A daily dose which is not anticipated to cause any adverse effects in a human population over a lifetime of exposure. These values are derived by the U.S. EPA.

Right-of-way -- A corridor of low growing shrubs or grasses that facilitate the maintenance and protection of utility power lines and provide transport pathways for humans or wildlife.

Route of exposure -- The way in which a chemical or biological agent enters the body. Most typical routes include oral (eating or drinking), dermal (contact of the agent with the skin), and inhalation.

Scientific notation -- The method of expressing quantities as the product of number between 1 and 10 multiplied by 10 raised to some power. For example, in scientific notation, 1 kg = 1,000 g would be expressed as 1 kg = 1 x 10^3 g and 1 mg = 0.001 would be expressed as 1 mg = 1 x 10^{-3}.

Sensitive subgroup -- Subpopulations that are much more sensitive than the general public to certain agents in the environment.

Sensitization – A condition in which one is or becomes hypersensitive or reactive to an agent through repeated exposure.

Site preparation -- The removal of competition and conditioning of the soil to enhance the survival and growth of seedlings or to enhance the seed germination.

Species-to-species extrapolation -- A method involving the use of exposure data on one species (usually an experimental mammal) to estimate the effects of exposure in another species (usually humans).

Subchronic exposure -- An exposure duration that can last for different periods of time, but 90 days is the most common test duration. The subchronic study is usually performed in two species (rat and dog) by the route of intended use or exposure.

Substrate -- With reference to enzymes, the chemical that the enzyme acts upon.

Synergistic effect -- A situation is which the combined effects of two chemicals is much greater than the sum of the effect of each agent given alone.

Systemic toxicity -- Effects that require absorption and distribution of a toxic agent to a site distant from its entry point at which point effects are produced. Systemic effects are the obverse of local effects.

Teratogenic -- Causing structural defects that affect the development of an organism; causing birth defects.

Teratology -- The study of malformations induced during development from conception to birth.

Terrestrial – Anything that lives on land as opposed to living in an aquatic environment.

Threshold -- The maximum dose or concentration level of a chemical or biological agent that will not cause an effect in the organism.

Thymus – A small gland that is the site of T-cell production. The gland is composed largely of lymphatic tissue and is situated behind the breastbone. The gland play an important role in the human immune system.

Toxicity -- The inherent ability of an agent to affect living organisms adversely.

Uncertainty factor (UF) -- A factor used in operationally deriving the RfD and similar values from experimental data. UFs are intended to account or (1) the variation in sensitivity among members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is less than lifetime exposure; and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10. See table 2-4 for additional details.

Vehicle -- A substance (usually a liquid) used as a medium for suspending or dissolving the active ingredient. Commonly used vehicles include water, acetone, and corn oil.

Vertebrate -- An animal that has a spinal column (backbone).

Volatile -- Referring to compounds or substances that have a tendency to vaporize. A material that will evaporate quickly.

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IMAZAPYR
APPENDICES

Appendix 1: Toxicity of imazapyr to mammals.
Appendix 2: Toxicity of imazapyr to birds after oral administration.
Appendix 3: Toxicity of imazapyr to non-target terrestrial plants.
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Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
ORAL			
Acute Oral			
Rats, Charles River, albino, 6-weeks-old, 5 males (bw=151-157 g) and 5 females (bw=120-124 g)	Single oral dose of 5000 mg/kg or 25 mL/kg. 14-day observation period. [Test material specified as AC 3532-149 or 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; 2 lb/gallon formulation.] Fiche contains CBI data on ingredients not summarized in this appendix.	No mortality among females. One male rat died (necropsy revealed congestion of liver, kidney, and intestinal tract, and hemorrhagic lungs). Surviving test animals showed no visible lesions. LD_{50} = >5000 mg/kg	Fischer 1983 MRID 00132031
Rats, Charles River, albino, 7-10 weeks old, 5 males (bw=167-173 g) and 5 females (bw=193-199 g)	Single oral dose of 5000 mg/kg or 4.8 mL/kg. [Test material specified as AC 5329-101-C or Imazethapyr and Imazapyr 170/ 6.5 gallon/L AS formulation.]	No mortality; no signs of toxicity, no gross lesions at necropsy. LD_{50} = >5000 mg/kg	Lowe 1988 MRID 40463402

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Chronic, Oral			
Dogs, Beagles, 5-6 months old, 6 males and 6 females per dose group, 4 dose groups	0, 1000, 5000, or 10,000 ppm in the diet for 1 year. Positive dose levels correspond to 27.6, 129.18, or 262.88 mg/kg for males, and 29.71,127.72, or 269.80 mg/kg for females (mg/kg doses based on midpoint food consumption and body weights reported in the study). [Test material specified as AC 243,997, purity = 99.5%]	No mortality; no clinical signs of toxicity attributed to treatment, 10,000 ppm considered to be “no-effect” level.	Shellenger 1987 MRID 41039502

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Mice, CD-1, approximately 42 days old, 65 males (mean bw=27 g) and 65 females (mean bw=21g) per dose level.	Dietary exposure to 0, 1000, 5000, or 10,000 ppm for 18 months. Test substance intake based on measured food consumption values ranged as follows: 126-254, 674-1194, and 1301-2409 mg/kg/day in males and 151-303, 776-1501, and 1639-3149 mg/kg/day in females.	No dose-related or statistically significant (Chi-square analysis) differences in mortality between controls and treated mice, but survival in treated males was slightly better than in control males and survival in mid- and high-dose females was slightly worse than in control females. Although there were no treatment-related effects on body weight; increased food consumption was statistically significant among treated mice but was not considered treatment related in the absence of a dose-response relationship No statistically significant adverse effects on hematology were observed. Organ weight data indicate a "few statistically significant differences," which occurred sporadically and were not considered treatment related. Gross pathology revealed a slightly higher incidence of enlarged mesenteric lymph nodes in all treated mice, but no dose-response relationship; a slightly increased incidence of kidney cysts in high dose males [5/33 (15%)] compared with controls [2/28 (7%); and a dose-related, but not statistically significant increase in the number of enlarged seminal vesicles: [0ppm 3/28 (11%); 1000ppm 6/35 (17%); 5000ppm 9/34 (27%); 10,000ppm 10/33 (30%)], which the investigators viewed as "common findings in old mice." Microscopic evaluation revealed changes that occurred with greater incidence in high dose mice, compared with controls. These mild inflammatory changes, which were not statistically significant and not considered treatment related, included plasma cell hyperplasia in the mesenteric lymph nodes and erythrocytes in the sinus of the mediastinal lymph nodes in females. There was no difference in the incidence of pathological findings in gonads between treated and control mice and no dose-related differences in incidence or degree of hydronephrosis.	Auletta 1988 MRID 41039504

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rats, Sprague-Dawley, 44 days old, 260 males (bw=158-221 g), 260 females (bw=121-174 g) 65 males and 65 females per dose group, control plus 3 dose groups.	0, 1000, 5000, or 10,000 ppm for 2 years. Partial sacrifice (10 per group) after 12 months of treatment; all remaining survivors sacrificed after 24 months. Mean test substance intake values calculated over the 2-year study duration, based on individual body weight and food consumption, and the purity of the test material were 49.9, 252.6, and 503.0 mg/kg/day for males and 64.2, 317.6, and 638.6 mg/kg/day for females (cf: pg 13 of study).	No differences in the number of deaths among control and treated animals. In males, there was a slight but statistically insignificant relationship between dose level and time to death. Females (in all treatment groups) showed a slight (and in most cases statistically significant) increase in food consumption during the first year; however, the effect, which did not always exhibit a dose response, was not considered toxicologically significant. In control and all treated groups there was a random distribution of gross lesions considered to be incidental changes unrelated to exposure to test material. There were no treatment-related effects on hematology, clinical chemistry or urinalysis, mean organ weights, organ/body weight or organ/brain weight ratios; however, there was an increased incidence of C-cell carcinomas of the thyroid gland in high dose males. [See section 3.1.5 for a detailed discussion of the significance of these findings.]	Daly 1988 MRID 41039503

Reproduction/Teratogenicity

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rabbits, New Zealand White, albino, females, nominally 18 per dose (only data for gravid females are summarized; VC=17; T-1=18; T-2=16; T-3=17)	0, 25, 100, or 400 mg/kg bw by gavage on days 6-18 of gestation. [Test material specified as AC 243,997].	Two rabbits in the control group and two rabbits in the 400 mg/kg died; gross pathology revealed only pulmonary changes. All other does survived to final sacrifice. A slightly increased incidence of common and expected pulmonary and hepatic changes was observed in the treated does but was not considered treatment related. There was no evidence of reproductive effects in the dams; there were no statistically significant differences in fetal body weight and crown-rump length compared with controls. EXTERNAL ANOMALIES: There was one external anomaly observed in the 25 mg/kg group and four in the 400 mg/kg group. In the 25 mg/kg group (152 fetuses; 17 litters), one fetus had a short tail. [Another fetus had a left eye that appeared larger than normal, but appeared to be normal in size during internal examination.] In the 400 mg/kg group (144 fetuses; 16 litters), one fetus had a kink at the tip of the tail; there were two fetuses (from the same litter) with talipes; and one anurous fetus (from a different litter) with talipes and spina bifida. Evaluations of fetal internal, skeletal, and internal head development indicated no consistent, adverse effects resulting from exposure to AC 243,997.	Salamon et al. 1983c MRID 00131613

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rabbits, New Zealand White, albino, females, nominally 5 per dose (only data for gravid females are summarized; VC=4; T-1=5; T-2=3; T-3=5; T-4=5)	0, 250, 1000, or 2000 mg/kg bw by gavage on days 6-18 of gestation. [Test material specified as AC 243,997].	Mortality in does = 2/5 (250 mg/kg); 4/5 (1000 mg/kg); and 5/5 (2000 mg/kg). At 250 mg/kg, necropsy revealed fluid in the trachea and chronic non-suppurative pneumonia in one animal and pulmonary exudate and discoloration, gastric mucosal depressions and ulcers in the other. At 1000 mg/kg, necropsy revealed stomach lesions (discolorations/depressions) in all four animals. At 2000 mg/kg, necropsy revealed gastric mucosal changes (erosive lesions) in four animals and gastric and pyloric mucosal discolorations in the other animal. In animals that survived to final sacrifice, there were no treatment-related adverse effects on body weight, mean numbers of corpora lutea, implantation sites, resorption sites, viable fetuses, and gross pathology. Exposure levels of 1000 and 2000 mg/kg resulted in maternal death; exposure levels of 250 and 500 mg/kg did not produce exaggerated pharmacological or embryocidal effects.	Salamon et al. 1983d MRID 00131614 This is a pilot study for Salamon et al. 1983c.
Rats, Charles River, female, 25 per dose group (only data for gravid females are summarized; VC=22; T-1=24; T-2=23; T-3=22)	0, 100, 300, or 1000 mg/kg bw by gavage on days 6-15 of gestation. [Test material specified as AC 243,997].	No mortality; no teratogenicity; salivation was observed in 6/22 animals treated with 1000 mg/kg bw/day.	Salamon et al. 1983a MRID 00131611
Rats, Charles River, female, 5 per dose group	0, 250, 500, 1000, or 2000 mg/kg bw on days 6-15 of gestation. [Test material specified as AC 243,997].	No mortality; no pharmacological or embryocidal effects; only recurring effect was salivation: 1/5 (250 mg/kg); 2/5 (500 mg/kg); 3/5 (1000 mg/kg); 5/5 (2000 mg/kg)	Salamon et al. 1983b MRID 00131612 This is a pilot study for Salamon et al. 1983a.

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rats, Sprague-Dawley, 25 males (bw=187-240 g) and 25 females (bw=128-166 g) forming F_0 generation in a 2-generation reproduction study.	0, 1000, 5000, or 10,000 ppm in the diet. Rats were treated for 64 days prior to mating, throughout the two mating periods and for approximately 3 weeks after the end of the second mating period. Ranges of achieved intake of AC 243,997 between weeks 1 to 10 and 18 to 19 were as follows: **males:** 48.3 to 142.8, 252.8 to 720.8, and 483.4 to 1471.8 mg/kg/day, corresponding to 1000, 5000, and 10,000 ppm, respectively; **females:** 80.2 to 149.9, 404.7 to 736.1, and 761.3 to 1537.1 mg/kg/day, corresponding to 1000, 5000, and 10,000 ppm, respectively;	**In the F_0 and F_{1b} adult generations**: There were no treatment-related effects on mortality, or pathology, and no clinical signs of toxicity. There were no adverse effects on body weights or food consumption in any of the dose groups. There were no significant differences in fertility indices, day of mating, or other parameters of parental performance. The incidence of dead pups at birth varied markedly among groups and was occasionally statistically significant but did not show a clear dose-response relationship. Other parameters of reproductive toxicity (i.e., gestation index, length of gestation, number of live pups at birth, and sex ratio) were similar to control values. **In the F_{1a}, F_{1b}, F_{2a}, F_{2b} pups**: There were no adverse effects on viability, survival, or lactation indices, or on the clinical condition of the pups. Except for one occasion, the body weights of pups in the treated group were not significantly different from controls. There were no pathology findings related to treatment.	Robinson 1987 MRID 41039505

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
DERMAL			
Rabbits, New Zealand, white, albino, young adults, 10 per sex per dose	0, 100, 200, or 400 mg/kg/day to close-clipped, intact or abraded, occluded backs, 5 days/week for 3 weeks	Two rabbits died with gross evidence (confirmed microscopically) of pneumonia; no systemic toxicity (i.e., no adverse effects on body weight, food consumption, hematology, serum chemistry or organ weights). Microscopic evaluation of all tissues from control and high dose group rabbits and all remarkable tissues from low and middle dose group rabbits did not indicate consistent or distinct treatment-related effects.	Larson and Kelly 1983 MRID 00131609
Rabbits, New Zealand, white, albino, males (mean bw 3.09) and females (mean bw 2.64), 12-14 weeks old, 5 per sex per dose.	Single dermal dose of 2.0 mL/kg or 2148 mg/kg applied to shaved skin using an impervious plastic cuff that provided 24-hour contact. [Test material specified as AC 3532-149 or 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; 2 lb/gallon formulation.] Fiche contains CBI data on ingredients not summarized in this appendix.	No mortality among females. One male died (necropsy revealed pneumonic areas of the lungs). Of survivors, 1/9 had mottled and pale liver; 1/9 had moderate congestion of the lungs; 7/9 had no visible lesions. LD_{50}=>2000 mg/kg or 2 mL/kg	Fischer 1983 MRID 00132031

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rabbits, New Zealand, white, albino, 5 males (mean bw=2.59 g), 5 females (mean bw = 2.56 g)	Single dermal dose of 1.92 mL/kg or 2000 mg/kg applied by application to dorsal surface (area = approx. 10% of body surface) to nonfasted, shaved animals. Test material held under impervious plastic cuff for 24-hour continuous contact. After 24-hour exposure, cuff removed, treated site wiped with moistened gauze pad, and animals fitted with fiber collars to prevent further ingestion of remaining test material. [Test material specified as AC 5329-101-C or Imazethapyr/Imazapyr 170/6.5 gallon/L AS formulation.]	One male rabbit died on day 12 of study due apparently to an incurrent respiratory infection. Necropsy revealed pale kidneys, consolidation and adhesions in the lungs and fluid in the pleural cavity. No other deaths occurred and no other gross lesions were observed in the surviving animals. No overt signs of toxicity were observed during the study. LD_{50}=>2000 mg/kg or 1.92 mL/kg. Investigators indicate that the product is considered to be “no more than slightly toxic by single skip applications.”	Lowe 1988 MRID 40763402

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
Rabbits, New Zealand, white, albino, 6 males	0.5 mL applied to shaved, abraded or intact skin (intact and abraded sites were on opposite side of the midline of the same animal) for 24 hours. [Test material specified as AC 3532-149 or 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; 2 lb/gallon formulation.] Fiche contains CBI data on ingredients not summarized in this appendix.	Skin irritation was scored according to the Draize scoring system. At 24 hours, mean scores for erythema were 1.00 (intact skin) and 1.67 (abraded skin); means scores for edema were 0.00 (intact skin) and 1.50 (abraded skin) At 72 hours, mean scores for erythema were 0.33 (intact skin) and 0.67 (abraded skin); means scores for edema were 0.00 (intact skin) and 0.00 (abraded skin). The total mean score = 5.17; Primary Irritation Score (total score/4) = 1.29. The test material is considered to be mildly irritating to rabbit skin.	Fischer 1983 MRID 00132031
Rabbits, New Zealand, white, albino, 6 males	0.5 mL applied to shaved, 1" squares of intact skin on dorsal surface (opposite side of the midline of the same animal served as control). Test material was covered with gauze pad, occluded with plastic wrap, and left in contact with skin for 4 hours. [Test material specified as AC 5329-101-C or Imazethapyr/Imazapyr 170/6.5 gallon/L AS formulation.]	Skin irritation was scored according to the Draize scoring system. The maximum possible score for skin irritation is 4. Sites were scored for irritation at 4, 24, 48, and 72 hours. The test material was not irritating to the skin of rabbits.	Lowe 1988 MRID 40763402

Appendix 1: Toxicity to experimental mammals.

Animal	Dose	Response	Reference
EYES			
Rabbits, New Zealand, white, albino, males, 6 in group without rinsing, 3 in group with rinsing	0.1 mL instilled into conjunctival sac of right eye (left eye served as control) with or with out rinsing after 20 seconds [Test material specified as AC 3532-149 or 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; 2 lb/gallon formulation.] Fiche contains CBI data on ingredients not summarized in this appendix.	Eye irritation was scored according to the Draize scoring system. The maximum possible scores for eye irritation reactions are: cornea (80); iris (10), conjunctiva (20). Observations of the cornea, iris, and conjunctiva at 24, 48, and 72 hours and 4 and 7 days indicated that the test material was irritating to the rabbit eye with complete recovery by 7days. The group without rinsing had substantially higher mean irritation scores, compared with the group with rinsing.	Fischer 1983 MRID 00132031
Rabbits, New Zealand, white, albino, 6 males	0.1 mL instilled into conjunctival sac of right eye (left eye served as control) without rinsing for 24 hours, after which time, treated eyes were rinsed with tap water. [Test material specified as AC 5329-101-C or Imazethapyr/Imazapyr 170/6.5 gallon/L AS formulation.]	Eye irritation was scored according to the Draize scoring system. The maximum possible scores for eye irritation reactions are: cornea (80); iris (10), conjunctiva (20). Examinations of the cornea, iris, and conjunctiva at 1 hour, 24, 48, and 72 hours (with the aid of ultraviolet light and fluorescein) indicated that the test material was “nonirritating” to the rabbit eye.	Lowe 1988 MRID 40763402

Appendix 2: Toxicity to birds after oral administration.

Animal	Dose	Response	Reference
Ducks, Mallard, 4 days old at start, 10 per dose	0, 312, 625, 1250, 2500, or 5000 ppm in diet for 5 days. [0, 64, 145, 273, 595, or 1149 mg/kg bw based on measured food consumption.]	No mortality [Study included one control group for each test group]	Fletcher 1983b MRID 00133553
Ducks, Mallard, approximately 23 weeks old, 16 per dose per sex.	0, 500, 1000, or 2000 ppm in diet for 18 weeks. [50, 100, or 200 mg/kg bw based on measured food consumption (birds consumed approximately 10% body weight as specified in Table II of fiche)] [Test material specified as AC 243,997 Technical]	No significant reductions for any of the reproductive endpoints examined (i.e., egg production, hatchability, survival of hatchlings). NOEC for reproductive effects = 2000 ppm AC 243,997.	Fletcher et al. 1995b MRID 43831402
Quail, Bobwhite, 11-17 days old at start,10 per dose, body weight of 20-35 g	0, 312, 625, 1250, 2500, or 5000 ppm in diet for 5 days. [0, 38, 72, 148, 322, and 674 mg/kg bw based on measured food consumption.] [Test material specified as AC 243,997]	No mortality. [Study included one control group for each test group]	Fletcher 1983a MRID 0133552
Quail, Northern Bobwhite, young adults, 12 males and 24 females per dose,	0, 500, 1000, or 2000 ppm in diet for 18 weeks. [50, 100, or 200 mg/kg bw based on measured food consumption (birds consumed approximately 10% body weight as specified in Table I of fiche)] [Test material specified as AC 243,997 Technical]	No significant reductions for any of the reproductive endpoints examined (i.e., egg production, hatchability, survival of hatchlings). NOEC for reproductive effects = 2000 ppm AC 243,997. Mortality among the birds was as follows: 0 ppm = 2M, 5F 500 ppm = 1M, 4F 1000 ppm =1M, 3F 2000 ppm = 0M, 5F	Fletcher et al. 1995a MRID 43831401

Appendix 3: Toxicity to experimental plants.

Plant	Exposure	Response	Reference
Tier II non-target terrestrial plants Expresses data in units of a.i. but indicates that assays were conducted on the acid. ∴a.i. == a.e.	Seed germination: cucumber, soybean, wheat, onions, peas, tomato, corn, sugarbeets, sunflower, and oats. Seeds on filter paper in petri dish. Chemical dissolved in acetone/water. Each dish sprayed at rates from 0.035 kg/ha to 1.12 kg/ha.	Tomatoes: EC_{50} 1.120 kg/ha Sugarbeet EC_{25} 0.140 kg/ha	American Cyanamid 1988. MRID 40811801.
	Seedling emergence: corn, wheat, sugarbeets, sunflower, tomato, cucumber, oats, onions, soybeans, and green peas. Each crop planted in 4 inch dixie cups filled with sand. 10 seeds per cup. Spray applications of 0.00219 to 1.12 kg/ha in acetone water solution.	Sugarbeet: EC_{25} 0.00219 kg/ha Corn and Onions: EC_{25} 1.12 kg/ha No significant effect on other species.	

Post-emergence/foliar applications. Green peas, soybeans, onions, corn, wheat, oats, sugarbeets, sunflowers, tomatoes and cucumbers. [All on fiche 2 of 2]. Green house at 24°C. Technical grade acid in 1:1 (v/v) solution of acetone and water and sprayed at 400 L/ha with laboratory belt sprayer. Tween 20 surfactant added to spray solution at 0.25% (v/v). Five seedlings per pot, 3 replicate pots per application rate. Two series of studies. In first, seedlings grown 13 days prior to treatment with application rates of 0.00219 to 1.12 kg/ha. In second part of study, used only corn, wheat, oats, sugarbeets, sunflowers, cucumbers, and tomatoes. Larger seedlings grown for 28 days with application rates of 0.000068 to 0.01750 kg/ha.	All crops tested EC_{25} 0.00219-0.00875 kg/ha EC_{50} 0.00219-0.0175 kg/ha **Most tolerant:** green peas. 100% injury at 0.14 kg/ha and higher. No significant injury at 0.00438 kg/ha and lower. **Study 1:** Based on heights, no significant injury at <0.0085 kg/ha. Based on weights, no significant injury at <0.035 kg/ha. Height is most sensitive objective endpoint. All plants died at 0.28 kg/ha and above. **Most Sensitive:** sugarbeets affected at rates of >0.000548 kg/ha. **Study 1:** Table 19 shows visual injury (50%) at lowest conc. tested, 0.00219 kg/ha. Table 20 shows about 80% inhibition based on fresh weight at 0.00219 kg/ha. Table 21 shows about 40% inhibition based on height at 0.00219.] All plants died at 0.00875 kg/ha and above. **Study 2:** Table 40 shows visual injury (50%) at about 0.001 kg/ha, similar to study 1. Table 41 shows about 50% inhibition based on height at 0.00219 kg/ha, again consistent with Study 1. Table 22 shows about 50% inhibition based on weight at 0.00219.] All plants died at 0.00875 kg/ha and above. Large seedlings tolerated higher levels than smaller seedlings. Monocots could tolerate up to 0.00875 kg/ha without damage. Dicots were more variable.	American Cyanamid 1988. MRID 40811801. *(Continued)*

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801

Raw Data on Green Peas from American Cyanamid (1988) MRID 40811802

Application Rate (kg/ha)	Height (cm)	Weight (g)
0.14	3	0.41
0.14	7	0.90
0.14	7	0.58
0.07	9	7.23
0.07	10	12.31
0.07	10	13.44
0.035	26	10.10
0.035	11	15.18
0.035	22	7.70
0.0175	30	20.33
0.0175	22	23.18
0.0175	40	23.33
0.00875	31	16.22
0.00875	37	22.56
0.00875	43	26.66
0.00438	33	20.94
0.00438	34	27.70
0.00438	35	34.72
0.00219	34	26.50
0.00219	31	10.20
0.00219	33	30.63
0.00	42	14.96
0.00	33	28.86
0.00	32	14.00

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801 *(continued)*.

Raw Data on Sugarbeets from American Cyanamid (1988) MRID 40811802

Application Rate (kg/ha)	Height (cm)	Weight (g)
0.00438	8	15.80
0.00438	10	49.30
0.00438	3	19.00
0.00219	13	67.80
0.00219	16	43.30
0.00219	12	58.20
0.001095	15	108.30
0.001095	18	72.90
0.001095	19	109.90
0.000548	24	120.00
0.000548	23	132.60
0.000548	27	127.80
0.000274	20	116.10
0.000274	20	119.00
0.000274	18	96.70
0.000137	18	90.30
0.000137	21	127.00
0.000137	23	112.80
0.000068	23	162.00
0.000068	27	161.30
0.000068	24	161.00
0.00	24	114.50
0.00	26	111.50
0.00	26	122.70

EXPONENTIAL MODEL

Green Peas: Effect on **Height** Study #1
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Exponential model**: Y = exp(a + b*X)

Dependent variable: HEIGHT
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	3.55911	0.0702098	50.6924	0.0000
Slope	-14.5856	1.22845	-11.8731	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	10.5203	1	10.5203	140.97	0.0000
Residual	1.64179	22	0.0746269		
Lack-of-Fit	0.456712	6	0.0761187	1.03	0.4430
Pure Error	1.18508	16	0.0740675		
Total (Corr.)	12.1621	23			

Correlation Coefficient = -0.930058
R-squared = 86.5007 percent
Standard Error of Est. = 0.273179

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801 *(continued)*.

Green Peas: Effect on **Weight** Study #1
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Exponential model**: Y = exp(a + b*X)

Dependent variable: WGT_G
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	3.29476	0.124837	26.3925	0.0000
Slope	-24.3872	2.18426	-11.165	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	29.4106	1	29.4106	124.66	0.0000
Residual	5.19049	22	0.235931		
Lack-of-Fit	3.11944	6	0.519907	4.02	0.0121
Pure Error	2.07104	16	0.12944		
Total (Corr.)	34.601	23			

Correlation Coefficient = -0.921949
R-squared = 84.999 percent
Standard Error of Est. = 0.485728

Sugar Beets Effect on **Height** Study #2
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Exponential model:** Y = exp(a + b*X)

Dependent variable: HEIGHT
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	3.18998	0.0601464	53.0369	0.0000
Slope	-300.977	33.6371	-8.94776	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	4.38471	1	4.38471	80.06	0.0000
Residual	1.20486	22	0.0547661		
Lack-of-Fit	0.239648	6	0.0399413	0.66	0.6811
Pure Error	0.965207	16	0.0603255		
Total (Corr.)	5.58957	23			

Correlation Coefficient = -0.885689
R-squared = 78.4446 percent
Standard Error of Est. = 0.234022

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801 *(continued)*.

Sugar Beets Effect on **Weight** Study #2
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Exponential model:** Y = exp(a + b*X)

Dependent variable: WGT_G
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	4.89943	0.0658323	74.4229	0.0000
Slope	-385.097	36.817	-10.4598	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	7.17819	1	7.17819	109.41	0.0000
Residual	1.44343	22	0.0656103		
Lack-of-Fit	0.389361	6	0.0648936	0.99	0.4672
Pure Error	1.05406	16	0.065879		
Total (Corr.)	8.62162	23			

Correlation Coefficient = -0.912459
R-squared = 83.2581 percent
Standard Error of Est. = 0.256145

LINEAR MODEL

Green Peas: Effect on **Height** Study #1
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Linear model:** Y = a + b*X

Dependent variable: HEIGHT
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	33.7991	1.63089	20.7243	0.0000
Slope	-235.378	28.5355	-8.24862	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	2739.75	1	2739.75	68.04	0.0000
Residual	885.874	22	40.267		
Lack-of-Fit	451.874	6	75.3123	2.78	0.0479
Pure Error	434.0	16	27.125		
Total (Corr.)	3625.63	23			

Correlation Coefficient = -0.869289
R-squared = 75.5663 percent
Standard Error of Est. = 6.34563

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801 *(continued)*.

Green Peas: Effect on **Weight** Study #1
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Linear model:** Y = a + b*X

Dependent variable: WGT_G
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	22.7913	1.59118	14.3235	0.0000
Slope	-165.995	27.8407	-5.9623	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	1362.6	1	1362.6	35.55	0.0000
Residual	843.263	22	38.3301		
Lack-of-Fit	264.386	6	44.0644	1.22	0.3475
Pure Error	578.876	16	36.1798		
Total (Corr.)	2205.86	23			

Correlation Coefficient = -0.78595
R-squared = 61.7717 percent
Standard Error of Est. = 6.19113

Analysis of Dose/Response Relationships in Non-target Terrestrial Plants from American Cyanamid 1988, MRID 40811801 *(continued)*.

Sugar Beets Effect on **Height** Study #2
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Linear model:** Y = a + b*X

Dependent variable: HEIGHT
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	23.3244	0.751989	31.0169	0.0000
Slope	-3903.39	420.553	-9.28156	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	737.495	1	737.495	86.15	0.0000
Residual	188.339	22	8.56085		
Lack-of-Fit	109.672	6	18.2787	3.72	0.0166
Pure Error	78.6667	16	4.91667		
Total (Corr.)	925.833	23			

Correlation Coefficient = -0.89251
R-squared = 79.6574 percent
Standard Error of Est. = 2.92589

Sugar Beets Effect on **Weight** Study #2
Note: Excludes data on dead plants,
reported as zero in American Cyanamid 1988 MRID 40811801
Regression Analysis - **Linear model:** Y = a + b*X

Dependent variable: WGT_G
Independent variable: RATE_KGHA

Parameter	Estimate	Standard Error	T Statistic	P-Value
Intercept	127.62	5.39683	23.6472	0.0000
Slope	-24661.6	3018.2	-8.17098	0.0000

Analysis of Variance with Lack-of-Fit

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Model	29438.7	1	29438.7	66.76	0.0000
Residual	9700.48	22	440.931		
Lack-of-Fit	6709.66	6	1118.28	5.98	0.0019
Pure Error	2990.82	16	186.926		
Total (Corr.)	39139.2	23			

Correlation Coefficient = -0.867268
R-squared = 75.2154 percent
Standard Error of Est. = 20.9984

Appendix 4: Toxicity to fish, aquatic invertebrates, and aquatic plants.

Animal	Exposure	Response	Reference
FRESHWATER			
Fish			
Trout, Rainbow Sunfish, Bluegill Catfish, Channel	96-hours	LC_{50} >100 mg/L	Peoples 1984 Gagne et al. 1991
Trout, Rainbow, early life-stage (28-day post swim-up) 20 trout per concentration.	Measured concentrations of 0, 6.59, 12.1, 24.0, 43.1, or 92.4 mg/L for 62 days. Flow-through freshwater toxicity test. [Test material specified as AC 243,997]	No statistical effects on hatching, survival, or growth. Investigators report a "nearly significant effect on hatching in the 92.4 mg/L concentration and an observed reduction on survival at the same concentration"; however, in the conclusion of the study, the investigators discount the significance of the effects due to a "lack of a correlation to test concentration and lack of corresponding reductions in wet and dry weights."	Manning 1989a MRID 41315804
Invertebrates			
Daphnia magna, <24 hours old, 5 replicates per concentration, 10 animals per replicate	0, 10, 18, 32, 56, or 100 mg/L for 24 or 48 hours, static, no aeration. [Test material specified as AC 243,997 Technical]	No mortality at 24 or 48 hours of exposure 24-hour LC_{50} = >100 mg/L 48-hour LC_{50} = >100 mg/L	Kintner and Forbis, 1983 MRID 00133550
Daphnia magna, <26-hours old, 4 replicates per concentration, 10 animals per replicate	Measured concentrations of <2.63 (control) 5.73, 11.7, 23.8, 45.6, or 97.1 mg/L in a 21-day flow-through test. [Test material specified as AC 243,997, 99.5% a.i.]	No adverse effects on survival, reproduction, or growth of 1st generation. 7-, 14- and 21-day LC_{50} =>97.1; NOEC =97.1 mg/L; MATC =>97.1 mg/L	Manning 1989b MRID 41315805

Plants

Selenastrum capriconutum, a green algae	Nominal concentrations of 10-100 mg a.e./L. Mean measured concentrations of 9.4-101.2 mg/L. 7 day exposure	Only highest conc. caused inhibition (99.9%). Lower conc. (56 mg/L and less) caused stimulation. Based on cell density, EC_{25} of 48 mg/L and EC_{50} of 71mg/L. Confidence intervals not provided.	Hughes 1987 MRID 40811802
Anabaen flosaquae, a blue-green algae	Nominal concentrations of 0, 5.6, 10, 18, 32, 52, and 100 mg a.e./L for 7 days. Note: Study says a.i. but only identifies the material as AC243,997. The water solubility that they give is that of the acid.	EC_{25} for Cell Count 7.3 (<0.0001-51.4) mg/L EC_{50} for Cell Count 11.7 (<0.0001-105.5) mg/L	Hughes 1987 MRID 40811802
Naviculla pelliculosa, a freshwater diatom	Concentrations of 10 to 100 mg a.e./L for 7 days. Static.	All concentrations caused stimulation rather than inhibition of cell number. Extent of stimulation was 1.6% to 17% with no apparent dose/response relationship.	Hughes. 1987 MRID 40811802
Chlorella emersonii, an green algae	Concentrations ranging from 1 µM [0.261 mg/L] to about 100 µM [26.1 mg/L]	IC_{50} for growth of about 0.8 µM [≈0.2 mg/L] taken from Figure 1, p. 2. Resistant strains of Chlorella had about 10 fold higher IC_{50}s	Landstein et al. 1993
Lemna gibba, a macrophyte	Nominal concentrations of 0, 0.01, 0.018, 0.032, 0.056, and 0.100 mg a.e./L for 14 days. Static. Measured concentrations not reported.	Frond Counts $EC_{25:}$ 0.013 (0.009-0.019) mg/L $EC_{50:}$ 0.024 (0.016-0.033) mg/L	Hughes. 1987 MRID 40811802

SALTWATER

Skeletonema costatum, marine diatom	Nominal concentrations of 10-100 mg a.e./L. Mean measured concentrations of 8.9-90.5 mg/L. 7 day exposure	Cell Density EC_{25}: 42.2 mg/L $EC_{50:}$ 85.5 mg/L Confidence limits could not be determined.	Hughes. 1987 MRID 40811802

Appendix 5: GLEAMS modeling of imazapyr.

A5.1. General Considerations -- GLEAMS is a root zone model that can be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions (Knisel et al. 1992). As with many environmental fate and transport models, the input and output files for GLEAMS can be complex. The input files used for this analysis have been provided to the Forest Service. Only the most relevant information is detailed in the following paragraphs.

In the exposure assessments, two types of estimates are needed: off-site (i.e., application site) movement of imazapyr to estimate potential concentrations of imazapyr in water or soil and on-site soil residues of imazapyr to estimate the duration of potential effects on non-target plant species.

A5.2. Runoff from and Percolation Through 3 Foot Soil Layer -- For off-site movement, preliminary model runs indicated that both runoff and percolation could be significant depending on the soil type and estimates of imazapyr binding to soil (K_d). This impacts one of the key parameters on the GLEAMS model, the depth of the soil horizon being modeled. This is referred to at the routing depth in the GLEAMS documentation (Knisel et al. 1992). The shallower the depth of the horizon, the greater the amount of runoff from and percolation through the soil layer (Knisel et al. 1992, p. 32). For a generic exposure assessment, the selection of the rooting depth is arbitrary. For this part of the modeling, a routing depth of 3 feet is used. Any percolation losses below this layer are assumed to contaminate ground water - i.e., the water table is 3 feet deep. The selection of shallower or deeper routing depths - i.e., shallower or deeper water table - has a great impact on percolation loss and a lesser but still substantial impact on runoff, depending on the soil type.

The key chemical-specific parameters for imazapyr are water solubility, $K_{o/c}$, and soil halftime. The water solubility of imazapyr is taken as 13,100 mg/L (Cortes 1990). Other reported values (Table 2-2 of main document) are reasonably close to this value and would have minimal impact on the modeled results.

The $K_{o/c}$ is the soil-water distribution coefficient (K_d) based on organic carbon and is typically calculated as:

$$K_{o/c} = K_d/oc,$$

where *oc* is the organic carbon content of the soil (mg organic carbon/mg soil) (Winegardner 1996, p. 116-117).

The K_d, also by definition, is the ratio of the concentration of a chemical adhered to soil particles to the concentration of the chemical in soil water and is typically expressed in units of mL/g - i.e., µg of chemical/g of soil ÷ µg of chemical/mL of water = mL water/g soil). The actual value of a particular K_d will depend on the physicochemical properties of both the soil as well as the chemical being bound to the soil (Winegardner 1996).

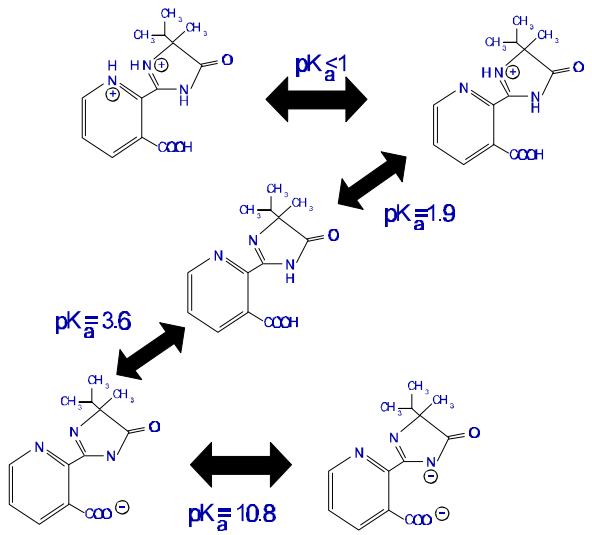

Figure A5-1: Various ionic states of imazapyr at different pH's (modified from Pusino et al. 1997).

For the GLEAMS modeling, K_d values are used for both sandy and clay soils. For sandy soil, the measured K_d values of 0.06-0.09 for imazapyr taken from Mangels (1994) are used as the basis of a central estimate of 0.075 mL/g. Measured K_d values for clay have not been encountered in the literature. Mangels (1994) reports K_d values of 0.23-1.12 for loam or silt loam soil and K_d values of 4.55 for pond sediment. Kd values in the range of 1.24 to 3.02 have also been reported for silt loam soil by McDowell et al. (1997). Pusino et al. (1997) provide Freundlich adsorption and desorption parameters for a variety of soil types ranging from sandy loam to clay loam but did not assay clay soils. For the GLEAMS modeling, a K_d of 10 mL/g is selected judgmentally as a plausible upper range for clay.

The use of these measured K_d values is admittedly an over-simplification. The binding of imazapyr to soil, however, is very complex because of the different charge configurations that imazapyr at different pH's (Figure A5-1). As detailed by Pusino et al. (1997), imazapyr adsorption to a variety of different soil types will increase as the pH decreases - i.e., the soil becomes more acidic. Thus, for example, soils with high levels of humic acid with tend to bind imazapyr more strongly. In addition, soils with high levels of iron oxides will bind imazapyr more strongly, particularly at lower pH (see Pusino et al. 1997, Table 5, p. 1015). Also at lower pH (i.e.,pH<5), increased organic matter will increase soil binding. Higher soil adsorption at lower pH has also been noted by Tjitrosemito et al. (1992) in different soils in Indonesia. The results of Pusino et al. (1997) may also explain the observations that imazapyr bound more strongly to sand (pH 6.4) than clay (pH 6.9 to 7.7) (Wehtje et al. 1987) but also more strongly to clay (pH 7.4) than loam (7.75) (Vizantinopoulos and Lolos 1994). Decreasing the water content of the soil will also tend to enhance soil binding (Wehtje et al. 1987).

Thus, while the K_d values of 0.075 mL/g for sandy soil and 10 mL/g for clay may be reasonable, site specific factors such as soil pH, iron oxides, and organic carbon and a number of other factors

can substantially impact the K_d and this in turn will substantially impact the transport of imazapyr in soil. If site-specific assessments were to be conducted - i.e., as part of an EA - there are adequate data in the above publications to reasonably estimated the K_d of imazapyr in most soil types. GLEAMS considered both pH and soil organic carbon. Soil pH, however, is only used in estimating levels of phosphorous and thus was not considered in the modeling. The organic carbon of both the sand and clays soils was set at 1%. As indicated above, this has a direct linear effect on the $K_{o/c}$ used in the model.

The persistence of imazapyr in soil is also highly variable. As indicated in Table 2-2, a number of different studies are available on the persistence of imazapyr in soil and reported halftimes in soil range from about 30 days (Michael et al. 1996; Michael and Neery1993) to over 500 days (17 months, American Cyanamid 1983b). Based on a number of different studies (American Cyanamid 1991; Mallipudi et al. 1985; Mallipudi et al. 1983b; McDowell et al. 1996, 1997; Vizantinoupulos and Lolos 1994) factors such as temperature, pH, aeration, organic matter, and soil depth may all impact the rate of degradation in soil. Much shorter halftimes, 5 to 7 days, have been reported in the tropics under ambient temperatures of 35°C [98.6°F] (Ismail and Ahmad 1994).

The most influential factor in the persistence of imazapyr in soil, however, that may underlie all of these other experimental variables, in microbial activity. This assertion is based on the study by McDowell et al. (1996) in which imazapyr was applied at a rate of 0.5 kg/ha in silt loam soil and residues assayed by bioassay using lentil (*Lens culinaris*). Halftimes for imazapyr in soil with low organic matter (3.5%) was 155 (±10) days at 15°C [59°F] and 77 (±8.7) days at 30°C [86°F]. In soil with high with high organic matter (6.4%), halftimes were and 125 (±8.5) days at 15°C and 99 (±9.3) at 30°C. In Table 1 of this publication (p. 200 of McDowell et al. 1996), these investigators also provide information on microbial biomass. For this exposure assessment, the reported halftimes were converted to degradation coefficients ($k = \log_e(2) \div t_{1/2}$) and these coefficients were regressed against microbial biomass (MBm) as the independent variable using the simply linear model. The resulting regression equation:

$$k\ (\text{days}^{-1}) = 6.2\times10^{-6}\ \text{Mbm}_{(\mu\text{gC/g soil})} + 0.0020\ (\text{days}^{-1})$$

was significant at p=0.029 with a squared correlation coefficient of 0.94 - i.e., the model, in this case the linear relationship to biomass, accounts for 94% of the scatter in the data. The intercept from this relationship, 0.002 days^{-1}, corresponds to a halftime of about 350 days, which is reasonably close to the halftime of 17 months or about 510 days for imazapyr in anaerobic soil kept in the dark incubated in the laboratory (American Cyanamid 1983b). The speculation that the persistence of imazapyr in soil may be primarily controlled by levels of soil microorganisms is also consistent with the observation by Ismail and Ahmad (1994) that imazapyr is degrades more rapidly in grass covered soil than bare soil.

For this risk assessment, soil halftimes of 30 to 155 days will be used. This range encompasses all of the field studies on the persistence of imazapyr in soil and excludes only the 17-month halftime

reported by (American Cyanamid 1983b). This value can be reasonably excluded from this risk assessment because of the conditions under which the study was conducted - i.e., anaerobic incubation in the dark. Such studies are typically designed to detected significant chemical degradation in soil. For imazapyr as well as most other herbicides, the rate of chemical degradation is very slow. The very low halftimes of 5 to 7 days reported by (Ismail and Ahmad 1994) are also excluded because of the tropical conditions under which these have times were obtained. The halftimes of 30 to 155 days are likely to reflect a plausible range of persistence under field conditions that could apply to Forest Service applications.

For the GLEAMS model, a soil halftime of 70 days was used. This is approximately the geometric mean of the range [$(30\times155)^{0.5} \approx 68.2$]. While this range varies by only a factor of 3, the relative difference that this makes to the modeled concentrations increases with time. For a simple exponential model [$k=\ln(2)\div t_{1/2}$], the magnitude of the difference is:

$$\frac{e^{(k+\delta)t}}{e^{kt}} = e^{\delta t} \qquad \text{Equ. A4-1}$$

where δ is the different in the two coefficients. Thus, if degradation rather than dissipation were the primary mechanism for the removal of imazapyr from soil, changing the halftime form 70 days [$k\approx0.009$ days^{-1}] to 155 days [$k\approx0.0045$ days^{-1}], the value of δ is [0.009 days^{-1} - 0.0045 days^{-1} = 0.0045 days^{-1}] and the difference after one year (365 days) is a factor of about 5.2 [$e^{0.0045\times365}$] - i.e., after 365 days, about five times more imazapyr would be projected to remain at the longer halftime relative to the amount remaining at the shorter halftime.

The only other noteworthy chemical-specific parameters required by GLEAMS involve foliar interception, foliar wash-off, and foliar half-time. For all GLEAMS models used in this exposure assessment, foliar interception is set to 0.5 - i.e., half of all of the applied imazapyr reaches the soil surface immediately after application. Foliar wash-off is taken at 0.9 and foliar half-time is set to 30 days. These values are consistent with the high water solubility of imazapyr and reported halftimes on vegetation (Knisel et al. 1992; Michael and Neary 1993).

As indicated above, two types of soils are modeled: clay (high runoff potential) and sand (low runoff potential). Two erosion parameter files and two hydrology parameter files are used, one each for clay and sand. Both sets of files specify a 10 acre (435,600 sq. ft.) area that is 50 feet wide and 8712 feet long - e.g., a right-of-way.

For estimating runoff to water, it is assumed that a body of water runs along the length of the right-of-way and that the slope toward the water is 10 percent. This moderate value for slope is intended to balance the potential for both runoff and percolation.

Because of the general rather than site-specific nature of this exposure assessment, only a single overland profile is used. Additional parameters specified in this file are consistent with a clay or sand with little resistance to runoff. The most sensitive hydrological parameters affecting runoff are organic carbon and runoff curve numbers, both of which are directly related to runoff and

inversely related to percolation. As with the parameters used in the pesticide file, the parameters used in these files are set in the mid-range to balance the potential for runoff and percolation. Specific parameter values were selected based on reference tables provided in the documentation for GLEAMS (Knisel et al. 1992) as well as texts dealing with runoff (Boulding 1995; Leng et al. 1995; Nix 1994; Winegardner 1996).

Rainfall also has a substantial influence on runoff and GLEAMS requires daily rainfall data files. National monthly rainfall statistics covering the period from 1961 to 1990 were obtained from the U.S. National Weather Service (1998). Based on these files, national annual summary statistics were generated in a DBASE file. Average annual rainfall ranged from a low of 0.3 inches (lower range for Yuma, Arizona) to 172.2 inches (upper range for Yakutat, Alaska) with a mean average annual rainfall of 27.69 inches. Based on these statistics, model runs for both clay and sandy soil were conducted using precipitation rates of 5, 10, 25, 50, 100, 150, 200, and 250 inches per year.

Each GLEAMS model run was conducted over a 6 year period, with applications of imazapyr contaminated herbicide on Julian day 180 of years 2 through 6. The first year of the simulation was used to condition the soil and the average annual rainfall was simply divided equally among each day. In subsequent years, equal amounts of rainfall were generated every tenth day to yield the average annual rainfall. This approach was taken because most runoff and percolation will occur during periods of relatively intense rainfall. Combined with the pesticide, erosion, and hydrology parameters discussed above, this should yield relatively high but still plausible estimates of runoff and percolation.

Table A5-1: Summary of GLEAMS estimates of the annual off-site transport of imazapyr as a proportion of the applied amount.

Annual Rainfall (inches)	Proportion	
	Clay (Runoff)	Sand (Percolation)
5	0	0
10	0	0
25	0.0066	0.0757
50	0.0573	0.4468
100	0.1544	0.6914
150	0.2318	0.7708
200	0.2952	0.8003
250	0.3483	0.8175

A summary of the results are given in Table A5-1 and illustrated in Figure A5-2. Under conditions of low rainfall (≈10 inches per year or less), neither runoff nor percolation is anticipated under the conditions modeled. Thus, under relatively arid conditions, the loss of imazapyr from the soil is likely to be due solely to microbial degradation. At higher annual precipitation rates, the transport of imazapyr will depend on the characteristics of the soil. For clay, all of the modeled loss of imazapyr from soil was attributed with runoff. For sand, all of the loss was attributed to percolation. For intermediate soil types - e.g., loam, sandy loam, clay loam etc. - both runoff and percolation are plausible. At least under the conditions used in the GLEAMS modeling, the losses from percolation through sand are likely to exceed losses from runoff from clay.

All of the rates given in Table A4-1 and illustrated in Figure A4-2 are averages over the 5 year simulation cycle used in the GLEAMS modeling. For each year, rates varied by no more than 1% and no accumulation occurred in soil, runoff, or percolation.

Given the general rather than site-specific nature of this modeling exercise and the complexities of estimating both the persistence and movement of imazapyr in soil, these estimates of runoff and percolation should be considered only as crude approximations of environmentally plausible rates.

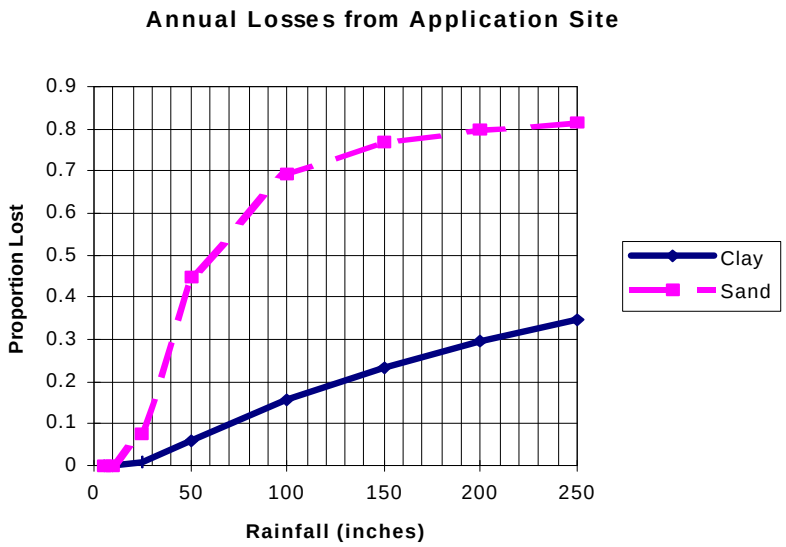

Figure A5-2: Imazapyr runoff from clay and percolation through sand as a fraction of the applied amount at various annual precipitation rates.

A5.3. Estimated Concentrations in Water Associate with Runoff from Clay or Percolation from Sand Using a 3 Foot Soil Layer -- While the data presented in the previous section are useful for assessing the types of loss (percolation vs runoff) from various sites and the magnitude of yearly losses relative to the amount applied at the treated site, these cannot be used directly to project concentrations in ambient water. By making certain assumptions concerning the persistence of imazapyr in water and the amounts of imazapyr that could be transported to surface water, however, such estimates can be made and are illustrated in Figures A5-3 (runoff from clay) and A5-4 (percolation from sand.

These estimated concentrations of imazapyr in water require estimates of the daily amount of imazapyr in runoff or percolation that is transported to water, the volume of water into which the imazapyr is mixed, and the persistence of imazapyr in the water.

Although imazapyr is chemically stable in water with a halftime for hydrolysis of 325

Table A5-2: Kinetics of the breakdown of imazapyr and photolysis products of imazapyr to CO_2 in pond water.

Time (days)	Proportion converted to $C0_2$
0	0
7	0.287
14	0.399
21	0.42
28	0.521

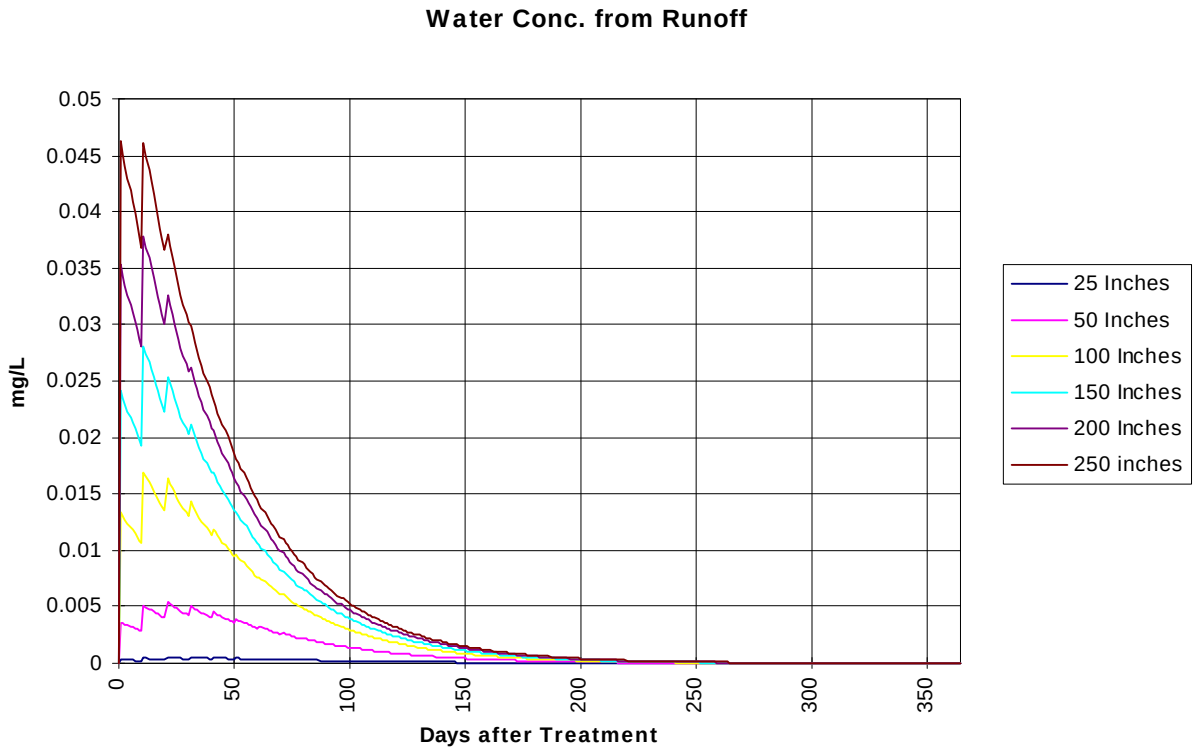

Figure A5-3: Imazapyr concentrations in a small pond as a result of runoff from clay at an application rate of 0.15 lb a.e./acre and various annual rainfall rates.

days at pH 9 (American Cyanamid 1983b), both photolysis and biodegradation may occur in natural water. For this exposure assessment, a halftime in water of 28 days is used based on the study conducted by American Cyanamid (1991) on the photolysis and breakdown of imazapyr in pond water and water sediment (Table A4-2). In this study, ^{14}C-labelled imazapyr was irradiated at 0.25 watts/m^2 at 340 nm for 96 hours and then incubated in pond water and pond sediment for 28-days. Degradation was assayed as the proportion of the imazapyr and imazapyr photolysis products converted to $C0_2$. These data fit an simple exponential decay model (r^2=0.92, p=0.0089) with a decay coefficient of 0.025 days^{-1}, corresponding to a halftime of about 27.7 days [$\ln(2)/t_{1/2}$].

GLEAMS simulations were conducted at an application rate of 0.15 lb a.e./acre, the typical application rate anticipated by the Forest Service (Section 2), as detailed in the previous section. GLEAMS output files were read for output fields 601 (runoff loss in g/ha) and 701 (percolate loss in g/ha) for the clay and sand simulations, respectively.

Based on a 50 foot wide ROW, one hectare (10,760 ft^2) is about 215 feet long [10,760 ft^2÷50 ft =215.2 feet]. Using a 50 foot wide standing body of water adjacent to the ROW, the volume of water can be calculated from the dimensions - 215 ft (65.532 meters) by 50 ft (15.24 meters) by 1 meter deep - as 1,000,000 liters::

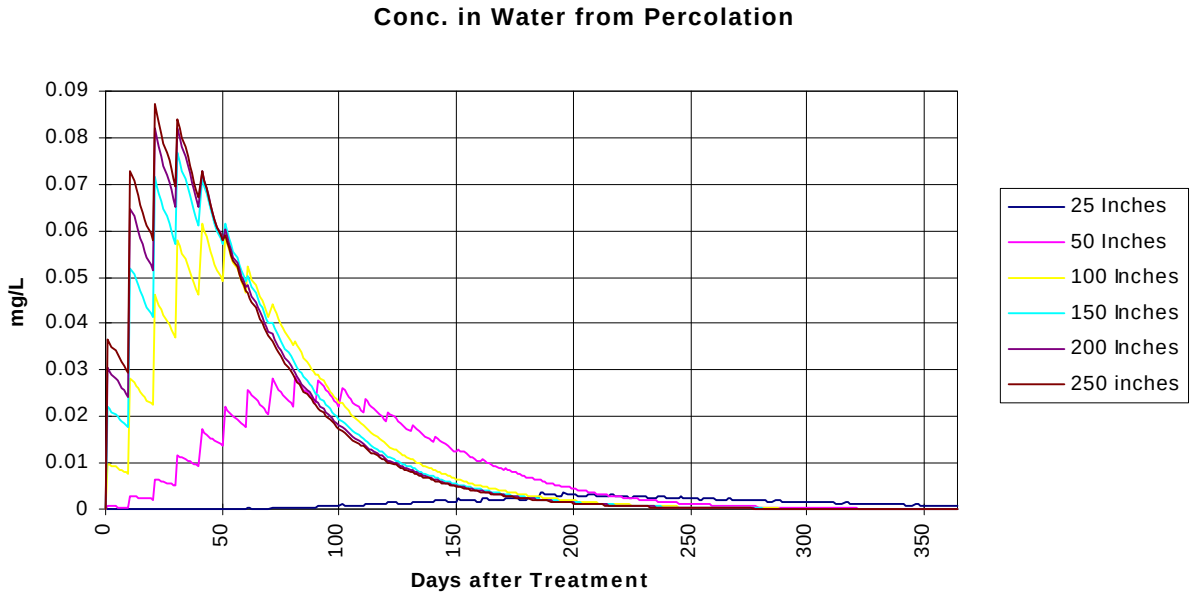

Figure A5-4: Imazapyr concentrations in a small pond as a result of percolation from sand at an application rate of 0.15 lb a.e./acre and various annual rainfall rates.

$$65.532 \text{ m} \times 15.24 \text{ m} \times 1 \text{ m} = 998.70 \text{ m}^3 \approx 1000 \text{ m}^3 \times 1000 \text{ L/m}^3 = 1{,}000{,}000 \text{ L}.$$

For any time, *t*, amount of imazapyr in water A_t in units of g/ha is calculated as:

$$A_t = A_{t-1} - (A_{t-1} * k_e) + \delta$$

where δ is the amount added at time *t* by runoff or percolation read from the GLEAM output files. The concentration in water at time *t* in units of mg/L is then calculated as:

$$A_{t\,(g/ha)} \times 1000 \text{ mg/g} \div 1{,}000{,}000 \text{ L/ha}.$$

Following this approach, the concentrations in water over a one year period following the application of imazapyr at a rate of 0.15 lb/acre are illustrated in Figures A5-3 (clay) and A5-4 (sand).

As illustrated in Figures A5-3 and A5-4, peak water concentrations will vary substantially with rainfall rates. Below annual rainfall rates of 10 inches per year, no runoff is anticipated. At annual rainfall rates of 25 to 250 inches per year, peak water concentrations vary from about 0.005 mg/L to 0.045 mg/L. These rates encompass the EC_{50} values for growth inhibition in most sensitive species of aquatic plants - i.e., 0.013 (0.009-0.019) mg/L - as discussed further in the risk characterization (Section 4.4.3.2 of main document).

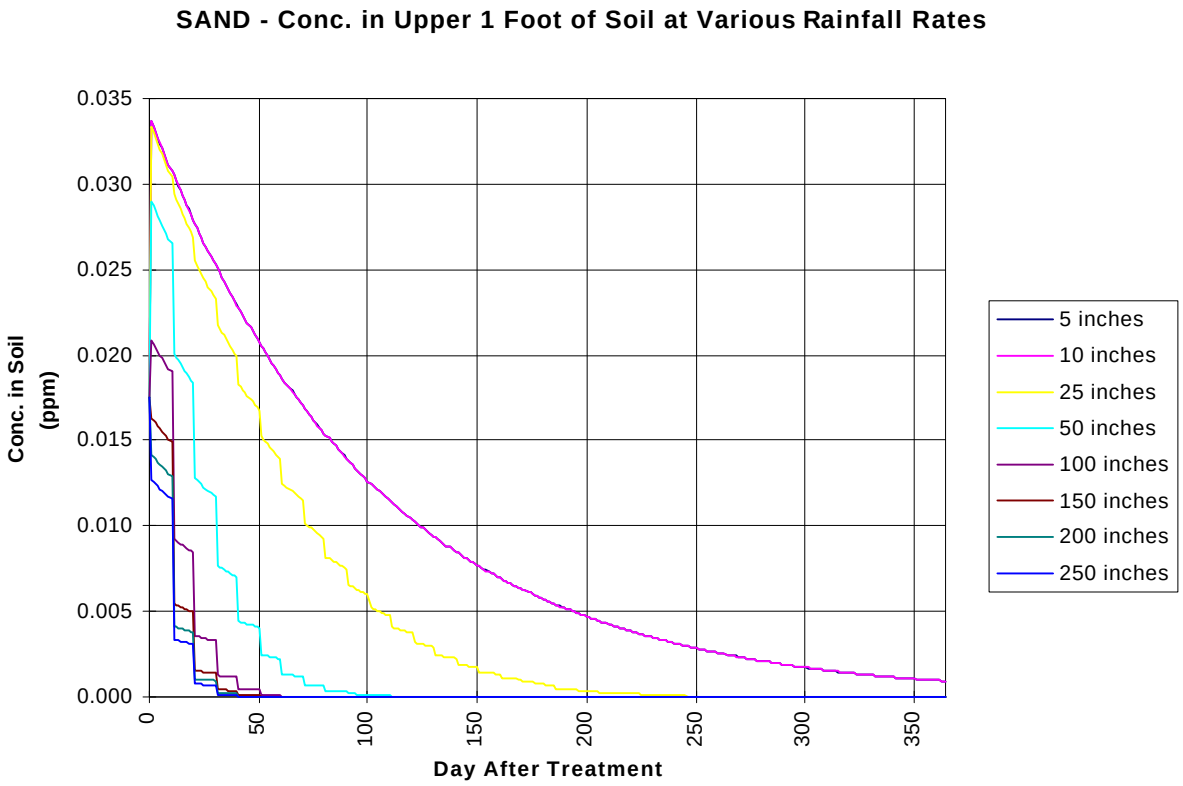

Figure A5-5: Concentrations of imazapyr applied at a rate of 0.15 lb a.e./acre in the top 1 foot of sandy soil at various annual precipitation rates.

At comparable rainfall rates, higher concentrations of imazapyr are anticipated from percolation, at least if it is assumed that the percolate will quickly and directly mix with ambient standing water (Figure A5-4). At rainfall rates ranging from 25 to 250 inches per year, peak levels of about 0.003 to 0.09 mg/L are projected. As with the results for runoff from clay, these concentrations encompass the EC_{50} values for growth inhibition in most sensitive species of aquatic plants - i.e., 0.013 (0.009-0.019) mg/L as discussed further in Section 4.4.3.2 of main document.

A5.4. Persistence in 1 Foot Soil Layer -- For assessing the impact of on-site soil residues, a routing depth of one foot is used and the soil concentration is expressed as the average concentration within the one foot deep soil layer[1]. A depth of one foot was

[1]If only a single soil horizon is specified in the input file, as was done in all cases in this exposure assessment, output files from the GLEAMS model still give soil concentrations (parameter 811) for four soil horizons. The first horizon is the effective mixing depth - one cm for surface applications. The next three horizons are equally divided amount the remaining routing depth. Thus, for a 1(30.48 cm) foot routing depth, the first soil horizon is1 cm and the next three

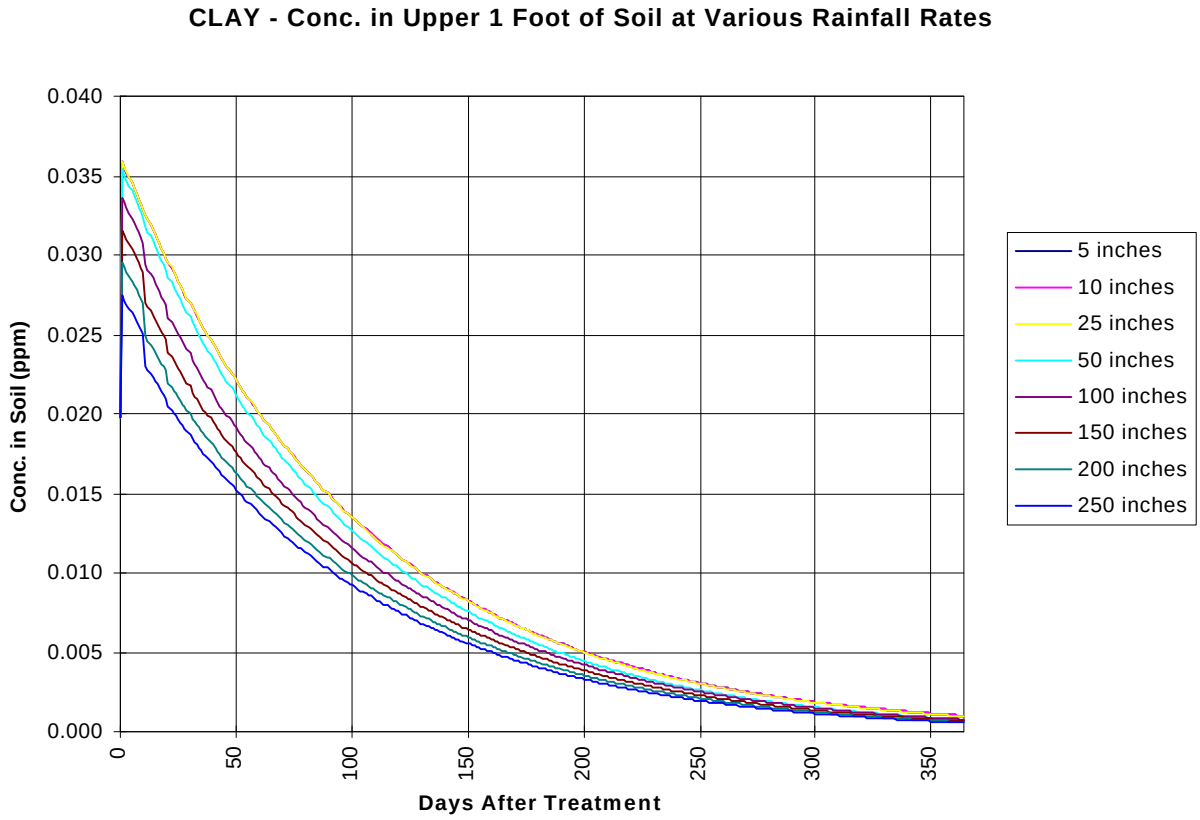

Figure A5-6: Concentrations of imazapyr applied at a rate of 0.15 lb a.e./acre in the top 1 foot of clay soil at various annual precipitation rates.

selected as a reasonable routing depth for non-target plant species. Selecting a deeper layer would decrease the average concentration but increase the duration of exposure. Conversely, selecting a shallower layer would increase the average concentration but decrease the duration of exposure. As with any 'generic' application of a model such as GLEAMS, the choice of a specific depth is arbitrary. Except of the change in rooting depth, all of the model parameters where identical to those described in section A5.2 for the 3 foot deep soil layer.

The results of the GLEAMS modeling for sand and clay soils are illustrated in Figures A5-5 and A5-6, respectively.

In sandy soil under arid conditions - i.e., annual rainfall of 5 inches or less - there is no percolation or runoff and the rate of decrease is attributable solely to presumed microbial breakdown. For example, in Figure A5-5 the time to a 50% decrease in soil concentrations is about 70 days, identical to the soil halftime used in the GLEAMS modeling. At higher precipitation rates, percolation becomes increasing significant and is clearly the dominant factor at rainfall rates of 50

`horizons are about 9.83 cm deep.`

inches/year or more. Note that the stepped appearance of the time plots for higher rainfall rates simply reflects the *every tenth day* rainfall pattern used in the GLEAMS modeling. In an extremely arid environment in which the microbial activity of the soil is very low, soil halftimes of much greater than 70 days - i.e., that used in the GLEAMS modeling - are plausible. In some cases, the 'sterile' soil halftime of 17 months or about 500 days (American Cyanamid 1983b) could be approximated.

In clay soil (Figure A5-6), the modeling results under arid conditions are essentially identical to those of sand. In an arid environment (annual precipitation of 5 inches per year or less), runoff from clay soil will be negligible and the rate of degradation in soil will depend primarily on microbial activity. Thus, in Figure A5-6, the line for a 5-inch annual rainfall is virtually identical to the corresponding line for sandy soil (Figure A5-5) and reflects the soil halftime of 70 days used in the modeling. The *every tenth day* rainfall pattern used in the GLEAMS modeling is less apparent for clay (Figure A5-6) than sand (Figure A5-5) primarily because the amount of runoff from clay is less than the amount of percolation in sand. The one sharp step at day 10 reflects the higher foliar washoff coefficient (0.9) used in the GLEAMS modeling.

As with the modeling results given in the previous section of this appendix, these estimates of persistence in soil should be considered only as crude approximations of environmentally plausible rates. Site-specific considerations - particularly microbial activity and soil binding of imazapyr - could lead to substantial variations form the modeled values. There are adequate data in the publications cited in this appendix to conducted more precise site-specific exposure assessments.

WORKSHEETS FOR
Imazapyr

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GENERAL ASSUMPTIONS, VALUES, and MODELS

Worksheet A01: Constants and conversion factors used in calculations [CONST]		
Conversion	ID	Value
mg/lb	mg_lb	453,600
mL/gallon	ml_gal	3,785
lb/gallon to mg/mL	lbg_mgml	119.8
lb/acre to µg/cm^2	lbac_ugcm	11.21
lb/acre to mg/cm^2	lbac_mgcm	0.01121
gallons to liters	gal_lit	3.785

Worksheet A02: General Assumptions Used in Worker Exposure Assessments [STD]				
Parameter	ID	Value	Units	Reference
Body Weight (General)	BW	70	kg	ICRP (1975), p. 13
Surface area of hands	Hands	840	cm^2	U.S. EPA 1992
Surface area of lower legs	LLegs	2070	cm^2	U.S. EPA 1992
Weight of liquid adhering to surface of skin after a spill	Liq	0.008	mg/cm^2	Mason and Johnson 1987

Worksheet A03a: Directed Ground Sprays (includes backpack, cut surface, and streamline applications) - General Assumptions Used in Worker Exposure Assessments [BACKPACK]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		0.625	acres/hour	USDA 1989a,b,c
Lower estimate		0.25		
Upper estimate		1		
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	N/A[1]
Lower estimate	ACREL	1.5		
Upper estimate	ACREU	8		
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.0003		
Upper estimate	RATEU	0.01		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A03b: Hydraulic/Broadcast Ground Sprays - General Assumptions Used in Worker Exposure Assessments [HYDSPRAY]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		16	acres/hour	USDA 1989a,b,c
Lower estimate		11		
Upper estimate		21		
Acres treated per day				
Central estimate	ACREC	112	acres/day	N/A[1]
Lower estimate	ACREL	66		
Upper estimate	ACREU	168		
Absorbed dose rate				
Central estimate	RATEC	0.0002	(mg agent/kg bw) ÷ (lbs agent handled per day) [2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.00001		
Upper estimate	RATEU	0.0009		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A03c: Aerial Broadcast Sprays (includes pilots, mixers, and loaders) - General Assumptions Used in Worker Exposure Assessments.[AERIAL]

Parameter/Assumption	Code	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		70	acres/hour	USDA 1989a,b,c
Lower estimate		40		
Upper estimate		100		
Acres treated per day				
Central estimate	ACREC	490	acres/day	N/A[1]
Lower estimate	ACREL	240		
Upper estimate	ACREU	800		
Absorbed dose rate				
Central estimate	RATEC	0.00003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.000001		
Upper estimate	RATEU	0.0001		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of value are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Body Weights				
Male, Adult	BWM	70	kg	ICRP (1975), p. 13.
Female, Adult	BWF	64	kg	Burnmaster 1998; U.S. EPA 1985[1]
Child, 2-3 years old	BWC	13.3	kg	U.S. EPA, 1996, page 7-1, Table 7-2
Body Surface Areas				
Female, feet and lower legs	SAF1	2915	cm^2	U.S. EPA, 1992, p. 8-11, Table 8-3, total for feet and lower legs
Female, exposed skin when wearing shorts and a T-shirt	SAF2	5300	cm^2	U.S. EPA, 1992, p. 8-11, Table 8-3, total for arms, hands, lower legs, and feet.
Child, male, 2-3 years old, total body surface area	SAC	6030	cm^2	U.S. EPA, 1996, p. 6-15, Table 6-6, 50th percentile.
Water Intake				
Adult				
typical	WCAT	2	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (1.4 L/day) and 90th percentile (2.4 L/day) rounded to one significant place.
lower range for exposure assessment	WCAL	1.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCAH	2.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile
Child, <3 years old				
typical	WCT	1	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (0.61L/day) and 90th percentile (1.5 L/day) rounded to one significant place.
lower range for exposure assessment	WCL	0.61	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCH	1.50	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of value are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Fish Consumption				
Freshwater anglers, typical intake per day over a prolonged period	FAT	0.010	kg/day	U.S. EPA, 1996, p. 10-51, average of means from four studies
Freshwater anglers, maximum consumption for a single day	FAU	0.158	kg/day	Ruffle et al. 1994
Native American subsistence populations, typical intake per day	FNT	0.081	kg/day	U.S. EPA, 1996, p. 10-51, median value of 94 individuals
Native American subsistence populations, maximum for a single day	FNU	0.770	kg/day	U.S. EPA, 1996, p. 10-51, highest value of 94 individuals
Consumption of Fruits or Vegetables				
Amount of food consumed per kg bw per day for longer term exposures scenarios.				
Typical	VT	0.0043	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, mean intake of vegetables
Upper	VU	0.01	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, 95th percentile for intake of vegetables
Worst-case scenario for consumption in a single day, acute exposure scenario only.	VAcute	0.454	kg food	1 lb. The approximate mid range of the above typical and upper limits based on the 64 kg body weight.
Miscellaneous				
Estimate of dislodgeable residue as a proportion of application rate shortly after application.	DisL	0.1	none	Harris and Solomon 1992, data on 2,4-D

[1]This is the average value (63.79 kg), rounded to the nearest kg for 3 different groups of women between 15-49 years old: control (62.07 kg), pregnant (65.90 kg), and lactating (63.48 kg) (Burnmaster 1998). This is identical to the body weight for females, 45-55 years old, 50th percentile from U.S. EPA, 1985, page 5, Table 2-2, rounded to nearest kilogram.

Worksheet A05a: Estimated concentrations of pesticides on or in various types of vegetation shortly after application at 1 lb a.i./acre [from Hoerger and Kenaga (1972), Table 9, p. 22]. [HK]

Type of Vegetation	Concentration (mg chemical/kg vegetation)			
	Typical		Upper Limit	
	ID	Value	ID	Value
Range grass	RGT	125	RGU	240
Grass	GST	92	GSU	110
Leaves and leafy crops	LVT	35	LVU	125
Forage crops	FCT	33	FCU	58
Pods containing seeds	PDT	3	PDU	12
Grain	GNT	3	GNU	10
Fruit	FRT	1.5	FRU	7

Worksheet A05b: Concentrations of chemical on spheres (berries) at the specified application rate. [FRUIT]

Diameter (cm)	Planar Surface Area (cm^2)[a]	Amount deposited (mg)[b]	Weight of sphere (kg)[c]	Concentration (mg/kg)[d]
1	0.7853981634	0.008796459	0.0005236	16.8
5	19.6349540849	0.21991148575	0.065449847	3.36
10	78.5398163397	0.87964594301	0.5235987756	1.68
	Application rate	1 lb/acre =	0.0112	mg/cm^2

a Planar surface area of a sphere = πr^2 where r is the radius in cm.

b Amount deposited is calculated as the application rate in mg/cm^2 multiplies by the planar surface area.

c Assumes a density of 1 g/cm^3 for the fruit. The volume of a sphere is$(1\div6)\times \pi \times d^3$ where d is the diameter in cm. Assuming a density of 1 g/cm^3, the weight of the sphere in kg is equal to:

$$kg= (1\div6)\times \pi \times d^3 \div 1000$$

d Amount of chemical in mg divided by the weight of the sphere in kg.

Worksheet A06: Central estimates of off-site drift associated with aerial application of pesticides (from Bird 1995, p. 205) [OFFSITE]

Distance Down Wind (meters)	ID	Drift as a proportion of application rate
100	DRFT100	0.05
200	DRFT200	0.02
300	DRFT300	0.01
400	DRFT400	0.008

Worksheet A07a: Estimate of first-order absorption rate (k_a in hours^{-1}) and 95% confidence intervals (from Durkin et al. 1998). `[KAMODEL]`

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.233255	
Coefficient for MW	C_MW	0.005657	
Model Constant	C	1.49615	
Number of data points	DP	29	
Degrees of Freedom (d.f.)	DF	26	
Critical value of $t_{0.025}$ with 26 d.f.[1]	CRIT	2.056	
Standard error of the estimate	SEE	16.1125	
Mean square error or model variance	MDLV	0.619712	
Standard deviation of model (s)	MSD	0.787218	$MDLV^{0.5}$
X′X, cross products matrix	0.307537	-0.00103089	0.00822769
	-0.00103089	0.000004377	-0.0000944359
	0.0082	-0.0000944359	0.0085286

[1] Mendenhall and Scheaffer, 1973, Appendix 3, 4, p. A31.

Central (maximum likelihood) estimate:

$$\log_{10} k_a = 0.233255 \log_{10}(k_{o/w}) - 0.005657\ MW - 1.49615$$

95% Confidence intervals for $\log_{10} k_a$

$$\log_{10} k_a \pm t_{0.025} \times s \times (a' X' X\ a)^{0.5}$$

where a is a column vector of {1, MW, $\log_{10}(k_{o/w})$}.

NB: Although the equation for the central estimate is presented with $k_{o/w}$ appearing before MW to be consistent with the way a similar equation is presented by EPA, MW must appear first in column vector a because of the way the statistical analysis was conducted to derive X′X .

See following page for details of calculating $a' X' X\ a$ without using matrix arithmetic.

Worksheet A07a (continued)
Details of calculating $a' X' X\, a$

The term $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ requires matrix multiplication. While this is most easily accomplished using a program that does matrix arithmetic, the calculation can be done with a standard calculator.

Letting

$$\mathbf{a} = \{a\_1, a\_2, a\_3\}$$

and

$$(\mathbf{X}'\mathbf{X})^{-1} = \{ \{b\_1, b\_2, b\_3\}, \{c\_1, c\_2, c\_3\}, \{d\_1, d\_2, d\_3\} \},$$

$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ is equal to

Term 1: {a_1 ×([a_1×b_1] + [a_2×c_1] + [a_3×d_1])} +
Term 2: {a_2 ×([a_1×b_2] + [a_2×c_2] + [a_3×d_2])} +
Term 3: {a_3 ×([a_1×b_3] + [a_2×c_3] + [a_3×d_3])}.

Worksheet A07b: Estimate of dermal permeability (K_p in cm/hr) and 95% confidence intervals (data from U.S. EPA 1992). [PKMODEL]

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.706648	
Coefficient for MW	C_MW	0.006151	
Model Constant	C	2.72576	
Number of data points	DP	90	
Degrees of Freedom (d.f.)	DF	87	
Critical value of $t_{0.025}$ with 87 d.f.[1]	CRIT	1.96	
Standard error of the estimate	SEE	45.9983	
Mean square error or model variance	MDLV	0.528716	
Standard deviation of model (s)	MSD	0.727129	$MDLV^{0.5}$
X′X, cross products matrix	0.0550931	-0.0000941546	-0.0103443
	-0.0000941546	0.0000005978	-0.0000222508
	-0.0103443	-0.0000222508	0.00740677

[1] Mendenhall and Scheaffer, 1973, Appendix 3, Table 4, p. A31.

NOTE: The data for this analysis is taken from U.S. EPA (1992), Dermal Exposure Assessment: Principles and Applications, EPA/600/8-91/011B, Table 5-4, pp. 5-15 through 5-19. The EPA report, however, does not provide sufficient information for the calculation of confidence intervals. The synopsis of the above analysis was conducted in STATGRAPHICS Plus for Windows, Version 3.1 (Manugistics, 1995) as well as Mathematica, Version 3.0.1.1 (Wolfram Research, 1997). Although not explicitly stated in the EPA report, 3 of the 93 data points are censored from the analysis because they are statistical outliers: [Hydrocortisone-21-yl]-hemipimelate, n-nonanol, and n-propanol. The model parameters reported above are consistent with those reported by U.S. EPA but are carried out to greater number of decimal places to reduce rounding errors when calculating the confidence intervals. See notes to Worksheet A07a for details of calculating maximum likelihood estimates and confidence intervals.

CHEMICAL SPECIFIC VALUES

Worksheet B01: Anticipated Application and Dilution Rates for imazapyr [WSB01]				
Item	Code	Value	Units	Reference/Source
Typical application rate	Typ	0.15	lb a.e./acre	Section 2.4
Lowest application rate	Low	0.08	lb a.e./acre	Section 2.4
Highest application rate	Hi	2.5	lb a.e./acre	Section 2.4
Lowest dilution	LDil	20	gal./acre	C&P Press 1998*
Highest dilution	Hdil	40	gal./acre	C&P Press 1998*
*Product label for Transline				

Typical concentration in applied solution:

Typical application rate divided by the average of the lowest and highest dilutions, converted to mg/mL, and rounded to two significant places after the decimal.

0.15 lb/acre ÷ [(20 gal/acre + 40 gal/acre)/2] × 119.8 (mg/mL)/(lb/gal) = **0.6 mg/mL** [TypDr]

Lowest estimated concentration in applied solution:

Lowest application rate divided by the highest dilution, converted to mg/mL, and rounded to two significant places after the decimal.

0.08 lb/acre ÷ 40 gal/acre) × 119.8 (mg/mL)/(lb/gal) = **0.24 mg/mL** [LowDr]

Highest estimated concentration in applied solution:

Highest application rate divided by the lowest dilution, converted to mg/mL, and rounded to two significant decimal places after the decimal.

2.5 lb/acre ÷ 20 gal/acre × 119.8 (mg/mL)/(lb/gal) = **15.0 mg/mL** [HI_Dr]

Worksheet B02: Summary of central estimate and range of concentrations of imazapyr in field solutions.				
Parameter	ID	Value	Units	Reference/Source
Typical	TypDR	0.6	mg/mL	See calculations above
Low	LowDR	0.24	mg/mL	
High	Hi_DR	15	mg/mL	

Worksheet B03: Summary of chemical specific values used for imazapyr in exposure assessment worksheets. [WSB03]

Parameter	ID	Value	Units	Source/Reference
Molecular weight (acid)	MW	261	grams/mole	Budavari 1989
Water Solubility, pH 7	WS	11000	mg/L	Knisel et al. 1992
$K_{o/w}$	Kow	1.3	unitless	Reichert and Stanley-Millner. 1983
Foliar half-time ($t_{½}$)	FT12	30	days	[c] Knisel et al. 1992
Halftime on vegetation, central	FrT12C	26	days	Michael and Neary 1993
composite of different lower	FrT12L	15	days	
types upper	FrT12U	37	days	
Measured bioconcentration factor (***BCF***$_{(kg\ fish/L)}$)	BCFM	0.5	kg fish/L	McAllister et al. 1985
Calculated bioconcentration factor [a]	BCFC	1.53	kg fish/L	see footnote a below.
Bioconcentration factord use in exposure assessments	BCFT	1	kg fish/L	McAllister et al. 1985
EPA RfD[b]	RfDP	2.5	mg/kg bw/day	Section 3.3.3

[a] Calculate from the following equation given by Calabrese and Baldwin (1993, p. 17, eq. 2.14) for bioconcentration in fish muscle:

$$\log_{10} BCF = 0.542 \log_{10} K_{o/w} + 0.124$$

[b] No RfD for imazapyr is listed on IRIS. This RfD is that derived by EPA/OPP (U.S. EPA 1997).

Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for imazapyr.							
Parameters	Value	Units	Reference				
Molecular weight	261	g/mole					
$K_{o/w}$ at pH 7	1.3	unitless					
$\log_{10} K_{o/w}$	0.11						
Column vector ***a*** for calculating confidence intervals (see Worksheet 08 for definitions.)							
a_1	1						
a_2	261						
a_3	0.11						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07a for details of calculation.							
Term 1	0.03937671						
Term 2	0.0263920723						
Term 3	-0.001703013						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.0641	calculation verified in Mathematica 3.0.1.1					
$\log_{10} k_a = 0.233255 \log_{10}(k_{o/w}) - 0.005657\ MW - 1.49615$			WSA07a				
$\log_{10}$ of first order absorption rate (k_a)							
Central estimate	-2.94604914336	±	$t_{0.025}$	×	s	×	$(\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a})^{0.5}$
Lower limit	-3.35582573035	-	2.0560	×	0.787218	×	0.25317977802
Upper limit	-2.53627255637	+	2.0560	×	0.787218	×	0.25317977802
First order absorption rates (i.e., antilog or 10^x of above values).							
Central estimate	0.001132272	$hours^{-1}$					
Lower limit	0.00044073	$hours^{-1}$					
Upper limit	0.002908891	$hours^{-1}$					

Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for imazapyr.							
Parameters	Value	Units	Reference				
Molecular weight	261	g/mole					
$K_{o/w}$ at pH 7	1.3	unitless					
$\log_{10} K_{o/w}$	0.11394335231						
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)							
a_1	1						
a_2	261						
a_3	0.11394335231						
Calculation of $\mathbf{a'} \cdot (\mathbf{X'X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07b for details of calculation.							
Term 1	0.0293400852						
Term 2	0.0154866619						
Term 3	-0.001744223						
$\mathbf{a'} \cdot (\mathbf{X'X})^{-1} \cdot \mathbf{a}$	0.0431	calculation verified in Mathematica 3.0.1.1					
$\log_{10} k_p = 0.706648 \log_{10}(\boldsymbol{k_{o/w}}) - 0.006151\ \boldsymbol{MW} - 2.72576$						Worksheet A07b	
$\log_{10}$ of dermal permeability							
Central estimate	-4.25065315798	±	$\boldsymbol{t}_{0.025}$	×	$\boldsymbol{s}$	×	$\mathbf{a'} \cdot (\mathbf{X'X})^{-1} \cdot \mathbf{a}^{0.5}$
Lower limit	-4.54652672826	-	1.9600	×	0.727129	×	0.20760539492
Upper limit	-3.9547795877	+	1.9600	×	0.727129	×	0.20760539492
Dermal permeability							
Central estimate	0.0000562	cm/hour					
Lower limit	0.0000284	cm/hour					
Upper limit	0.0001110	cm/hour					

Worksheet B06: Summary of chemical specific dermal absorption values used for imazapyr dermal absorption. [WSB06]

Description	Code	Value	Units	Reference/Source
Zero-order absorption (K_p)				
Central estimate	KpC	0.00005610	cm/hour	Worksheet B05, values rounded to two significant figures
Lower limit	KpL	0.00002841	cm/hour	
Upper limit	KpU	0.00011100	cm/hour	
First-order absorption rates (k_a)				
Central estimate	AbsC	0.00113	$hour^{-1}$	Worksheet B04, values rounded to two significant figures
Lower limit	AbsL	0.00044	$hour^{-1}$	
Upper limit	AbsU	0.0029	$hour^{-1}$	

Worksheet B07: Estimates of the concentration of imazapyr in ambient water per lb a.i. applied per acre based on monitoring data. [Used in chronic contaminated water exposure assessment.][a]

Scenario	Ambient Conc. mg/L	Appl. Rate (lb a.e./acre)	ID	WCR[b] (mg/L) ÷ (lb a.e./acre)	Reference
Typical	0.130	1.59	AWT	0.082	Neary and Michael 1996. See section 3.2.3.4.
Low	0.001	0.082	AWL	0.012	
High	0.680	1.59	AWU	0.428	

[a] See appendix 5 for estimates based on GLEAMS modeling.
[B] Expected water contamination rate - mg/L in water after the application of imazapyr at a given rate in lb a.e./acre.

WORKER EXPOSURE ASSESSMENTS

Worksheet C01a: Worker exposure estimates for directed foliar (backpack) applications of imazapyr				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	ApplC	0.15	lbs a.e./day	WSB01.TYP
Lower estimate	ApplL	0.08	lbs a.e./day	WSB01.LOW
Upper estimate	ApplU	2.5	lbs a.e./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	WSA03.ACREC
Lower estimate	ACREL	1.5	acres/day	WSA03.ACREL
Upper estimate	ACREU	8	acres/day	WSA03.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	0.65625	lb/day	
Lower estimate	HANDLL	0.12	lb/day	
Upper estimate	HANDLU	20	lb/day	
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA03.RATEC
Lower estimate	RATEL	0.0003		WSA03.RATEL
Upper estimate	RATEU	0.01		WSA03.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.0020	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000036		
Upper estimate	DOSEU	0.200		

Worksheet C01b: Worker exposure estimates for boom spray (hydraulic ground spray) applications of imazapyr [WSC01]				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	APPLC	0.15	lbs a.e./day	WSB01.TYP
Lower estimate	APPLL	0.08	lbs a.e./day	WSB01.LOW
Upper estimate	APPLU	2.5	lbs a.e./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	112	acres/day	WSA04.ACREC
Lower estimate	ACREL	66	acres/day	WSA04.ACREL
Upper estimate	ACREU	168	acres/day	WSA04.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	16.8	lb/day	
Lower estimate	HANDLL	5.28	lb/day	
Upper estimate	HANDLU	420	lb/day	
Absorbed dose rate				
Central estimate	RATEC	0.00020	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA04.RATEC
Lower estimate	RATEL	0.00001		WSA04.RATEL
Upper estimate	RATEU	0.00090		WSA04.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.00336	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000053		
Upper estimate	DOSEU	0.378		

WSC01c: Worker exposure estimates for aerial applications of imazapyr [WKAREXP01]

NOTE: The upper and lower estimates of dose are based on the typical application rate. Variability is encompassed by differences in the number of acres treated and the absorbed dose rate.

Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	WS10C	0.15	lbs a.e./day	APPL.TYP
Lower estimate	WS10L	0.08	lbs a.e./day	APPL.LOW
Upper estimate	WS10U	2.5	lbs a.e./day	APPL.HI
Acres treated per day				
Central estimate	ACREC	520	acres/day	AERIAL.ACREC
Lower estimate	ACREL	240	acres/day	AERIAL.ACREL
Upper estimate	ACREU	800	acres/day	AERIAL.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	78	lb/day	N/A[1]
Lower estimate	HANDLL	36	lb/day	
Upper estimate	HANDLU	120	lb/day	
Absorbed dose rate				
Central estimate	RATEC	0.00003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	AERIAL.RATEC
Lower estimate	RATEL	0.000001		AERIAL.RATEL
Upper estimate	RATEU	0.0001		AERIAL.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.00234	mg/kg bw	N/A
Lower estimate	DOSEL	0.0000360		
Upper estimate	DOSEU	0.012		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet C02: Workers: Accidental Dermal Exposure Assessments Using Zero-Order Absorption			
Parameter	Value	Units	Source
Body weight (*W*)	70	kg	WSA02.BW
Surface Area of hands (*S*)	840	cm^2	WSA02.Hands
Dermal permeability (K_p, cm/hour) [see Worksheet B05]			
Typical	0.0000561	cm/hour	WSB06.KpC
Lower	0.00002841	cm/hour	WSB06.KpL
Upper	0.0001110	cm/hour	WSB06.KpU
Concentration in solution (*C*) [see Worksheet B02]			
Typical	0.6	mg/mL	WSB02.TypDr
Lower	0.24	mg/mL	WSB02.LowDr
Upper	15	mg/mL	WSB02.HI_Dr

Note that 1 mL is equal to 1 cm^3 and thus mg/mL = mg/cm^3.

Details of calculations for worker zero-order dermal absorption scenarios.

Equation (U.S. EPA 1992)

$$K_p \cdot C \cdot Time(hr) \cdot S \cdot \div W = Dose(mg/kg)$$

where: C = concentration in mg/cm^3 or mg/mL, S = Surface area of skin in cm^2, W = Body weight in kg.

Immersion of Hands or Wearing Contaminated Gloves for One-Minute

Typical Value: Use typical concentration and central estimate of K_p.
0.0000561 cm/hr × 0.6 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 6.73e-06 mg/kg [WZHT1M]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0000284 cm/hr × 0.24 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 1.36e-06 mg/kg [WZHL1M]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0001110 cm/hr × 15 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 0.000333 mg/kg [WZHU1M]

Wearing Contaminated Gloves for One-Hour

Typical Value: Use typical concentration and central estimate of K_p.
0.0000561 cm/hr × 0.6 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.00040392 mg/kg [WZHT1H]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0000284 cm/hr × 0.24 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 8.18e-05 mg/kg [WZHL1H]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0001110 cm/hr × 15 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.01998 mg/kg [WZHU1H]

Worksheet C03: Worker Accidental Spill Based on the Assumption of First-Order Absorption			
Parameter	Value	Units	Source
Liquid adhering to skin after a spill (***L***)	0.008	mg/mL	WSA02.Liq
Body weight (***W***)	70	kg	WSA02.BW
Surface Areas (**A**)			
Hands	840	cm^2	WSA02.Hands
Lower legs	2070	cm^2	WSA02.LLegs
First-order dermal absorption rates (k_a)			
Central Estimate	0.00113	$hour^{-1}$	WSB06.ABSC
Lower limit of range	0.000440	$hour^{-1}$	WSB06.ABSL
Upper limit of range	0.00290	$hour^{-1}$	WSB06.ABSU
Concentration in solution (***C***) [see Worksheet B01]			
Typical	0.6	mg/mL	TypDr
Lower	0.24	mg/mL	LowDr
Upper	15	mg/mL	HI_Dr

Details of calculations.

Equation (from Durkin et al. 1995)

$$Dose_{(mg/kg\ bw)} = k_{a\ (1/hours)} \times L_{(mg/cmsq)} \times C_{(mg/mL)} \times T_{(hours)} \times A_{(cm\ sq)} \div W_{(kg)}$$

where ***T*** is the duration of exposure in hours and other terms are defined as above.

Lower Legs: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFLT1H],
0.0011300 h^{-1} × 0.008 mL/cm × 0.6 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 1.6e-04 mg/kg
Lower range [WFLL1H],
0.0004400 h^{-1} × 0.008 mL/cm × 0.24 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 2.5e-05 mg/kg
Upper range [WFLU1H],
0.0029000 h^{-1} × 0.008 mL/cm × 15 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 1.0e-02 mg/kg

Hands: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFHT1H],
0.0011300 h^{-1} × 0.008 mL/cm × 0.6 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 6.5e-05 mg/kg
Lower range [WFHL1H],
0.0004400 h^{-1} × 0.008 mL/cm × 0.24 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.0e-05 mg/kg
Upper range [WFHU1H],
0.0029000 h^{-1} × 0.008 mL/cm × 15 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 4.2e-03 mg/kg

EXPOSURE ASSESSMENTS for the GENERAL PUBLIC

Worksheet D01: Direct spray of child.			
Verbal Description*: A naked child is accidentally sprayed over the entire body surface with a field dilution as it is being applied. The child is effectively washed - i.e., all of the compound is removed - after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	13.3	kg	WSA04.BWC
Exposed surface area (***A***)	6030	cm^2	WSA04.SAC
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	0.6	mg/mL	WSB02.TYPDR
Low	0.24	mg/mL	WSB02.LOWDR
High	15	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00113	$hour^{-1}$	WSB06.AbsC
Low	0.000440	$hour^{-1}$	WSB06.AbsL
High	0.0029	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.00246	mg/kg	SPRYC
Low	0.000383	mg/kg	SPRYL
High	0.158	mg/kg	SPRYH

Details of calculations

Equation: $L \times C \times A \times k_a \times T \div W$

Central Estimate [SPRYCC]:
0.008 mg/mL × 0.6 mg/mL × 6030 cm^2 × 0.00113 h^{-1} × 1 h ÷ 13.3 kg = 0.00246 mg/kg

Lower Range of Estimate [SPRYCL]:
0.008 mg/mL × 0.24 mg/mL × 6030 cm^2 × 0.00044 h^{-1} × 1 h ÷ 13.3 kg = 0.000383 mg/kg

Upper Range of Estimate [SPRYCH]:
0.008 mg/mL × 15 mg/mL × 6030 cm^2 × 0.0029 h^{-1} × 1 h ÷ 13.3 kg = 0.158 mg/kg

Worksheet D02: Direct spray of woman.			
Verbal Description*: A woman is accidentally sprayed over the feet and legs with a field dilution as it is being applied. The woman washes and removes all of the compound after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	2915	cm^2	WSA04.SAF1
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	0.6	mg/mL	WSB02.TYPDR
Low	0.24	mg/mL	WSB02.LOWDR
High	15	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00113	$hour^{-1}$	WSB06.AbsC
Low	0.000440	$hour^{-1}$	WSB06.AbsL
High	0.0029	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.000247	mg/kg	SPRYWC
Low	0.000039	mg/kg	SPRYWL
High	0.0159	mg/kg	SPRYWH

Details of calculations

Equation: $L \times C \times S \times k_a \times T \div W$

Central Estimate [SPRYWC]:
0.008 mg/mL × 0.6 mg/mL × 2915 cm^2 × 0.00113 h^{-1} × 1 h ÷ 64 kg = 0.000247 mg/kg

Lower Range of Estimate [SPRYWL]:
0.008 mg/mL × 0.24 mg/mL × 2915 cm^2 × 0.00044 h^{-1} × 1 h ÷ 64 kg = 0.0000385 mg/kg

Upper Range of Estimate [SPRYWH]:
0.008 mg/mL × 15 mg/mL × 2915 cm^2 × 0.0029 h^{-1} × 1 h ÷ 64 kg = 0.0159 mg/kg

Worksheet D03: Dermal contact with contaminated vegetation.			
Verbal Description*: A woman wearing shorts and a short sleeved shirt is in contact with contaminated vegetation for 1 hour shortly after application of the compound - i.e. no dissipation or degradation is considered. The chemical is effectively removed from the surface of the skin - i.e., washing - after 24 hours.*			
Parameter/Assumption	Value	Units	Source/Reference
Contact time (***Tc***)	1	hour	N/A
Exposure time (***Te***)	24	hours	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	5300	cm^2	WSA04.SAF2
Dislodgeable residue (***Dr***) as a proportion of application rate	0.1	none	WSA04.DisL
Application Rates(***R***)			
Typical/Central	0.15	lb a.i/acre	WSB01.TYP
Low	0.08	lb a.i/acre	WSB01.LOW
High	2.5	lb a.i/acre	WSB01.HI
First-order dermal absorption rate (k_a)			
Central	0.00113	$hour^{-1}$	WSB06.AbsC
Low	0.000440	$hour^{-1}$	WSB06.AbsL
High	0.00290	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations on next page.***			
Central	0.004450	mg/kg	VEGDWC
Low	0.000870	mg/kg	VEGDWL
High	0.2447	mg/kg	VEGDWH

Description of Calculations:

Step 1:

Use method of Durkin et al. (1995, p. 68, equation 4) to calculate dislodgeable residue (Dr) in units of µg/(cm^2·hr)) after converting application rate in lb a.e./acre to units of µg/cm^2:

$x = \log(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(\boldsymbol{R} \times \text{WSA01.lbac\_ugcm})) + 0.05$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^x$

Step 2:

Convert Dr from units of µg/(cm^2·hr)) to units of mg/(cm^2·hr)) by dividing by 1000:

$\boldsymbol{Dr}(mg/(cm^2 \cdot hr)) = \boldsymbol{Dr}(\mu g/(cm^2 \cdot hr))/1000$

Step 3:

Estimate amount (*Amnt*) transferred to skin in mg during the exposure period:

$\boldsymbol{Amnt}(mg) = \boldsymbol{Dr}(mg/(cm^2 \cdot hr)) \times \boldsymbol{Tc}\ (hours) \times \boldsymbol{A}\ (cm^2)$

Step 4:

Estimate the absorbed dose ($\boldsymbol{D_{Abs}}$) in mg/kg bw as the product of the amount on the skin , the first-order absorption rate, and the duration of exposure divided by the body weight:

$\boldsymbol{D_{Abs}} = \boldsymbol{Amnt}(mg) \times \mathbf{k_a}\ (hours^{-1}) \times \boldsymbol{Te}\ (hours) \div \boldsymbol{W}\ (kg)$

See next page for details of calculations.

Worksheet D03 Details of calculations: *Dermal Exposure to Contaminated Vegetation*

Central Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)))0.296 = (1.09 \times \log_{10}(0.15 \times 11.21)) + 0.05 = 0.296\ \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{0.296} = 1.98\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Dr}\ (mg/(cm^2 \cdot hr)) = 1.98\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 0.00198\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 0.00198\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 10.494\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 10.494\ mg \times 0.00113\ hr^{-1} \times 24\ hours \div 64\ kg = 0.00445$ [VEGDWC]

Lower Range of Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(0.08 \times 11.21)) + 0.05 = -0.002 \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-0.002} = 0.995\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Dr}\ (mg/(cm^2 \cdot hr)) = 0.995\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 0.000995\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 0.000995\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 5.27\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 5.27\ mg \times 0.00044\ hr^{-1} \times 24\ hours \div 64\ kg = 0.0008696$ [VEGDWL]

Upper Range of Estimate:

0.008Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(2.5 \times 11.21)) + 0.05 = 1.628\ \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{1.628} = 42.46\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Dr}\ (mg/(cm^2 \cdot hr)) = 42.46\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 0.04246\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 0.04246\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 225\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 225\ mg \times 0.0029\ hr^{-1} \times 24\ hours \div 64\ kg = 0.2447$ [VEGDWH]

Worksheet D04: Consumption of contaminated fruit, acute exposure scenario.			
Verbal Description*: A woman consumes 1 lb (0.4536 kg) of contaminated fruit shortly after application of the chemical - i.e. no dissipation or degradation is considered. Residue estimates based on relationships from Hoerger and Kenaga (1972) summarized in WSA07.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	64	kg	`WSA04.BWF`
Amount of fruit consumed (***A***)	0.454	kg	`N/A`
Application rates (***R***)			
Typical	0.15	lb a.e./acre	`WSB01.Typ`
Lower	0.08	lb a.e./acre	`WSB01.Low`
Upper	2.5	lb a.e./acre	`WSB01.Hi`
Residue rates (***rr***)			
Typical	1.5	RUD[1]	`WSA05a.FRT`
Upper	7	RUD[1]	`WSA05a.FRU`
Dose estimates (***D***) - **see details of calculations below**			
Typical	0.0016	mg/kg bw	`VEGCWAT`
Lower	0.00085	mg/kg bw	`VEGCWAL`
Upper	0.124	mg/kg bw	`VEGCWAU`
[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on vegetation (mg chemical per kg of vegetation) for each l lb a.e./acre applied.			

Equation (terms defined in above table):

D (mg/kg bw) = ***A***(kg) × ***R***(lb a.e./acre) × ***rr***(mg/kg÷lb a.e./acre) ÷***W***(kg bw)

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.454 kg × 0.15 lb a.e./acre × 1.5 mg/kg÷lb a.e./acre ÷ 64 kg = 0.0016 mg/kg bw

Lower: Use lowest estimated application rate. Use typical RUD because no lower estimate of the RUD is available.

D = 0.454 kg × 0.08 lb a.e./acre × 1.5 mg/kg÷lb a.e./acre ÷ 64 kg = 0.00085 mg/kg bw

Upper: Use highest estimated application rate and highest RUD.

D = 0.454 kg × 2.5 lb a.e./acre × 7 mg/kg÷lb a.e./acre ÷ 64 kg = 0.124 mg/kg bw

Worksheet D05: Consumption of contaminated fruit, chronic exposure scenario.			
***Verbal Description**: A woman consumes contaminated fruit for a 90 day period starting shortly after application of the chemical. Initial residue estimates are based on relationships from Hoerger and Kenaga (1972) summarized in Worksheet A05a. The foliar half-time is used to estimate the concentration on vegetation after 90 days. The geometric mean of the initial and 90 day concentrations is used as a central/typical dose.*			
Parameters/Assumptions	Value	Units	Source/Reference
Halftime on vegetation ($t_{½}$) central	26	days	WSB03.FrT12C
lower	15	days	WSB03.FrT12L
upper	37	days	WSB03.FrT12U
Duration of exposure (***t***)	90	days	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Amount of vegetation consumed per unit body weight(***A***)			
Typical	0.0043	kg veg./kg bw	WSA04.VT
Upper	0.01	kg veg./kg bw	WSA04.VU
Application rates (***R***)			
Typical	0.15	lb a.e./acre	WSB01.Typ
Lower	0.08	lb a.e./acre	WSB01.Low
Upper	2.5	lb a.e./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	1.5	RUD[1]	WSA05a.FRT
Upper	7	RUD[1]	WSA05aFRU
Dose estimates (***D***) - **see details of calculations on next page**			
Typical	0.00079	mg/kg bw/day	VEGCWCT
Lower	0.000360	mg/kg bw/day	VEGCWCL
Upper	0.075	mg/kg bw/day	VEGCWCU
[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on fruit (mg chemical per kg of vegetation) for each l lb a.e./acre applied.			

Details of calculations on next page

Subchronic consumption of vegetation: Details of calculations

Equations (terms defined below or in table on previous page):

Step 1: Calculate $C_{0,}$ concentration in vegetation on Day 0 - i.e., day of application- as the product of the application rate (***R***) and the residue rate (***rr***):

C_0 (mg/kg) = ***R***(lb a.e./acre) × ***rr***(mg/kg÷lb a.e./acre)

Step 2: Calculate $C_{90,}$ concentration in vegetation on Day 90 (t=90 days) based on dissipation coefficient (k) derived from foliar half-life ($t_{½}$).

k ($days^{-1}$) = ln(2) ÷ $t_{½}$ (days)

C_{90} (mg/kg) = C_0 (mg/kg) × e^{-tk}

Step 3: Use the geometric mean of C_0 and C_{90} to get a central estimate of concentration in vegetation (mg/kg veg.) and multiply this value by the vegetation consumption (kg veg/kg bw) to calculate the daily dose (mg/kg bw) over the exposure period.

D (mg/kg bw) = $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw × ***W*** kg bw ÷ ***B***(kg bw)

= $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw

Central Estimate:

Use the typical application rate, the typical vegetation consumption rate, and the typical residue rate along with the central estimate of half-time on vegetation.

Step 1:

C_0 = 0.15 lb a.e./acre × 1.5 mg/kg veg. = 0.225 mg/kg veg.

Step 2:

k = ln(2) ÷26 $days^{-1}$ = 0.027

C_{90} = 0.225 mg/kg × $e^{-0.027 \times 90}$ = 0.15 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(0.225 \times 0.15)^{0.5}$ (mg/kg veg.) × 0.0043 kg veg/kg bw = 0.00079 mg/kg bw

Lower Estimate:

Use the lowest anticipated application rate along with the lower limit of the half-time of vegetation. Also the typical vegetation consumption rate and the typical residue rate because lower limits on these estimates are not available.

Step 1:

C_0 = 0.08 lb a.e./acre × 1.5 mg/kg veg. = 0.12 mg/kg veg.

Step 2:

k = ln(2) ÷15 $days^{-1}$ = 0.046

C_{90} = 0.12 mg/kg × $e^{-0.046 \times 90}$ = 0.06 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (0.12 \times 0.06)^{0.5}{}_{(mg/kg\ veg.)} \times 0.0043_{(kg\ veg/kg\ bw)} = 0.00036_{(mg/kg\ bw)}$

Upper Estimate:

Use the highest anticipated application rate, the upper range of the vegetation consumption rate and the upper range of the residue rate along with the upper limit of the half-time on vegetation.

Step 1:

C_0 = 2.5 lb a.e./acre × 7 mg/kg veg. = 17.5 mg/kg veg.

Step 2:

k = ln(2) ÷37 $days^{-1}$ = 0.019

C_{90} = 17.5 mg/kg × $e^{-0.019 \times 90}$ = 3.2 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (17.5 \times 3.2)^{0.5}{}_{(mg/kg\ veg.)} \times 0.01_{(kg\ veg/kg\ bw)} = 0.075_{(mg/kg\ bw)}$

Worksheet D06: Consumption of contaminated water, acute exposure scenario.			
Verbal Description*: A young child (2-3 years old) consumes 1 liter of contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
	757	liters	1 gallon = 3.785 Liters
Concentrations in solution (***C*** $_{(mg/L)}$)			
Central	600	mg/L	WSB02.TypDR
Low	240	mg/L	WSB02.LowDR
High	15000	mg/L	WSB02.Hi_DR
Concentrations in ambient water ***C*** × VS(liters) ÷ LV)			
Central	0.4542	mg/L	WSB02.TypDR
Low	0.18168	mg/L	WSB02.LowDR
High	11.355	mg/L	WSB02.Hi_DR
Body weight (***W***)	13.3	kg	WSA04.BWC
Amount of water consumed (***A***)			
Typical	1	L/day	WSA04.WCT
Lower	0.61	L/day	WSA04.WCL
Upper	1.5	L/day	WSA04.WCH
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	0.034	mg/kg bw	WATCCAT
Lower	0.0083	mg/kg bw	WATCCAL
Upper	1.28	mg/kg bw	WATCCAU

Details of calculations on next page

Acute Consumption of Contaminated Water from an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: Calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$Conc._{(mg/L)} = VS_{(gal.)} \times 3.785_{L/gal} \times C_{(mg/L)} \div VL_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the amount of water consumed, and the body weight.

$$D_{(mg/kg\ bw)} = Conc._{(mg/L)} \times A_{(L)} \div W_{(kg)}$$

Calculations

Central Estimate:

Use the typical field dilution, and the typical water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 0_{(mg/L)} \div 1000000_{(liters)} = 0.45_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.45_{(mg/L)} \times 1_{(L)} \div 13.3_{(kg)} = 0.034_{(mg/kg\ bw)}$$ [WATCCAT]

Lower Estimate:

Use the lowest estimated field dilution and the lower range of water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 240_{(mg/L)} \div 1000000_{(liters)} = 0.182_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.182_{(mg/L)} \times 0.61_{(L)} \div 13.3_{(kg)} = 0.0083_{(mg/kg\ bw)}$$ [WATCCAL]

Upper Estimate:

Use the highest estimated field concentration and the upper range of water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 15000_{(mg/L)} \div 1000000_{(liters)} = 11.36_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 11.36_{(mg/L)} \times 1.5_{(L)} \div 13.3_{(kg)} = 1.28_{(mg/kg\ bw)}$$ [WATCCAU]

Worksheet D07: Consumption of contaminated water, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates (***R*** $_{(\text{lb a.e./acre})}$)			
Central	0.15	lb a.e./gal	WSB01.Typ
Low	0.08		WSB01.Low
High	2.5		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(\text{mg/L})}$÷***R*** $_{(\text{lb a.e./gal})}$)			
Central	0.082	mg/L/lb a.e./acre	WSB07.AWT
Low	0.011		WSB07.AWL
High	0.43		WSB07.AWU
Body weight (***W***)	70	kg	WSA046.BWM
Amount of water consumed (***A*** $_{(\text{L/day})}$)			
Typical	2	L/day	WSA04.WCAT
Lower	1.4	L/day	WSA04.WCAL
Upper	2.4	L/day	WSA04.WCAH
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	0.00035	mg/kg bw/day	WATCMCT
Lower	0.0000176	mg/kg bw/day	WATCMCL
Upper	0.0369	mg/kg bw/day	WATCMCU

Details of calculations on next page

Chronic Consumption of Contaminated Ambient Water
Details of calculations

Equations (terms defined in table on previous page)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{\text{(lb a.e./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.e./gal))}}$) to get the concentration in ambient water. This product is in turn multiplied by the amount of water consumed per day ($\boldsymbol{A}_{\text{(L/day)}}$) and then divided by the body weight ($\boldsymbol{W}_{\text{(kg)}}$)to get the estimate of the absorbed dose ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.e./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.e./gal))}} \times \boldsymbol{A}_{\text{(L/day)}} \div \boldsymbol{W}_{\text{(kg)}}$$

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), and the typical water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.15_{\text{(lb a.e./acre)}} \times 0.082_{\text{((mg/L)×(lb a.e./gal))}} \times 2_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.00035_{\text{(mg/kg bw)}}$$ [WATCMCT]

Lower Range of Estimate:

Use the lowest anticipated application rate, the low end of the range of the water contamination rate (WCR), and the low end of the range for water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.08_{\text{(lb a.e./acre)}} \times 0.011_{\text{((mg/L)×(lb a.e./gal))}} \times 1.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0000176_{\text{(mg/kg bw)}}$$ [WATCMCL]

Upper range of Estimate:

Use the lowest anticipated application rate, the low end of the range of the water contamination rate (WCR), and the low end of the range for water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 2.5_{\text{(lb a.e./acre)}} \times 0.43_{\text{((mg/L)×(lb a.e./gal))}} \times 2.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0369_{\text{(mg/kg bw)}}$$ [WATCMCU]

Worksheet D08: Consumption of contaminated fish, acute exposure scenario.

Verbal Description*: An adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered. Because of the available and well documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations, separate exposure estimates are made for these two groups.*

Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in spilled solution (***C*** $_{(mg/L)}$)			
Central	600	mg/L	WSB02.TYPDR×1000
Low	240	mg/L	WSB02.LOWDR×1000
High	15000	mg/L	WSB02.HI_DR×1000
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population	0.158	kg/day	WSA04.FAU
Native American subsistence populations	0.77	kg/day	WSA04.FNU
Bioconcentration factor (***BCF*** $_{(kg\ fish/L)}$)	1	kg fish/L	WSB03.BCFT
Dose estimates (***D***) - **see details of calculations on next page.**			
General Population			
Typical	0.0010	mg/kg bw	FISHAMGPT
Lower	0.00041	mg/kg bw	FISHAMGPL
Upper	0.0256	mg/kg bw	FISHAMGPU
Native American subsistence populations			
Typical	0.005	mg/kg bw	FISHAMNAT
Lower	0.00198	mg/kg bw	FISHAMNAL
Upper	0.125	mg/kg bw	FISHAMNAU

Details of calculations on next page

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: As in the acute drinking water scenario, calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$\textit{Conc.}_{(mg/L)} = \textit{VS}_{(gal.)} \times 3.785_{L/gal} \times \textit{C}_{(mg/L)} \div \textit{VL}_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the bioconcentration factor, the amount of fish consumed, and the body weight.

$$\textit{D}_{(mg/kg\ bw)} = \textit{Conc.}_{(mg/L)} \times \textit{BCF}_{(kg\ fish/L)} \times \textit{A}_{(kg\ fish)} \div \textit{W}_{(kg\ bw)}$$

General Public

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 600_{(mg/L)} \div 1000000_{(liters)} = 0.45_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 0.45_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.00100_{(mg/kg\ bw)}$$ `[FISHAMGPT]`

Lower End of Range for the Estimate:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 240_{(mg/L)} \div 1000000_{(liters)} = 0.182_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 0.182_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.00041_{(mg/kg\ bw)}$$ `[FISHAMGPL]`

Upper End of Range for the Estimate:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 15000_{(mg/L)} \div 1000000_{(liters)} = 11.36_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 11.36_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.0256_{(mg/kg\ bw)}$$ `[FISHAMGPU]`

(continued on next page)

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations (continued)

Native American Subsistence Populations

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 600 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 0.45 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 0.45 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.005 $_{(mg/kg\ bw)}$ [FISHAMNAT]

Estimate of Lower End of Range:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 240 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 0.180 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 0.18 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.00198 $_{(mg/kg\ bw)}$ [FISHAMNAL]

Estimate of Upper End of Range:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 15000 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 11.360 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 11.36 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.125 $_{(mg/kg\ bw)}$ [FISHAMNAU]

Worksheet D09: Consumption of contaminated fish, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes fish taken from contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates (***R*** $_{(\text{lb a.e./acre})}$)			
Central	0.15	lb a.e./gal	WSB01.Typ
Low	0.08		WSB01.Low
High	2.5		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(\text{mg/L})}$÷***R*** $_{(\text{lb a.e./gal})}$)			
Central	0.082	mg/L/lb a.e./acre	WSB07.AWT
Low	0.011		WSB07.AWL
High	0.43		WSB07.AWU
Bioconcentration factor (***BCF*** $_{(\text{kg fish/L})}$)	1	kg fish/L	WSB03.BCFT
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population typical	0.01	kg/day	WSA04.FAT
upper limit	0.158	kg/day	WSA04.FAU
Native American subsistence populations typical	0.081	kg/day	WSA04.FNT
upper limit	0.77	kg/day	WSA04.FNU
Dose estimates (***D***) - **see details of calculations on next page.**			
General Public			
Typical	0.00000176	mg/kg bw/day	FISHMCT
Lower	0.000000126	mg/kg bw/day	FISHMCL
Upper	0.00243	mg/kg bw/day	FISHMCU
Native American Subsistence Population			
Typical	0.0000142	mg/kg bw/day	FISHNMCT
Lower	0.00000102	mg/kg bw/day	FISHNMCL
Upper	0.01183	mg/kg bw/day	FISHNMCU

Details of calculations on next page

Chronic Consumption of Contaminated Fish, Details of calculations

Equations (terms defined below or in table on previous page)

Verbal Description: Multiply the application rate ($R_{(\text{lb a.e./acre})}$) by the water contamination rate ($WCR_{((\text{mg/L})\times(\text{lb a.e./gal}))}$) to get the concentration in ambient water. This product is in turn multiplied by the bioconcentration factor ($BCF_{(\text{kg fish/L})}$) and the amount of fish consumed per day ($A_{(\text{kg fish/day})}$) and then divided by the body weight ($W_{(\text{kg bw})}$) to get the estimate of the absorbed dose ($D_{(\text{mg/kg bw})}$).

$$D_{(\text{mg/kg bw})} = R_{(\text{lb a.e./acre})} \times WCR_{((\text{mg/L})\times(\text{lb a.e./gal}))} \times A_{(\text{kg/day})} \times BCF_{(\text{kg fish/L})} \div W_{(\text{kg})}$$

General Public

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), the typical fish consumption, the measured bioconcentration factor, and standard body weight.

$D_{(\text{mg/kg bw})} = 0.15_{(\text{lb a.e./acre})} \times 0.082_{((\text{mg/L})\times(\text{lb a.e./gal}))} \times 1_{(\text{kg fish/L})} \times 0.01_{(\text{kg fush/day})} \div 70_{(\text{kg bw})} = 0.00000176_{(\text{mg/kg bw})}$ `[FISHMCT]`

Lower Range of Estimate:

Use the lowest anticipated application rate, lower range of contamination rate (WCR), the typical fish consumption, the measured bioconcentration factor, and standard body weight. Typical fish consumption is used because there is no published lower estimate.

$D_{(\text{mg/kg bw})} = 0.08_{(\text{lb a.e./acre})} \times 0.011_{((\text{mg/L})\times(\text{lb a.e./gal}))} \times 1_{(\text{kg fish/L})} \times 0.01_{(\text{kg fush/day})} \div 70_{(\text{kg bw})} = 0.000000126_{(\text{mg/kg bw})}$ `[FISHMCL]`

Upper Range of Estimate:

Use the highest labelled application rate, upper range of contamination rate (WCR), the maximum l fish consumption, the measured bioconcentration factor, and standard body weight.

$D_{(\text{mg/kg bw})} = 2.5_{(\text{lb a.e./acre})} \times 0.43_{((\text{mg/L})\times(\text{lb a.e./gal}))} \times 1_{(\text{kg fish/L})} \times 0.158_{(\text{kg fush/day})} \div 70_{(\text{kg bw})} = 0.00243_{(\text{mg/kg bw})}$ `[FISHMCU]`

Chronic Consumption of Contaminated Fish
Details of calculations (continued)

Native American Subsistence Populations

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), the typical fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.15_{\text{(lb a.e./acre)}} \times 0.082_{\text{((mg/L)×(lb a.e./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.081_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.0000142_{\text{(mg/kg bw)}}$$ `[FISHNMCT]`

Lower Range of Estimate:

Use the lowest anticipated application rate, lower range of contamination rate (WCR), the typical fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight. Typical fish consumption is used because there is no published lower estimate.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.08_{\text{(lb a.e./acre)}} \times 0.011_{\text{((mg/L)×(lb a.e./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.081_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.00000102_{\text{(mg/kg bw)}}$$ `[FISHNMCL]`

Upper Range of Estimate:

Use the highest labelled application rate, upper range of contamination rate (WCR), the maximum l fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 2.5_{\text{(lb a.e./acre)}} \times 0.43_{\text{((mg/L)×(lb a.e./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.77_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.01183_{\text{(mg/kg bw)}}$$ `[FISHNMCU]`

SUMMARY TABLES FOR HUMAN HEALTH RISK ASSESSMENT

Worksheet E01: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.002	0.000036	0.2	WSC01a
Broadcast ground spray (Boom spray)	0.0034	0.0000528	0.38	WSC01b
Aerial applications	0.0023	0.000036	0.012	WSC01c
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	6.73e-06	1.36e-06	0.00033	WSC02
Contaminated Gloves, 1 hour	4.04e-04	8.18e-05	0.01998	WSC02
Spill on hands, 1 hour	6.50e-05	1.01e-05	0.0042	WSC03
Spill on lower legs, 1 hour	0.00016	2.50e-05	0.0103	WSC03

Worksheet E02: Summary of risk characterization for workers[1]

RfD	2.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.001	0.00001	0.08	WSC01a
Broadcast ground spray (Boom spray)	0.001	0.00002	0.15	WSC01b
Aerial applications	0.0009	0.00001	0.005	WSC01c
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	3e-06	5e-07	0.00013	WSC02
Contaminated Gloves, 1 hour	0.0002	3e-05	0.01	WSC02
Spill on hands, 1 hour	0.00003	4e-06	0.002	WSC03
Spill on lower legs, 1 hour	0.0001	0.00001	0.004	WSC03

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Worksheet E01 for summary of exposure assessment.

Worksheet E03: Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00246	0.000383	0.158	WSD01
Direct spray, lower legs	Woman	0.000247	0.0000385	0.0159	WSD02
Dermal, contaminated vegetation	Woman	0.00445	0.000870	0.2447	WSD03
Contaminated fruit, acute exposure	Woman	0.0016	0.00085	0.124	WSD04
Contaminated water, acute exposure	Child	0.034	0.0083	1.28	WSD06
Consumption of fish, general public	Man	0.001	0.00041	0.0256	WSD08
Consumption of fish, subsistence populations	Man	0.005	0.00198	0.125	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.00079	0.00036	0.075	WSD05
Consumption of water	Man	0.00035	1.76e-05	0.0369	WSD07
Consumption of fish, general public	Man	1.76e-06	1.26e-07	0.00243	WSD09
Consumption of fish, subsistence populations	Man	1.42e-05	1.02e-06	0.01183	WSD09

Worksheet E04: Summary of risk characterization for the general public [1] .

Provisional RfD		2.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.001	0.0002	0.1	WSD01
Direct spray, lower legs	Woman	0.0001	0.00002	0.01	WSD02
Dermal, contaminated vegetation	Woman	0.002	0.0003	0.1	WSD03
Contaminated fruit, acute exposure	Woman	0.001	0.0003	0.05	WSD04
Contaminated water, acute exposure	Child	0.01	0.003	0.5	WSD06
Consumption of fish, general public	Man	0.0004	0.0002	0.01	WSD08
Consumption of fish, subsistence populations	Man	0.002	0.0008	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0003	0.00014	0.03	WSD05
Consumption of water	Man	0.0001	7.00e-06	0.01	WSD07
Consumption of fish, general public	Man	7.00e-07	5.00e-08	0.001	WSD09
Consumption of fish, subsistence populations	Man	0.00001	4.00e-07	0.005	WSD09

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Worksheet E03 for summary of exposure assessments.

Worksheet F01: Direct spray of small mammal assuming first order absorption kinetics.			
Verbal Description*: A 20 g mammal is directly sprayed over one half of the body surface as the chemical is being applied. The absorbed dose over the first day - i.e., a 24 hour period) is estimated using the assumption of first-order dermal absorption. In the absence of any data on dermal absorption in a small mammal, the estimated absorption rate for humans is used. An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.020	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	87	cm^2	
Application rate (***R***)			
Typical/Central	0.15	lb a.e. /acre	WSB01.TYP
Low	0.08		WSB01.LOW
High	2.5		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
First-order dermal absorption rate (k_a)			
Central	0.00113	$hour^{-1}$	WSB06.AbsC
Low	0.000440	$hour^{-1}$	WSB06.AbsL
High	0.00290	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.098	mg/kg	SMDSDC
Low	0.02049	mg/kg	SMDSDL
High	4.1	mg/kg	SMDSDH

Details of calculations on next page.

Direct Spray of Small Mammal, first-order absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \times 1^{-ka \times T} \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Get the proportion of the amount that is absorbed using the assumption of first order absorption kinetics. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate and dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.15 lb/acre × 87 cm^2
× 1-e$^{-0.00113/h \times 24h}$ ÷ 0.02 kg = 0.098 mg/kg [SMDSDC]

Lower Range of Estimate: Use the lowest anticipated application rate and lower 95% limit of the estimated dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.08 lb/acre × 87 cm^2
× 1-e$^{-0.00044/h \times 24 h}$ ÷ 0.02 kg = 0.02049 mg/kg [CMDSDL]

Upper Range of Estimate: Use the highest anticipated application rate and upper 95% limit of the estimated dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 2.5 lb/acre × 87 cm^2
× 0.0029/h × 24 h) ÷ 0.02 kg = 4.1 mg/kg [DMDSDH]

Worksheet F02: Direct spray of small mammal assuming 100% absorption over the first 24 hour period.			
Verbal Description*: A 20 g mammal is directly sprayed over one half of the body surface as the chemical is being applied. The deposited dose is assumed to be completely absorbed during the first day. An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.020	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	87	cm^2	
Application rate (***R***)			
Typical/Central	0.15	lb a.e. /acre	WSB01.TYP
Low	0.08		WSB01.LOW
High	2.5		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	3.7	mg/kg	SMDS2DC
Low	1.95	mg/kg	SMDS2DL
High	61	mg/kg	SMDS2DH

Direct Spray of Small Mammal, Complete absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 0.15 lb/acre $\times$ 87 $cm^2 \div$ 0.02 kg = 3.7 mg/kg [SMDS2DC]

Lower Range of Estimate [WSE042DL]: Use the lowest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 0.08 lb/acre $\times$ 87 $cm^2 \div$ 0.02 kg = 1.95 mg/kg [SMDS2DL]

Upper Range of Estimate [WSE042DH]: Use the highest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 2.5 lb/acre $\times$ 87 $cm^2 \div$ 0.02 kg = 61 mg/kg [SMDS2DU]

Worksheet F03: Direct spray of bee assuming 100% absorption over the first 24 hour period.			
Verbal Description*: A 0.093 g bee is directly sprayed over one half of the body surface as the chemical is being applied. The deposited dose is assumed to be completely absorbed during the first day. An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.000093	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	2.7	cm^2	
Application rate (***R***)			
Typical/Central	0.15	lb a.e. /acre	WSB01.TYP
Low	0.08		WSB01.LOW
High	2.5		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	24	mg/kg	BEEDS2DC
Low	13	mg/kg	BEEDS2DL
High	407	mg/kg	BEEDS2DH

Direct Spray of Bee, Complete absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 0.15 lb/acre $\times$ 2.7 $cm^2 \div$ 0.000093 kg = 24 mg/kg [BEEDS2DC]

Lower Range of Estimate: Use the lowest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 0.08 lb/acre $\times$ 2.7 $cm^2 \div$ 0.000093 kg = 13 mg/kg [BEEDS2DL]

Upper Range of Estimate: Use the highest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div$ lb/acre) $\times$ 2.5 lb/acre $\times$ 2.7 $cm^2 \div$ 0.000093 kg = 407 mg/kg [BEEDS2DH]

Worksheet F04: Consumption of contaminated vegetation by a small mammal, acute exposure scenario.

Verbal Description*: A 20 g mammal consumes vegetation shortly after application of the chemical - i.e. no dissipation or degradation is considered. The contaminated vegetation accounts for 100% of the diet. Residue estimates based on relationships for leaves and leafy vegetables from Hoerger and Kenaga (1972) summarized in Worksheet A05a.*

Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	0.020	kg	N/A
Food consumed per day (***A***)	0.003	kg	U.S. EPA 1989
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.15	lb a.e./acre	WSB01.Typ
Lower	0.08	lb a.e./acre	WSB01.Low
Upper	2.5	lb a.e./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Dose estimates (***D***) - **see details of calculations below**			
Typical	0.79	mg/kg bw	VGCSMAC
Lower	0.42	mg/kg bw	VGCSMAL
Upper	46.9	mg/kg bw	VGCSMAU

[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on vegetation (mg chemical per kg of vegetation) for each l lb a.e./acre applied.

Equation (terms defined in above table):

D (mg/kg bw) = ***A***(kg) × ***R***(lb a.e./acre) × ***rr***(mg/kg veg.÷lb a.e./acre) ÷ ***W***(kg bw)

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.003 kg × 0.15 lb a.e./acre × 35 mg/kg÷lb a.e./acre ÷ 0.02 kg = 0.79 mg/kg bw [VGCSMAC]

Lower: Use lowest estimated application rate. Use typical RUD because no lower estimate of the RUD is available.

D = 0.003 kg × 0.08 lb a.e./acre × 35 mg/kg÷lb a.e./acre ÷ 0.02 kg = 0.42 mg/kg bw [VGCSMAL]

Upper: Use highest estimated application rate and highest RUD.

D = 0.003 kg × 2.5 lb a.e./acre × 125 mg/kg÷lb a.e./acre ÷ 0.02 kg = 46.9 mg/kg bw [VGCSMAU]

Worksheet F05: Consumption of contaminated vegetation by a small mammal, chronic exposure scenario.

Verbal Description*: A 20 g mammal consumes contaminated vegetation for a 90 day period starting shortly after application of the chemical. It is assumed that 100% of the diet is contaminated. Initial residue estimates are based on relationships for leaves and leafy vegetables from Hoerger and Kenaga (1972) summarized in Worksheet A05a. The foliar half-time is used to estimate the concentration on vegetation after 90 days. The geometric mean of the initial and 90 day concentrations is used as the estimate of the dose.*

Parameters/Assumptions	Value	Units	Source/Reference
Duration of exposure (***D***)	90	days	N/A
Body weight (***W***)	0.02	kg	N/A
Food consumed per day (***A***)	0.003	kg	U.S. EPA 1989
kg food consumed per kg bw	0.15	Unitless	0.003/0.02
Foliar halftimes ($t_{½}$) Central	26	$days^{-1}$	Worksheet B03
Low	15	$days^{-1}$	
High	37	$days^{-1}$	
Application rates (***R***)			
Typical	0.15	lb a.e./acre	WSB01.Typ
Lower	0.08	lb a.e./acre	WSB01.Low
Upper	2.5	lb a.e./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Dose estimates (***D***) - **see details of calculations on next page**			
Typical	0.05	mg/kg bw	VGCSMCT
Lower	0.0001	mg/kg bw	VGCSMCL
Upper	0.39	mg/kg bw	VGCSMCU

[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on fruit (mg chemical per kg of vegetation) for each l lb a.e./acre applied.

Equations (terms defined below or in above table):

Step 1: Calculate $C_{0,}$ concentration in vegetation on Day 0 - i.e., day of application.

C_0 (mg/kg) = ***R***(lb a.e./acre) × ***rr***(mg/kg÷lb a.e./acre)

Step 2: Calculate $C_{90,}$ concentration in vegetation on Day 90 (t=90 days) based on dissipation coefficient (k) derived from foliar half-life ($t_{½}$).

k ($days^{-1}$) = ln(2) ÷ $t_{½}$ (days)

C_{90} (mg/kg) = C_0 (mg/kg) × e^{-tk}

Step 3: Use the geometric mean of C_0 and C_{90} to get a central estimate of concentration in vegetation (mg/kg veg.) and multiply this value by the vegetation consumption (kg veg/kg bw) to calculate the daily dose (mg/kg bw) over the exposure period.

D (mg/kg bw) = $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw

Details of calculations on next page

Subchronic consumption of vegetation by a small mammal:
Details of calculations

Central Estimate:

Use the typical application rate, the typical vegetation consumption rate, and the typical residue rate along with the central estimate of half-time on vegetation.

Step 1:

C_0 = 15 lb a.e./acre × 0.08 mg/kg veg. = 1.2 mg/kg veg.

Step 2:

k = ln(2) ÷ 26 $days^{-1}$ = 0.027

C_{90} = 1.2 mg/kg × $e^{-0.027 \times 90}$ = 0.11 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(1.2 \times 0.11)^{0.5}$ (mg/kg veg.) × 0.15 kg veg/kg bw = 0.05 mg/kg bw [VGCSMCT]

Lower Estimate:

Use the lowest anticipated application rate along with the upper estimate of the half-time on vegetation. Also the typical vegetation consumption rate and the typical residue rate because lower limits on these estimates are not available.

Step 1:

C_0 = 0.08 lb a.e./acre × 0.08 mg/kg veg. = 0.0064 mg/kg veg.

Step 2:

k = ln(2) ÷15 $days^{-1}$ = 0.046

C_{90} = 0.0064 mg/kg × $e^{-0.046 \times 90}$ = 0.0001 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (0.0064 \times 0.0001)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 0.00012_{(mg/kg\ bw)}$ [VGCSMCL]

Upper Estimate:

Use the highest anticipated application rate, the upper range of the vegetation consumption rate and the upper range of the residue rate along with the lower range of the estimated of half-time on vegetation.

Step 1:

C_0 = 2.5 lb a.e./acre × 2.5 mg/kg veg. = 6.25 mg/kg veg.

Step 2:

k = ln(2) ÷37 $days^{-1}$ = 0.019

C_{90} = 6.25 mg/kg × $e^{-0.019 \times 90}$ = 1.1 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (6.25 \times 1.1)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 0.39_{(mg/kg\ bw)}$ [VGCSMCU]

Worksheet F06: Consumption of contaminated water by a small mammal, acute exposure scenario.			
Verbal Description*: A small (20g) mammal consumes contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in solution ($C_{(mg/L)}$)			
Central	600	mg/L	WSB02.TYPDR×1000
Low	240	mg/L	WSB02.LOWDR×1000
High	15000	mg/L	WSB02.HI_DR×1000
Body weight (***W***)	0.02	kg	N/A
Amount of water consumed (***A***)	0.005	L/day	U.S. EPA 1989
Dose estimates (***D***) - **see details of calculations below.**			
Typical	0.113	mg/kg bw	WTCSMAT
Lower	0.0460	mg/kg bw	WTCSMAL
Upper	2.84	mg/kg bw	WTCSMAU

Equations (terms defined below or in table)

Step 1: Calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$\text{Conc.}_{(mg/L)} = \text{VS}_{(gal.)} \times 3.785_{L/gal} \times \text{C}_{(mg/L)} \div \text{VL}_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the amount of water consumed, and the body weight.

$$\text{D}_{(mg/kg\ bw)} = \text{Conc.}_{(mg/L)} \times \boldsymbol{A}_{(L)} \div \text{W}_{(kg)}$$

Central Estimate: Use the typical field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 600_{(mg/L)} \div 1000000_{(liters)} = 0.45_{(mg/L)}$

Step 2: $\text{D}_{(mg/kg\ bw)} = 0.45_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.113_{(mg/kg\ bw)}$ [WTCSMAT]

Lower Estimate: Use the lowest estimated field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 240_{(mg/L)} \div 1000000_{(liters)} = 0.182_{(mg/L)}$

Step 2: $\text{D}_{(mg/kg\ bw)} = 0.182_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.046_{(mg/kg\ bw)}$ [WTCSMAL]

Upper Estimate: Use the highest estimated field concentration,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 15000_{(mg/L)} \div 1000000_{(liters)} = 11.36_{(mg/L)}$

Step 2: $\text{D}_{(mg/kg\ bw)} = 11.36_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 2.84_{(mg/kg\ bw)}$ [WTCSMAU]

Worksheet F07: Consumption of contaminated water by a small mammal, chronic exposure scenario.			
Verbal Description*: A small (20 g) mammal consumes contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates ($\boldsymbol{R}_{\text{(lb a.e./acre)}}$)			
Central	0.15	lb a.e./gal	WSB01.Typ
Low	0.08		WSB01.Low
High	2.5		WSB01.Hi
Water Contamination Rate (WCR)($\boldsymbol{C}_{\text{(mg/L)}} \div \boldsymbol{R}_{\text{(lb a.e./gal)}}$)			
Central	0.082	mg/L/lb a.e./acre	WSB07.AWT
Low	0.011		WSB07.AWL
High	0.43		WSB07.AWU
Body weight ($\boldsymbol{W}$)	0.02	kg	U.S. EPA 1989
Amount of water consumed ($\boldsymbol{A}_{\text{(L/day)}}$)	0.005	L/day	U.S. EPA 1989
Dose estimates ($\boldsymbol{D}$) - **see details of calculations on next page.**			
Typical	0.0031	mg/kg bw	WTCSMCT
Lower	0.000220	mg/kg bw	WTCSMCL
Upper	0.269	mg/kg bw	WTCSMCU

Equations (terms defined in table)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{\text{(lb a.e./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.e./gal))}}$) to get the concentration in ambient water. This product is in turn multiplied by the amount of water consumed per day ($\boldsymbol{A}_{\text{(L/day)}}$) and then divided by the body weight ($\boldsymbol{W}_{\text{(kg)}}$)to get the estimate of the absorbed dose ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.e./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.e./gal))}} \times \boldsymbol{A}_{\text{(L/day)}} \div \boldsymbol{W}_{\text{(kg)}}$$

Central Estimate: Use the typical application rate and typical water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.15_{\text{(lb a.e./acre)}} \times 0.082_{\text{((mg/L)×(lb a.e./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.0031_{\text{(mg/kg bw)}}$$ [WTCSMCT]

Lower Range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.08_{\text{(lb a.e./acre)}} \times 0.011_{\text{((mg/L)×(lb a.e./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.00022_{\text{(mg/kg bw)}}$$ [WTCSMCL]

Upper range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 2.5_{\text{(lb a.e./acre)}} \times 0.43_{\text{((mg/L)×(lb a.e./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.269_{\text{(mg/kg bw)}}$$ [WTCSMCU]

Worksheet G01: Summary of Exposure Scenarios for terrestrial animals

Scenario	Dose (mg/kg/day)			Worksheet
	Typical	Lower	Upper	
Acute/Accidental Exposures				
Direct spray, small mammal, first-order absorption	0.098	0.02049	4.1	WSF01
Direct spray, small animal, 100% absorption	3.7	1.95	61	WSF02
Direct spray, bee, 100% absorption	24	13	407	WSF03
Consumption of contaminated vegetation, acute exposure	0.79	0.42	46.9	WSF04
Consumption of contaminated water, acute exposure	0.113	0.046	2.84	WSF06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.05	0.00012	0.39	WSF05
Consumption of contaminated water, chronic exposure	0.0031	0.00022	0.269	WSF07

Worksheet G02: Summary of quantitative risk characterization for terrestrial animals[1]

Scenario	Hazard Quotient[2]		
	Typical	Lower	Upper
Acute/Accidental Exposures			
Direct spray, small mammal, first-order absorption	0.0004	0.00008	0.02
Direct spray, small animal, 100% absorption	0.01	0.008	0.2
Direct spray, bee, 100% absorption[3]	0.02	0.01	0.4
Consumption of contaminated vegetation, acute exposure	0.003	0.002	0.2
Consumption of contaminated water, acute exposure	0.0005	0.0002	0.003
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.0002	5.00e-07	0.002
Consumption of contaminated water, chronic exposure	0.00001	9e-07	0.001
Toxicity value for mammal [2]		250	mg/kg/day
Toxicity value for bee [3]		1000	mg/kg

[1] See Worksheet G01 for details of exposure assessment.
[2] Except for the honey bee, the hazard quotient is calculated as the estimated exposure divided by the chronic dogs NOAEL of 250 mg/kg/day and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on LD_{50} of >1000 mg/kg (Gagne et al. 1991) .