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ISOXABEN-
ABBREVIATED Human Health and Ecological Risk Assessment
Final Report

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TABLE OF CONTENTS

LIST OF TABLES v

LIST OF FIGURES v

ACRONYMS, ABBREVIATIONS, AND SYMBOLS vi

COMMON UNIT CONVERSIONS AND ABBREVIATIONS viii

CONVERSION OF SCIENTIFIC NOTATION ix

EXECUTIVE SUMMARY x

1. INTRODUCTION 1-1

2. PROGRAM DESCRIPTION 2-1

2.1. OVERVIEW 2-1

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS 2-1

2.3. APPLICATION METHODS 2-2

2.4. MIXING AND APPLICATION RATES 2-2

3. HUMAN HEALTH RISK ASSESSMENT 3-1

3.1. HAZARD IDENTIFICATION 3-1

3.1.1. Overview 3-1
3.1.2. Acute Oral Toxicity 3-1
3.1.3. Subchronic or Chronic Systemic Toxic Effects 3-1
3.1.4. Reproductive and Teratogenic Effects 3-1
3.1.5. Carcinogenicity and Mutagenicity 3-2
3.1.6. Effects on the Skin and Eyes 3-3
3.1.7. Systemic Toxic Effects from Dermal Exposure 3-4
3.1.8. Inhalation Exposure 3-4
3.1.9. Impurities, Metabolites, and Formulation Additives 3-4
3.1.10. Toxicological Interactions 3-5
3.1.11. Mechanism of Action 3-5

TABLE OF CONTENTS (*continued*)

3.2. EXPOSURE ASSESSMENT 3-6

3.2.1. Overview 3-6
3.2.2. Workers 3-6
3.2.3. General Public 3-8

3.3. DOSE-RESPONSE ASSESSMENT 3-13

3.3.1. Overview 3-13
3.3.2. Existing Guidelines 3-13
3.3.3. Dose-Response and Dose-Severity Relationships 3-14
3.3.4. Cancer Potency 3-14

3.4. RISK CHARACTERIZATION 3-15

3.4.1. Overview 3-15
3.4.2. Workers 3-16
3.4.3. General Public 3-17
3.4.4. Sensitive Subgroups 3-18
3.4.5. Connected Actions 3-18
3.4.6. Cumulative Effects 3-18

4. ECOLOGICAL RISK ASSESSMENT 4-1

4.1. HAZARD IDENTIFICATION 4-1

4.1.1. Overview 4-1
4.1.2. Toxicity to Terrestrial Organisms 4-1
4.1.3. Aquatic Organisms 4-3

4.2. EXPOSURE ASSESSMENT 4-4

4.2.1. Overview 4-4
4.2.2. Terrestrial Animals 4-5
4.2.3. Terrestrial Plants 4-9
4.2.4. Aquatic Organisms 4-9

4.3. DOSE-RESPONSE ASSESSMENT 4-10

4.3.1. Overview 4-10
4.3.2. Toxicity to Terrestrial Organisms 4-10

TABLE OF CONTENTS (*continued*)

4.3.3. Aquatic Organisms 4-11

4.4. RISK CHARACTERIZATION 4-11

4.4.1. Overview 4-11
4.4.2. Terrestrial Organisms 4-12
4.4.3. Aquatic Organism 4-13

5. REFERENCES 5-1

WORKSHEETS

LIST OF TABLES

Table 2-1 Selected Physical and Chemical properties 2-4

Table 3-1 Summary of Worker Exposure Scenarios 3-19

Table 3-2 Summary of Exposure Scenarios for the General Public 3-20

Table 3-3 Summary of risk characterization for workers 3-21

Table 3-4 Summary of risk characterization for the general public 3-22

Table 3-5 Summary of carcinogenic risks associated with chronic exposures scenarios for members of the general public 3-23

Table 4-1 Summary of Exposure Scenarios for Terrestrial Animals 4-14

Table 4-2 Summary of quantitative risk characterization for terrestrial animals . . . 4-15

LIST OF FIGURES

Figure 2-1 Region in which isoxaben will be applied 2-6

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

a.e.	acid equivalents
a.i.	active ingredient
AEL	adverse-effect level
AP	alkaline phosphatase
AST	aspartate aminotransferase
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
cm	centimeter
DMSO	dimethyl sulfoxide
EC_{50}	concentration causing 50% inhibition of a process
EC_{100}	concentration causing complete inhibition of a process
EIS	environmental impact statement
F	female
F_1	first filial generation
FS	Forest Service
g	gram
GC	gas chromatography
GRAS	generally recognized as safe
HQ	hazard quotient
IARC	International Agency for Research on Cancer
i.p.	intraperitoneal
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% mortality
LD_{50}	lethal dose, 50% mortality
LD_{95}	lethal dose, 95% mortality
LOAEL	lowest-observed-adverse-effect level
m	meter
M	male
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
MW	molecular weight
MTD	maximum tolerated dose
NCI	National Cancer Institute
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NRC	National Research Council

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

ppm	parts per million
RBC	red blood cells
RfD	reference dose
UF	uncertainty factor
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
USDA	United States Department of Agriculture
$>$	greater than
$\geq$	greater than or equal to
$<$	less than
$\leq$	less than or equal to
$=$	equal to
$\simeq$	approximately equal to

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
hectares (ha)	square meters	10,000
inches (in)	centimeters (cm)	2.540
kilograms (kg)	ounces, (oz)	35.274
kilograms (kg)	pounds, (lb)	2.2046
kilograms per hectare (hg/ha)	pounds per acre (lb/acre)	0.892
kilometers (km)	miles (mi)	0.6214
liters (L)	cubic centimeters (cm^3)	1,000
liters (L)	gallons (gal)	0.2642
liters (L)	ounces, fluid (oz)	33.814
miles (mi)	kilometers (km)	1.609
miles per hour (mi/hr)	cm/sec	44.70
milligrams (mg)	ounces (oz)	0.000035
meters (m)	feet	3.281
ounces (oz)	grams (g)	28.3495
ounces per acre (oz/acre)	grams per hectare (g/ha)	70.1
ounces per acre (oz/acre)	kilograms per hectare (kg/ha)	0.0701
ounces fluid	cubic centimeters (cm^3)	29.5735
pounds (lb)	grams (g)	453.6
pounds (lb)	kilograms (kg)	0.4536
pounds per acre (lb/acre)	kilograms per hectare (kg/ha)	1.121
pounds per acre (lb/acre)	mg/square meter (mg/m^2)	112.1
pounds per acre (lb/acre)	µg/square centimeter ($\mu g/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

Introduction

The USDA Forest Service is proposing to use isoxaben in its vegetation management programs. The Forest Service is proposing to use only one commercial formulation of isoxaben, Gallery 75 Dry Flowable. The present document provides abbreviated risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using isoxaben in Forest Service programs.

Program Description

Isoxaben is a soil active preemergence herbicide that acts by absorption through the roots of the plant as opposed to foliar absorption. Thus, isoxaben must be applied to the soil and then activated by rainfall. The Forest Service proposes to use only one commercial formulation of isoxaben, Gallery 75 Dry Flowable. This formulation is produced by Dow AgroSciences and contains 75% (w/w) isoxaben and 25% (w/w) inerts. The Forest Service is proposing to apply isoxaben only in boom spray (broadcast foliar) operations.

Currently, the Forest Service plans to used Gallery at only one nursery, which is located on the northwest coast of California near McKinleyville. In addition, the Forest Service plans on treating only 60-80 acres per year. As discussed further in sections 3 and 4, this limited use has a substantial impact on the exposure assessments and risk characterizations for both the human health and ecological risk assessments.

The labeled application rates for Gallery 75 DF range from 0.66 to 1.33 lbs a.i./acre. The Forest Service plans to use a typical application rate of 0.75 lbs a.i./acre, once per season. The highest single application rate would be1.0 lbs a.i./acre and the Forest Service may apply Gallery 75 DF twice per year.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification

Although the mechanism for the herbicidal activity of isoxaben is characterized in some detail, the mechanism of toxic action in mammals or other animal species is not well characterized. Isoxaben has a low order of acute toxicity with acute oral LD_{50} values >5000 mg/kg and acute dermal LD_{50} values >200 mg/kg and acute inhalation LC_{50} values >1.99 mg/L or 1990 mg/m^3. In addition, isoxaben may cause moderate eye irritation, transient corneal injury, and slight skin irritation. Longer-term exposures to isoxaben are associated with signs of liver and kidney damage, enlargement of the heart, and decreases in food conversion efficiency. Isoxaben has the potential to cause both reproductive and developmental effects at doses that cause signs of maternal toxicity. The U.S. EPA classified isoxaben as a possible human carcinogen. This assessment is based on a statistically significant increase in and dose-response trend for a non-malignant and malignant liver tumors combined.

Exposure Assessment
There are no occupational exposure studies in the available literature that are associated with the application of isoxaben. Consequently, worker exposure rates are estimated from an empirical relationship between absorbed dose per kilogram of body weight and the amount of chemical handled. For broadcast ground applications, estimated worker exposures are 0.0074 mg/kg/ day with a range of 0.00027 to 0.058 mg/kg/day.

Except in the case of accidental exposure, the levels of isoxaben to which the general public might be exposed should be far less than the levels for workers. Longer-term exposure scenarios for the general public lead to central estimates of daily doses that range from about 0.00005 to about 0.003 mg/kg/day with upper limits of exposure in the range of 0.001-0.05 mg/kg/day. Given the limited use of isoxaben proposed by the Forest Service, some of the exposure scenarios on which both the longer-term doses are based are highly implausible. This is discussed in greater detail in the risk characterization.

Accidental exposure scenarios result in central estimates of exposure of up to about 0.075 mg/kg/day with upper ranges in the area of about 0.11 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. Again, given the limited use of isoxaben, some of these standard accidental exposure scenarios are excluded in the risk characterization.

Dose-Response Assessment
The U.S. EPA (1993a) derived an RfD for isoxaben of 0.05 mg/kg/day. This is based on a dietary NOAEL of 125 ppm in the diet corresponding to estimated daily doses of 5 mg/kg/day and using an uncertainty factor of 100. In the same study, the LOAEL was about 50 mg/kg/day (1250 ppm in the diet), and the observed effects included signs of liver and kidney damage, enlargement of the heart, and an apparent decrease in food conversion efficiency. No acute RfD for isoxaben has been derived by the U.S. EPA.

While isoxaben is classified as a possible human carcinogen by the U.S. EPA, the U.S. EPA did not derive a cancer potency estimate for this compound. In documents submitted to U.S. EPA as part of the registration process, however, two oncogenic potency parameters were derived, one based on adenomas and carcinomas combined and the other based on nodular hyperplasia, adenomas, and carcinomas combined. The recent U.S. EPA guidelines for cancer risk assessment do permit the combining of benign and malignant tumors for the assessment of cancer risks. For this risk assessment, the higher potency parameter, 0.0021 $(mg/kg/day)^{-1}$, is used to illustrate the potential risks of benign and malignant liver tumors combined.

Risk Characterization
Based on the central estimate of exposures associated with hydraulic spray applications, the hazard quotient is 0.1, below the level of concern by a factor of 10. At the upper range of the estimated exposure, however, the hazard quotient is 1.2, somewhat above the chronic RfD. The lack of an acute RfD or some other similar measure of ‘acceptable’ short-tern exposure limits this

quantitative characterization of risk. The currently proposed use of isoxaben by the Forest Service will involve at most, exposure periods of 30 hours per year for a worker. Thus, using a chronic RfD as the basis for characterizing risks from a 30-hour exposure is likely to be grossly conservative. Accidental exposures for workers also lead to central estimates of hazard quotients that are below the level of concern. The upper limit for the contaminated glove scenario involving a 1-hour exposure is 2, in the range of concern for subclinical systemic toxic effects but not frank signs of toxicity or reproductive effects. Again, the lack of an acute RfD limits the characterization of risk.

Under the conditions of use proposed by the Forest Service and at the single location where the Forest Service is proposing to use isoxaben, there is no apparent risk in terms of systemic toxicity or reproductive effects for members of the general public. However, if the Forest Service were to use isoxaben in a different area where the contamination of edible vegetation or spills into surface water were plausible, risks to the general public would be of concern.

The potential risks of both benign and malignant liver tumors are based on the potency parameter of 0.0021 $(mg/kg/day)^{-1}$. The calculated risks are factors of up to about 25 above the risk level of 1 in one million. A risk level of 1 in one million has been used by the Forest Service as an administrative trigger for action to reduce exposure. The proximity of the estimated risks to the risk level of 1 in one million as well as the substantial uncertainties in the exposure assessments raise concern for the potential cancer risks that could be associated with the use of isoxaben if individuals were to be chronically exposed to contaminated water from this site. Based on information provided by the Forest Service, however, chronic exposure to contaminated water or vegetation is not plausible.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification

The mammalian toxicity of isoxaben is relatively well characterized in experimental mammals; however, there is relatively little information regarding nontarget wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., liver and kidney damage).

Several acute toxicity studies and two reproduction studies are available on the toxicity of isoxaben to birds. Isoxaben is relatively non-toxic to birds after acute oral exposure: the acute oral LD_{50} is >2000 mg/kg. On the other hand, birds may be somewhat more sensitive than experimental mammals to the reproductive effects of isoxaben: the NOAEL and LOAEL are 45 and 150 mg/kg/day, respectively, for birds and 125 and 625 mg/kg bw/day, respectively, for mammals. Isoxaben seems also to have a low order of toxicity to terrestrial invertebrates. This assessment is based on the only two available acute toxicity studies, one in bees and one in earthworms.

The toxicity of isoxaben to terrestrial plants is well characterized. Isoxaben inhibits the incorporation of glucose into cellulose, the major structural polysaccharide in plants. As part of

the registration process for herbicides the U.S. EPA requires toxicity assays on nontarget plant species. Isoxaben is much more toxic after soil incorporation, compared with surface application. Effects on nontarget terrestrial plants are considered more quantitatively in the dose-response assessment.

The potential for toxic effects on aquatic species, either plants or animals, exposed to isoxaben appears to be remote. The solubility of isoxaben in water is reported to range from 1 to 2 mg/L. Standard toxicity bioassays suggest that no acute effects are likely at concentrations in the range of 1 mg/L and that no chronic effects are likely in the range of 0.4-0.7 mg/L.

Exposure Assessment

As in the human health risk assessment, the exposure assessments presented in this document are based on a standard set of scenarios and assumptions that are uniformly applied in all Forest Service risk assessments. Given the very limited use of isoxaben proposed by the Forest Service and the specific characteristics of the single site where isoxaben will be applied, not all of these exposure assessments may be relevant to the Forest Service program. This is discussed further in the risk characterization.

Terrestrial animals might be exposed to any applied pesticide 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 estimated for terrestrial animals involve the direct spray of a bee, assuming 100% absorption. This scenario leads to estimates of absorbed dose ranging from 122 to 163 mg/kg.

Central estimates of absorbed dose for several other acute exposure scenarios—direct spray of a small mammal assuming 100% absorption and the consumption of contaminated vegetation, insects or fish — range from 0.25 to 21 mg/kg bw. The upper limits of exposure for these scenarios range from 0.25 to 40 mg/kg bw.

In chronic exposure scenarios, central estimates of daily doses for birds and mammals range from 0.006 to 2.2 mg/kg/day. Based on upper ranges of exposure, the highest doses are estimated for the consumption of contaminated vegetation by a large mammal or birds, with estimated doses ranging from about 18 to 28 mg/kg bw/day. Other exposure scenarios lead to upper estimates of absorbed doses that range from about 0.011 to 0.48 mg/kg bw/day.

The potential for longer-term effects on aquatic species are based on estimated concentrations of isoxaben in water, which are identical to those used in the human health risk assessment. A longer-term water contamination rate adopted from an exposure assessment made by the U.S. EPA is used in all the exposure assessments involving the contamination of ambient water. For all acute exposure scenarios, peak water concentrations of 1 mg/L are estimated based on the water solubility of isoxaben.

Dose-Response Assessment
For mammals, the lowest NOAEL for systemic toxicity is 5 mg/kg/day and the lowest NOAEL for reproductive toxicity is 125 mg/kg/day, the same values used in the human health risk assessment. These two values are used to characterize risk quantitatively. The value of 5 mg/kg/day for systemic toxicity is used to calculate the hazard quotient. The ratio of the reproductive toxicity NOAEL to the NOAEL for systemic toxicity (i.e., 25 or 125 mg/kg/day ÷ 5 mg/kg/day) is used to characterize the potential for reproductive toxicity for scenarios that exceed a hazard quotient of unity for systemic toxicity. Birds may be somewhat more sensitive than experimental mammals to the adverse effects of isoxaben on reproduction, with a NOAEL and LOAEL of 60 and 200 mg/kg/day, respectively. These values are used to characterize risk quantitatively in exposure scenarios involving birds.

Isoxaben is a herbicide and causes adverse effects in various nontarget plant species. A soil incorporation assay employing an application rate of 0.25 lbs a.i./acre resulted in substantial growth inhibition in winter wheat. More sensitive plant species could be adversely affected at functional application rates of 0.008 lbs a.i./acre.

At the solubility of isoxaben in test water (i.e., about 1 mg/L) the level of mortality did not permit the calculation of LC_{50} values. Thus, there appears to be a very low potential for isoxaben to cause adverse effects in aquatic species after acute exposure. NOAELs for chronic toxicity are approximately 0.4 mg/L or higher.

Risk-Characterization
Standard acute exposure scenarios reach or exceed a level of concern for the direct spray of a small mammal under the assumption of 100% dermal absorption and the consumption of contaminated vegetation by a large mammal. In addition, the upper limit of the hazard index exceeds the level of concern for the consumption of contaminated vegetation by a small mammal. For longer-term exposures, none of the hazard quotients reach a level of concern. The highest hazard quotients are associated with the consumption of contaminated vegetation. The longer-term consumption of contaminated water or fish lead to hazard quotients that are far below a level of concern. At the upper ranges of exposure, the only hazard index to exceed a level of concern is that associated with the chronic consumption of contaminated vegetation by a large mammal. For this scenario, the upper range of the hazard quotient for systemic toxicity is 3.5 but the upper range of the hazard quotient for reproductive effects is 0.1 - i.e., below the level of concern by a factor of10.

Isoxaben is an effective preemergence herbicide, and numerous plant species will be affected in areas directly treated with this compound. Although some damage to nontarget vegetation might be anticipated in areas close to the application site (i.e., <100 meters), damage to nontarget vegetation at greater distances does not appear to be likely. Notwithstanding this assertion, off site damage to nontarget vegetation could be more substantial if conditions during application favor greater rates of drift or if local species of vegetation are highly sensitive to isoxaben.

The potential for damage to aquatic species appears to be remote, based on the low solubility of isoxaben in water and the relatively low proportion of isoxaben that is estimated by U.S. EPA to runoff of the application site. In addition, the risks to aquatic species are further reduced because of the 1000 to 3000 foot distance between the treated area and nearest permanent body of surface water in the area in which the Forest Service proposes to apply this herbicide.

1. INTRODUCTION

The USDA Forest Service uses the herbicide, isoxaben, in its vegetation management programs. The Forest Service is proposing to use only one commercial formulation of isoxaben, Gallery 75 Dry Flowable. The present document provides abbreviated risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using isoxaben in Forest Service programs.

The Forest Service proposes to use isoxaben at only one facility, as discussed further in section 2. Because of the proposed limited use of the herbicide and in the interest of economy, the Forest Service requested an abbreviated risk assessment for this compound. There are some differences between a standard risk assessment and this abbreviated risk assessment. As in a standard risk assessment, this abbreviated risk assessment involves accessing the published and CBI (confidential business information) literature. A complete search of the U.S. EPA files was conducted in the preparation of this risk assessment. Full text copies of the most relevant studies [n=80] were kindly provided by the U.S. EPA Office of Pesticide Programs. Unlike a standard risk assessment, however, no CBI appendices were prepared. To the extent necessary, summaries of relevant information from CBI studies are incorporated into the text but not to the level of detail found in SERA's standard CBI appendices.

In addition, U.S. EPA's RfD (U.S. EPA 1993a), cancer classification of isoxaben (U.S. EPA 1990), and risk assessments (U.S. EPA 1988a,b) were accepted; however, the conclusions and supporting literature were not reviewed and independently evaluated to the extent found in a standard risk assessment. The CBI and open literature were consulted primarily to clarify existing U.S. EPA risk assessments. In addition to the U.S. EPA risk assessment and other related documents on isoxaben, a risk assessment of isoxaben was conducted for the California Department of Transportation (Jones and Stokes 1991). Relevant sections of this document also were consulted in the preparation of this abbreviated risk assessment. More recent studies published in the open literature and summarized in the current report do not provide information that contradicts the existing U.S. EPA risk assessments.

Like a standard risk assessment, 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 isoxaben, an assessment of potential exposure to this compound, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. 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.

This is a technical support document and it addresses some specialized technical areas. Nevertheless an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical

concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 1998a).

The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. The information presented in chapters 2, 3, and 4 of the risk assessment are intended to be detailed enough to support a review of the risk analyses; however, they are not intended to be as detailed as the information generally presented in Chemical Background documents or other comprehensive reviews.

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 (1998a), 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 isoxaben 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 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

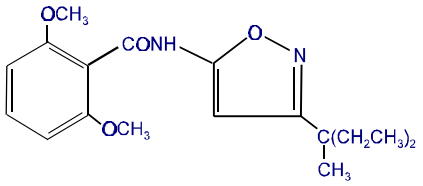
Isoxaben is a soil active preemergence herbicide that acts by absorption through the roots of the plant as opposed to foliar absorption. Thus, isoxaben must be applied to the soil and then activated by rainfall. The Forest Service proposes to use only one commercial formulation of isoxaben, Gallery 75 Dry Flowable. This formulation is produced by Dow AgroSciences and contains 75% (w/w) isoxaben and 25% (w/w) inerts. The Forest Service is proposing to apply isoxaben only in boom spray operations.

Currently, the Forest Service plans to used Gallery at only one nursery, which is located on the northwest coast of California near McKinleyville. In addition, the Forest Service plans on treating only 60-80 acres per year. As discussed further in sections 3 and 4, this limited use has a substantial impact on the exposure assessments and risk characterizations for both the human health and ecological risk assessments.

The labeled application rates for Gallery 75 DF range from 0.66 to 1.33 lbs a.i./acre. The Forest Service plans to use a typical application rate of 0.75 lbs a.i./acre, once per season. The highest single application rate would be1.0 lbs a.i./acre and the Forest Service may apply Gallery 75 DF twice per year.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Isoxaben is the common name for N-[3-(1-ethyl-1-methylpropyl)-5-isoxazolyl]-2,6-dimethoxybenzamide:



Selected chemical and physical properties of isoxaben are summarized in Table 2-1. The values from Table 2-1 that are directly used in this risk assessment are summarized in worksheet B03.

The Forest Service proposes to use only one commercial formulation of isoxaben, Gallery 75 Dry Flowable. This formulation is produced by Dow AgroSciences and contains 75% (w/w) isoxaben and 25% (w/w) inerts (C&P Press 1999a). The inerts include kaolin and crystalline silica that is contained in kaolin (C&P Press 1999b), as discussed further in section 3.1.9.3.

This formulation of isoxaben is recommended as a preemergence herbicide for the control of broadleaf weeds in turf, nursery stock, ground covers, and non-cropland areas. To be effective, this formulation must be applied before weeds emerge and must be activated in the soil by rainfall or irrigation (C&P Press 1999a).

2.3. APPLICATION METHODS

Currently, the Forest Service plans to used Gallery at only one nursery, which is located on the northwest coast of California near McKinleyville, California and north of Arcata and Eureka, California. In addition, the Forest Service plans to treat only 60-80 acres per year. As discussed further in sections 3 and 4, this limited use has a substantial impact on the exposure assessments and risk characterizations for both the human health and ecological risk assessments.

The Forest Service proposes to apply isoxaben only in boom spray operations. The spray equipment is mounted on tractors or trucks and applied over the area to be treated. At the nursery where isoxaben will be used, the actual rate of application will range from 6 to 8 acres per hour, including turnaround time, loading, and moving from location to location. This rate of application is somewhat less than values that are typically used in Forest Service risk assessments for broadcast ground applications (i.e., approximately 8-21 acres/hour) (USDA 1989b, p 2-9 to 2-10) (Worksheet A03b). Nonetheless, because these lower rates of application reflect the conditions under which isoxaben will be applied by the Forest Service, a range of 6-8 acres per hour (Worksheet A03b) is used to estimate the exposure for workers involved in boom spray applications (Worksheet C01b).

It should also be noted that only 60-80 acres will be treated, possibly twice, per year. Thus, at treatment rates of 6-8 acres per hour, applications would be completed in only 7.5 [60÷8] to 13.3 [80÷6] hours. Even with two applications per year, at most 26.6 hours spent would be spent by a worker applying this herbicide. Thus, all exposure scenarios for workers essentially involve short-term exposures. This is discussed further in the risk characterization for workers (section 3.4.2).

In the area where the Forest Service plans to apply isoxaben, there is one small stream about 1,000-3,000 feet from the nursery site. The Forest Service has indicated that slope of terrain at the nursery is such that water contamination of the creek from nursery operations is not plausible. The nursery site does include two sumps that are used to collect water from the nursery water collection system. These sumps, which are dry in summer months, each have a capacity of about 1,000,000 liters and may occasionally overflow into private property. The Forest Service has indicated that these sumps are not likely to be used as sources of drinking water (Bakke 2000).

2.4. MIXING AND APPLICATION RATES

The labeled application rates for Gallery 75 DF range from 0.66 to 1.33 lbs a.i./acre. The label specifies that repeated applications may be made after an interval of at least 60 days but that the total amount that may be applied in one season is 4 lbs a.i./acre. (C&P Press 1999a).

The Forest Service plans to use a typical application rate of 0.75 lbs a.i./acre, once per season. The highest single application rate would be 1.0 lbs a.i./acre, and the Forest Service may apply Gallery 75 DF twice per year. Thus, for this risk assessment, the typical as well as the lower limit of the application rate is taken at 0.75 lbs a.i./acre. The upper range of the application rate is taken at 2 lbs a.i./acre (i.e., 1 lb a.i./acre twice per year).

The labeled application volumes for Gallery 75 DF range from 10 to 200 gallons per acre (C&P Press 1999a). The Forest Service plans to use a typical application volume of 33 gallons per acre, with a possible range of 25-40 gallons per acre. For this risk assessment, the extent to which a formulation is diluted prior to application primarily influences dermal and direct spray scenarios, both of which depend on 'field dilution'(i.e., the concentration of the compound in the applied spray). In all cases, the higher the concentration of the compound, the greater the risk. Details regarding the calculation of field dilution rates are provided in worksheet B01, and the calculations following this worksheet are summarized in worksheet B02.

Table 2-1. Selected physical and chemical properties of isoxaben.

Synonyms	N-[3-(1-ethyl-1-methylpropyl)-5-isoxazolyl]-2,6-dimethoxybenzamide (Budavari 1989) EL-107 (Budavari 1989) benzamizole (Budavari 1989) NA 8318 (Budavari 1989) Flexidor (Budavari 1989)
U.S. EPA Reg. No.	62719-145 (C&P Press 1999a)
Commercial Formulations	Gallery 75 Dry Flowable
CAS number	82558-50-7 (C&P Press 1999b; U.S. EPA 1993a) 8255-50-7 (Budavari 1989) *[This CAS number is incorrect.]*
Molecular weight (g/mole)	332.40 (Budavari 1989)
Appearance, ambient	white crystalline solid
Bulk density (g/mL)	0.52 to 0.56 (Rutherford 1986)
pH	3 for 1% slurry (Rutherford 1986)
Vapor pressure (mm Hg)	4×10^{-7} (Jones and Stokes 1991) $<3.9\times10^{-7}$ at 26°C (Rutherford 1986)
Water solubility (mg/L)	1-2 @ 25°C (Budavari 1989) 1 @ 25°C and pH 7 (Rutherford 1986)
Environmental metabolites	six metabolites identified, demethylation of aromatic carboxymethyl groups and/or hydroxylation of methyl groups on nonaromatic ring.
Bioconcentration factor (L/kg)	14 (edible tissue after 28 day exposure) (U.S. EPA 1989a,b) 134 (nonedible tissues after 28 day exposure) (U.S. EPA 1989a,b) 70 (whole fish after 28 day exposure) (U.S. EPA 1989a,b) 420 to 620 (Jones and Stokes 1991) 10.3 in edible tissue of bluegill sunfish over 7 to 28 days at 0.243 µg/L (Rainey 1986) 122.4 in viscera of bluegill sunfish over 7 to 28 days at 0.243 µg/L (Rainey 1986) 60.4 in whole bluegill sunfish over 7 to 28 days at 0.243 µg/L (Rainey 1986)
log $K_{o/w}$	2.64 ($K_{o/w}$ = 434) (U.S. EPA 1989a; Rutherford 1986)
Limits of detection	0.005 ppm, soil, liquid chromatography (Rutherford 1990)
Soil adsorption, K_d (L/kg)	8.4 (sand), 10 (sandy loam), 16 (loam) and 30 (clay loam) (column leaching) U.S. EPA 1989b)
Soil sorption, $K_{o/c}$ (ml/g)	2980 to 4370 (Jones and Stokes 1991) 1400 to 1700 (column leaching) (U.S. EPA 1989b) 730 (clay loam) to 1300 (sand)(batch equilibrium) (U.S. EPA 1989b)
Field dissipation half-time (days)	30 to 40 (sand and loam in spring) (U.S. EPA 1989b) 60 to 182 (sand and loam in fall) (U.S. EPA 1989b) 28 to 70 (4 to 10 weeks) (Rainey 1986)
Soil half-time (days)	21 (Jones and Stokes 1991, p. IS-1) 150 to 180 (Jones and Stokes 1991, p. IS-2) ≈129 (4.3 months in clay loam) (U.S. EPA 1989a, Rainey 1986) ≈168 (5.6 months in loam) (U.S. EPA 1989a, Rainey 1986) ≈318 (10.6 months in sandy loam) (U.S. EPA 1989a, Rainey 1986) 146 days (sandy loam, Texas, fall) (Rutherford and Decker 1986) 87 days (sand/turf, Florida, fall) (Rutherford and Decker 1986) 34 days (sand/turf, Florida, spring) (Rutherford and Decker 1986) 56 days (loam clay/loam, Indiana, spring) (Rutherford and Decker 1986) 92 days (Rouchaud et al. 1993)
Foliar halftime (days)	No data found. Foliar halftime is typically ≤ soil halftime (Knisel et al. 1992).
Photolysis in water, halftime (days)	7 to 15 (U.S. EPA 1989b) 3.9 to 63 days depending on season/amount of sunlight (Rainey 1986)
Hydrolysis	stable (U.S. EPA 1989a) no significant hydrolysis at pH 5, 7, or 10 over 32 days (Rainey 1986)

Figure 2-1: Area in which isoxaben will be applied by the Forest Service.

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview. Although the mechanism for the herbicidal activity of isoxaben is characterized in some detail, the mechanism of toxic action in mammals or other animal species is not well characterized. Isoxaben has a low order of acute toxicity with acute oral LD_{50} values >5000 mg/kg and acute dermal LD_{50} values >200 mg/kg and acute inhalation LC_{50} values >1.99 mg/L or 1990 mg/m^3. In addition, isoxaben may cause moderate eye irritation, transient corneal injury, and slight skin irritation. Longer-term exposures to isoxaben are associated with signs of liver and kidney damage, enlargement of the heart, and decreases in food conversion efficiency. Isoxaben has the potential to cause both reproductive and developmental effects at doses that cause signs of maternal toxicity. The U.S. EPA classified isoxaben as a possible human carcinogen. This assessment is based on a statistically significant increase in, and dose-response trend for, non-malignant tumors.

3.1.2. Acute Toxicity. As reviewed by Jones and Stokes (1991), isoxaben has a low order of acute toxicity with acute oral LD_{50} values >5000 mg/kg and acute dermal LD_{50} values >200 mg/kg and acute inhalation LC_{50} values >1.99 mg/L or 1990 mg/m^3.

3.1.3. Subchronic or Chronic Systemic Toxic Effects. The subchronic or chronic toxicity of isoxaben to humans or mammals is not documented in the published literature, and all of the available toxicological data comes from unpublished studies that were conducted to support the registration of isoxaben as a herbicide.

The critical effects for chronic exposure to isoxaben that were identified by the U.S. EPA (1993a) include increased blood urea nitrogen (BUN), decreased serum alkaline phosphatase (AP), and aspartate aminotransferase (AST), decreased “food consumption efficiency”, and increased relative heart weight. These endpoints were noted in a 2-year rat feeding study at a dietary concentration of isoxaben in the diet of 1250 ppm corresponding to estimated daily doses of 50.7 mg/kg/day for males and 61.8 mg/kg/day for females. The NOAEL for this effect was 125 ppm in the diet corresponding to estimated daily doses of 5 mg/kg/day for males and 6.2 mg/kg/day for females (Lake et al. 1985). As discussed in section 3.3, this study forms the basis of the U.S. EPA (1993a) RfD for isoxaben.

Other effects that can be caused by chronic or subchronic exposure to isoxaben at higher dose levels include increases in the size and number of liver cells, decreased body weight gain and food conversion efficiency, liver microsomal enzyme induction, and increased liver weight (U.S. EPA 1993a).

3.1.4. Reproductive and Teratogenic Effects. Isoxaben was tested for its ability to cause birth defects (i.e., teratogenicity) as well as its ability to cause reproductive impairment. These studies are reviewed in U.S. EPA (1993a).

Teratogenicity studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Two such studies were conducted on isoxaben: one in rats (Byrd 1984a) and one in rabbits (Byrd 1984b). In the rat study, increases in preimplantation losses, resorptions, and the number of runt fetuses as well as smaller litter sizes were noted at a dose of 1000 mg/kg/day. The NOAEL for both reproductive and maternal toxicity was 320 mg/kg/day. This dose also caused signs of maternal toxicity. No signs of fetal toxicity or teratogenicity were noted in rabbits.

Another type of reproduction study involves exposing more than one generation of the test animal to the compound. One such study (Hoyt 1984) was conducted on isoxaben, a three-generation reproduction study in rats in which the compound was administered at dietary concentrations of 500 ppm (25 mg/kg bw/day), 2500 ppm (125 mg/kg/day), and 12,500 ppm (625 mg/kg/day). Effects included decreases in the number of viable pups, lower body weight of the pups on postpartum day 21, and increased incidences of two birth defects: hydroureter (a urinary tract malformation) and microphthalmia (smaller than normal eyes). The NOAEL and LOAEL for these effects were 125 and 625 mg/kg bw/day respectively. The NOAEL and LOAEL for maternal toxicity were 25 and 125 mg/kg bw/day, respectively.

Taken together, the teratology and reproduction studies in rats (Byrd 1984a; Hoyt 1984) suggest that isoxaben has the potential to cause both reproductive and developmental effects at doses that cause signs of maternal toxicity. These studies are discussed further in the dose-response assessment (section 3.3). Single generation reproduction studies also were conducted in two species of birds (Cochrane 1984a,b), as discussed in section 4.1.2.2.

3.1.5. Carcinogenicity and Mutagenicity. The U.S. EPA (U.S. EPA 1990; U.S. EPA 1993a) conducted an extensive review on the potential carcinogenicity of isoxaben and concluded that isoxaben should be classified as “C; possible human carcinogen”. This assessment is based on 2-year dietary studies in mice (Lake and Usher 1985a) and rats (Lake et al. 1985). In the mouse study, isoxaben was administered in the diet at concentrations of 0, 100, 1000, and 12,500 ppm.. A statistically significant trend in the incidence of hepatocellular adenoma (a non-malignant tumor) was noted in both sexes, and the incidence of this tumor type was significantly increased in the high dose groups of both sexes relative to the respective control groups. There was, however, no increase in dose-related trend or incidence of hepatocellular carcinoma (a malignant tumor) in either dose group. When the incidences of both of these tumor types were combined, a significant dose-related trend was apparent in both sexes and the incidence of the combined tumors was significantly higher in the high-dose females (9/52), compared with the female control group (0/52). Using the Fisher Exact test, these differences are significant at $p=0.001335$. In the rat study, no oncogenic effects were observed in females. In males, a dose-related trend as well as an increase in the incidence of benign adrenal tumors (high dose compared to controls) was observed.

As reviewed by the U.S. EPA (1993a), supporting data for the assessment of the carcinogenicity of isoxaben includes equivocal results in an initial micronucleus assay in mice (Soiu 1984) but

positive results in a repeat micronucleus assay in mice (Siou 1987a,b). No evidence of genotoxicity was noted in an Ames assay for mutagenicity (Gries et al. 1987a,b), a forward mutation assay in mouse lymphoma cells (Oberly et al. 1983), and an assay for unscheduled DNA synthesis in rat hepatocytes (Hill et al. 1983).

The weight of the evidence as articulated by the U.S. EPA is:

> *... the weight of evidence is adequate for a Group C classification based on the following: 1) although chronic compound-induced hepatotoxicity can cause histopathological alterations, the mechanism involved in the compound-induced histopathological alterations is not the primary issue of consideration, 2) an MTD* [maximum tolerated dose] *was not exceeded solely because there was target organ toxicity, and 3) the noted liver tumors are most likely compound-induced* (U.S. EPA 1993a).

According to the IRIS entry for isoxaben, this carcinogenicity assessment was entered on September 1, 1991.

3.1.6. Effects on the Skin and Eyes. Based on information summarized in the material safety data sheet (C&P Press 1999b), isoxaben may cause moderate eye irritation that is slow to heal, transient corneal injury, and slight skin irritation.

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

As noted in section 3.1.2, the dermal LD_{50} of isoxaben is >200 mg/kg and the oral LD_{50} is >5000 mg/kg. This, however, does not indicate that isoxaben is necessarily more toxic by the dermal route of administration compared with the oral route. The designation of LD_{50} or LC_{50} values as greater than a particular value generally means that less than 50% mortality and often no mortality was observed at the highest dose tested in a particular study. In general, pesticides are more toxic after oral than dermal administration (Gaines 1969).

The kinetics of dermal absorption of isoxaben are not documented in the available literature. Although there are several dermal toxicity studies in the U.S. EPA/CBI files for isoxaben, no kinetic studies on dermal absorption were identified in the U.S. EPA/CBI files.

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. Using the method recommended by U.S. EPA (1992), the estimated dermal permeability coefficient for isoxaben is 0.0012 cm/hour with a 95% confidence interval of 0.00081-0.0019 cm/hour based on the molecular weight of 332.4 g/mole and the K_{ow} of 434 (see Table 2-1). 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 0.0017 $hour^{-1}$ with 95% confidence intervals of 0.00080 to 0.0037 $hour^{-1}$ based on the molecular weight and the $K_{o/w}$ as specified above. The calculations for these estimates are presented in worksheet B04.

3.1.8. Inhalation Exposure. As discussed in section 3.1.2, the acute inhalation LC_{50} value for isoxaben is >1.99 mg/L or 1990 mg/m^3 (Jones and Stokes 1991). There are many acute inhalation studies on isoxaben formulations in the U.S. EPA/CBI files. These kinds of studies (i.e., acute inhalation studies on each formulation) are required as part of the registration process.

3.1.9. Impurities, Metabolites, and Formulation Additives.

3.1.9.1. Impurities -- There is no published information regarding the impurities in technical grade isoxaben or any of its commercial formulations. Information on all of the impurities in technical grade isoxaben were disclosed to the U.S. EPA (Day and Rutherford 1986), and the information was obtained as part of this risk assessment. Because this information is classified as confidential business information (CBI), details about the impurities cannot be disclosed. Nonetheless, all of the toxicology studies on isoxaben involve technical isoxaben, which is presumed to be the same as or comparable to the active ingredient in the formulation used by the Forest Service. Thus, if toxic impurities are present in technical isoxaben, they are likely to be encompassed by the available toxicity studies using technical grade isoxaben.

3.1.9.2. Metabolites -- As reviewed by the U.S. EPA (U.S. EPA. 1988a,b), there are numerous metabolites and/or degradation products of isoxaben that involve hydroxylation of the aliphatic side chain or demethylation of the carboxy-side chains. Furthermore, any number of different breakdown products may occur on photolysis, including a benzamide, a pyrazolone, and isoquinolone, and a benzopyrrolidone (Mamouni et al. 1992; Saunders and Powers 1989a).

Thus, in the environment, isoxaben may be transformed to many different compounds by kinetics that are complex and likely to be highly variable under different environmental conditions. In any event, release of isoxaben to the environment will result in exposure to a mixture of many different compounds. Unlike the case with impurities, discussed above, exposure to the

metabolites is not necessarily encompassed by the available toxicity data on isoxaben, at least with respect to humans and other mammals.

There is no assessment of the toxicity of isoxaben metabolites in the open literature or U.S. EPA files (U.S. EPA 1988a,b, 1990, 1993a). Thus, the toxicity of the environmental metabolites cannot be addressed in the human health risk assessment. Concern for the potential toxicity of isoxaben metabolites is reduced somewhat by a study indicating that the phytotoxicity of isoxaben analogs are the same or less than that of isoxaben (Brinkmeyer et al. 1991) and that the soil metabolites of isoxaben are less phytotoxic than the parent compound (Rouchaud et al. 1993). Nonetheless, no studies were encountered on the toxicity of environmental metabolites to mammals. This limitation is common to many compounds that are released to the environment.

3.1.9.3. Inerts -- Gallery 75, the commercial formulation of isoxaben used by the Forest Service, contains materials other than isoxaben. Two inerts are listed on the MSDS for Gallery 75 (C&P Press 1999b): kaolin and crystalline silica which is one of the components in kaolin. The U.S. EPA (1998) lists kaolin as a List 4A inert. List 4A inerts are those classified by the U.S. EPA as posing *minimal risk* (U.S. EPA 1995). Crystalline silica, when inhaled in the form of quartz or cristobalite, is classified by IARC as a human carcinogen (Farrar 2000). No discussion of the possible risks associated with exposure to crystalline silica as a component of kaolin has been encountered in the literature.

No inerts other than kaolin and crystalline silica are listed on the MSDS for Gallery 75 (C&P Press 1999b). This indicates that no other compounds that are classified as toxic under 29 CFR 1910.1200 are contained in this formulation.

3.1.10. Toxicological Interactions. The open literature and U.S. EPA files do not contain information about the toxicological interactions of isoxaben with other compounds. As noted in section 3.1.3, subchronic exposure to isoxaben is associated with liver microsomal enzyme induction (U.S. EPA 1993a), which is generally associated with the induction of mixed-function oxidases. In turn, this effect can change the rates of metabolism of many different compounds (Moslen 1996), which may increase or decrease the toxicity of the compound whose metabolism is affected. Thus, there is a potential for isoxaben to influence the toxicity of other compounds; however, it is not possible to make generalizations regarding the nature of the influence (i.e., antagonism or synergism).

3.1.11. Mechanism of Action. Although the mechanism for the herbicidal activity of isoxaben is characterized in some detail (section 4.1.2.4), the mechanism of toxic action in mammals or other animal species is not well characterized. As noted in section 3.1.3, isoxaben causes biochemical indicators that are indicative of damage to the liver and kidney. In addition, exposure to isoxaben is associated with decreased food conversion efficiency and increased relative heart weight. While isoxaben affects glucose metabolism in plants by inhibiting the incorporation of glucose molecules into cellulose, a glucose polymer, there is no apparent relationship between this effect in plants and decreased food conversion efficiency in mammals. An increase in heart weight can

be associated with many different mechanisms (Van Vleet et al. 1991). Hypertension secondary to kidney damage is a possible cause of enlargement of the heart. This speculation is at least consistent with the apparent toxicity of isoxaben to the kidney.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. There are no occupational exposure studies in the available literature that are associated with the application of isoxaben. Consequently, worker exposure rates are estimated from an empirical relationship between absorbed dose per kilogram of body weight and the amount of chemical handled. For broadcast ground applications, estimated worker exposures are 0.0074 mg/kg/ day with a range of 0.00027 to 0.058 mg/kg/day.

Except in the case of accidental exposure, the levels of isoxaben to which the general public might be exposed should be far less than the levels for workers. Longer-term exposure scenarios for the general public lead to central estimates of daily doses that range from about 0.00005 to about 0.003 mg/kg/day with upper limits of exposure in the range of 0.001-0.05 mg/kg/day. Given the limited use of isoxaben proposed by the Forest Service, some of the exposure scenarios on which both the longer-term doses are based are highly implausible. This is discussed in greater detail in the risk characterization.

Accidental exposure scenarios result in central estimates of exposure of up to about 0.075 mg/kg/day with upper ranges in the area of about 0.11 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. Again, given the limited use of isoxaben, some of these standard accidental exposure scenarios are excluded in the risk characterization.

3.2.2. Workers. A summary of the exposure assessments for workers is presented in Table 3-1. 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 worksheets that accompany this risk assessment, as indicated in Table 3-1.

***3.2.2.1. General Exposures* --** The assumptions used in worker exposure assessments are detailed in worksheet A03b (boom spray). As discussed in section 2, the treatment rate will be in the range of 6 to 8 acres per hour at the nursery where isoxaben will be used. These treatment rates have been put into worksheet A03b and are used in the calculation of worker exposure (worksheet C01b). Although worksheets are provided as place holders for backpack (Worksheet A03a and C01a) and aerial applications (Worksheet A03c and C01c), these application methods are not proposed for isoxaben and are not considered in this risk assessment.

The range of acres treated per hour and hours worked per day are 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 and boom spray workers, the use of the arithmetic mean rather than some other measure of central tendency, like the geometric mean, has no marked effect on the risk assessment.

3.2.2.2. Accidental Worker 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 to involve various dermal exposure scenarios.

Isoxaben can cause irritant effects to the skin and eyes (see section 3.1.6). The available literature does not include quantitative methods for characterizing exposure or responses associated with splashing a solution of a chemical into the eyes; furthermore, there appear to be no reasonable approaches to modeling this type of exposure scenario quantitatively. 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). 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. As specified in Table 3-1, the details of these exposure estimates are presented in the worksheets appended to this risk assessment.

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.

3.2.3. General Public.

3.2.3.1. General Considerations **--** Under normal circumstances, members of the general public should not be exposed to substantial levels of isoxaben. 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 3-2, and the details regarding the assumptions and calculations involved in these exposure assessments are provided in worksheets D01-D09. The remainder of this section focuses on a qualitative description of the data supporting each of the assessments.

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.

In a typical Forest Service risk assessment, a scenario is presented in which a naked child is sprayed directly during a ground application. The scenario also assumes that the child is completely covered (that is, 100% of the surface area of the body is exposed), which makes this an extremely conservative exposure scenario that is likely to represent the upper limits of plausible exposure. For isoxaben, the hydraulic sprayer will be only 20 inches from the ground surface. Consequently, this exposure scenario is not plausible and is not used in the risk characterization. This scenario, nonetheless, is included in Worksheet D01.

An additional scenario included in Forest Service risk assessments involves a young woman who is accidentally sprayed over the feet and legs. While perhaps only marginally plausible for members of the general public, this exposure assessment is both included in the worksheets (D02) and quantitatively used in this risk assessment.

For each exposure scenario, certain assumptions are made regarding the surface area of the skin and body weight. These assumptions are taken from various U.S. EPA reports (1992, 1996) and are relatively well documented.

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 the exposure scenarios, estimates of dislodgeable residue and the rate of transfer from the contaminated vegetation to the surface of the skin must be available. Because no such data are directly available for isoxaben, 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.

3.2.3.4. Contaminated Water **--** Water can be contaminated from runoff, as a result of leaching from contaminated soil, from a direct spill, or from unintentional contamination from drift. Although isoxaben is chemically stable in pure aqueous solutions, it is degraded in natural waters by photolysis, and concentrations of isoxaben in water are further reduced by dispersal. For this risk assessment, the two types of estimates made for the concentration of isoxaben in ambient water are acute/accidental exposure and longer-term exposure.

3.2.3.4.1. ACUTE EXPOSURE -- A standard scenario used in Forest Service risk assessments involves an acute exposure assuming 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 isoxaben 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.

In addition, it should be noted that all of the estimates of the concentration of isoxaben in water from the spill of 200 gallons of a field solution (Worksheet D06) exceeds the solubility of isoxaben in water. In other words, some of the isoxaben would precipitate from solution and would not be ingested under any plausible scenario. Consequently, for estimating the ingested dose, the highest plausible concentration of isoxaben in water is taken as the water solubility (i.e., 1 mg/L at 25°C and pH 7) (Rutherford 1986 as summarized in Table 2-1). This same approach is taken for all accidental spill scenarios involving water contamination in the ecological risk assessment (section 4).

As with the accidental direct spray of a child (see section 3.2.3.2.), this standard exposure scenario is not plausible for the specific application of isoxaben currently proposed by the Forest Service because there is no small body of water in the area in which isoxaben will be applied. Consequently, this standard exposure scenario is not used in the characterization of risk; nonetheless, it is presented here in the event that the Forest Service elects to broaden the use of this herbicide.

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

There are no monitoring studies available on isoxaben that permit an assessment of concentrations in ambient water associated with ground applications of the compound. Isoxaben has an extremely low potential for leaching from the soil surface to groundwater and is classified as essentially immobile in terms of leaching potential (Jamet and Thoisy-Dur 1988).

The Office of Pesticides (U.S. EPA 1988a, p. 12) has estimated the concentration of isoxaben that might occur in ambient water under the assumption that 0.01 of the applied isoxaben is lost in runoff into a 1 acre (4047 m^2) pond that is 6 feet deep. This is equivalent to a volume of water of about 7 million liters [4047 m^2 × 6 feet × 0.305 m/foot ≈ 7400 m^3 = 7,400,000 L]. Thus, under the assumption that a 10 acre area is treated at 1 lb/acre [10 lbs = 4.536 kg = 4536 g = 4,536,000 mg], the estimated concentration in ambient water is estimated at about 0.006 mg/L:

$$0.01 \times 4{,}536{,}000 \div 7{,}400{,}000 \text{ L} = 0.00613 \text{ mg/L}.$$

The estimated concentration of isoxaben in ambient water is generic, and the amount of isoxaben that may actually occur in ambient water or groundwater would depend on many site-specific conditions relating to soil, topography, and climate/rainfall.

Some published studies report that much higher proportions of runoff may exist under certain circumstances. For example, a runoff proportion of 0.23 was noted after irrigation with 1.6 cm (≈0.6 inch) of water (Briggs et al. 1998). Similarly, runoff proportions of 0.12-0.16 for granular isoxaben and 0.06-0.18 for sprayable isoxaben were noted over a 9-day period from nursery sites with a daily irrigation rate of 1.3 cm (about 0.5 inches) (Wilson et al. 1995). The potential importance of runoff is also suggested by the reduced efficacy of isoxaben when 25 cm (9.8 inches) of rainfall occurred within 2 weeks of application - i.e., about 1.8 cm/day [25 cm/14 days] (Chandran et al. 1998).

In order to better assess the discrepancies between the EPA estimate of a 0.01 runoff proportion and the published values of 0.06 to 0.23, preliminary GLEAMS model runs were made using a slope of 3%. The proportion of runoff was 0.01, identical to the EPA estimate, at an annual rainfall rate of 50 inches or about 0.1 inches (0.25 cm) per day. At an annual rainfall of 250 inches or about 0.68 inches (1.74 cm) per day, the proportion of runoff loss was 0.38. This is a factor of 1.65 higher than the 0.23 runoff proportion noted by Briggs et al. (1998) after 0.6 inches of rainfall. Thus, the U.S. EPA (1988a, p. 12) runoff estimate of 0.01 may underestimate runoff potential in areas of heavy rainfall.

Nonetheless, the runoff proportion of 0.01 used by the U.S. EPA may be a reasonable approximation for the current risk assessment because of the buffer zone between the application site and the stream in the area that the Forest Service proposes to treat. For example, Lowrance et al. (1997) found that a three zone buffer (field, grass, hardwood forest) reduced the concentrations of two herbicides in runoff to a stream by factors of about 10 to over 30 relative to the concentrations at the edge of field. Thus, for an edge of field runoff proportion of 0.4, the maximum estimated in the GLEAMS modeling, runoff to a stream would be estimated at about 0.013 to 0.04 [0.4 ÷ 30 to 0.4 ÷ 10].

In this abbreviated human risk assessment, site-specific exposure assessments have not been conducted and the approach used by the U.S. EPA (1988a) is used to estimate ambient water levels of isoxaben, based on the application rates proposed by the Forest Service and the number of acres that might be treated. These calculations are detailed in Worksheet B07. The potential impact of uncertainties in the estimates of runoff is discussed further in the risk characterization.

3.2.3.5. Oral Exposure from Contaminated Fish **--** Many chemicals may 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]. As with most absorption processes, bioconcentration

depends initially on the duration of exposure but eventually reaches steady state. Details regarding the relationship of bioconcentration factor to standard pharmacokinetic principles are provided in Calabrese and Baldwin (1993).

The only available study regarding the bioconcentration of isoxaben is a standardized test using bluegill sunfish that is required as part of the registration process (Magnussen and Rainey 1986). At a water concentration of 0.243 mg/L, bioconcentration factors were 7.24 (edible tissue) and 42.5 (whole fish). After 28 days, bioconcentration factors were 13.79 (edible tissue) and 70.5 (whole fish).

For both the acute and longer-term exposure scenarios involving the consumption of contaminated fish, the water concentrations of isoxaben used are identical to the concentrations used in the contaminated water scenarios (see section 3.2.3.4). For all of the human health exposure assessments, only bioconcentration factors for the edible portion of the fish are used with the values rounded to 7 for acute exposure scenarios and 14 for chronic exposure scenarios.

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. Because this is an acute exposure scenario, the short term BCF of 7 is used and 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 isoxaben concentrations in ambient water are based on the U.S. EPA estimates discussed in section 3.2.3.4.2. and a longer-term BCF of 14, for the edible portion of fish, is used.

3.2.3.6. Oral Exposure from Contaminated Vegetation -- Given the currently proposed use of isoxaben by the Forest Service, it is extremely unlikely that humans will consume vegetation contaminated with isoxaben. In most standard Forest Service risk assessments, exposure scenarios are developed involving either accidental spraying of crops or the spraying of edible wild vegetation like berries.

For consistency with other Forest Service risk assessments and in the event that the Forest Service may wish to use isoxaben in other applications, two accidental exposure scenarios are developed, including one scenario for acute exposure (worksheet D04) and one scenario for longer-term exposure (worksheet D05). In both scenarios, the concentration of isoxaben 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, and the dissipation on the vegetation is estimated using a foliar half-time of 56 days with a range of 34-87 days (worksheet B03). There is no direct information available on the foliar half-time of isoxaben. The estimates presented in worksheet B03 are by analogy to the soil half-times from Rutherford and Decker (1986) as summarized in Table 2-1. In general, foliar half-times tend to be equal to or less than soil half-times (e.g., Knisel et al. 1992).

Although the duration of exposure appears to be somewhat arbitrarily chosen, it is intended to represent the consumption of contaminated vegetation that might be available over one season. Longer durations could be used for certain kinds of vegetation but would lower the estimated dose (i.e., would result in a less conservative exposure assessment). The central estimate of dose for the longer-term exposure period is taken as the geometric mean of the initial concentration and concentration after 90 days.

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 (1996a) 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 3-2 is based on the range of concentrations on vegetation from Hoerger and Kenaga (1972) and the range of application rates for isoxaben. 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 and the range of application rates for isoxaben.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The U.S. EPA (1993a) derived an RfD for isoxaben of 0.05 mg/kg/day. This is based on a dietary NOAEL of 125 ppm in the diet corresponding to estimated daily doses of 5 mg/kg/day and using an uncertainty factor of 100. In the same study, the LOAEL was about 50 mg/kg/day (1250 ppm in the diet), and the observed effects included signs of liver and kidney damage, enlargement of the heart, and an apparent decrease in food conversion efficiency. No acute RfD for isoxaben has been derived by the U.S. EPA.

While isoxaben is classified as a possible human carcinogen by the U.S. EPA, the U.S. EPA did not derive a cancer potency estimate for this compound. In documents submitted to U.S. EPA as part of the registration process, however, two oncogenic potency parameters were derived, one based on adenomas and carcinomas combined and the other based on nodular hyperplasia, adenomas, and carcinomas combined. The recent U.S. EPA guidelines for cancer risk assessment do permit the combining of benign and malignant tumors for the assessment of cancer risks. For this risk assessment, the higher potency parameter, 0.0021 $(mg/kg/day)^{-1}$, is used to illustrate the potential risks of benign and malignant liver tumors combined.

3.3.2. Existing Guidelines.
The RfD for isoxaben is based on a 2- year feeding study in which male and female Fischer rats were exposed to concentrations of 0, 125, 1250, or 12,500 ppm isoxaben in the diet, which corresponded to daily doses of 0, 5, 50.7, and 526.5 mg/kg bw/day for males and 0, 6.2, 61.8, and 646.6 mg/kg bw/day for females (Lake et al. 1985). No effects were observed at the lowest dose. In the mid-dose group, effects included increased BUN, decreased serum levels of alkaline phosphatase (AP) and aspartate aminotransferase (AST), decreased food consumption efficiency (males and females), and increased heart-to-body weight (males). In the high-dose group, effects included decreased body weight and body weight gains; increased alkaline phosphatase; increased liver-to-body weight ratios, kidney-to-body weight, and brain-to-body weight (males and females); increased creatinine; decreased prostate weights; increased liver weights; and increased heart-to-body weight (males)

In deriving the RfD, the U.S. EPA accepted the 5 mg/kg/day group as a NOAEL and used an uncertainty factor of 100. The uncertainty factor consists of two components: a factor of 10 for extrapolating from animals to humans and a factor of 10 for extrapolating to sensitive individuals within the human population.

3.3.3. Dose-Severity Relationships. As noted above, adverse effects were observed in the study by Lake et al. (1985) at dietary levels of 1250 ppm, which is a factor of 10 above the NOAEL. In addition, at a factor of 100 above the NOAEL, frank signs of toxicity were not apparent. Thus, hazard quotients of 10 or higher would be a clear cause for concern although frank signs of toxicity might not be expected.

As discussed in section 3.1.4, isoxaben caused developmental and fetotoxic effects in rats at 625 mg/kg bw/day (Hoyt 1984), a factor of 125 above the NOAEL of 5 mg/kg/day. The NOAEL for reproductive/teratogenic effects was 25 mg/kg bw/day (Hoyt 1984), a factor of 5 above the NOAEL for systemic toxicity. Thus, hazard quotients above unity but less than 5 could be of concern for toxic effects but not reproductive/developmental effects. Hazard quotients above 125 (i.e., corresponding to the reproductive LOAEL) would be of clear and substantial concern for reproductive and developmental effects. Between hazard quotients of 5 and 125, the level of concern is indeterminate although obviously increasing as the hazard quotients approach 125.

3.3.4. Cancer Potency. As discussed in section 3.1.5, the U.S. EPA (U.S. EPA 1990, 1993a) classifies isoxaben as a possible human carcinogen. Nonetheless, no statistically significant increases were apparent in dose-related trend for malignant tumors or the incidence of malignant tumors in any of the individual dose groups relative to the appropriate control group. Thus, U.S. EPA (1993a) did not derive a cancer potency factor for this compound. A risk assessment conducted for the California Department of Transportation also did not conduct a quantitative risk assessment for the potential carcinogenicity of isoxaben (Jones and Stokes 1991).

As detailed in the most recent draft of U.S. EPA's cancer risk assessment guidelines (U.S. EPA/ORD 1996),

> ...*the default* [approach] *is to include benign tumors observed in animal studies in the assessment of animal tumor incidence if they have the capacity to progress to the malignancies with which they are associated.* (U.S. EPA/ORD 1996, p. 28)

Two analyses were submitted to U.S. EPA in which potency factors were derived based on a combination of benign and malignant tumors. An analysis by Lilly Research Laboratories (Bjerregaard and Lake 1985) derived a potency estimate of 0.00053 $(mg/kg/day)^{-1}$ based on the combined incidences of nodular hyperplasia, adenomas, and carcinomas in mouse liver from the study by Lake and Usher (1985a). Environ Corporation (Youngren et al. 1989) derived a potency parameter of 0.0021 $(mg/kg/day)^{-1}$ using only liver adenomas and carcinomas in female mice from the study by Lake and Usher (1985a). This potency parameter is about a factor of about 4 higher than the potency parameter derived by Bjerregaard and Lake (1985). This increased potency parameter probably reflects differences in the control response rates relative to the positive dose-response rates between adenomas and carcinomas combined and nodular hyperplasia, adenomas, and carcinomas combined.

For isoxaben, the available data are not sufficient to assert whether or not the benign tumors have the capacity to progress to malignant tumors. Consequently, the combination of benign and malignant tumors in the analyses by Bjerregaard and Lake (1985) and Youngren et al. (1989) appears to be prudent. For this risk assessment, the higher potency parameter, 0.0021 $(mg/kg/day)^{-1}$, will be used to characterize the potential risks of benign and malignant liver tumors. In a full risk assessment, an alternative potency parameter would be derived based on the lower 95% confidence limit of the ED_{10} as recommended in the most recent EPA guidelines (U.S. EPA/ORD 1996). Whether this would increase or decrease the cancer potency cannot be determined at this time.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. Based on the central estimate of exposures associated with hydraulic spray applications, the hazard quotient is 0.1, below the level of concern by a factor of 10. At the upper range of the estimated exposure, however, the hazard quotient is 1.2, somewhat above the chronic RfD. The lack of an acute RfD or some other similar measure of ‘acceptable’ short-tern exposure limits this quantitative characterization of risk. The currently proposed use of isoxaben by the Forest Service will involve at most, exposure periods of 30 hours per year for a worker. Thus, using a chronic RfD as the basis for characterizing risks from a 30-hour exposure is likely to be grossly conservative. Accidental exposures for workers also lead to central estimates of hazard quotients that are below the level of concern. The upper limit for the contaminated glove scenario involving a 1-hour exposure is 2, in the range of concern for subclinical systemic toxic effects but not frank signs of toxicity or reproductive effects. Again, the lack of an acute RfD limits the characterization of risk.

Under the conditions of use proposed by the Forest Service and at the single location where the Forest Service is proposing to use isoxaben, there is no apparent risk in terms of systemic toxicity or reproductive effects for members of the general public. However, if the Forest Service were to use isoxaben in a different area where the contamination of edible vegetation or spills into surface water were plausible, risks to the general public would be of concern.

The potential risks of both benign and malignant liver tumors are based on the potency parameter of 0.0021 $(mg/kg/day)^{-1}$. The calculated risks are factors of up to about 25 above the risk level of 1 in one million. A risk level of 1 in one million has been used by the Forest Service as an administrative trigger for action to reduce exposure. The proximity of the estimated risks to the risk level of 1 in one million as well as the substantial uncertainties in the exposure assessments raise concern for the potential cancer risks that could be associated with the use of isoxaben if individuals were to be chronically exposed to contaminated water from this site. Based on information provided by the Forest Service, however, chronic exposure to contaminated water or vegetation is not plausible.

3.4.2. Workers. A quantitative summary of the risk characterization for workers is presented in Table 3-3. The quantitative risk characterization is expressed as the hazard quotient, which is the ratio of the estimated exposure doses from Table 3-1 to the chronic RfD of 0.05 mg/kg/day, as derived in section 3.3.2.

For both workers and members of the general public, the lack of an acute RfD or some other similar measure of 'acceptable exposure' is an important factor in the quantitative characterization of risk. As discussed in the dose-response assessment (see section 3.3), the only available RfD for isoxaben is based on a 2-year rat feeding study that involved essentially lifetime exposure. The currently proposed use of isoxaben by the Forest Service, however, will involve at most two applications per year. Even if the same worker were involved in both applications, the total time spent applying isoxaben would be less than, at most, 30 hours per year. Thus, using a lifetime exposure study as the basis for characterizing risks from a 30-hour exposure is likely to be grossly conservative.

Based on the central estimate of exposures associated with hydraulic spray applications, the hazard quotient is 0.1, below the level of concern by a factor of 10. At the upper range of the estimated exposure, however, the hazard quotient is 1.2, marginally above the level of concern. Typically, the hazard quotient is rounded to 1 significant decimal or digit. Thus, the hazard quotient of 1.2 rounds to 1.0, indicating that the level of exposure is at but not above the level of concern. In practical terms, the very limited exposures for any one worker - i.e., a maximum of 30 hours - as well as the use of a chronic RfD to assess the impact of an essentially acute exposure suggest that risks to workers are likely to be insubstantial. As with the handling of any chemical, prudence dictates that steps be taken to ensure that worker exposures are minimized.

Central estimates for accidental exposures to workers also lead to hazard quotients that are below the level of concern. The upper limit for the contaminated glove scenario involving a 1-hour

exposure is 2, in the range of concern for subclinical systemic toxic effects but not frank signs of toxicity or reproductive effects. 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. As discussed in section 3.2, confidence in this assessment is diminished by the lack of information regarding the dermal absorption kinetics of isoxaben 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.

As discussed in section 3.1.6, isoxaben can cause irritation 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 isoxaben. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

3.4.3. General Public. The quantitative hazard characterization for the general public is summarized in Table 3-4. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the U.S. EPA (1993a) chronic RfD of 0.05 mg/kg/day. The limitations of this approach for assessing the consequences of exposures to isoxaben, most of which involve only acute exposures, are substantial, as detailed in the previous section on risk characterization for workers.

None of the longer-term exposure scenarios exceed a level of concern even at the upper estimates of exposure. As noted in the summary worksheet for the general public (worksheet E04), the chronic exposure scenario for the consumption of contaminated vegetation does lead to a level of concern at the upper range of plausible exposures. This exposure scenario is acknowledged but is not used to characterize risk because the site at which the Forest Service will apply isoxaben does not have any vegetation that humans might consume.

Excluding the chronic consumption of contaminated vegetation, the highest chronic hazard quotient in the remaining scenarios involves the consumption of contaminated fish by subsistence populations. The upper range of this hazard quotient, 0.1, is a factor of 10 below the level of concern. Although this hazard quotient does not reach a level of concern, there are, as discussed in section 3.2.3.4.2, some substantial uncertainties in the exposure assessment associated with this scenario (i.e., estimates of the concentration of isoxaben in ambient water for longer-term periods after application).

As in the chronic assessments, several acute exposure scenarios are not applicable to the risk characterization for the proposed Forest Service activity because they are implausible given the location, method of application, and limited use of isoxaben proposed by the Forest Service. Specifically, the acute exposure scenarios for the direct spray of a child, the consumption of contaminated fruit, and the consumption of contaminated water or fish taken from water after an accidental spill are not relevant to the specific Forest Service program proposed by the Forest

Service. Table 3-4 gives the full set of hazard quotients, several of which exceed unity, for generic exposures used in standard Forest Service risk assessments. Notably, however, none of the hazard quotients for members of the general public exceed 2, which is below the range of concern for potential reproductive effects (i.e., a hazard quotient greater than 5 as discussed in section 3.3.3).

The simplest verbal interpretation for the risk characterization for the general public is that, under the conditions of use proposed by the Forest Service and at the single location where the Forest Service is proposing to use isoxaben, there is no apparent risk to members of the general public for either systemic toxic effects or reproductive effects. If the Forest Service were to use isoxaben in a different area where the contamination of edible vegetation were plausible, risks to the general public would be of concern in terms of systemic toxicity but not reproductive effects.

The potential risks of benign and malignant liver tumors combined from chronic exposure scenarios are summarized in Table 3-5. The top part of Table 3-5 gives the cancer risk as the product of the potency parameter provided in section 3.3.4 and the estimated dose provided in Table 3-2. The bottom part of the table gives the ratio of this calculated risk to a risk level of 1 in one million. A risk level of 1 in one million has been used by the Forest Service as an administrative trigger. Cancer risks above 1 in one million typically will cause the Forest Service to take administrative programmatic measures to reduce or eliminate exposure.

The cancer risks in Table 3-5 are factors of 10 below to 25 above a risk level of 1 in one million. A major factor that needs to be considered in the interpretation of these risks is the exposure assessment for ambient water. As noted in section 3.2.3.4.2, the estimated concentrations of isoxaben in ambient water, which drive the cancer risk for water ingestion and the ingestion of contaminated fish, are based on rather general estimates of runoff made by the U.S. EPA (1989a). Certain studies suggest that greater runoff and hence greater water contamination may be plausible (see section 3.2.3.4.2). Conversely, the Forest Service proposes to use this compound only to a very limited extent in a single area where the potential for the consumption of contaminated water may be remote and where the local conditions could result in water contamination that is much less than the generic estimate made by the U.S. EPA (1989a). Nonetheless, the proximity of the currently estimated risks to the risk level of 1 in one million as well as the substantial uncertainties in the exposure assessments raise concern for the potential cancer risks that could be associated with the use of isoxaben if individuals were to be chronically exposed to contaminated water from a site treated with isoxaben.

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 isoxaben. As indicated in section 3.1.3, the most sensitive effects for isoxaben appear to be liver and kidney damage. Thus, it is possible that individuals with pre-existing liver or kidney disease could be at increased risk.

3.4.5. Connected Actions. The Forest Service does not propose to use isoxaben in combination with other herbicides. As discussed in section 3.1.10, isoxaben may induce liver mixed-function

oxidases, which may lead to various toxicological interactions with other compounds. Nonetheless, it is impossible to make generalizations concerning the nature of any such interactions (i.e., antagonism or synergism).

3.4.6. Cumulative Effects. This risk assessment specifically considers the effect of repeated exposure in that the chronic RfD is used as an index of acceptable exposure even for acute exposure scenarios. As noted in section 3.4.2, this is a very conservative approach. Consequently, the risk characterizations presented in this risk assessment encompass the potential impact of long-term exposure and cumulative effects.

Table 3-1: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)[a]			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	**Not Applicable**			
Broadcast ground spray (Boom spray)	0.0074	0.00027	0.058	WSC01b
Aerial applications	**Not Applicable**			
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	0.00065	0.00036	0.0018	WSC02
Contaminated Gloves, 1 hour	0.039	0.022	0.11	WSC02
Spill on hands, 1 hour	0.00044	0.00017	0.0017	WSC03
Spill on lower legs, 1 hour	0.0011	0.00043	0.0042	WSC03

[a] All values rounded to two significant digits.

Table 3-2: Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)[a]			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.017	0.00652	0.064	WSD01
Direct spray, lower legs	Woman	0.0017	0.00065	0.0065	WSD02
Dermal, contaminated vegetation	Woman	0.0031	0.0015	0.0093	WSD03
Contaminated fruit, acute exposure	Woman	0.008	0.0080	0.050	WSD04
Contaminated water, acute exposure	Child	0.075	0.046	0.11	WSD06
Consumption of fish, general public	Man	0.0010	0.0010	0.016	WSD08
Consumption of fish, subsistence populations	Man	0.0081	0.0081	0.077	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0028	0.0020	0.049	WSD05
Consumption of water	Man	0.00073	0.00051	0.0016	WSD07
Consumption of fish, general public	Man	0.000051	0.000051	0.0014	WSD09
Consumption of fish, subsistence populations	Man	0.00041	0.00041	0.0070	WSD09

[a] All values rounded to two significant digits.

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

RfD	0.05	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	**Not Applicable**			
Broadcast ground spray (Boom spray)	0.1	0.005	**1.2**	WSC01b
Aerial applications	**Not Applicable**			
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	0.01	0.007	0.04	WSC02
Contaminated Gloves, 1 hour	0.8	0.4	**2**	WSC02
Spill on hands, 1 hour	0.009	0.003	0.03	WSC03
Spill on lower legs, 1 hour	0.02	0.009	0.08	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 3-1 for a summary of the exposure assessment.

Table 3-4: Summary of risk characterization for the general public [1] .

Chronic RfD		0.05	mg/kg/day	Sect. 3.3.3.	
Acute RfD		0.05	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.3	0.1	**1.3**	WSD01
Direct spray, lower legs	Woman	0.03	0.01	0.1	WSD02
Dermal, contaminated vegetation	Woman	0.06	0.03	0.2	WSD03
Contaminated fruit, acute exposure	Woman	0.2	0.2	**1.0**	WSD04
Contaminated water, acute exposure	Child	**1.5**	0.9	**2**	WSD06
Consumption of fish, general public	Man	0.02	0.02	0.3	WSD08
Consumption of fish, subsistence populations	Man	0.2	0.2	**1.5**	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.06	0.04	**1.0**	WSD05
Consumption of water	Man	0.01	0.01	0.03	WSD07
Consumption of fish, general public	Man	0.001	0.001	0.03	WSD09
Consumption of fish, subsistence populations	Man	0.008	0.008	0.1	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 3-2 for a summary of the exposure assessments.

Table 3-5: Summary of carcinogenic risks associated with chronic exposures scenarios for members of the general public [1] .

Potency factor		0.0021	(mg/kg/day)$^{-1}$	Sect. 3.3.4.	
Scenario	Target	Risk			Worksheet
		Typical	Lower	Upper	
Contaminated fruit[2]	Woman	**1.5e-06**	**1.0e-06**	**2.5e-05**	WSD05
Consumption of water	Man	**1.5e-06**	**1.1e-06**	**3.3e-06**	WSD07
Consumption of fish, general public	Man	1.1e-07	1.1e-07	**3.0e-06**	WSD09
Consumption of fish, subsistence populations	Man	8.7e-07	8.7e-07	**1.5e-05**	WSD09

Scenario	Target	Risk ÷ (1 in one million)			Worksheet
		Typical	Lower	Upper	
Contaminated fruit	Woman	**1.5**	**1.0**	**25**	WSD05
Consumption of water	Man	**1.5**	**1.1**	**3.3**	WSD07
Consumption of fish, general public	Man	0.1	0.1	**3.0**	WSD09
Consumption of fish, subsistence populations	Man	0.9	0.9	**15**	WSD09

[1] Risk calculated as the product of the potency factor and the daily dose. See Table 3-2 for summary of exposure assessments.
[2] 90-Day doses from Worksheet D05 (Table 3-2) adjusted for 365 days in a year.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. The mammalian toxicity of isoxaben is relatively well characterized in experimental mammals; however, there is relatively little information regarding nontarget wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., liver and kidney damage).

Several acute toxicity studies and two reproduction studies are available on the toxicity of isoxaben to birds. Isoxaben is relatively non-toxic to birds after acute oral exposure: the acute oral LD_{50} is >2000 mg/kg. On the other hand, birds may be somewhat more sensitive than experimental mammals to the reproductive effects of isoxaben: the NOAEL and LOAEL for birds are 60 and 200 mg/kg/day, respectively, and the corresponding values for mammals are 125 and 625 mg/kg bw/day. Isoxaben seems also to have a low order of toxicity to terrestrial invertebrates. This assessment is based on the only two available acute toxicity studies, one in bees and one in earthworms.

The toxicity of isoxaben to terrestrial plants is well characterized. Isoxaben inhibits the incorporation of glucose into cellulose, the major structural polysaccharide in plants. As part of the registration process for herbicides the U.S. EPA requires toxicity assays on nontarget plant species. Isoxaben is much more toxic after soil incorporation, compared with surface application. Effects on nontarget terrestrial plants are considered more quantitatively in the dose-response assessment.

The potential for toxic effects on aquatic species, either plants or animals, exposed to isoxaben appears to be remote. The solubility of isoxaben in water is reported to range from 1 to 2 mg/L. Standard toxicity bioassays suggest that no acute effects are likely at concentrations in the range of 1 mg/L and that no chronic effects are likely in the range of 0.4-0.7 mg/L.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals– As summarized in the human health risk assessment (see section 3.1), the mode of action of isoxaben in mammals is not well understood. There are several standard toxicity studies in experimental mammals that were conducted as part of the registration process. The most consistent effects observed in mammals after exposure to isoxaben are consistent with damage to the kidney and liver. In addition, isoxaben was shown to cause adverse reproductive and developmental effects, which would be consistent with a decrease in reproductive capacity in wildlife species. There are no field studies that would permit an assessment of this endpoint in free ranging populations.

4.1.2.2. Birds– The toxicity studies involving the exposure of birds to isoxaben were reviewed and evaluated by the U.S. EPA Ecological Effects Branch of the Office of Pesticides (U.S. EPA 1988a). Isoxaben is relatively non-toxic to birds after acute oral exposure: the acute oral LD_{50} is >2000 mg/kg. As with mammals, exposure to isoxaben is associated with adverse reproductive

effects in birds. The NOEL for this effect in mallard ducks is 300 mg/kg in the diet. The LOAEL, associated with a reduction in hatchability, is 1000 mg/kg in the diet. These data are from a study by Cochrane (1984b). Based on average measured food consumption and body weight (Tables 4 and 5 in Cochrane 1984b), the daily food consumption of the birds during the exposure period was approximately 20% of the body weight. Thus, the dietary values of 300 mg/kg and 1000 mg/kg correspond to 60 mg/kg bw/day (NOAEL) and 200 mg/kg bw/day (LOAEL). For comparison, the NOAEL and LOAEL for reproductive effects in mammals is 125 and 625 mg/kg bw/day respectively (see section 3.1.4), suggesting that birds may be somewhat more sensitive than mammals to the reproductive effects of isoxaben.

4.1.2.3. Terrestrial Invertebrates– A standard bioassay was conducted on the toxicity of isoxaben to honey bees (Cocke 1986). The acute oral LD_{50} for isoxaben was >101.7 μg/bee. Using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993), this value corresponds to a dose of >1093 mg/kg [0.1017 mg ÷ 0.000093 kg].

The toxicity of isoxaben also was evaluated using earthworms. Soil concentrations up to 100 ppm caused no effects on growth or mortality and no other overt signs of toxicity over 14-day exposure periods (Francis et al. 1983a).

4.1.2.4. Terrestrial Plants (Macrophytes)– The toxicity of isoxaben to terrestrial plants was studied extensively and is well characterized (e.g., Fisher and Cyr 1998; Heim et al. 1991, 1993). Isoxaben inhibits the incorporation of glucose into cellulose, a polymer of glucose and a basic structural polysaccharide in plants. Most woods are about 50% cellulose, and certain substances, like cotton, are virtually all cellulose. Isoxaben is a soil active preemergence herbicide that acts by absorption through the roots of the plant as opposed to foliar absorption (e.g., Schneegurt et al. 1994b). Thus, isoxaben must be applied to the soil and then activated by rainfall (C&P Press 1999a).

As part of the registration process for herbicides the U.S. EPA requires toxicity assays on nontarget plant species. One such study was submitted to U.S. EPA (Saunders et al. 1987), and it is the basis of the U.S. EPA (1989a) assessment of the toxicity of isoxaben to nontarget plants. A summary provided by U.S. EPA (1989a) indicates that isoxaben caused a 50% reduction in emergence at soil concentrations of 0.5-1.3 ppm in several species, including annual ryegrass, barley, barnyardgrass, black nightshade, blackgrass, browntop panicum cheatgrass, cocklebur, common ragweed, corn, cotton, cucumber, grain sorghum, green foxtail jimsonweed, lambsquarters, morning glory, prickly sida, redroot pigweed, rice, socklepod soybean, velvetleaf, wheat, and wild oats. Except for winter wheat, all of the bioassays involved only soil incorporation. A review of the full-text copy of this study indicates that two application methods were used, direct preemergence surface application on soil and soil incorporation. Isoxaben was much more toxic after soil incorporation, compared with surface application. For example, in a surface application assay, at an application rate of 0.25 lbs a.i./acre, isoxaben had no effects on top growth or root growth in winter wheat. In the soil incorporation assay, however, 35% inhibition in top growth and 72% inhibition in root growth was noted at the same application rate

(Saunders et al. 1987, Table 1, p. 12). Based on statistical estimates of EC_{50} values from the soil incorporation assays, the most sensitive species was cocklebur (0.02 ppm in soil) and the least sensitive species was wild oats (1.3 ppm in soil). Wheat was relatively tolerant with a soil EC_{50} of 0.58 ppm in soil.

At application rates of 0.8 kg/ha (about 0.7 lbs a.i./acre) isoxaben had no effect on the growth of strawberries or raspberries (Lawson and Wiseman 1987). And since this experiment involved foliar application without soil incorporation, adverse effects would not be anticipated.

Bhandary et al. (1997) evaluated the potential for isoxaben to affect nursery crops when irrigation water is contaminated. Nominal concentrations of 1 and 10 mg/L isoxaben reduced fresh shoot weight of fountain grass but not daylily. At 10 mg/L, isoxaben reduced root weight in dwarf gardenia and Hellers holly. Significantly, the reported water solubility of isoxaben is only 1 mg/L. Although the Bhandary et al. (1997) publication does not address the issue of water solubility explicitly, it appears that the concentrations reported in this study are nominal rather than measured values.

Varieties of the same plant species may be tolerant to isoxaben. The basis for this tolerance does not appear to be related to differences in metabolism either within or among plant species and thus may involve differences at a specific receptor site (Corio-Costet et al. 1991a,b; Heim et al. 1989, 1990a,b, 1991, 1993; Salihu et al. 1998; Schneegurt et al. 1994a). Among different plant species— as opposed to different strains or varieties of the same species— differences in sensitivity may be related to differences in the rate of absorption of isoxaben by the plant roots (Salihu et al. 1998).

Other herbicides that inhibit cellulose synthesis include the triazole carboxamides, flupoxam, and triazofenamide. There are plants that are resistant to these compounds and not necessarily cross-resistant to isoxaben, which suggests that there are different mechanisms of action between the triazoles and isoxaben (Heim et al. 1998).

4.1.2.5. Terrestrial Microorganisms– Studies regarding the toxicity of isoxaben to soil microorganisms were not available in the U.S. EPA files or the open literature. The soil biodegradation of isoxaben is enhanced by repeated applications (Rouchaud et al. 1997) suggesting that isoxaben may induce its own metabolism rather than have a toxic effect on soil microorganisms.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish– Standard toxicity bioassays to assess the effects of isoxaben on fish are summarized in U.S. EPA (1989a). The LC_{50} values reported by U.S. EPA (1989a) for freshwater and estuarine fish are greater than about 1 mg/L, the highest concentration tested for carp, bluegills, trout, and sheepshead minnow. As noted in Table 2-1, the water solubility limit for isoxaben is about 1 mg/L. Thus, the potential for acute lethal effects seems remote, which is consistent with the assessment by U.S. EPA (1989a). The NOAEL for early life-stage (egg and

fry) toxicity in fathead minnow and trout is 0.4 mg/L, the highest concentration tested (U.S. EPA 1989a).

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

4.1.3.3. Aquatic Invertebrates– Standard toxicity bioassays to assess the effects of isoxaben on aquatic invertebrates are summarized in U.S. EPA (1989a). The acute LC_{50} value for immobility in *Daphnia* is >1 mg/L, which is both the highest concentration tested and the approximate value for the solubility of isoxaben in water. This is also the acute LC_{50} value for the grass shrimp, an estuarine invertebrate. Thus, the potential for acute lethal exposure appears to be remote for aquatic invertebrates, as it does for fish.

The reported NOEL for reproduction in *Daphnia* is 0.69 mg/L with a LOAEL of 1.01 mg/L. In an embryo-larvae study using the Quahog clam, another estuarine invertebrate, exposure to 0.96 mg/L was associated with a 40% mortality. A NOAEL for this species is not reported in U.S. EPA (1989a).

4.1.3.4. Aquatic Plants– A standard toxicity bioassay to assess the effects of isoxaben on aquatic plants was submitted to the U.S. EPA in support of the registration of isoxaben and is summarized in U.S. EPA (1989a). At the solubility limit of isoxaben in the test water (reported as 1.4 mg/L), no growth inhibition was apparent in the freshwater algae, *Selenastrum capricornutum*.

4.1.3.5. Other Aquatic Microorganisms– The U.S. EPA files do not contain information on toxicity of isoxaben to aquatic microorganisms. In a series of bioassays of various herbicides to assess toxicity to *Oscillatoria* cf. *chatbyea*, an undesirable freshwater cyanobacteria, Schrader et al. (1998) report that 0.1 µM isoxaben (i.e., 33.24 µg/L or about 0.03 mg/L) caused growth inhibition in *O. chatbyea* but no growth inhibition was observed in *Selenastrum capricornutum*, a freshwater green algae, at a reported concentration of 10 µM or about 3.3 mg/L. The nominal concentration of 3.3 mg/L exceeds the water solubility of isoxaben but was achieved in this study by the addition of DMSO.

4.2. EXPOSURE ASSESSMENT

4.2.1 Overview. As in the human health risk assessment, the exposure assessments presented in this document are based on a standard set of scenarios and assumptions that are uniformly applied in all Forest Service risk assessments. Given the very limited use of isoxaben proposed by the Forest Service and the specific characteristics of the single site where isoxaben will be applied, not all of these exposure assessments may be relevant to the Forest Service program. This is discussed further in the risk characterization.

Terrestrial animals might be exposed to any applied pesticide 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 estimated for terrestrial animals involve the direct spray of a bee, assuming 100% absorption. This scenario leads to estimates of absorbed dose ranging from 122 to 163 mg/kg.

Central estimates of absorbed dose for several other acute exposure scenarios—direct spray of a small mammal assuming 100% absorption and the consumption of contaminated vegetation, insects or fish —range from 0.25 to 21 mg/kg bw. The upper limits of exposure for these scenarios range from 0.25 to 40 mg/kg bw.

In chronic exposure scenarios, central estimates of daily doses for birds and mammals range from 0.006 to 2.2 mg/kg/day. Based on upper ranges of exposure, the highest doses are estimated for the consumption of contaminated vegetation by a large mammal or birds, with estimated doses ranging from about 18 to 28 mg/kg bw/day. Other exposure scenarios lead to upper estimates of absorbed doses that range from about 0.011 to 0.48 mg/kg bw/day.

The potential for longer-term effects on aquatic species are based on estimated concentrations of isoxaben in water, which are identical to those used in the human health risk assessment. A longer-term water contamination rate adopted from an exposure assessment made by the U.S. EPA is used in all the exposure assessments involving the contamination of ambient water. For all acute exposure scenarios, peak water concentrations of 1 mg/L are estimated based on the water solubility of isoxaben.

4.2.2. Terrestrial Animals. Terrestrial animals might be exposed to any applied pesticide 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. 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 (e.g., Boxenbaum and D'Souza 1990). These relationships dictate that, for a fixed level of exposure (e.g., concentrations 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.

The available information on isoxaben suggests that this compound has a low order of acute toxicity to birds and mammals (sections 4.2 and 4.3). Birds, however, may be more sensitive than mammals to the adverse effects of isoxaben on reproduction. Therefore, separate exposure assessments are conducted for birds and mammals.

Generic estimates of exposure are given for a small mammal. A body weight of 20 g is used for a small mammal, which approximates the body weight of small mammals like mice, voles, shrews, and bats. Other body weights, food consumption, and caloric requirements for mammals and birds are taken from U.S. EPA (1993b).

The exposure assessments for terrestrial animals are summarized in Table 4-1. The computational details for each exposure assessment presented in this section are provided in the attached worksheets (worksheets F01 through F13). Details of each of these exposure assessments are described in the following subsections.

4.2.2.1. Direct Spray **–** In the broadcast application of any pesticide, 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 isoxaben.

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 is likely to 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 isoxaben 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 for body surface area proposed by Boxenbaum and D'Souza (1990). Because there is no information regarding the dermal absorption rate of isoxaben by bees, 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.

Thus, no quantitative exposure assessment is made for this scenario. As discussed in the risk characterization for ecological effects (section 4.4), the direct spray scenarios result in exposure levels below those of toxicological concern, which somewhat diminishes concern about the inability to model this scenario directly.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey **–** Since isoxaben will be applied to vegetation, uptake from contaminated vegetation is an obvious concern and separate exposure scenarios are developed for mammals and birds. Separate acute and chronic exposure scenarios are developed for a small mammal (worksheets F04 and F05) and large mammal (worksheets F10

and F11). In addition, the potential for isoxaben to cause adverse reproductive effects in birds after the consumption of contaminated insects is evaluated for acute exposures (worksheet F14).

A small mammal is used because allometric relationships indicate that small mammals will ingest greater amounts of food per unit body weight, compared with large mammals. 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 (U.S. EPA 1989a). When applied generally, this value may overestimate or underestimate exposure in some circumstances. For example, a 20 g herbivore has a caloric requirement of about 13.5 kcal/day. If the diet of the herbivore consists largely of seeds (4.92 kcal/g), the animal would have to consume a daily amount of food equivalent to approximately 14% of its body weight [(13.5 kcal/day ÷ 4.92 kcal/g)÷20g = 0.137]. Conversely, if the diet of the herbivore consists largely of vegetation (2.46 kcal/g), the animal would have to consume a daily amount of food equivalent to approximately 27% of its body weight [(13.5 kcal/day ÷ 2.46 kcal/g)÷20g = 0.274] (U.S. EPA 1993b, pp.3-5 to 3-6). While it is possible to model this kind of variability, the results might profoundly increase the apparent complexity of the risk assessment by adding several additional scenarios involving various species consuming various diets. A simpler approach is taken in this risk assessment by making the conservative assumption that 100% of the diet is contaminated and that the small mammal consumes leaves and leafy vegetables.

A large herbivorous mammal is included because empirical relationships of concentrations of pesticides in vegetation, discussed below, indicate that grasses may have substantially higher pesticide residues than other types of vegetation such as forage crops or fruits (worksheet A05a). Grasses are an important part of the diet for some large herbivores, but small mammals do not consume grasses as a substantial proportion of their diet. So, even though using residues from grass to model exposure for a small mammal is the most conservative approach, it is not generally applicable to the assessment of potential adverse effects. Hence, in the exposure scenarios for large mammals, the consumption of contaminated range grass is modeled for a 70 kg herbivore, like a deer. Caloric requirements for herbivores and the caloric content of vegetation are used to estimate food consumption based on data from U.S. EPA (1993b). Details of these exposure scenarios are given in worksheets F10 and F11.

The consumption of contaminated vegetation is also modeled for a large bird. This scenario is included because, as discussed in section 4.1.2.2, available studies indicate that isoxaben may cause reproductive impairment in some birds. For this exposure scenario, the consumption of range grass by a 4 kg herbivorous bird, like a Canada Goose, is modeled for both acute (worksheet F12) and chronic (worksheet F13) exposures.

For this component of the exposure assessment, the estimated amounts of pesticide residue in vegetation are based on the relationship between application rate and residue rates on different types of vegetation. As summarized in worksheet A05a, these residue rates are based on the relationships derived by Hoerger and Kenaga (1972). This is the same approach taken by U.S. EPA (1988a) in their ecological risk assessment of isoxaben. For chronic exposures, dissipation

from vegetation is incorporated explicitly into the exposure assessment as detailed in worksheets F11 and F13.

Similarly, the consumption of contaminated insects is modeled for a small bird. There are no monitoring data on the concentrations of isoxaben in insects. The empirical relationships for residues in vegetation developed by Hoerger and Kenaga (1972) are used as surrogates, as detailed in worksheet F14.

In addition to the consumption of contaminated vegetation and insects, isoxaben may reach ambient water and bioconcentrate in fish. Thus, a separate exposure scenario is developed for the consumption of contaminated fish by a predatory bird in both acute (worksheet F08) and chronic (worksheet F09) exposures. Because predatory birds usually consume more food per unit body weight than do predatory mammals (U.S. EPA 1993b, pp. 3-4 to 3-6), a separate exposure scenario for a predatory mammal is not developed. The bioconcentration factors used for these risk assessments are based on the study by Magnussen and Rainey (1986) in which bioconcentration factors in whole fish were 42.5 after 1 day and 70.5 after 28 days in fish exposed to a concentration of 0.243 mg/L isoxaben in water. The bioconcentration factors are rounded to 40 for acute exposure scenarios and 70 for chronic exposure scenarios..

4.2.2.4. Ingestion of Contaminated Water **–** Estimated concentrations of isoxaben in water are identical to those used in the human health risk assessment (worksheet B07). As discussed in section 3.2.3.4.1, the maximum concentration in water after an accidental spill is limited by the solubility of isoxaben in water. 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 (1989a)]. 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 in the human health risk assessment, in the ecological risk assessment there are no available estimates for the variability of water consumption. 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. The amount of the spilled solution is taken as 200 gallons, which is the same value used in the acute exposure scenario for the human health risk assessment,. In the chronic exposure scenario, the factors that affect the variability are the water contamination rate (see 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. Unintended direct spray will result in an exposure level equivalent to the application rate. As summarized in section 2, the typical application rate used in this risk assessment is 0.75-1.0 lbs a.i./acre with up to two applications per year. 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. Using hydraulic ground spray applications, no more than 0.1% (prop = 0.001) herbicide drift was noted 100 m off site at wind speeds between 2.5

m/second (5.6 miles/hour) and 3.5 m/sec (7.8 miles/hour) (Marrs et al. 1989). Thus, functional application rates associated with drift 100 m off site would range from 0.0075 to 0.001 lbs a.i./acre.

4.2.4. Aquatic Organisms. The potential for effects on aquatic species are based on estimated concentrations of isoxaben in water, which are identical to those used in the human health risk assessment. Short-term exposure scenarios are based on 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 isoxaben is considered. Like the accidental spill scenarios used in the human health risk assessment (see section 3.2.3.4.1), in the assessment of exposure of mammals and birds that consume contaminated water or fish (sections 4.2.2.3 and 4.2.2.4.), the maximum concentration of isoxaben in water is limited by the solubility of isoxaben in water.

The longer-term water contamination rate in all exposure assessments involving the contamination of ambient water are detailed in worksheet B07. This approach is identical to the approach used in the exposure assessment for human health risk assessment as well as the exposure assessments for terrestrial species involving contaminated water or fish taken from contaminated water.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview. For mammals, the lowest NOAEL for systemic toxicity is 5 mg/kg/day and the lowest NOAEL for reproductive toxicity is 125 mg/kg/day, the same values used in the human health risk assessment. These two values are used to characterize risk quantitatively. The value of 5 mg/kg/day for systemic toxicity is used to calculate the hazard quotient. The ratio of the reproductive toxicity NOAEL to the NOAEL for systemic toxicity (i.e., 25 or 125 mg/kg/day ÷ 5 mg/kg/day) is used to characterize the potential for reproductive toxicity for scenarios that exceed a hazard quotient of unity for systemic toxicity. Birds may be somewhat more sensitive than experimental mammals to the adverse effects of isoxaben on reproduction, with a NOAEL and LOAEL of 60 and 200 mg/kg/day, respectively. These values are used to characterize risk quantitatively in exposure scenarios involving birds.

Isoxaben is a herbicide and causes adverse effects in various nontarget plant species. A soil incorporation assay employing an application rate of 0.25 lbs a.i./acre resulted in substantial growth inhibition in winter wheat. More sensitive plant species could be adversely affected at functional application rates of 0.008 lbs a.i./acre.

At the solubility of isoxaben in test water (i.e., about 1 mg/L) the level of mortality did not permit the calculation of LC_{50} values. Thus, there appears to be a very low potential for isoxaben to cause adverse effects in aquatic species after acute exposure. NOAELs for chronic toxicity are approximately 0.4 mg/L or higher.

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, the lowest NOAEL in experimental mammals is 5 mg/kg/day (see section 3.3.3.) and the lowest NOAEL for reproductive toxicity is 125 mg/kg/day (see section 3.3.3.). These two values are used in the quantitative risk characterization provided in section 4.4. The value of 5 mg/kg/day for systemic toxicity is used to calculate the hazard quotient. The ratio of the reproductive toxicity NOAEL to the NOAEL for systemic toxicity (i.e., 25 or 125 mg/kg/day ÷ 5 mg/kg/day) is used to characterize the potential for reproductive toxicity for scenarios that exceed a hazard quotient of unity for systemic toxicity.

4.3.2.2. Birds – As noted in section 4.1.2.2, oral toxicity studies suggest that birds are no more sensitive than mammals to the systemic toxic effects of isoxaben. Nevertheless, birds may be somewhat more sensitive than experimental mammals to the adverse effects of isoxaben on reproduction, with a NOAEL and LOAEL of 60 and 200 mg/kg/day, respectively. These values are used to characterize risk quantitatively in exposure scenarios involving birds. Hazard quotients greater than unity raise concern for potential effects on reproduction and at hazard quotients greater than about 3 [200 mg/kg/day ÷ 60 mg/kg/day ≈ 3.3], adverse effects on reproduction would be anticipated.

4.3.2.3. Terrestrial Invertebrates– There is relatively little information available on the toxicity of isoxaben to terrestrial invertebrates (see section 4.1.2.3). Following the approach adopted by the U.S. EPA (1988a), the LD_{50} value of >1093 mg/kg in the honey bee is used quantitatively to characterize risk to terrestrial invertebrates.

4.3.2.4. Terrestrial Plants (Macrophytes)– Isoxaben is a herbicide and causes adverse effects in a variety of nontarget plant species. As summarized in section 4.1.2.4, a soil incorporation assay employing an application rate of 0.25 lbs a.i./acre caused substantial growth inhibition in winter wheat (Saunders et al. 1987). Winter wheat was among the least sensitive species, with a soil EC_{50} for growth inhibition of 0.58 ppm in soil. The most sensitive species was cocklebur with a soil EC_{50} of 0.02 ppm. Taking the ratio of these two EC_{50} values—0.58 ppm /0.02 ppm. = 29—off site functional application rates of about 0.008 lbs a.i./acre [0.25 lb/acre ÷ 29] could be associated with adverse effects in sensitive nontarget species.

4.3.2.5. Terrestrial Microorganisms– No data were encountered on the toxicity of isoxaben to terrestrial microorganisms. Thus, no dose-response assessment for this group is possible.

4.3.3. Aquatic Organisms *(Fish, Invertebrates, and Plants)*.

As indicated in sections 4.1.3.1 through 4.1.3.3, an assessment of the toxicity of isoxaben to aquatic species is limited by the solubility of isoxaben in water. At the functional solubility in test water reported in the available bioassays (i.e., about 1 mg/L) the level of mortality did not permit the calculation of LC_{50} values. Thus, there appears to be a very little potential for isoxaben to cause adverse effects in aquatic species after acute exposure.

For chronic exposures, the lowest reported NOAEL is 0.4 mg/L, for an early life-stage study in fathead minnows and trout. This value is used to characterize risks associated with chronic

exposure to aquatic species. Because ambient levels of exposure are estimated to be far below this value (section 4.4), it is not necessary to elaborate further on the dose-response relationships.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. Standard acute exposure scenarios reach or exceed a level of concern for the direct spray of a small mammal under the assumption of 100% dermal absorption and the consumption of contaminated vegetation by a large mammal. In addition, the upper limit of the hazard index exceeds the level of concern for the consumption of contaminated vegetation by a small mammal. For longer-term exposures, none of the hazard quotients reach a level of concern. The highest hazard quotients are associated with the consumption of contaminated vegetation. The longer-term consumption of contaminated water or fish lead to hazard quotients that are far below a level of concern. At the upper ranges of exposure, the only hazard index to exceed a level of concern is that associated with the chronic consumption of contaminated vegetation by a large mammal. For this scenario, the upper range of the hazard quotient for systemic toxicity is 3.5 but the upper range of the hazard quotient for reproductive effects is 0.1 - i.e., below the level of concern by a factor of10.

Isoxaben is an effective preemergence herbicide, and numerous plant species will be affected in areas directly treated with this compound. Although some damage to nontarget vegetation might be anticipated in areas close to the application site (i.e., <100 meters), damage to nontarget vegetation at greater distances does not appear to be likely. Notwithstanding this assertion, off site damage to nontarget vegetation could be more substantial if conditions during application favor greater rates of drift or if local species of vegetation are highly sensitive to isoxaben.

The potential for damage to aquatic species appears to be remote, based on the low solubility of isoxaben in water and the relatively low proportion of isoxaben that is estimated by U.S. EPA to runoff of the application site. In addition, the risks to aquatic species are further reduced because of the 1000 to 3000 foot distance between the treated area and nearest permanent body of surface water in the area in which the Forest Service proposes to apply this herbicide.

4.4.2. Terrestrial Organisms

4.4.2.1. Terrestrial Animals– The quantitative risk characterization for terrestrial animals is summarized in Table 4-2. For mammals, the hazard quotients are based on the levels of exposure summarized in Table 4-1 and the long-term NOAEL of 5 mg/kg/day that was used in the human health risk assessment to derive the RfD. Only two of the acute exposure scenarios for mammals lead to central estimates of hazard quotients that are above unity: direct spray of a small mammal and the consumption of contaminated vegetation by a large mammal. The latter scenario has limited applicability to the very specific use of isoxaben proposed by the Forest Service. As detailed in section 4.2.2.3, this exposure scenario is based on a large mammal, like a deer, consuming contaminated range grass. The area where the Forest Service will apply isoxaben does not contain substantial quantities of range grass. Thus, it is unlikely that animals like deer would be exposed to significant amounts of isoxaben. Direct spray of a small mammal is a plausible scenario. In either of these scenarios, the exposure is sufficient for systemic toxic effects that would probably be transient and without signs of overt toxicity. The only chronic hazard quotient

that is above unity is the upper range of the hazard quotient for a large mammal consuming contaminated vegetation. Again, this exposure scenario does not appear to relevant to the specific location where the Forest Service proposes to apply isoxaben. All hazard quotients are less than 25. Consequently there is no concern for reproductive toxicity (see section 4.3.2.1). For birds, none of the exceed unity.

The simple verbal interpretation of this quantitative risk characterization for terrestrial animals is that there is little evidence that terrestrial animals would be exposed to levels of concern given the specific location of and types of vegetation in the area in which the Forest Service proposes to apply isoxaben.

4.4.2.2. Terrestrial Plants– Isoxaben is an effective preemergence herbicide and numerous plant species will be affected in areas directly treated with this compound. At the application rates proposed by the Forest Service, the germination and emergence of several kinds of vegetation will be suppressed in the treated area. This is the basic point of applying the compound.

The impact of herbicide drift can be evaluated at least indirectly from the available dose-response data. As discussed in section 4.3.2.4, functional application rates of 0.008 lbs a.i./acre may substantially inhibit the development of sensitive species such as cocklebur. At an application rate of 1 lb a.i./acre and assuming a 100 m off site drift of 0.001, the functional application rate would be 0.001 lbs a.i./acre. Thus, while some damage to nontarget vegetation might be anticipated in areas close to the application site (i.e., <100 m), damage to nontarget vegetation at greater distances does not seem likely. Notwithstanding this assertion, off site damage to nontarget vegetation could be more substantial if conditions during application favor greater rates of drift or if local species of vegetation are highly sensitive to isoxaben.

4.4.2.3. Terrestrial Microorganisms – The risks to terrestrial microorganisms cannot be characterized because no data were located on the toxicity of isoxaben to terrestrial microorganisms. As noted in section 4.1.2.5, repeated soil applications of isoxaben enhance rather than inhibit the biodegradation of this compound. This at least suggests that isoxaben may not be generally toxic to soil microorganisms at normal application rates.

4.4.3. Aquatic Organisms. Given the low solubility of isoxaben in water and based on the runoff estimates provided by the U.S. EPA (1988a), the potential for damage to aquatic species appears to be remote. This evaluation is consistent with the risk characterization of isoxaben by the U.S. EPA (1988a). In terms of the application site under consideration by the Forest Service, the risks are further reduced because the nearest body of surface water is 1000 to 3000 feet from the treatment site. Thus, there is no apparent basis for asserting that isoxaben will cause adverse effects in aquatic organisms in the area to be treated by the Forest Service.

Table 4-1: Summary of Exposure Scenarios for Terrestrial Animals.

Scenario	Dose (mg/kg/day) Typical	Lower	Upper	Worksheet
Acute/Accidental Exposures				
Direct spray				
small mammal, first-order absorption	0.73	0.35	2.1	WSF01
small animal, 100% absorption	18	18	24	WSF02
bee, 100% absorption	122	122	163	WSF03
Contaminated vegetation				
small mammal	3.9	3.9	19	WSF04
large mammal	5.3	5.3	25	WSF10
large bird	8.4	8.4	40	WSF12
Contaminated water				
small mammal	0.25	0.25	0.25	WSF06
Contaminated insects				
small bird	21	1.9	48	WSF14
Contaminated fish				
predatory bird	4.0	2.0	6.0	WSF08
Longer-term Exposures				
Contaminated vegetation				
small mammal	2.2	0.034	0.11	WSF05
large mammal	0.91	0.21	18	WSF11
large bird	1.4	0.34	28	WSF13
Contaminated water				
small mammal	0.006	0.006	0.011	WSF07
Contaminated fish				
predatory bird	0.18	0.09	0.48	WSF08

[a] All values rounded to two significant digits.

Table 4-2: 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	0.1	0.07	0.4
small animal, 100% absorption	**3.7**	**3.7**	**4.9**
bee, 100% absorption	0.1	0.1	0.15
Contaminated vegetation			
small mammal, toxicity	0.8	0.8	**3.8**
small mammal, reproduction	0.03	0.03	0.2
large mammal, toxicity	**1.1**	**1.1**	**5**
large mammal, reproduction	0.04	0.042	0.2
large bird, reproduction	0.1	0.1	0.7
Contaminated water			
small mammal, toxicity	0.1	0.1	0.1
small mammal, reproduction	0.002	0.002	0.00
Contaminated insects			
small bird, reproduction	0.3	0.03	0.8
Contaminated fish			
predatory bird, reproduction	0.07	0.03	0.1
Longer-term Exposures			
Contaminated vegetation			
small mammal, toxicity	0.4	0.007	0.0
small mammal, reproduction	0.02	0.0003	0.001
large mammal, toxicity	0.2	0.04	**3.5**
large mammal, reproduction	0.007	0.002	0.1
large bird, reproduction	0.02	0.006	0.5
Contaminated water			
small mammal	0.001	0.001	0.002
Contaminated fish			
predatory bird	0.003	0.001	0.01
Toxicity Indices [3]			
General toxicity value for mammal - NOAEL		5	mg/kg/day
Reproductive toxicity value for mammal - NOAEL		125	mg/kg/day
Reproductive toxicity value for bird - NOAEL		60	mg/kg/day
Toxicity value for bee - not lethal		1075	mg/kg

[1] See Table 4-1 for summary of exposure assessment.
[2] Estimated dose ÷ toxicity index then round to one significant digit or decimal place.
[3] See Section 4.3 for a discussion of the toxicity indices.

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WORKSHEETS FOR ISOXABEN

SPECIAL NOTE:
As detailed in the document that accompanies these worksheets, the abbreviated risk assessment for isoxaben is being conducted in support of a very specific application at a single nursery. These worksheets summarized standard exposure scenarios used in Forest Service risk assessments. Several of these exposure assessments may not be applicable to the current use of this compound by the Forest Service. Specifically, only ground broadcast (hydraulic spray) applications are planned. The exposure assessments for backpack and aerial sprays are included only as place holders. Similarly, given the limited use and the area in which isoxaben is being used, several of the exposure scenarios for the general public may not apply or may be only marginally relevant. This is discussed further in the exposure assessment (Section 3.2) and risk characterization (3.3).

At the nursery where isoxaben will be used, the actual rate of application will range from 6 to 8 acres per hour rather than 8-21 acres/hour, the. rate of application typically used in Forest Service risk assessments for broadcast ground applications. The lower rates have been put into worksheet A03b and are used in the calculation of worker exposure (C01b).

As indicated in Table 2-1, the water solubility of isoxaben is 1 mg/kg at 25°C and pH 7. All of the standard accidental spill scenarios for a small pond in the human health and ecological exposure assessment lead to calculated concentrations greater than 1 mg/L. For these acute exposure assessments, 1 mg/L is used as the maximum concentration of isoxaben in water.

Worksheet Table of Contents

Section/Title	Page No.
GENERAL ASSUMPTIONS, VALUES, and MODELS	
Worksheet A01: Constants and conversion factors used in calculations	WS-4
Worksheet A02: General Assumptions Used in Worker Exposure Assessments	WS-4
Worksheet A03a: Directed Ground Sprays (includes backpack, cut surface, and streamline applications) - General Assumptions Used in Worker Exposure Assessments	WS-5
Worksheet A03b: Hydraulic/Broadcast Ground Sprays - General Assumptions Used in Worker Exposure Assessments	WS-6
Worksheet A03c: Aerial Applications - General Assumptions Used in Worker Exposure Assessments	WS-7
Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public	WS-8
Worksheet A05a: Estimated concentrations of pesticides on various types of vegetation immediately after application at 1 lb a.i./acre	WS-10
Worksheet A05b: Concentrations of chemical on spheres (berries) at the specified application rate. [FRUIT]	WS-10
Worksheet A06: Central estimates of off-site drift associated with aerial application of pesticides (from Bird 1995)	WS-10
Worksheet A07a: Estimate of first-order absorption rate (k_a in hours^{-1}) and 95% confidence intervals	WS-11
Worksheet A07b: Estimate of dermal permeability (K_p in cm/hr) and 95% confidence intervals	WS-13
CHEMICAL SPECIFIC VALUES and ESTIMATES	
Worksheet B01: Anticipated Application and Dilution Rates for isoxaben	WS-14
Worksheet B02: Summary of central estimate and range of concentrations of isoxaben in field solutions	WS-14
Worksheet B03: Chemical specific values used for isoxaben in exposure assessment worksheets.	WS-15
Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for isoxaben.	WS-16
Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for isoxaben.	WS-17
Worksheet B06: Summary of chemical specific dermal absorption values used for isoxaben dermal absorption.	WS-18
Worksheet B07: Estimates of the concentration of isoxaben in ambient water per lb a.e. applied per acre based on monitoring data.	WS-18

Worksheet Table of Contents

Section/Title	Page No.
EXPOSURE ASSESSMENTS for WORKERS	
Worksheet C01a: Worker exposure estimates for directed foliar (backpack) applications of isoxaben	WS-19
Worksheet C01b: Worker exposure estimates for boom spray (hydraulic ground spray) applications of isoxaben	WS-20
Worksheet C01c: Worker exposure estimates for aerial applications of isoxaben	WS-21
Worksheet C02: Workers: Dermal Exposure Assessments Using Zero-Order Absorption	WS-22
Worksheet C03: Worker Accidental Dermal Exposure Assessments Based on the Assumption of First-Order Absorption	WS-23
EXPOSURE ASSESSMENTS for the GENERAL PUBLIC	
Worksheet D01: Direct spray of child.	WS-24
Worksheet D02: Direct spray of woman.	WS-25
Worksheet D03: Dermal contact with contaminated vegetation.	WS-26
Worksheet D04: Consumption of contaminated fruit, acute exposure scenario.	WS-28
Worksheet D05: Consumption of contaminated fruit, chronic exposure scenario.	WS-29
Worksheet D06: Consumption of contaminated water, acute exposure scenario.	WS-31
Worksheet D07: Consumption of contaminated water, chronic exposure scenario.	WS-33
Worksheet D08: Consumption of contaminated fish, acute exposure scenario.	WS-35
Worksheet D09: Consumption of contaminated fish, chronic exposure scenario.	WS-38
HUMAN HEALTH EFFECTS SUMMARY TABLES	
Worksheet E01: Summary of worker exposure scenarios	WS-41
Worksheet E02: Summary of risk characterization for workers	WS-42
Worksheet E03: Summary of exposure scenarios for the general public	WS-43
Worksheet E04: Summary of risk characterization for the general public	WS-44
Worksheet E05: Summary of cancer risks for the general public for chronic exposure scenarios	WS-45

Worksheet Table of Contents

Section/Title	Page No.
EXPOSURE ASSESSMENTS for Terrestrial Species	
Worksheet F01: Direct spray of small mammal assuming first order absorption kinetics.	WS-46
Worksheet F02: Direct spray of small mammal assuming 100% absorption over the first 24 hour period.	WS-48
Worksheet F03: Direct spray of bee assuming 100% absorption over the first 24 hour period.	WS-49
Worksheet F04: Consumption of contaminated fruit by a small mammal, acute exposure scenario.	WS-50
Worksheet F05: Consumption of contaminated vegetation by a small mammal, chronic exposure scenario.	WS-51
Worksheet F06: Consumption of contaminated water by a small mammal, acute exposure scenario	WS-53
Worksheet F07: Consumption of contaminated water, chronic exposure scenario.	WS-54
Worksheet F08: Consumption of contaminated fish by bird, acute exposure scenario.	WS-55
Worksheet F09: Consumption of contaminated fish by bird, chronic exposure scenario.	WS-56
Worksheet F10: Consumption of contaminated vegetation by a large mammal, acute exposure scenario.	WS-57
Worksheet F11: Consumption of contaminated vegetation by a large mammal, chronic exposure scenario.	WS-58
Worksheet F12: Consumption of contaminated vegetation by a large bird, acute exposure scenario.	WS-60
Worksheet F13: Consumption of contaminated vegetation by a large bird, chronic exposure scenario.	WS-61
Worksheet F14: Consumption of contaminated insects by a small bird, acute exposure scenario.	WS-63
Summary Tables for Terrestrial Species	
Worksheet G01: Summary of Exposure Scenarios for terrestrial animals	WS-64
Worksheet G02: Summary of quantitative risk characterization for terrestrial animals.	WS-65

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]	SERA 1996, 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		7	acres/hour	This is less than the range of 8 to 21 acres per hour used in most FS risk assessments. See Section 2.3.
Lower estimate		6		
Upper estimate		8		
Acres treated per day				
Central estimate	ACREC	49	acres/day	N/A[1]
Lower estimate	ACREL	36		
Upper estimate	ACREU	64		
Absorbed dose rate				
Central estimate	RATEC	0.0002	(mg agent/kg bw) ÷ (lbs agent handled per day) [2]	SERA. 1996, 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]	SERA 1996, 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). See Burnmaster 1998, p.218, Table III., Risk Analysis. 18(2): 215-219. 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/cm²

a Planar surface area of a sphere = ð r^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÷6)× ð × 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:

$$kg = (1 \div 6) \times ð \times d^3 \div 1000$$

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 $\boldsymbol{t}_{0.025}$ 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:

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

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

$$\log_{10} k_a \pm \boldsymbol{t}_{0.025} \times \boldsymbol{s} \times (\boldsymbol{a'X'X\,a})^{0.5}$$

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

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 $\boldsymbol{a}$ because of the way the statistical analysis was conducted to derive X′X .

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

Worksheet 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 isoxaben [WSB01]				
Item	Code	Value	Units	Reference/Source
Typical application rate	Typ	0.75	lb a.i./acre	Section 2.4
Lowest application rate	Low	0.75	lb a.i./acre	Section 2.4
Highest application rate	Hi	1	lb a.i./acre	Section 2.4
Typical dilution	CDil	33	gal./acre	Bakke 2000
Lowest dilution	LDil	25	gal./acre	
Highest dilution	HDil	40	gal./acre	

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.

0.75 lb/acre ÷ 33 gal/acre] × 119.8 (mg/mL)/(lb/gal) = **2.72 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.

0.75 lb/acre ÷ 40 gal/acre) × 119.8 (mg/mL)/(lb/gal) = **2.25 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.

1 lb/acre ÷ 25 gal/acre × 119.8 (mg/mL)/(lb/gal) = **4.79 mg/mL** [HI_Dr]

Worksheet B02: Summary of central estimate and range of concentrations of isoxaben in field solutions.				
Parameter	ID	Value	Units	Reference/Source
Typical	TypDR	2.72	mg/mL	See calculations above
Low	LowDR	2.25	mg/mL	
High	Hi_DR	4.79	mg/mL	

Worksheet B03: Summary of chemical specific values used for isoxaben in exposure assessment worksheets. [WSB03]				
Parameter	ID	Value	Units	Source/Reference
Molecular weight (acid)	MW	332.4	grams/mole	Table 2-1
Water Solubility, pH 7	WS	1	mg/L	
$K_{o/w}$, pH 7	Kow	434	unitless	
Foliar half-time ($t_{½}$)	FT12	56	days	No direct information available. These are by analogy to the soil halftimes from Rutherford and Decker 1986 as summarized in Table 2-1.
Halftime on vegetation, central	FrT12C	56	days	
composite of different lower	FrT12L	34	days	
types upper	FrT12U	87	days	
Dissipation coefficients on vegetation				
central	VgKC	0.01238	$days^{-1}$	ln(2)/half-time. The upper limit on half-time is used to calculate the lower limit on dissipation coefficient.
lower	VgKL	0.008	$days^{-1}$	
upper	VgKU	0.02039	$days^{-1}$	
Bioconcentration factor, edible portion, acute exposure	BCFT	7	kg fish/L	Section 3.2.3.5. Used for all human exposures
Bioconcentration factor, edible portion, chronic exposure	BCFCh	14	kg fish/L	
Bioconcentration factor, whole fish, acute	BCFWA	40	kg fish/L	Section 4.2.2.3. Used for all exposures of wildlife
Bioconcentration factor, whole fish, chronic	BCFWC	70	kg fish/L	
EPA RfD[b]	RfDP	0.05	mg/kg bw/day	Section 3.3.3
[a] This the RfD on IRIS.				

Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for isoxaben.							
Parameters	Value	Units					Reference
Molecular weight	332.4	g/mole					
$K_{o/w}$ at pH 7	434	unitless					
$\log_{10} K_{o/w}$	2.64						
Column vector ***a*** for calculating confidence intervals (see Worksheet 08 for definitions.)							
a_1	1						
a_2	332.4						
a_3	2.64						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet Worksheet A07a for details of calculation.							
Term 1	-0.013482836						
Term 2	0.0580749416						
Term 3	-0.00170887						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.0429	calculation verified in Mathematica 3.0.1.1					
$\log_{10} k_a = 0.233255 \log_{10}(\boldsymbol{k_{o/w}}) - 0.005657\ \boldsymbol{MW} - 1.49615$							WSA07a
$\log_{10}$ of first order absorption rate (k_a)							
Central estimate	-2.76132913314	±	$\boldsymbol{t}_{0.025}$	×	$\boldsymbol{s}$	×	$(\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a})^{0.5}$
Lower limit	-3.09656213983	-	2.0560	×	0.787218	×	0.20712315177
Upper limit	-2.42609612645	+	2.0560	×	0.787218	×	0.20712315177
First order absorption rates (i.e., antilog or 10^x of above values).							
Central estimate	0.001732491	$hours^{-1}$					
Lower limit	0.00080064	$hours^{-1}$					
Upper limit	0.0037489	$hours^{-1}$					

Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for isoxaben.							
Parameters	Value	Units					Reference
Molecular weight	332.4	g/mole					
$K_{o/w}$ at pH 7	434	unitless					
$\log_{10} K_{o/w}$	2.63748972951						
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)							
a_1	1						
a_2	332.4						
a_3	2.63748972951						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07b for details of calculation.							
Term 1	-0.003486874						
Term 2	0.0152464778						
Term 3	0.004733803						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.0165	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	-2.90657555762	±	$\boldsymbol{t}_{0.025}$	×	$\boldsymbol{s}$	×	$\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a}^{0.5}$
Lower limit	-3.08964232357	-	1.9600	×	0.727129	×	0.12845232579
Upper limit	-2.72350879167	+	1.9600	×	0.727129	×	0.12845232579
Dermal permeability							
Central estimate	0.0012400	cm/hour					
Lower limit	0.0008135	cm/hour					
Upper limit	0.0018901	cm/hour					

Worksheet B06: Summary of chemical specific dermal absorption values used for isoxaben dermal absorption. [WSB06]				
Description	Code	Value	Units	Reference/Source
Zero-order absorption (K_p)				
Central estimate	KpC	0.0012	cm/hour	Worksheet B05, values rounded to two significant figures
Lower limit	KpL	0.00081	cm/hour	
Upper limit	KpU	0.0019	cm/hour	
First-order absorption rates (k_a)				
Central estimate	AbsC	0.0017	$hour^{-1}$	Worksheet B04, values rounded to two significant figures
Lower limit	AbsL	0.00080	$hour^{-1}$	
Upper limit	AbsU	0.0037	$hour^{-1}$	

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

Scenario	Acres Treated	Appl. Rate (lb a.e./acre)	mg Applied	Prop. Runoff	Vol. Water (L)	Conc. in Water (mg/L)	ID	WCR [b] (mg/L) ÷ (lb a.e./acre)
Typical	60	0.75	2.04e+07	0.01	8,000,000	0.026	AWT	0.034
Low	60	0.75	2.04e+07	0.01	8,000,000	0.026	AWL	0.034
High	80	1	3.63e+07	0.01	8,000,000	0.045	AWU	0.045

[a] Calculated as 453,600 mg/lb.
[a] The U.S. EPA uses a value of 0.01 for the expected proportion of runoff (U.S. EPA 1988a).
[a] The U.S. EPA uses a volume of about 8,000,000 L based on a 1 acre pond that is six feed deep in their generic risk assessment.
[b] Expected water contamination rate - mg/L in water after the application of isoxaben at a given rate in lb a.e./acre.

WORKER EXPOSURE ASSESSMENTS

Worksheet C01a: Worker exposure estimates for directed foliar (backpack) applications of isoxaben				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	ApplC	0.75	lbs a.i./day	WSB01.TYP
Lower estimate	ApplL	0.75	lbs a.i./day	WSB01.LOW
Upper estimate	ApplU	1	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	WSA03a.ACREC
Lower estimate	ACREL	1.5	acres/day	WSA03a.ACREL
Upper estimate	ACREU	8	acres/day	WSA03a.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	3.28125	lb/day	
Lower estimate	HANDLL	1.125	lb/day	
Upper estimate	HANDLU	8	lb/day	
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA03a.RateC
Lower estimate	RATEL	0.0003		WSA03a.RateL
Upper estimate	RATEU	0.01		WSA03a.RateU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.0098	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000338		
Upper estimate	DOSEU	0.080		

Worksheet C01b: Worker exposure estimates for boom spray (hydraulic ground spray) applications of isoxaben [WSC01]				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	APPLC	0.75	lbs a.i./day	WSB01.TYP
Lower estimate	APPLL	0.75	lbs a.i./day	WSB01.LOW
Upper estimate	APPLU	1	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	49	acres/day	WSA03b.ACREC
Lower estimate	ACREL	36	acres/day	WSA03b.ACREL
Upper estimate	ACREU	64	acres/day	WSA03b.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	36.75	lb/day	
Lower estimate	HANDLL	27	lb/day	
Upper estimate	HANDLU	64	lb/day	
Absorbed dose rate				
Central estimate	RATEC	0.0002	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA03b.RateC
Lower estimate	RATEL	0.00001		WSA03b.RateL
Upper estimate	RATEU	0.0009		WSA03b.RateU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.00735	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000270		
Upper estimate	DOSEU	0.0576		

WS01c: Worker exposure estimates for aerial applications of isoxaben [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	0.75	lbs a.e./day	APPL.TYP
Lower estimate	WS10L	0.75	lbs a.e./day	APPL.LOW
Upper estimate	WS10U	1	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	390	lb/day	N/A[1]
Lower estimate	HANDLL	180	lb/day	
Upper estimate	HANDLU	600	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	0.0117	mg/kg bw	N/A
Lower estimate	DOSEL	0.0001800		
Upper estimate	DOSEU	0.06		

[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	0.0012	cm/hour	WSB06.KpC
Lower	0.00081	cm/hour	WSB06.KpL
Upper	0.0019	cm/hour	WSB06.KpU
Concentration in solution (*C*) [see Worksheet B02]			
Typical	2.72	mg/mL	WSB02.TypDr
Lower	2.25	mg/mL	WSB02.LowDr
Upper	4.79	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.
0.0012000 cm/hr × 2.72272727273 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 6.53e-04 mg/kg [WZHT1M]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0008100 cm/hr × 2.24625 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 3.64e-04 mg/kg [WZHL1M]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0019000 cm/hr × 4.792 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 0.00182096 mg/kg [WZHU1M]

Wearing Contaminated Gloves for One-Hour

Typical Value: Use typical concentration and central estimate of K_p.
0.0012000 cm/hr × 2.72272727273 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.0392072727 mg/kg [WZHT1H]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0008100 cm/hr × 2.24625 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 2.18e-02 mg/kg [WZHL1H]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0019000 cm/hr × 4.792 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.10926 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	mL/cm^2	`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	0.00170	hour^{-1}	`WSB06.ABSC`
Lower limit of range	0.000800	hour^{-1}	`WSB06.ABSL`
Upper limit of range	0.00370	hour^{-1}	`WSB06.ABSU`
Concentration in solution (***C***) [see Worksheet Worksheet B01]			
Typical	2.72272727273	mg/mL	`TypDr`
Lower	2.24625	mg/mL	`LowDr`
Upper	4.792	mg/mL	`HI_Dr`

Details of calculations.

Equation (from Durkin et al. 1995)

$$\boldsymbol{Dose}_{\text{(mg/kg bw)}} = \boldsymbol{k_a}_{\text{(1/hours)}} \times \boldsymbol{L}_{\text{(mL/cmsq)}} \times \boldsymbol{C}_{\text{(mg/mL)}} \times \boldsymbol{T}_{\text{(hours)}} \times \boldsymbol{A}_{\text{(cm sq)}} \div \boldsymbol{W}_{\text{(kg)}}$$

where ***T*** is the duration of exposure in hours and other terms are defined as above. Note: 1 mL = cm^3.

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

Typical Value `[WFLT1H]`,
0.0017000 h^{-1} × 0.008 mL/cm^2 × 2.72272727273 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 1.1e-03 mg/kg
Lower range `[WFLL1H]`,
0.0008000 h^{-1} × 0.008 mL/cm^2 × 2.24625 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 4.3e-04 mg/kg
Upper range `[WFLU1H]`,
0.0037000 h^{-1} × 0.008 mL/cm^2 × 4.792 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 4.2e-03 mg/kg

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

Typical Value `[WFHT1H]`,
0.0017000 h^{-1} × 0.008 mL/cm^2 × 2.72272727273 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 4.4e-04 mg/kg
Lower range `[WFHL1H]`,
0.0008000 h^{-1} × 0.008 mL/cm^2 × 2.24625 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.7e-04 mg/kg
Upper range `[WFHU1H]`,
0.0037000 h^{-1} × 0.008 mL/cm^2 × 4.792 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.7e-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	2.722727273	mg/mL	WSB02.TYPDR
Low	2.24625	mg/mL	WSB02.LOWDR
High	4.792	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.0017	$hour^{-1}$	WSB06.AbsC
Low	0.000800	$hour^{-1}$	WSB06.AbsL
High	0.0037	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.01679	mg/kg	SPRYC
Low	0.006518	mg/kg	SPRYL
High	0.064	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 × 2.72272727273 mg/mL × 6030 cm^2 × 0.0017 h^{-1} × 1 h ÷ 13.3 kg = 0.01679 mg/kg

Lower Range of Estimate [SPRYCL]:
0.008 mg/mL × 2.24625 mg/mL × 6030 cm^2 × 0.0008 h^{-1} × 1 h ÷ 13.3 kg = 0.006518 mg/kg

Upper Range of Estimate [SPRYCH]:
0.008 mg/mL × 4.792 mg/mL × 6030 cm^2 × 0.0037 h^{-1} × 1 h ÷ 13.3 kg = 0.064 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	2.722727273	mg/mL	`WSB02.TYPDR`
Low	2.24625	mg/mL	`WSB02.LOWDR`
High	4.792	mg/mL	`WSB02.HI_DR`
First-order dermal absorption rate (k_a)			
Central	0.0017	$hour^{-1}$	`WSB06.AbsC`
Low	0.000800	$hour^{-1}$	`WSB06.AbsL`
High	0.0037	$hour^{-1}$	`WSB06.AbsU`
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.001687	mg/kg	`SPRYWC`
Low	0.000655	mg/kg	`SPRYWL`
High	0.0065	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 × 2.72272727273 mg/mL × 2915 cm^2 × 0.0017 h^{-1} × 1 h ÷ 64 kg = 0.001687 mg/kg

Lower Range of Estimate `[SPRYWL]`:
0.008 mg/mL × 2.24625 mg/mL × 2915 cm^2 × 0.0008 h^{-1} × 1 h ÷ 64 kg = 0.0006548 mg/kg

Upper Range of Estimate `[SPRYWH]`:
0.008 mg/mL × 4.792 mg/mL × 2915 cm^2 × 0.0037 h^{-1} × 1 h ÷ 64 kg = 0.0065 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	0.75	lb a.i/acre	WSB01.TYP
Low	0.75	lb a.i/acre	WSB01.LOW
High	1	lb a.i/acre	WSB01.HI
First-order dermal absorption rate (k_a)			
Central	0.00170	$hour^{-1}$	WSB06.AbsC
Low	0.000800	$hour^{-1}$	WSB06.AbsL
High	0.00370	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations on next page.***			
Central	3.14e-03	mg/kg	VEGDWC
Low	1.48e-03	mg/kg	VEGDWL
High	9.35e-03	mg/kg	VEGDWH

Description of Calculations:

Step 1:

Use method of Durkin et al. (1995, p. 68, equation 4) to calculate the transfer rate (***Tr***) units of µg/(cm^2·hr)) based on the dislodgeable residue (***Dr***) in units of µg/cm^2. Estimate *Dr* based on 0.1 of the application rate after converting application rate (***R***) in lb a.i./acre to units of µg/cm^2:

$$x = \log(\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(\boldsymbol{R} \times \text{WSA01.lbac_ugcm} \times 0.1)) + 0.05$$

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

Step 2:

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

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

Step 3:

Estimate amount (*Amnt*) transferred to a specified surface are of skin (***A***) in mg during the exposure period (contact time or ***Tc***):

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

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 (***Te***) 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:

$x = \log_{10}(\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(0.75 \times 11.21 \times 0.1)) + 0.05 = -3.21e\text{-}02\ \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-3.21e-02} = 9.29e\text{-}01\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Tr}\ (mg/(cm^2 \cdot hr)) = 9.29e\text{-}01\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 9.29e\text{-}04\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 9.29e\text{-}04\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 4.92e+00\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 4.92e+00\ mg \times 0.0017\ hr^{-1} \times 24\ hours \div 64\ kg = 3.14e\text{-}03$ `[VEGDWC]`

Lower Range of Estimate:

Step 1:

$x = \log_{10}(\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(0.75 \times 11.21 \times 0.1)) + 0.05 = -3.21e\text{-}02 \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-3.21e-02} = 9.29e\text{-}01\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Tr}\ (mg/(cm^2 \cdot hr)) = 9.29e\text{-}01\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 9.29e\text{-}04\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 9.29e\text{-}04\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 4.92e+00\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 4.92e+00\ mg \times 0.0008\ hr^{-1} \times 24\ hours \div 64\ kg = 1.48e\text{-}03$ `[VEGDWL]`

Upper Range of Estimate:

Step 1:

$x = \log_{10}(\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(1 \times 11.21 \times 0.1)) + 0.05 = 1.04e\text{-}01\ \mu g/(cm^2 \cdot hr)$

$\boldsymbol{Tr}\ (\mu g/(cm^2 \cdot hr)) = 10^{1.04e-01} = 1.27e+00\ \mu g/(cm^2 \cdot hr)$

Step 2:

$\boldsymbol{Tr}\ (mg/(cm^2 \cdot hr)) = 1.27e+00\ \mu g/(cm^2 \cdot hr) \div 1000\ \mu g/mg = 1.27e\text{-}03\ mg/(cm^2 \cdot hr)$

Step 3:

$\boldsymbol{Amnt}(mg) = 1.27e\text{-}03\ mg/(cm^2 \cdot hr) \times 1\ hr \times 5300\ cm^2 = 6.74e+00\ mg$

Step 4:

$\boldsymbol{D_{Abs}}\ (mg/kg\ bw) = 6.74e+00\ mg \times 0.0037\ hr^{-1} \times 24\ hours \div 64\ kg = 9.35e\text{-}03$ `[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	0.75	lb a.i./acre	`WSB01.Typ`
Lower	0.75	lb a.i./acre	`WSB01.Low`
Upper	1	lb a.i./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	0.008	mg/kg bw	`VEGCWAT`
Lower	0.00798	mg/kg bw	`VEGCWAL`
Upper	0.05	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.i./acre applied.			

Equation (terms defined in above table):

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

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.454 kg × 0.75 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.008 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 × 0.75 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.00798 mg/kg bw

Upper: Use highest estimated application rate and highest RUD.

D = 0.454 kg × 1 lb a.i./acre × 7 mg/kg÷lb a.i./acre ÷ 64 kg = 0.05 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	56	days	WSB03.FrT12C
lower	34	days	WSB03.FrT12L
upper	87	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	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./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	2.82e-03	mg/kg bw/day	VEGCWCT
Lower	1.97e-03	mg/kg bw/day	VEGCWCL
Upper	4.88e-02	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.i./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.i./acre) × ***rr***(mg/kg÷lb a.i./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 = 0.75 lb a.i./acre × 1.5 mg/kg veg. = 1.125 mg/kg veg.

Step 2:

k = ln(2) ÷56 days^{-1} = 0.012

C_{90} = 1.125 mg/kg × $e^{-0.012 \times 90}$ = 3.82e-01 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(1.125 \times 3.82e\text{-}01)^{0.5}$ (mg/kg veg.) × 0.0043 kg veg/kg bw = 2.82e-03 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 = 0.75 lb a.i./acre × 1.5 mg/kg veg. = 1.125 mg/kg veg.

Step 2:

k = ln(2) ÷34 days^{-1} = 0.02

C_{90} = 1.125 mg/kg × $e^{-0.02 \times 90}$ = 1.86e-01 mg/kg veg.

Step 3:

$D_{\text{(mg/kg bw)}} = (1.125 \times 1.86e\text{-}01)^{0.5}{}_{\text{(mg/kg veg.)}} \times 0.0043_{\text{(kg veg/kg bw)}} = 1.97e\text{-}03_{\text{(mg/kg bw)}}$

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 = 1 lb a.i./acre × 7 mg/kg veg. = 7 mg/kg veg.

Step 2:

k = ln(2) ÷87 days^{-1} = 0.008

C_{90} = 7 mg/kg × $e^{-0.008 \times 90}$ = 3.41e+00 mg/kg veg.

Step 3:

$D_{\text{(mg/kg bw)}} = (7 \times 3.41e{+}00)^{0.5}{}_{\text{(mg/kg veg.)}} \times 0.01_{\text{(kg veg/kg bw)}} = 4.88e\text{-}02_{\text{(mg/kg bw)}}$

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 field solution (***C*** $_{(mg/L)}$)			
Central	2722.72727	mg/L	WSB02.TypDR
Low	2246.25	mg/L	WSB02.LowDR
High	4792	mg/L	WSB02.Hi_DR
Concentrations in ambient water ***C*** × VS(liters) ÷ LV)			
Central	2.06	mg/L	These calculated values are not used. The concentration in water is limited by the solubility of isoxaben in water - i.e., 1 mg/L. See discussion in Section 3.2.3.4.1.
Low	1.70	mg/L	
High	3.63	mg/L	
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	0.075	mg/kg bw	WATCCAT
Lower	0.046	mg/kg bw	WATCCAL
Upper	0.11	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:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2722.73_{(mg/L)} \div 1000000_{(liters)} = 2.06_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 1_{(L)} \div 13.3_{(kg)} = 0.075_{(mg/kg\ bw)}$$ [WATCCAT]

Lower Estimate:

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

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2246.25_{(mg/L)} \div 1000000_{(liters)} = 1.7_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 0.61_{(L)} \div 13.3_{(kg)} = 0.046_{(mg/kg\ bw)}$$ [WATCCAL]

Upper Estimate:

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

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 4792_{(mg/L)} \div 1000000_{(liters)} = 3.63_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 1.5_{(L)} \div 13.3_{(kg)} = 0.11_{(mg/kg\ bw)}$$ [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*** $_{(\text{lb a.i./acre})}$)			
Central	0.75	lb a.e./gal	WSB01.Typ
Low	0.75		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(\text{mg/L})}$÷***R*** $_{(\text{lb a.i./gal})}$)			
Central	3.40e-02	mg/L/lb a.e./acre	WSB07.AWT
Low	3.40e-02		WSB07.AWL
High	4.54e-02		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	7.29e-04	mg/kg bw/day	WATCMCT
Lower	5.10e-04	mg/kg bw/day	WATCMCL
Upper	1.56e-03	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 ($\boldsymbol{R}_{\text{(lb a.i./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}}$) 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 ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.i./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}} \times \boldsymbol{A}_{\text{(L/day)}} \div \boldsymbol{W}_{\text{(kg)}}$$

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), and the typical water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.75_{\text{(lb a.i./acre)}} \times 3.40\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 2_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 7.29\text{e-}04_{\text{(mg/kg bw)}}$$ [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.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.75_{\text{(lb a.i./acre)}} \times 3.40\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 1.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 5.10\text{e-}04_{\text{(mg/kg bw)}}$$ [WATCMCL]

Upper range of Estimate:

Use the highest anticipated application rate, the upper end of the range of the water contamination rate (WCR), and the upper end of the range for water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 1_{\text{(lb a.i./acre)}} \times 4.54\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 2.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 1.56\text{e-}03_{\text{(mg/kg bw)}}$$ [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.* **NOTE:** For all of these calculations, the calculated concentration in water exceeds the water solubility. Thus, the water solubility of 1 mg/L is used rather than the calculated concentrations. See Section 3.2.3.4.1. Also note that the BCF used is based on a 24 hour exposure in fish.

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	2722.72727	mg/L	WSB02.TYPDR×1000
Low	2246.25	mg/L	WSB02.LOWDR×1000
High	4792	mg/L	WSB02.HI_DR×1000
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population, typical	0.01	kg/day	WSA04.FAU
upper range	0.158		
Subsistence populations, typical	0.081	kg/day	WSA04.FNU
upper range	0.77		
Bioconcentration factor (***BCF***$_{(kg\ fish/L)}$)	7	kg fish/L	WSB03.BCFE
Dose estimates (***D***) - **see details of calculations on next page.**			
General Population			
Typical	0.0010	mg/kg bw	FISHAMGPT
Lower	0.00100	mg/kg bw	FISHAMGPL
Upper	0.0158	mg/kg bw	FISHAMGPU
Native American subsistence populations			
Typical	0.0081	mg/kg bw	FISHAMNAT
Lower	0.0081	mg/kg bw	FISHAMNAL
Upper	0.077	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.

$$\textbf{\textit{Conc.}}_{(mg/L)} = \textbf{\textit{VS}}_{(gal.)} \times 3.785_{L/gal} \times \textbf{\textit{C}}_{(mg/L)} \div \textbf{\textit{VL}}_{(liters)}$$

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

$$\textbf{\textit{D}}_{(mg/kg\ bw)} = \textbf{\textit{Conc.}}_{(mg/L)} \times \textbf{\textit{BCF}}_{(kg\ fish/L)} \times \textbf{\textit{A}}_{(kg\ fish)} \div \textbf{\textit{W}}_{(kg\ bw)}$$

General Public

Central Estimate:

Use the typical field dilution as well as the experimental BCF and typical daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2722.72727273_{(mg/L)} \div 1000000_{(liters)} = 2.06_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$\text{D}_{(mg/kg\ bw)} = 1_{(mg/L)} \times 7_{(L/kg)} \times 0.01_{(kg\ fish)} \div 70_{(kg)} = 0.001_{(mg/kg\ bw)}$$ `[FISHAMGPT]`

Lower End of Range for the Estimate:

Use the lower field dilution as well as the experimental BCF and daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2246.25_{(mg/L)} \div 1000000_{(liters)} = 1.7_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$\text{D}_{(mg/kg\ bw)} = 1_{(mg/L)} \times 7_{(L/kg)} \times 0.01_{(kg\ fish)} \div 70_{(kg)} = 0.00100_{(mg/kg\ bw)}$$ `[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:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 4792_{(mg/L)} \div 1000000_{(liters)} = 3.63_{(mg/L)}$$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

$$\text{D}_{(mg/kg\ bw)} = 1_{(mg/L)} \times 7_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.0158_{(mg/kg\ bw)}$$ `[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 typical daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 2722.72727273 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 2.06 $_{(mg/L)}$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

D $_{(mg/kg\ bw)}$ = 1 $_{(mg/L)}$ × 7 $_{(L/kg)}$ × 0.081 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.0081 $_{(mg/kg\ bw)}$ `[FISHAMNAT]`

Estimate of Lower End of Range:

Use the lower field dilution as well as the experimental BCF and typical daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 2246.25 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 1.700 $_{(mg/L)}$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

D $_{(mg/kg\ bw)}$ = 1 $_{(mg/L)}$ × 7 $_{(L/kg)}$ × 0.081 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.0081 $_{(mg/kg\ bw)}$ `[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 $_{L/gal}$ × 4792 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 3.630 $_{(mg/L)}$

Step 2: ***NOTE: Use water solubility of 1 mg/L rather than nominal concentration. See Section 3.2.3.4.1.***

D $_{(mg/kg\ bw)}$ = 1 $_{(mg/L)}$ × 7 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.077 $_{(mg/kg\ bw)}$ `[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*** $_{(\text{lb a.i./acre})}$)			
Central	0.75	lb a.i./gal	WSB01.Typ
Low	0.75		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(\text{mg/L})}$÷***R*** $_{(\text{lb a.i./gal})}$)			
Central	3.40e-02	mg/L/lb a.i./acre	WSB07.AWT
Low	3.40e-02		WSB07.AWL
High	4.54e-02		WSB07.AWU
Bioconcentration factor (***BCF***$_{(\text{kg fish/L})}$)	14	kg fish/L	WSB03.BCFCh
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	5.10e-05	mg/kg bw/day	FISHMCT
Lower	5.10e-05	mg/kg bw/day	FISHMCL
Upper	1.43e-03	mg/kg bw/day	FISHMCU
Native American Subsistence Population			
Typical	4.13e-04	mg/kg bw/day	FISHNMCT
Lower	4.13e-04	mg/kg bw/day	FISHNMCL
Upper	6.99e-03	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*** $_{\text{(lb a.i./acre)}}$) by the water contamination rate (***WCR*** $_{\text{((mg/L)×(lb a.i./gal))}}$) 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***$_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.i./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}} \times \boldsymbol{A}_{\text{(kg/day)}} \times \boldsymbol{BCF}_{\text{(kg fish/L)}} \div \boldsymbol{W}_{\text{(kg)}}$$

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.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.75_{\text{(lb a.i./acre)}} \times 3.40\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 14_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fish/day)}} \div 70_{\text{(kg bw)}} = 5.10\text{e-}05_{\text{(mg/kg bw)}}$ `[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.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.75_{\text{(lb a.i./acre)}} \times 3.40\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 14_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fish/day)}} \div 70_{\text{(kg bw)}} = 5.10\text{e-}05_{\text{(mg/kg bw)}}$ `[FISHMCL]`

Upper Range of Estimate:

Use the highest labeled application rate, upper range of contamination rate (WCR), the maximum l fish consumption, the measured bioconcentration factor, and standard body weight.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 1_{\text{(lb a.i./acre)}} \times 4.54\text{e-}02_{\text{((mg/L)×(lb a.i./gal))}} \times 14_{\text{(kg fish/L)}} \times 0.158_{\text{(kg fish/day)}} \div 70_{\text{(kg bw)}} = 1.43\text{e-}03_{\text{(mg/kg bw)}}$ `[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.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.75_{(\text{lb a.i./acre})} \times 3.40\text{e-}02_{((\text{mg/L})\times(\text{lb a.i./gal}))} \times 14_{(\text{kg fish/L})} \times 0.081_{(\text{kg fish/day})} \div 70_{(\text{kg bw})} = 4.13\text{e-}04_{(\text{mg/kg bw})}$$ [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.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.75_{(\text{lb a.i./acre})} \times 3.40\text{e-}02_{((\text{mg/L})\times(\text{lb a.i./gal}))} \times 14_{(\text{kg fish/L})} \times 0.081_{(\text{kg fish/day})} \div 70_{(\text{kg bw})} = 4.13\text{e-}04_{(\text{mg/kg bw})}$$ [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.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 1_{(\text{lb a.i./acre})} \times 4.54\text{e-}02_{((\text{mg/L})\times(\text{lb a.i./gal}))} \times 14_{(\text{kg fish/L})} \times 0.77_{(\text{kg fish/day})} \div 70_{(\text{kg bw})} = 6.99\text{e-}03_{(\text{mg/kg bw})}$$ [FISHNMCU]

SUMMARY TABLES FOR HUMAN HEALTH RISK ASSESSMENT

Worksheet E01: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)[a]			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.0098	0.00034	0.080	WSC01a
Broadcast ground spray (Boom spray)	0.0074	0.00027	0.058	WSC01b
Aerial applications	0.012	0.00018	0.060	WSC01c
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	0.00065	0.00036	0.0018	WSC02
Contaminated Gloves, 1 hour	0.039	0.022	0.11	WSC02
Spill on hands, 1 hour	0.00044	0.00017	0.0017	WSC03
Spill on lower legs, 1 hour	0.0011	0.00043	0.0042	WSC03

[a] All values rounded to two significant digits.

Worksheet E02: Summary of risk characterization for workers[1]

RfD	0.05	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.2	0.007	1.6	WSC01a
Broadcast ground spray (Boom spray)	0.1	0.005	**1.2**	WSC01b
Aerial applications	0.2	0.004	1.2	WSC01c
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	0.01	0.007	0.04	WSC02
Contaminated Gloves, 1 hour	0.8	0.4	**2**	WSC02
Spill on hands, 1 hour	0.009	0.003	0.03	WSC03
Spill on lower legs, 1 hour	0.02	0.009	0.08	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)[a]			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.017	0.00652	0.064	WSD01
Direct spray, lower legs	Woman	0.0017	0.00065	0.0065	WSD02
Dermal, contaminated vegetation	Woman	0.0031	0.0015	0.0093	WSD03
Contaminated fruit, acute exposure	Woman	0.008	0.0080	0.050	WSD04
Contaminated water, acute exposure	Child	0.075	0.046	0.11	WSD06
Consumption of fish, general public	Man	0.0010	0.0010	0.016	WSD08
Consumption of fish, subsistence populations	Man	0.0081	0.0081	0.077	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0028	0.0020	0.049	WSD05
Consumption of water	Man	0.00073	0.00051	0.0016	WSD07
Consumption of fish, general public	Man	0.000051	0.000051	0.0014	WSD09
Consumption of fish, subsistence populations	Man	0.00041	0.00041	0.0070	WSD09

[a] All values rounded to two significant digits.

Worksheet E04: Summary of risk characterization for the general public [1] .

Chronic RfD		0.05	mg/kg/day	Sect. 3.3.3.	
Acute RfD		0.05	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.3	0.1	**1.3**	WSD01
Direct spray, lower legs	Woman	0.03	0.01	0.1	WSD02
Dermal, contaminated vegetation	Woman	0.06	0.03	0.2	WSD03
Contaminated fruit, acute exposure	Woman	0.2	0.2	**1.0**	WSD04
Contaminated water, acute exposure	Child	**1.5**	0.9	**2**	WSD06
Consumption of fish, general public	Man	0.02	0.02	0.3	WSD08
Consumption of fish, subsistence populations	Man	0.2	0.2	**1.5**	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.06	0.04	**1.0**	WSD05
Consumption of water	Man	0.01	0.01	0.03	WSD07
Consumption of fish, general public	Man	0.001	0.001	0.03	WSD09
Consumption of fish, subsistence populations	Man	0.008	0.008	0.1	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 E02 for summary of exposure assessments.

Worksheet E05: Summary of carcinogenic risks associated with chronic exposures scenarios for members of the general public [1] .

Cancer potency		0.0021	(mg/kg/day)$^{-1}$	Sect. 3.3.4.	
Scenario	Target	Risk			Worksheet
		Typical	Lower	Upper	
Contaminated fruit[2]	Woman	**1.5e-06**	**1.0e-06**	**2.5e-05**	WSD05
Consumption of water	Man	**1.5e-06**	**1.1e-06**	**3.3e-06**	WSD07
Consumption of fish, general public	Man	1.1e-07	1.1e-07	**3.0e-06**	WSD09
Consumption of fish, subsistence populations	Man	8.7e-07	8.7e-07	**1.5e-05**	WSD09

Scenario	Target	Risk ÷ (1 in one million)			Worksheet
		Typical	Lower	Upper	
Contaminated fruit	Woman	**1.5**	**1.0**	**25**	WSD05
Consumption of water	Man	**1.5**	**1.1**	**3.3**	WSD07
Consumption of fish, general public	Man	0.1	0.1	**3.0**	WSD09
Consumption of fish, subsistence populations	Man	0.9	0.9	**15**	WSD09

[1] Risk calculated as the product of the potency factor and the daily dose. See Worksheet E02 for summary of exposure assessments.
[2] 90-Day doses from Worksheet D05 adjusted for 365 days in a year.

EXPOSURE ASSESSMENTS for Terrestrial Species

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	0.75	lb a.i. /acre	WSB01.TYP
Low	0.75		WSB01.LOW
High	1		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	0.00170	$hour^{-1}$	WSB06.AbsC
Low	0.000800	$hour^{-1}$	WSB06.AbsL
High	0.00370	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.7461	mg/kg	SMDSDC
Low	0.3511	mg/kg	SMDSDL
High	2.165	mg/kg	SMDSDH

Details of calculations on next page.

Direct Spray of Small Mammal, first-order absorption, Details of calculations

Equation: *0.5 × F × R × A ÷ 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 and dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.75 lb/acre × 87 cm^2 × -0.0017/h × 24h ÷ 0.02 kg = 0.7461 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) × 0.75 lb/acre × 87 cm^2 × 0.0008/h × 24 h ÷ 0.02 kg = 0.3511 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) × 1 lb/acre × 87 cm^2 × 0.0037/h × 24 h ÷ 0.02 kg = 2.165 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	0.75	lb a.i. /acre	WSB01.TYP
Low	0.75		WSB01.LOW
High	1		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	18.3	mg/kg	SMDS2DC
Low	18.29	mg/kg	SMDS2DL
High	24.4	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 ($mg/cm^2 \div lb/acre$) $\times$ 0.75 lb/acre $\times$ 87 $cm^2 \div 0.02$ kg = 18.3 mg/kg [SMDS2DC]

Lower Range of Estimate [WSE042DL]: Use the lowest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div lb/acre$) $\times$ 0.75 lb/acre $\times$ 87 $cm^2 \div 0.02$ kg = 18.29 mg/kg [SMDS2DL]

Upper Range of Estimate [WSE042DH]: Use the highest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div lb/acre$) $\times$ 1 lb/acre $\times$ 87 $cm^2 \div 0.02$ kg = 24.4 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	0.75	lb a.i. /acre	WSB01.TYP
Low	0.75		WSB01.LOW
High	1		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	122	mg/kg	BEEDS2DC
Low	122	mg/kg	BEEDS2DL
High	163	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 ($mg/cm^2 \div lb/acre$) $\times$ 0.75 lb/acre $\times$ 2.7 $cm^2 \div 0.000093$ kg = 122 mg/kg [BEEDS2DC]

Lower Range of Estimate: Use the lowest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div lb/acre$) $\times$ 0.75 lb/acre $\times$ 2.7 $cm^2 \div 0.000093$ kg = 122 mg/kg [BEEDS2DL]

Upper Range of Estimate: Use the highest anticipated application rate,
0.5×0.01121 ($mg/cm^2 \div lb/acre$) $\times$ 1 lb/acre $\times$ 2.7 $cm^2 \div 0.000093$ kg = 163 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 1989a
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./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	3.94	mg/kg bw	VGCSMAC
Lower	3.94	mg/kg bw	VGCSMAL
Upper	18.8	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.i./acre applied.			

Equation (terms defined in above table):

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

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.003 kg × 0.75 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 3.94 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 × 0.75 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 3.94 mg/kg bw [VGCSMAL]

Upper: Use highest estimated application rate and highest RUD.

D = 0.003 kg × 1 lb a.i./acre × 125 mg/kg÷lb a.i./acre ÷ 0.02 kg = 18.8 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 1989a
kg food consumed per kg bw	0.15	Unitless	0.003/0.02
Foliar halftimes ($t_{½}$) Central	56	$days^{-1}$	Worksheet B03
Low	34	$days^{-1}$	
High	87	$days^{-1}$	
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./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	2.23e+00	mg/kg bw	VGCSMCT
Lower	3.43e-02	mg/kg bw	VGCSMCL
Upper	0.11	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.i./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.i./acre) × ***rr***(mg/kg÷lb a.i./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 = 34 lb a.i./acre × 0.75 mg/kg veg. = 25.5 mg/kg veg.

Step 2:

k = ln(2) ÷ 56 $days^{-1}$ = 0.012

C_{90} = 25.5 mg/kg × $e^{-0.012 \times 90}$ = 8.65968590395 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(25.5 \times 8.65968590395)^{0.5}$ (mg/kg veg.) × 0.15 kg veg/kg bw = 2.229 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 = 0.75 lb a.i./acre × 0.75 mg/kg veg. = 0.5625 mg/kg veg.

Step 2:

k = ln(2) ÷34 $days^{-1}$ = 0.02

C_{90} = 0.5625 mg/kg × $e^{-0.02 \times 90}$ = 9.30e-02 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (0.5625 \times 9.30e\text{-}02)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 3.43e\text{-}02_{(mg/kg\ bw)}$ [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 = 1 lb a.i./acre × 1 mg/kg veg. = 1 mg/kg veg.

Step 2:

k = ln(2) ÷87 $days^{-1}$ = 0.008

C_{90} = 1 mg/kg × $e^{-0.008 \times 90}$ = 0.5 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (1 \times 0.5)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 0.11_{(mg/kg\ bw)}$ [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	2722.73	mg/L	WSB02.TYPDR×1000
Low	2246.25	mg/L	WSB02.LOWDR×1000
High	4792	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 1989a
Dose estimates (***D***) - **see details of calculations below.**			
Typical	0.25	mg/kg bw	WTCSMAT
Lower	0.25	mg/kg bw	WTCSMAL
Upper	0.25	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.

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

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

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

NOTE: All of the calculated concentrations of isoxaben in water exceed the water solubility of 1 mg/L (Section 3.2.3.4.1). Thus, the water solubility rather than the calculated concentration is used as the basis for estimating the dose.

Central Estimate: Use the typical field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2722.72727273_{(mg/L)} \div 1000000_{(liters)} = 2.06_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.25_{(mg/kg\ bw)}$ [WTCSMAT]

Lower Estimate: Use the lowest estimated field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 2246.25_{(mg/L)} \div 1000000_{(liters)} = 1.7_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.25_{(mg/kg\ bw)}$ [WTCSMAL]

Upper Estimate: Use the highest estimated field concentration,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 4792_{(mg/L)} \div 1000000_{(liters)} = 3.63_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 1_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.25_{(mg/kg\ bw)}$ [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 ($\boldsymbol{R}_{(lb\ a.i./acre)}$)			
Central	0.75	lb a.i./gal	WSB01.Typ
Low	0.75		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)($\boldsymbol{C}_{(mg/L)} \div \boldsymbol{R}_{(lb\ a.i./gal)}$)			
Central	0.03402	mg/L/lb a.i./acre	WSB07.AWT
Low	0.03402		WSB07.AWL
High	0.04536		WSB07.AWU
Body weight ($\boldsymbol{W}$)	0.02	kg	U.S. EPA 1989a
Amount of water consumed ($\boldsymbol{A}_{(L/day)}$)	0.005	L/day	U.S. EPA 1989a
Dose estimates ($\boldsymbol{D}$) - **see details of calculations below.**			
Typical	0.0064	mg/kg bw	WTCSMCT
Lower	0.006379	mg/kg bw	WTCSMCL
Upper	0.011	mg/kg bw	WTCSMCU

Equations (terms defined in table)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{(lb\ a.i./acre)}$) by the water contamination rate ($\boldsymbol{WCR}_{((mg/L)\times(lb\ a.i./gal))}$) to get the concentration in ambient water. This product is in turn multiplied by the amount of water consumed per day ($\boldsymbol{A}_{(L/day)}$) and then divided by the body weight ($\boldsymbol{W}_{(kg)}$)to get the estimate of the absorbed dose ($\boldsymbol{D}_{(mg/kg\ bw)}$).

$$\boldsymbol{D}_{(mg/kg\ bw)} = \boldsymbol{R}_{(lb\ a.i./acre)} \times \boldsymbol{WCR}_{((mg/L)\times(lb\ a.i./gal))} \times \boldsymbol{A}_{(L/day)} \div \boldsymbol{W}_{(kg)}$$

Central Estimate: Use the typical application rate and typical water contamination rate (WCR)

$$\boldsymbol{D}_{(mg/kg\ bw)} = 0.75_{(lb\ a.i./acre)} \times 0.03402_{((mg/L)\times(lb\ a.i./gal))} \times 0.005_{(L/day)} \div 0.02_{(kg\ bw)} = 0.0064_{(mg/kg\ bw)}$$ [WTCSMCT]

Lower Range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{(mg/kg\ bw)} = 0.75_{(lb\ a.i./acre)} \times 0.03402_{((mg/L)\times(lb\ a.i./gal))} \times 0.005_{(L/day)} \div 0.02_{(kg\ bw)} = 0.006379_{(mg/kg\ bw)}$$ [WTCSMCL]

Upper range of Estimate: Use the highest anticipated application rate and the upper end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{(mg/kg\ bw)} = 1_{(lb\ a.i./acre)} \times 0.04536_{((mg/L)\times(lb\ a.i./gal))} \times 0.005_{(L/day)} \div 0.02_{(kg\ bw)} = 0.011_{(mg/kg\ bw)}$$ [WTCSMCU]

Worksheet F08: Consumption of contaminated fish by predatory bird, acute exposure scenario. *[FISHBIRDACUTE]*

***Verbal Description**: A predatory bird consumes fish taken from contaminated water 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. The assumption is made that bioconcentration will reach equilibrium. This probably will overestimate exposure and subsequent risk.*

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 in gallons	200	gallons	N/A
Volume of spill in liters [VS]	757.8	liters	1 gal. = 3.789 L
Concentrations in field solution (***FC*** $_{(mg/L)}$)			
Central	2722.73	mg/L	WSB02.TypDR
Low	2246.25	mg/L	WSB02.LowDR
High	4792	mg/L	WSB02.Hi_DR
Concentrations in ambient water (WC) (***FC × VS /VL***)			
Central	2.06	mg/L	NOTE: All of the calculated values are about the solubility in water. See Section 3.2.3.4.1
Low	1.70	mg/L	
High	3.63	mg/L	
Bioconcentration factor (***BCF***$_{(kg\ fish/L)}$)	40	kg fish/L	WSB03.BCFWA
Concentrations in fish (FC) (***WC*** × ***BCF***) (mg/kg)			
Central	40	mg/kg fish	NOTE: Use water solubility of 1 mg/L for the concentration in water. See Section 3.2.3.4.1
Low	40		
High	40		
Fish consumed as a proportion of body weight (P_F)			
typical	0.1	g fish/g bw	Various species based on values from U.S. EPA (1993b).
lower	0.05		
upper limit	0.15		
Dose estimates (D) (**FC × P_F**)			
Typical	4.00	mg/kg bw/day	
Lower	2.00	mg/kg bw/day	
Upper	6.00	mg/kg bw/day	
Reproductive NOAEL	60	mg/kg/day	Section 4.1.2.2.
Hazard Quotient (HQ) ***(D÷NOAEL)***			
Typical	0.07	mg/kg bw/day	
Lower	0.03	mg/kg bw/day	
Upper	0.1	mg/kg bw/day	

Worksheet F09: Consumption of contaminated fish by predatory bird, chronic exposure scenario. *[FISHBIRDCHRONIC]*			
***Verbal Description**: An predatory bird consumes fish taken from contaminated ambient water for a lifetime. The levels in water are estimated from monitoring and modeling data and dissipation, degradation and other environmental processes are considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates (***R*** $_{\text{(lb a.i./acre)}}$)			
Central	0.75	lb a.i./gal	WSB01.Typ
Low	0.75		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{\text{(mg/L)}}$÷***R*** $_{\text{(lb a.i./gal)}}$)			
Central	0.03402	mg/L/lb a.i./acre	WSB07.AWT
Low	0.03402		WSB07.AWL
High	0.04536		WSB07.AWU
Water Concentrations (WC) (***WCR*** × ***R***) (mg/L)			
Central	0.025515	mg/L/lb a.i./acre	
Low	0.025515		
High	0.04536		
Bioconcentration factor (***BCF*** $_{\text{(kg fish/L)}}$)	70	kg fish/L	WSB03.BCFWhl
Concentrations in fish (FC) (***WC*** × ***BCP***) (mg/kg)			
Central	1.78605	mg/L/lb a.i./acre	
Low	1.78605		
High	3.1752		
Fish consumed as a proportion of body weight (P_F)			
typical	0.1	g fish/g bw	Various species based on values from U.S. EPA (1993b).
lower	0.05		
upper limit	0.15		
Dose estimates (D)			
Typical	0.178605	mg/kg bw/day	
Lower	0.0893025	mg/kg bw/day	
Upper	0.47628	mg/kg bw/day	
Reproductive NOAEL	60	mg/kg/day	Section 4.1.2.2.
Risk Quotient (RQ) ***(D÷NOAEL)***			
Typical	0.00297675	mg/kg bw/day	
Lower	0.001488375	mg/kg bw/day	
Upper	0.007938	mg/kg bw/day	

Worksheet F10: Consumption of contaminated vegetation by a large mammal, acute exposure scenario. *[VGCLMA]*			
***Verbal Description**: A 70 kg herbivore, such as a deer, consumes range grass 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 range grass from Hoerger and Kenaga (1972) summarized in Worksheet A05a. Caloric requirements are used to estimate food consumption from U.S. EPA (1993b).*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	70	kg	N/A
Caloric requirement (***KR***)	5226	kcal/day	U.S. EPA (1993b, p. 3-6)
	above based on following equation: $\boldsymbol{kcal/day = 1.518 \times W(g)^{0.73}}$		
Caloric content of vegetation (dry weight, ***KCD***)	2.46	kcal/g	U.S. EPA (1993b, p. 3-5)
Water content of vegetation (proportion, ***PW***)	0.85	unitless	U.S. EPA (1993b, p. 4-14)
Caloric content of vegetation (wet weight, ***KCW***)	0.37	kcal/g	***KCD*** × (1-***PW***)
Food consumed per day (wet weight, ***A***)	14	kg	(***KR*** ÷ ***KCW***)/1000 g/kg
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Conc. in Vegetation (***C***) [***R***×***rr***]			
Typical	26.25	mg/kg	Note: lower value based on typical ***rr*** and lower ***R***.
Lower	26.25	mg/kg	
Upper	125	mg/kg	
Dose estimates (***D***) ***[C × A ÷W]***			
Typical	5.3	mg/kg bw	VGCSMAC
Lower	5.3	mg/kg bw	VGCSMAL
Upper	25.3	mg/kg bw	VGCSMAU
NOAEL for Assessing Hazard (***NOAEL***)	5	mg/kg/day	Section 3.3.3.
Hazard Quotient (***HQ***) [***D ÷ NOAEL***]			
Typical	1.1	unitless	
Lower	1.1	unitless	
Upper	5	unitless	

[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.i./acre applied.

Worksheet F11: Consumption of contaminated vegetation by a large mammal, chronic exposure scenario. *[VGCLMC]*			
***Verbal Description**: A 70 kg herbivore, such as a deer, consumes range grass for a 90 day period after application of the chemical. The contaminated vegetation accounts for 10 to 100% of the diet. Residue estimates based on relationships for range grass from Hoerger and Kenaga (1972) summarized in Worksheet A05a.* Caloric requirements are used to estimate food consumption from U.S. EPA (1993b). *Dissipation is considered using the foliar halftime and taking the geometric mean of the initial and day-90 residues as the measure of dose.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	70	kg	N/A
Caloric requirement (***KR***)	5226	kcal/day	U.S. EPA (1993b, p. 3-6)
above based on following equation: $\boldsymbol{kcal/day = 1.518 \times W(g)^{0.73}}$			
Caloric content of vegetation (dry weight, ***KCD***)	2.46	kcal/g	U.S. EPA (1993b, p. 3-5)
Water content of vegetation (proportion, ***PW***)	0.85	unitless	U.S. EPA (1993b, p. 4-14)
Caloric content of vegetation (wet weight, ***KCW***)	0.37	kcal/g	***KCD*** × (1-***PW***)
Food consumed per day (wet weight, ***A***)	14	kg	(***KR*** ÷ ***KCW***)/1000 g/kg
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Day 0 Conc. in Vegetation (C_0) [***R***×***rr***]			
Typical	26.25	mg/kg	Note: lower value based on typical ***rr*** and lower ***R***.
Lower	26.25	mg/kg	
Upper	125	mg/kg	
Foliar dissipation coefficient (***k***)			
Typical	0.012378	$days^{-1}$	Worksheet B02
Lower	0.00797	$days^{-1}$	
Upper	0.020387	$days^{-1}$	
Day 90 Conc. in Vegetation (C_{90}) [$C_0 \times e^{-k \times 90\ days}$]			
Typical	8.6165041	mg/kg	
Lower	4.1906868	mg/kg	
Upper	61.02386	mg/kg	
Central Estimate of Conc. in Vegetation (C_{Ave}) [$(C_0 \times C_{90})^{0.5}$]			
Typical	15.039389	mg/kg	
Lower	10.488352	mg/kg	
Upper	87.34	mg/kg	

Worksheet F11 *(continued)*: Consumption of contaminated vegetation by a large mammal, chronic exposure scenario			
Proportion of diet contaminated (***P_D***)			
Typical	0.3	Unitless	See section 4.2.2.3.
Lower	0.1	Unitless	
Upper	1.0	Unitless	
Dose estimates (***D***) [***C_{Ave} × A ÷W***]			
Typical	0.9129	mg/kg bw	
Lower	0.21221505	mg/kg bw	
Upper	17.67	mg/kg bw	
Systemic Toxicity NOAEL (***$NOAEL_T$***)	5	mg/kg/day	Section 3.3.3.
Toxicity Hazard Quotient (***HQ***) [***D ÷ $NOAEL_T$***]			
Typical	0.183	unitless	
Lower	0.04244301	unitless	
Upper	3.5	unitless	
Repro. NOAEL (***$NOAEL_R$***)	125	mg/kg/day	Section 3.3.3.
Repro. Hazard Quotient (***rHQ***) [***D ÷ $NOAEL_R$***]			
Typical	0.0073	unitless	
Lower	2e-03	unitless	
Upper	0.14	unitless	
[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.i./acre applied.			

Worksheet F12: Consumption of contaminated vegetation by a large bird, acute exposure scenario. *[VGCLBA]*			
***Verbal Description**: A 4 kg herbivorous bird, such as a Canada Goose, consumes range grass 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 range grass from Hoerger and Kenaga (1972) summarized in Worksheet A05a.* from U.S. EPA (1993b).			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	4	kg	N/A
Caloric requirement (***KR***)	471	kcal/day	U.S. EPA (1993b, Eq. 3-35, p. 3-22)
above based on following equation: ***kcal/day = 3.12 × W(g)$^{0.604}$***			
Caloric content of vegetation (dry weight, ***KCD***)	2.46	kcal/g	U.S. EPA (1993b, p. 3-5)
Water content of vegetation (proportion, ***PW***)	0.85	unitless	U.S. EPA (1993b, p. 4-14)
Caloric content of vegetation (wet weight, ***KCW***)	0.37	kcal/g	***KCD*** × (1-***PW***)
Food consumed per day (wet weight, ***A***)	1.28	kg	(***KR*** ÷ ***KCW***)/1000 g/kg
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Conc. in Vegetation (***C***) [***R***×***rr***]			
Typical	26.25	mg/kg	Note: lower value based on typical ***rr*** and lower ***R***.
Lower	26.25	mg/kg	
Upper	125	mg/kg	
Dose estimates (***D***) ***[C × A ÷W***]			
Typical	8.4	mg/kg bw	VGCSMAC
Lower	8.4	mg/kg bw	VGCSMAL
Upper	39.9	mg/kg bw	VGCSMAU
Reproductive NOAEL (***NOAEL***)	60	mg/kg/day	Section 4.1.2.2.
Hazard Quotient (***HQ***) [***D ÷ NOAEL***]			
Typical	0.14	unitless	
Lower	0.14	unitless	
Upper	0.7	unitless	

[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.i./acre applied.

Worksheet F13: Consumption of contaminated vegetation by a large bird, chronic exposure scenario. *[VGCLBC]*			
***Verbal Description**: A 4 kg herbivorous bird, such as a Canada Goose, consumes range grass for a 90 day period after application of the chemical. The contaminated vegetation accounts for 10 to 100% of the diet. Residue estimates based on relationships for range grass from Hoerger and Kenaga (1972) summarized in Worksheet A05a.* Caloric requirements are used to estimate food consumption from U.S. EPA (1993b). *Dissipation is considered using the foliar halftime and taking the geometric mean of the initial and day-90 residues as the measure of dose.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	4	kg	N/A
Caloric requirement (***KR***)	471	kcal/day	U.S. EPA (1993b, p. 3-6)
	above based on following equation: $kcal/day = 3.12 \times W(g)^{0.604}$		
Caloric content of vegetation (dry weight, ***KCD***)	2.46	kcal/g	U.S. EPA (1993b, p. 3-5)
Water content of vegetation (proportion, ***PW***)	0.85	unitless	U.S. EPA (1993b, p. 4-14)
Caloric content of vegetation (wet weight, ***KCW***)	0.37	kcal/g	***KCD*** × (1-***PW***)
Food consumed per day (wet weight, ***A***)	1.3	kg	(***KR*** ÷ ***KCW***)/1000 g/kg
Duration of exposure (***D***)	90	days	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Day 0 Conc. in Vegetation (C_0) [$R \times rr$]			
Typical	26.25	mg/kg	Note: lower value based on typical ***rr*** and lower ***R***.
Lower	26.25	mg/kg	
Upper	125	mg/kg	
Foliar dissipation coefficient (***k***)			
Typical	0.012378	$days^{-1}$	Worksheet B02
Lower	0.00797	$days^{-1}$	
Upper	0.020387	$days^{-1}$	
Day 90 Conc. in Vegetation (C_{90}) [$C_0 \times e^{-k \times 90\ days}$]			
Typical	8.6165	mg/kg	
Lower	4.1906868	mg/kg	
Upper	61.02386	mg/kg	
Central Estimate of Conc. in Vegetation (C_{Ave}) [$(C_0 \times C_{90})^{0.5}$]			
Typical	15.039389	mg/kg	
Lower	10.488352	mg/kg	
Upper	87.34	mg/kg	

Worksheet F13 *(continued)*: Consumption of contaminated vegetation by a large bird, chronic exposure scenario			
Proportion of diet contaminated (***P_D***)			
Typical	0.3	Unitless	See section 4.2.2.3.
Lower	0.1	Unitless	
Upper	1.0	Unitless	
Dose estimates (***D***) ***[C_{Ave} × A ÷W***]			
Typical	1.4410	mg/kg bw	
Lower	0.3349822	mg/kg bw	
Upper	27.89	mg/kg bw	
Repro. NOAEL (***$NOAEL_R$***)	60	mg/kg/day	Section 4.1.2.2.
Repro. Hazard Quotient (***HQ***) [***D ÷ $NOAEL_R$***]			
Typical	0.0240	unitless	
Lower	6e-03	unitless	
Upper	0.46	unitless	
[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.i./acre applied.			

Worksheet F14: Consumption of contaminated insects by a small bird, acute exposure scenario. *[VGCSBA]*			
***Verbal Description**: A small insectivorous bird (10g) bird consumes insects shortly after application of the chemical - i.e. no dissipation or degradation is considered. The contaminated food accounts for 100% of the diet. Residue estimates in insects are based on relationships for seed containing pods and forage crops from Hoerger and Kenaga (1972) summarized in Worksheet A05a.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	0.01	kg	N/A
Caloric requirement (***KR***)	13	kcal/day	U.S. EPA (1993b, Eq. 3-35, p. 3-22)
	above based on following equation: ***kcal/day = 3.12 × W(g)$^{0.604}$***		
Caloric content of insects (dry weight, ***KCD***)	4.3	kcal/g	U.S. EPA (1993b, p. 3-5)
Water content of insects (proportion, ***PW***)[2]	0.65	unitless	U.S. EPA (1993b, p. 4-13)
Caloric content of insects (wet weight, ***KCW***)	1.51	kcal/g	***KCD*** × (1-***PW***)
Food consumed per day (wet weight, ***A***)	0.01	kg	(***KR*** ÷ ***KCW***)/1000 g/kg
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.75	lb a.i./acre	WSB01.Typ
Lower	0.75	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	33	RUD[1]	WSA05a.FCT
Lower	3	RUD[1]	WSA05a.PDT
Upper	58	RUD[1]	WSA05a.FCU
Conc. in Vegetation (***C***) [***R***×***rr***]			
Typical	24.75	mg/kg	Note: lower value based on typical ***rr*** for pods. Lower ranges not provided in Hoerger and Kenaga (1972)
Lower	2.25	mg/kg	
Upper	58	mg/kg	
Dose estimates (***D***) [***C*** × ***A*** ÷***W***]			
Typical	20.66	mg/kg bw	
Lower	1.878	mg/kg bw	
Upper	48.4	mg/kg bw	
Reproductive NOAEL (***NOAEL***)	60	mg/kg/day	Section 4.1.2.2.
Hazard Quotient (***HQ***) [***D*** ÷ ***NOAEL***]			
Typical	0.34	unitless	
Lower	0.031	unitless	
Upper	0.8	unitless	

[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.i./acre applied.
[2] Average of beetles (61%) and grasshoppers (69%) from U.S. EPA (1993b, Table 4-1, p. 4-13)

Worksheet G01: Summary of Exposure Scenarios for Terrestrial Animals.

Scenario	Dose (mg/kg/day) Typical	Lower	Upper	Worksheet
Acute/Accidental Exposures				
Direct spray				
small mammal, first-order absorption	0.73	0.35	2.1	WSF01
small animal, 100% absorption	18	18	24	WSF02
bee, 100% absorption	122	122	163	WSF03
Contaminated vegetation				
small mammal	3.9	3.9	19	WSF04
large mammal	5.3	5.3	25	WSF10
large bird	8.4	8.4	40	WSF12
Contaminated water				
small mammal	0.25	0.25	0.25	WSF06
Contaminated insects				
small bird	21	1.9	48	WSF14
Contaminated fish				
predatory bird	4.0	2.0	6.0	WSF08
Longer-term Exposures				
Contaminated vegetation				
small mammal	2.2	0.034	0.11	WSF05
large mammal	0.91	0.21	18	WSF11
large bird	1.4	0.34	28	WSF13
Contaminated water				
small mammal	0.006	0.006	0.011	WSF07
Contaminated fish				
predatory bird	0.18	0.09	0.48	WSF08

[a] All values rounded to two significant digits.

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	0.1	0.07	0.4
small animal, 100% absorption	**3.7**	**3.7**	**4.9**
bee, 100% absorption	0.1	0.1	0.15
Contaminated vegetation			
small mammal, toxicity	0.8	0.8	**3.8**
small mammal, reproduction	0.03	0.03	0.2
large mammal, toxicity	**1.1**	**1.1**	**5**
large mammal, reproduction	0.04	0.042	0.2
large bird, reproduction	0.1	0.1	0.7
Contaminated water			
small mammal, toxicity	0.1	0.1	0.1
small mammal, reproduction	0.002	0.002	0.00
Contaminated insects			
small bird, reproduction	0.3	0.03	0.8
Contaminated fish			
predatory bird, reproduction	0.07	0.03	0.1
Longer-term Exposures			
Contaminated vegetation			
small mammal, toxicity	0.4	0.007	0.0
small mammal, reproduction	0.02	0.0003	0.001
large mammal, toxicity	0.2	0.04	**3.5**
large mammal, reproduction	0.007	0.002	0.1
large bird, reproduction	0.02	0.006	0.5
Contaminated water			
small mammal	0.001	0.001	0.002
Contaminated fish			
predatory bird	0.003	0.001	0.01
Toxicity Indices [3]			
General toxicity value for mammal - NOAEL		5	mg/kg/day
Reproductive toxicity value for mammal - NOAEL		125	mg/kg/day
Reproductive toxicity value for bird - NOAEL		60	mg/kg/day
Toxicity value for bee - not lethal		1075	mg/kg

[1] See Worksheet G01 (Table 4-1 in text) for summary of exposure assessment.
[2] Estimated dose ÷ toxicity index then round to one significant digit or decimal place.
[3] See Section 4.3 for a discussion of the toxicity indices.