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Tebuthiuron:
Human Health and Ecological Risk Assessment
FINAL REPORT

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Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF Appendices

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ACR	acute-to-chronic ratio
AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
a.k.a.	also known as
a.s.	active substance
APHIS	Animal and Plant Health Inspection Service
ARI	Aggregate Risk Index
ASAE	American Society of Agricultural Engineers
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
CI	confidence interval
cm	centimeter
CNS	central nervous system
COC	crop oil concentrates
DAA	days after application
DAT	days after treatment
DER	data evaluation record
DF	dry flowable
d.f.	degrees of freedom
EC	emulsifiable concentrate
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
ECOTOX	ECOTOXicology (database used by U.S. EPA/OPP)
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FACTS	Forest ACtivity Tracking System
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FIRST	FQPA Index Reservoir Screening Tool
FOIA	Freedom of Information Act
FQPA	Food Quality Protection Act
g	gram
GLP	Good Laboratory Practices
GR_{50}	50% inhibition of growth (plant bioassays)
ha	hectare
HASPOC	Hazard and Science Policy Council
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient

HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IRED	Interim Reregistration Eligibility Decision
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEC	lowest-observed-adverse-effect concentration
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
LR_{50}	50% lethal response [EFSA/European term]
m	meter
M	male
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOE	margin of exposure
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MSO	methylated seed oil
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
NIOSH	National Institute for Occupational Safety and Health
NIS	nonionic surfactant
NK	Natural killer (immune cells)
NOAEC	no-observed-adverse-effect concentration
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
N.R.	not reported
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances

OSHA	Occupational Safety and Health Administration
Pa	Pascal
PBPK	physiologically-based kinetic
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
RQ	Risk Quotient
SERA	Syracuse Environmental Research Associates
SRBC	sheep red blood cells
TEP	typical end-use product
T.G.I.A.	Technical grade active ingredient
TRED	Tolerance Reassessment Eligibility Decision
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
VMD	volume median diameter (for droplet size distributions)
WCR	Water Contamination Rate
WG	water dispersible granule
WHO	World Health Organization
WWSA	Weed Science Society of America

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

Tebuthiuron is a soil active herbicide used in Forest Service programs primarily for the control of woody vegetation. The formulations most likely to be used in forestry related applications consist of either 20% a.i. pellets applied directly to soil (e.g., Spike 20P or Tebuthiuron 20 P) or 80% a.i. water dispersible granules/dry flowable formulations that are mixed with water prior to application (e.g., Spike 80DF; Tebuthiuron 80 WG). All formulations may be applied with ground equipment or aerially. Both ground and aerial applications are considered in this risk assessment.

The maximum labeled application rate for tebuthiuron is 6 lbs a.i./acre. This maximum application rate is substantially higher than application rates typically used in Forest Service programs. Based on use statistics from the Forest Service, the current risk assessment uses a typical application rate of 0.6 lb a.i./acre in the EXCEL workbooks that accompany this risk assessment.

Use of tebuthiuron and other pesticides by the Forest Service requires development of a risk assessment, which is used to evaluate whether the application of a pesticide might pose harm to humans or other species in the environment. The quantitative risk characterization in both the human health and in the ecological risk assessment is based on the hazard quotient (HQ), which is defined as the anticipated exposure divided by a toxicity value that is not likely to be associated with adverse effects. Thus, an HQ of greater than 1 is defined as the level of concern. For all non-accidental exposure scenarios, the HQs are linearly related to the application rate.

For workers, none of the central estimates of the HQs associated with anticipated applications of tebuthiuron exceeds the level of concern; however, the upper bound estimates of the HQs exceed the level of concern for backpack applications (HQ = 3) and aerial applications (HQ = 1.4). While these HQs are relatively modest exceedances above the level of concern, the toxicological endpoint for women of childbearing age involves fetal resorptions—i.e., early fetal death. This endpoint is, of course, a serious adverse effect. While HQs should not be considered predictive–i.e., an HQ of 1.3 to 3 might not necessarily lead to adverse effects on the fetus—the exceedances above the level of concern dictate that female workers of childbearing age should exercise extreme caution and implement all appropriate safety measures when applying tebuthiuron.

As with workers, none of the central estimates of HQs exceeds the level of concern for members of the general public. Even at the upper bounds of expected exposures, none of the HQs for granular/pellet applications of tebuthiuron exceeds the level of concern. The same is not true for liquid applications of tebuthiuron. At the upper bounds of anticipated exposures following liquid applications, exceedances in the level of concern occur for the acute consumption of contaminated fruit (HQ = 1.1), the acute consumption of contaminated broadleaf vegetation (HQ = 8), and the longer-term consumption of contaminated broadleaf vegetation (HQ = 3). For all of these exposure scenarios, the receptor is a young woman of childbearing age. Also as with the risk characterization for workers, exceedances in the level of concern for young women in the general public should be viewed with substantial concern for potential effects on the developing fetus. Without minimizing this concern, it must be stated that the upper bound exposure estimates which form the basis of these HQs are extreme and should be viewed as possible but not typical or expected levels of exposure in most cases. Moreover, undue exposure to tebuthiuron from consumption of contaminated fruit or vegetation would not ordinarily be expected under most uses of the herbicide by the Forest Service in sparsely inhabited areas (rangeland, woodlands, etc.). Qualitatively, the risk characterization for the general public involving non-accidental exposures clearly suggests that granular applications raise no substantial concerns, relative to those posed by liquid applications.

For both workers and members of the general public, several accidental exposure scenarios lead to HQs that exceed the level of concern. This finding is typical of most Forest Service pesticide risk assessments and reflects the extreme nature of the accidental exposure scenarios. As with virtually any pesticide, accidental exposures should be avoided. If accidental exposures occur, sensible steps should be taken to mitigate the exposure and ensure that exposed individuals receive prompt and effective medical care. As with the non-accidental exposures, women of childbearing age are the group that could be most severely affected.

While tebuthiuron is an effective herbicide for the control of woody vegetation, it is not exclusively selective, and the sensitivities of dicots and monocots to tebuthiuron overlap substantially. Consequently, tebuthiuron can adversely affect sensitive species of monocots as well as woody vegetation and other dicots. Nonetheless, the HQs for impacts on nontarget vegetation are not remarkably high for an effective herbicide. The highest HQ for sensitive species of vegetation is 10, which is associated with direct spray. For runoff scenarios, the upper bound HQ for sensitive species of vegetation is 7. If water contaminated with tebuthiuron is used for irrigation, the upper bound HQ for sensitive species of vegetation is 4. For all exposure scenarios, including direct spray, the HQs for tolerant species of vegetation are below the level of concern. The impact of tebuthiuron on vegetation, both target and nontarget, is documented in numerous field studies. The relatively modest HQs for tebuthiuron in the current risk assessment are due primarily to the relatively low typical application rate proposed by the Forest Service—i.e., 0.6 lb a.i./acre.

The most substantial nontarget impact of tebuthiuron applications made near surface water will involve effects on algae. Direct effects on fish and invertebrates are unlikely. The available toxicity data in algae indicate that differences in their sensitivities to tebuthiuron are much less than differences in the sensitivities of terrestrial macrophytes. Based on estimated peak concentrations in surface water, adverse effects in algae may be anticipated at the upper bounds of acute exposure for both sensitive and tolerant species and at the central and upper bound estimates of acute exposure for sensitive species. Over prolonged periods after tebuthiuron is applied at a rate of 0.6 lb a.i./acre, adverse effects could be apparent at the upper bounds of exposure for both sensitive and tolerant species of algae. In practical terms, the most important factor in refining the risk characterization for algae involves site-specific conditions. For instance, at sites or in regions where water contamination might be minimal due to weather or depending on the distance of surface water from the application site, risks to algae could be minimal.

The risk characterization for both mammals and birds differs depending on the type of formulation applied. Applications of granular formulations, relative to liquid formulations, will lead to lower concentrations of tebuthiuron in vegetation, the major route of exposure for mammals and birds. Following applications of granular formulations, risks to mammals and birds are minimal. Following applications of liquid formulations, risks to sensitive species of mammals and birds could substantially exceed the level of concern. The risk characterization for mammals is based on rabbits (Order Lagomorpha), the group of mammals apparently most sensitive to tebuthiuron. The available data indicate that rodents (Order Rodentia) are much less sensitive than rabbits to tebuthiuron and are not likely to be adversely affected. The sensitivities of other groups of mammals to tebuthiuron are not known.

The data on the toxicity of tebuthiuron to terrestrial invertebrates is sparse—i.e., limited to a single bioassay in honeybees and some field observations. Based on these data, effects on terrestrial invertebrates appear to be unlikely. No data are available on the toxicity of tebuthiuron to reptiles or amphibians (terrestrial or aquatic phase). Thus, no risk characterization for reptiles and amphibians has been developed for this risk assessment.

While the risk characterization for tebuthiuron focuses on the potential for direct toxic effects, there is also a potential for indirect effects in virtually all groups of nontarget organisms. The best documented indirect effect of tebuthiuron involves terrestrial vegetation. Consistent with the labelled uses of tebuthiuron, several efficacy studies indicate that tebuthiuron will reduce canopy cover (woody vegetation) and encourage the growth of grasses. Alterations in vegetation following the application of any effective herbicide, including tebuthiuron, could also have a cumulative impact on animals. These alterations in vegetation may be beneficial to some species and detrimental to others; moreover, the magnitude of the impact is likely to vary over time. The potential for cumulative impacts on animals is documented in field studies but to a much lesser extent than impacts on nontarget vegetation. If algae are adversely affected by tebuthiuron, indirect effects on aquatic invertebrates and fish could be detrimental due to a decrease in available food.

1. INTRODUCTION

1.1. Chemical Specific Information

Tebuthiuron is a herbicide used by the Forest Service in vegetation management programs. The present document provides human health and ecological risk assessments on the Forest Service use of this herbicide.

No relatively recent risk assessment on tebuthiuron has been developed by or for the Forest Service. A chemical background statement on tebuthiuron was prepared by the Forest Service in the mid-1980s (Sassaman and Jacobs 1986), and tebuthiuron is included in a risk assessment of Bonneville Power Administration Sites prepared for the Forest Service in the early 1990s (USDA/FS 1992). Other reviews and/or analyses of tebuthiuron have been prepared by or for the Canadian Council of Ministers of the Environment (1999a,b; Caux et al. 1997), the Bureau of Land Management (ENSR 2005), the Extension Toxicology Network (EXTOXNET 1993), the National Library of Medicine (HSDB 2015), the Department of Energy (DOE 2000). For the most part, these and other reviews of tebuthiuron are used primarily to identify key studies from the open literature and not as direct sources of information. Exceptions to this approach are discussed in the body of this risk assessment as appropriate.

The U.S. EPA's Office of Pesticide Programs (U.S. EPA/OPP) has the regulatory authority for the registration of pesticides. As discussed further in Section 2.2, tebuthiuron was originally registered in the United States in 1974 and reregistered in 1994 (U.S. EPA/OPP 1015, p. 11). Most of the studies required for registration and reregistration are summarized in the Reregistration Eligibility Decision (RED) document on tebuthiuron (U.S. EPA/OPP 1994). Further details of studies related to human health effects are given in the documentation for the tolerance reassessment of tebuthiuron (U.S. EPA/OPP/HED 2002). In addition to the initial reregistration of and tolerance reassessment for tebuthiuron, tebuthiuron is currently under registration review (U.S. EPA/OPP 2009a, p. 7). In support of the registration review, the EPA released initial risk assessments for both human health (U.S. EPA/OPP/HED 2014a) and ecological effects (U.S. EPA/OPP/EFED 2014a). In addition, the EPA conducted an endangered species assessment of the impact of tebuthiuron use on Pacific Salmon and Steelhead (U.S. EPA/OPP 2004). As discussed further in Section 1.2, the risk assessments and related documents from U.S. EPA/OPP include summaries of the required registrant studies submitted to the EPA. These studies are not available to the general public and were not available for the current risk assessment. Nonetheless, relevant information on these registrant-submitted studies is available in the EPA risk assessments cited above. The registrant-submitted studies are designated by the Master Record Identification Number (MRID number). In the appendices to this risk assessment, the registrant studies are identified by MRID number and the source of the information—i.e., the specific risk assessment from EPA—is specified for each of the studies summarized in the appendices.

The published literature on tebuthiuron was initially identified using TOXLINE (http://toxnet.nlm.nih.gov/). Additional information on tebuthiuron was identified through standard Internet search engines and databases (e.g., HSDB 2010; Kegley et al. 2014; USDA/ARS 1995). While the open literature on tebuthiuron is robust (Section 5, References), most of the published studies involve assays or field applications focused on evaluating the efficacy of tebuthiuron. As with all Forest Service risk assessments on herbicides, efficacy studies are not covered extensively; nevertheless, some of these studies are used to define differences in sensitivity between target and nontarget plants, as discussed further in Section 4.1.2.5.2. Open literature studies are also available on the environmental fate and toxicity of tebuthiuron; however, these studies are dominated by the studies submitted to EPA in support of the registration, reregistration, and registration review of tebuthiuron as specified above.

1.2. General Information

This document has four narrative sections, including the introduction (Section 1), program description (Section 2), risk assessment for human health effects (Section 3), and risk assessment for ecological effects or effects on wildlife species (Section 4). Each of the two risk assessment sections has four major subsections, including an identification of the hazards, an assessment of potential exposure, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure.

This is a technical support document which addresses some specialized technical areas. Nevertheless an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2014a). The human health and ecological risk assessments presented in this document are not and are intended to be comprehensive summaries of all of the available information. On the other hand, the information in the appendices as well as the discussions in Sections 2, 3, and 4 of the risk assessment are intended to be detailed enough to support an independent review of the risk analyses.

As noted in Section 1.1, the studies submitted in support of the registration of tebuthiuron are used extensively in this risk assessment based on information publically available from the U.S. EPA. In any risk assessment based substantially on registrant-submitted studies, the Forest Service is sensitive to concerns of potential bias. The general concern might be expressed as follows:

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

This concern is largely without foundation. While any study (published or unpublished) can be falsified, concerns regarding the design, conduct and reporting of studies submitted to the U.S. EPA for pesticide registration are misplaced. The design of the studies submitted for pesticide registration is based on strict guidelines for both the conduct and reporting of studies. These guidelines are developed by the U.S. EPA and not by the registrants. Full copies of the guidelines for these studies are available at http://www2.epa.gov/test-guidelines-pesticides-and-toxic-substances. Virtually all studies accepted by the U.S. EPA/OPP are conducted under Good Laboratory Practices (GLPs). GLPs are an elaborate set of procedures which involve documentation and independent quality control and quality assurance that substantially exceed the levels typically seen in open literature publications. As a final point, the EPA reviews each submitted study for adherence to the relevant study guidelines. These reviews most often take the form of Data Evaluation Records (DERs). While the nature and complexity of DERs varies according to the nature and complexity of the particular studies, each DER involves an independent assessment of the study to ensure that the EPA Guidelines are followed and that the results are expressed accurately. In many instances, the U.S. EPA/OPP will reanalyze raw data from the study as a check or elaboration of data analyses presented in the study. In addition, each DER undergoes internal review (and sometimes several layers of review). The DERs prepared by the U.S. EPA form the basis of EPA risk assessments and, when available, DERs are used in Forest Service risk assessments.

While data quality and data integrity are normally not substantial concerns, risk assessments may be limited by the nature and diversity of registrant-submitted studies. The studies from registrants required by the U.S. EPA are based on a relatively narrow set of criteria in a relatively small subset of species and follow standardized protocols. The relevance of this limitation to the current risk assessment on tebuthiuron is noted in various parts of this risk assessment as appropriate. As discussed in Section 1.1, the open literature on tebuthiuron is focused on efficacy studies. Nonetheless, the open literature is used quantitatively in the current risk assessment as appropriate. Any use of open literature data in preference to registrant studies used by the EPA is discussed in detail in the body of this risk assessment.

The Forest Service periodically updates pesticide risk assessments and welcomes input from the general public and other interested parties on the selection of studies included in risk assessments. This input is helpful, however, only if recommendations for including additional studies specify why and/or how the new or not previously included information would be likely to alter the conclusions reached in the risk assessments.

As with all Forest Service risk assessments, almost no risk estimates presented in this document are given as single numbers. Usually, risk is expressed as a central estimate and a range, which is sometimes quite large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations, most of which are relatively simple. Simple calculations are included in the body of the document [typically in brackets]. The results of some calculations within brackets may contain an inordinate number of significant figures in the interest of transparency— i.e., to allow readers to reproduce and check the calculations. In all cases, these numbers are not used directly but are rounded to the number of significant figures (typically two or three) that can be justified by the data.

Notwithstanding the above, some of the calculations used in this risk assessment are cumbersome. For those calculations, EXCEL workbooks (i.e., sets of EXCEL worksheets) are included as attachments to this risk assessment. The workbooks included with the current risk assessment are discussed in Section 2.4. The worksheets in these workbooks provide the detail for the estimates cited in the body of the document. Documentation for the use of these workbooks is presented in SERA (2011a).

The EXCEL workbooks are integral parts of the risk assessment. The worksheets contained in these workbooks are designed to isolate the numerous calculations from the risk assessment narrative. In general, all calculations of exposure scenarios and quantitative risk characterizations are derived and contained in the worksheets.

In these worksheets as well as in the text of this risk assessment, the hazard quotient (HQ) is used to characterize risk. The HQ is the ratio of the estimated exposure to a toxicity value, typically a no adverse effect level or concentration (e.g. RfD, NOAEL or NOAEC). Both the rationale for the calculations and the interpretation of the hazard quotients are contained in this risk assessment document. Additional details of the general use of HQs in Forest Service risk assessments are given in SERA (2014a).

2. PROGRAMS DESCRIPTION

2.1. Overview

Tebuthiuron is a soil active herbicide – i.e., the herbicide is intended to be applied to soil rather than to foliage – used primarily for the control of woody vegetation. Following application to soil, the herbicide is taken up by plant roots with resulting damage to the plants. While tebuthiuron is considered to be a nonselective herbicide, dicots appear to be somewhat more sensitive than monocots.

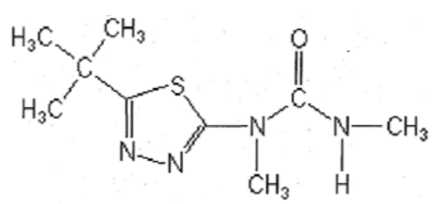
Tebuthiuron is not currently registered for either application to agricultural crops or residential use. The primary uses of tebuthiuron involve applications to pastures/rangeland. Tebuthiuron inhibits photosynthesis and is classified by the Herbicide Resistance Action Committee (HRAC) as a Group C_2 herbicide along with herbicides such as diuron. As discussed further in Section 4.1.2.5 (hazard identification terrestrial plants), the development of resistance by target plants is an issue with tebuthiuron and the HRAC resistance classifications are used as a guide to reduce the potential for resistance in long-term vegetation management programs.

The formulations most likely to be used in forestry related applications consist of either 20% a.i. pellets which are applied directly to soil (e.g., Spike 20P or Tebuthiuron 20 P) or 80% a.i. water dispersible granules/dry flowable formulations that are mixed with water prior to application (e.g., Spike 80DF; Tebuthiuron 80 WG). All formulations may be applied with ground equipment or aerially. Both ground and aerial applications are considered in this risk assessment.

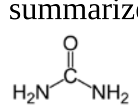
The maximum labeled application rate for tebuthiuron is 6 lbs a.i./acre; however, this application rate applies only to spot applications. This maximum application rate appears to be substantially higher than application rates that would be used in Forest Service programs. Based on use statistics from the Forest Service, the current risk assessment uses a typical application rate of 0.6 lb a.i./acre in the EXCEL workbooks that accompany this risk assessment.

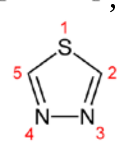
2.2. Chemical Description and Commercial Formulations

Tebuthiuron is the common name for N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N,N'-dimethylurea:

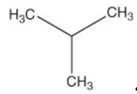


The chemical and physical properties of tebuthiuron are summarized in Table 1.

Structurally, tebuthiuron consists of a molecule of urea, 

, substituted with methyl groups on the two urea nitrogens as well as a thiadiazole (

) group on one of the urea

nitrogens. The thiadiazole is in turn substituted in the 5-carbon position with a 1,1-dimethylethyl group,  .

The herbicidal properties of tebuthiuron were first reported by Schwer (1974). As discussed in Section 4.1.2.5, tebuthiuron is an inhibitor of photosynthesis. Tebuthiuron is generally considered to be a nonselective herbicide (e.g., U.S. EPA/OPP 1994; U.S. EPA/OPP/EFED 2014a). While dicots, as a group, are somewhat more sensitive to tebuthiuron than monocots, the differences among species of dicots and species of monocots can be more or equally substantial than the differences between monocots as a group and dicots as a group (Section 4.1.2.5.1).

In terms of weed resistance, tebuthiuron is classified as Group 6 by the Weed Science Society of America or Group C_2 by the Herbicide Resistance Action Committee (HRAC). Other urea herbicides with this resistance classification include diuron, fluometuron, linuron, metbromuron, monolinuron, and siduron (Mallory-Smith and Retzinger 2003). While these herbicides share a common mechanism of phytotoxicity, specific sites of action may vary, leading to differences in species sensitivities (Diaz et al. 2005). Based on pesticides listed at the EPA pesticide search site (http://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:1:4620718240799::NO:1::) and the PAN Pesticide Database (http://www.pesticideinfo.org/), all of the photosystem II herbicides except metobromuron and monolinuron have active registrations in the United States. The Forest Service has not previously conducted recent risk assessments on any of the Group 6/Group C_2 herbicides.

The Forest Service has indicated that tebuthiuron will be used primarily to control shrubs (sagebrush, chaparral, etc.) and small trees (e.g., juniper) encroaching on grasslands or rangelands (e.g., Haywood 1993; Ruppel 2015; White 2015). Tebuthiuron is registered for these uses but is not registered for either agricultural crops used for human consumption or residential use (U.S. EPA/OPP/HED 2014a, p. 8). In the reregistration of tebuthiuron, agricultural commodities that could be treated with tebuthiuron were limited to hay and forage—i.e., commodities not consumed by humans (U.S. EPA/OPP 1994, p. 37). As noted in Section 2.5, use data from USGS indicates that tebuthiuron has been applied to soybeans. No EPA documents supporting the use of tebuthiuron on soybeans or other crops consumed by humans, however, have been identified.

The herbicidal properties of tebuthiuron were initially discovered by Air Products and Chemicals Incorporated (Loh et al. 1980) but the herbicide was introduced commercially in Brazil by Eli Lilly and Company, currently Dow AgroSciences (Tomlin 2004). The RED (Registration Eligibility Decision) for tebuthiuron indicates that this herbicide was registered in the United States in 1974 to Elanco Products Company and that the registration was transferred to DowElanco in 1989 (U.S. EPA/OPP 1994).

Tebuthiuron is currently off-patent. The Pesticide Action Network chemical database and the Greenbook label database (www.Greeenbook.net) indicate that there are 15 active product registrations in the United States from five manufacturers – i.e., Alligare, Dow AgroSciences, Celsius, Rainbow Technology Corporation, and SSI Maxim Co. (Kegley et al. 2014). The Forest

Service has indicated that Spike formulations will be used in Forest Service programs (Ruppel 2015; White 2015). Consistent with these statements and as summarized in Table 2, two Spike formulations of tebuthiuron from Dow AgroSciences are explicitly labelled for rangeland applications—i.e., Spike 20P, Spike 80 DF. As also summarized in Table 2, two additional formulations from Alligare are also explicitly considered—i.e., Tebuthiuron 20 P and Tebuthiuron 80 WG. All of these formulations are considered in the most recent risk human health risk assessment from the EPA (U.S. EPA/OPP/HED 2014a).

The formulations given in Table 2 are not intended to be exclusive. The Forest Service may elect to use any formulation of tebuthiuron registered for applications relevant to forestry. If other formulations are used in Forest Service programs, attempts should be made to identify information on the inerts in the formulations (i.e., ingredients other than tebuthiuron as discussed further in Section 3.1.14.1) as well as the toxicity of the formulations to ensure that the formulations under consideration are comparable to the formulations explicitly designated in Table 2. Material Safety Data Sheets (MSDSs) or Safety Data Sheets (SDSs) for formulations will contain some information on the toxicity of the formulation and/or ingredients in the formulation and additional information may be available from manufacturers or suppliers. For clarity, it should be noted that SDSs are a more recent formatting of information that was typically included in MSDSs. This organizational change is made as part of the Globally Harmonized System (GHS) for classification and labelling of chemicals (e.g., https://www.msdsonline.com/blog/compliance-education/2012/08/20/from-msds-to-sds). Although SDSs are gradually replacing MSDSs, the MSDS is still in common use. As discussed by NAS (2013, p. 120), standard acute mammalian toxicity studies on formulations are required by the U.S. EPA. These studies are typically summarized on MSDS/SDSs. A summary of the standard toxicity studies from MSDSs and SDSs is presented in Appendix 1, Table A1-8, for the representative formulations given in Table 2. These data are discussed in the appropriate subsections of the hazard identification (Section 3).

Some formulations of tebuthiuron are available as a mixture with diuron—e.g., Sprakil SK-13 and Sprakil SK-26 from SSI Maxim Co., Inc. As discussed above, diuron is another HRAC Group C_2 herbicide. As with all Forest Service risk assessments as well as recent EPA risk assessments of tebuthiuron (e.g., U.S. EPA/OPP/HED 2014a, U.S. EPA/OPP/EFED 2014a), applications of different active ingredients combined in a mixture with tebuthiuron are not considered in the current risk assessment. Pesticide mixtures can be considered at the program-specific level using a utility in the most recent version of WorksheetMaker (SERA 2011a).

Pesticide formulations may contain other than active ingredients, sometimes referred to as *inerts*. The identity of the other ingredients is typically classified as proprietary or Confidential Business Information (CBI). U.S. EPA/OPP (2010d, p. 5-13) encourages but does not require the disclosure of most inerts on product labels. No inerts are specified on product labels for Tebuthiuron 80 WG, Tebuthiuron 20 P, Spike 20P, and Spike 80 DF. In some cases, inert ingredients are specified on the Safety Data Sheets (SDS) or Material Safety Data Sheets (MSDS) for formulations. As summarized in Table 3, some inerts are specified on the SDS/MSDS's for the two Spike formulations. The disclosed inerts are discussed further in Section 3.1.14 and in the ecological risk assessment (Section 4) as warranted by the available data.

2.3. Application Methods

Different application methods involve different estimates of the amount of herbicide used by workers in a single day based on the number of acres treated per day and the application rate. Application rates are discussed in Section 2.4, and assumptions about the number of acres treated by a worker in a single day are discussed further in Section 3.2.2 (worker exposure assessments).

As detailed on product labels for tebuthiuron as well as in U.S. EPA/OPP (1994), tebuthiuron is a soil activated herbicide. In applications of tebuthiuron, the intent is to apply the herbicide to soil. Following adequate rainfall, the herbicide is absorbed by and exerts phytotoxic effects on the plant. All formulations of tebuthiuron listed in Table 2 are labeled for both ground and aerial applications. Although ground applications of tebuthiuron are commonly used in Forest Service programs (e.g., USDA/FS 2013), the Forest Service generally has not applied tebuthiuron aerially. However, Region 3 of the Forest Service has indicated that aerial applications of tebuthiuron are likely in the future (Hannemann 2015; White 2015). In addition, the Forest Service indicated that it would consider the use of pelleted formulations of tebuthiuron (i.e., Spike 20P) for use in aerial applications (Neal 2015a; Ruppel 2015a).

As discussed in Section 1.1, this risk assessment is accompanied by EXCEL workbooks that detail the exposure scenarios for tebuthiuron. Based on the anticipated uses of tebuthiuron in Forest Service programs, four EXCEL workbooks are provided. Applications of liquid solutions of tebuthiuron by directed and broadcast ground applications as well as aerial applications are included in Attachment 1. For granular applications of tebuthiuron, separate workbooks are provided for directed ground applications (Attachment 2), broadcast ground applications (Attachment 3), and aerial broadcast applications (Attachment 4).

As discussed above, aerial applications of tebuthiuron are likely to involve only pellet formulations. Nonetheless, the tebuthiuron formulations that are applied as a liquid (e.g., Spike 80DF and Tebuthiuron 80 WG) are labeled for aerial applications. Consequently, both Attachment 1 (liquids) and Attachment 4 (pellets) cover aerial applications in the event that the Forest Service may want to consider aerial applications of liquid solutions as well as pellets.

2.4. Mixing and Application Rates

As discussed above, tebuthiuron is a “soil activated” herbicide—i.e., it is applied to soil and is absorbed from the soil into the plant once the herbicide is dissolved in soil water (e.g., U.S. EPA/OPP 1994, p. iv). Spike 20P and Tebuthiuron 20 P, which are pellet formulations, are applied directly to soil—i.e., no mixing prior to application. Spike 80 DF (dry flowable) and Tebuthiuron 80 WG (water dispersible granule) are dry formulations that are mixed with water prior to application. No adjuvants are recommended on the product labels for Spike 80 DF and Tebuthiuron 80 WG. While application of the tebuthiuron formulations mixed with water are sometimes referred to as “foliar applications” (e.g., U.S. EPA/OPP/EFED 2014a, p. 26), applications of tebuthiuron are intended primarily to treat the soil rather than to apply the herbicide directly to foliage as specifically noted on the product labels for Spike 80 DF and Tebuthiuron 80 WG. As discussed in Section 2.3, the applications of liquid solutions of tebuthiuron—i.e., Spike 80 DF and Tebuthiuron 80 WG—are considered in Attachment 1 and applications of pellet formulations—i.e., Spike 20P and Tebuthiuron 20 P—are considered in Attachments 2-4.

The maximum application rate considered in the most recent EPA risk assessments is 6 lbs/acre (U.S. EPA/OPP/HED 20141; U.S. EPA/OPP/EFED 2014a). As summarized in Table 2, the product labels for the formulations of tebuthiuron explicitly considered for forestry or rangeland applications support an application rate of 6 lbs a.i./acre only for spot applications. As also summarized in Table 2, lower application rates must be used in some circumstances—e.g., a maximum application rate of 1 lb a.i./acre in areas with less than 20 inches/per year of rain under use restriction for ground water protection.

The workbooks that accompany the current Forest Service risk assessment consider a single application at a rate of 0.6 lb a.i./acre. As discussed further in Section 2.5, the range of application rates used in Forest Service projects ranges from about 0.2 to 2 lb a.i./acre and the application rate of 0.6 lb a.i./acre is approximately the geometric mean of this range [$(0.2 \times 2)^{0.5} \approx 0.63$]. The application rate of 0.6 lb a.i./acre is close to the typical application rate of 0.5 lb a.i./acre used in the recent risk assessment of tebuthiuron for the Bureau of Land Management (ENSR International 2005). While the workbooks that accompany this risk assessment are based on a typical rate of 0.6 lb a.i./acre, the impact of using lower and higher application rates is discussed in the sections addressing risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

For the formulations mixed with water, application volumes, meaning the number of gallons of pesticide solution applied per acre, have an impact on the estimates of potential risk. The extent to which a dry flowable or water dispersible granular formulation of tebuthiuron is diluted prior to application primarily influences dermal and direct spray exposure scenarios, both of which depend on 'field dilution' (i.e., the concentration of tebuthiuron in the applied spray). In all cases, the higher the herbicide concentration (i.e., the lower dilution of the herbicide), the greater is the risk. As summarized in Table 2, the application volumes for tebuthiuron formulations are specified only as greater than 5 gallons/acre. As discussed in Section 2.5, recent use reports from the Forest Service indicate application volumes of 7 to 80 gallons/acre (USDA/FS 2015a). In the workbooks that accompany this risk assessment, the central estimate of the application volume is taken as 20 gallons per acre with a range of 5 to 80 gallons per acre. The central estimate of the application volume is the approximate geometric mean of the application values reported by USDA/FS (2015a) [$(7 \times 80)^{0.5} \approx 23.6$]. The lower bound is based on the minimum application volume on the product labels and upper bound is based on the highest application volume reported by USDA/FS (2015a). Application volumes are used only with formulations that are applied as a liquid.

The selection of application rates and dilution volumes in this risk assessment is intended to reflect plausible estimates of potential exposures. In the assessment of specific program activities, the application rates and volumes can be changed in Worksheet A01 of the EXCEL workbooks to reflect the rates and volumes that are actually used in any specific application of tebuthiuron.

2.5. Use Statistics

Forest Service risk assessments attempt to characterize the use of a herbicide or other pesticide in Forest Service programs relative to the use of the herbicide or other pesticides in agricultural applications. Forest Service pesticide use reports up to the year 2004 are available on the Forest Service web site (http://www.fs.fed.us/foresthealth/pesticide/reports.shtml). No Forest Service uses of tebuthiuron are reported for the period of 2000 to 2004. Uses are reported in Region 2 for both 1999 (305 lbs at an average rate of 1.22 lbs/acre) and 1998 (0.6 lbs at an average rate of 0.12 lbs/acre) as well as Region 4 in 1999 (1650 lbs to 1100 acres in Forest 15 for an average rate of 1.5 lbs/acre). The relevance of this dated information to the current or future use of tebuthiuron by the Forest Service is not clear.

More recent use data for tebuthiuron from the Forest Service is available from an internal database, FACTS (Forest ACtivity Tracking System) (USDA/FS 2014). A summary of data from FACTS provided by the Forest Service (USDA/FS 2015b) documents 26 applications of tebuthiuron. Spike 20P was used in 24 of the applications and Spike 80DF was used in 2 of the applications. The application rates ranged from 0.004 lb a.i./acre to 1.4 lb a.i./acre. The low application rates are probably associated with spot applications. Most applications of Spike 20P were likely granular applications. For liquid applications, the application volumes are specified as 7 to 80 gallons/acre. Other project-specific documents provided by the Forest Service indicate application rates for tebuthiuron in the range of 0.2 to 2 lb a.i./acre (USDA/FS 2008, 2013, 2015b).

As noted in Section 2.2, tebuthiuron is not registered for agricultural applications to commodities consumed by humans. Nonetheless, agricultural applications of tebuthiuron are given by the U.S. Geological Survey (USGS), which provides low-end and high-end estimates of use (USGS 2015). The estimates for tebuthiuron are summarized in Figure 1 (low-end) and Figure 2 (high-end). As illustrated in these figures, the agricultural uses of tebuthiuron involve applications to soybeans in the eastern states—i.e., corresponding to Regions 8 (Southern Region) and 9 (Eastern Region)—and the agricultural uses of tebuthiuron have clearly declined from 1994 (an upper bound estimate of about 1.4 million pounds) to 2012 (an upper bound estimate of about 0.04 million pounds or about 40,000 lbs). As also noted in Section 2.2, no documents from EPA supporting the application of tebuthiuron to soybeans have been identified.

Detailed pesticide use statistics are compiled by the State of California. The use statistics from California for 2013, the most recent year for which statistics are available, indicate that a total of 7480.46 lbs of tebuthiuron was applied in California (CDPR 2015, p. 718-719). The major uses of tebuthiuron are landscape maintenance (3961.88 a.i. lbs) and rights-of-way management (3504.18 lbs a.i.). The number of acres treated in these applications is not reported. A minor use is reported only as “uncultivated non-ag” (14.40 lbs a.i. applied to 18 acres for an application rate of about 0.78 lb a.i./acre). No applications of tebuthiuron to crops are reported.

A screening level use analysis in the most recent ecological risk assessment from EPA indicates that about 8000 lbs a.i. of tebuthiuron were applied to pastureland in 2013 (U.S. EPA/OPP/EFED 2014, p. 16).

The amount of tebuthiuron that might be used in future Forest Service programs is unknown. Nonetheless, forestry or rangeland applications of tebuthiuron could be the dominant source of tebuthiuron in local areas, given that tebuthiuron is not currently registered for applications to agricultural commodities.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

Most of the available information on the mammalian toxicity of tebuthiuron comes from standard studies submitted to the U.S. EPA/OPP in support of its registration. Full copies of these studies, which are considered proprietary, were not available for the preparation of the current Forest Service risk assessment. The registrant studies relating to the hazard identification of potential human health effects are summarized in various EPA risk assessments and related documents, as specified in Section 1.1.

The U.S. EPA uses a classification system for acute responses ranging from Category I (most severe response) to Category IV (least severe response). The toxicity categories under EPA's system are Category I (highly toxic), Category II (moderately toxic), Category III (slightly toxic), and Category IV (practically non-toxic). Tebuthiuron is classified as Category II to Category III for acute oral toxicity, Category IV for acute dermal toxicity, and Category III for inhalation toxicity. Tebuthiuron is classified as Category IV for skin and eye irritation and does not appear to cause skin sensitization.

In longer-term exposures, tebuthiuron does not appear to be neurotoxic or immunotoxic. The most common signs of toxicity associated with exposure to tebuthiuron are decreased body weight, decreased weight gain, and decreased food consumption. Decreased body weight or weight gain accompanied by a decrease in food consumption can be secondary to other toxic effects (i.e., severely poisoned animals will often decrease their food consumption, which in turn leads to decreases in body weight and/or body weight gain). A decrease in food conversion efficiency (i.e., decreased weight gain greater than would be expected based on the level of food consumption) was observed in a reproduction study in rats; however, this effect is not noted in other subchronic or chronic toxicity studies. The decrease in food conversion efficiency noted in the rat reproduction study is the only indication that tebuthiuron might have effects on endocrine function. Slight vacuolization of pancreatic acinar cells was observed in a both a subchronic and chronic study in rats; however, effects on the islets of Langerhans cells (i.e., the cells in the pancreas associated with insulin release) are not reported in the available toxicity data. Effects on the pancreas have not been associated with an increase in blood glucose levels, although an unspecified increase in blood glucose is noted in a subchronic dermal study in rats.

3.1.2. Mechanism of Action

The specific mechanism of action of tebuthiuron in mammals is not identified or discussed in the open literature or EPA assessments (as identified in Section 1.1). As noted in Section 2.2 and discussed further in Section 4.1.2.5 (hazard identification for terrestrial plants), the phytotoxicity of tebuthiuron is based on the inhibition of photosynthesis, specifically photosystem II, and this mechanism of action is shared with several other urea herbicides. This mechanism of action is specific to plants and is not relevant to potential effects in humans. As discussed further in Section 3.4.6 (Cumulative Effects), the U.S. EPA/OPP had not determined a common mechanism of action with other pesticides for the potential human health effects of tebuthiuron (U.S. EPA/OPP/HED 2014a).

As discussed in the following sections of this hazard identification, the most commonly observed effect in mammals following exposure to tebuthiuron is decreased body weight gain. Decreases in body weight or body weight gain are common signs of toxicity observed with many pesticides and other toxic agents. Effects on body weight are often seen as secondary to reduced food consumption in animals adversely responding to pesticides due to a large number of different mechanisms. A decrease in food conversion efficiency—i.e., decreased weight gain that is greater than would be expected based on the level of food consumption—may be suggestive of metabolic or endocrine effects. As discussed further in the Section 3.1.9.2, decreased food conversion efficiency was observed in rat offspring during the course of a two-generation reproduction study (MRID 90108). Decreased food conversion efficiency is not noted in standard chronic toxicity studies in mice, rats, or dogs (Section 3.1.5).

Slight vacuolization of pancreatic acinar cells was observed in a subchronic study in rats. This study is published in the open literature (Todd et al. 1974) and was submitted to the EPA in support of the registration of tebuthiuron (i.e., MRID 00020662 as reviewed in U.S. EPA/OPP/HED 2014a). This effect was also noted in chronic toxicity study in rats (MRID 0020714), which is classified by the U.S. EPA/OPP/HED (2014a, pp. 42) as *Unacceptable*. As discussed further in Section 3.1.5, the effects on pancreatic acinar cells (i.e., slight vacuolization) in male and female rats were observed only in the high dose (2500 ppm dietary concentration or about 125 mg a.i./kg bw/day) group of the subchronic study. Neither the EPA nor Todd et al. (1974) indicates any effects on islets of Langerhans cells (i.e., the cells in the pancreas associated with insulin release); moreover, the data in Todd et al. (1974, Table 2) specifically indicate that tebuthiuron had no significant impact on blood glucose at any dose level. As discussed in Section 3.1.12, however, a subchronic dermal toxicity study in rats (MRID 00149733/00160796) conducted at a dose of 1000 mg a.i./kg bw reports an increase in blood glucose values but provides no information on the magnitude of the increase.

Effects on pancreatic cells have not been noted in other species and were not seen in rats over the course of a developmental study (MRID 00020803 discussed in Section 3.1.9.1). The pancreatic lesions may have been associated with reductions in the secretion of digestive enzymes which led to reductions in body weight or possibly a disruption of normal protein synthesis (Todd et al. 1974).

3.1.3. Pharmacokinetics and Metabolism

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

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

3.1.3.1. General Considerations

For pesticide registration, the U.S. EPA/OPP generally requires a relatively standard metabolism study in rats in which the compound is administered orally or a combination of oral and intravenous routes (U.S. EPA/OPPTS 1998a). One such study for tebuthiuron (MRID 42711701, 43129701) is summarized in U.S. EPA/OPP/HED (2004, p. 14) and U.S. EPA/OPP/HED (2014a, pp. 44-45). In this study, ^{14}C-tebuthiuron was administered at single oral doses of 10 or 100 mg a.i./kg bw and at 14-day repeated oral doses of 10 mg a.i./kg bw. As summarized in Table 4, the EPA identified six metabolites of concern, the most abundant of which were hydroxylated metabolites (i.e., 109-OH and 104-OH). Other metabolites were formed by demethylation of the urea group (metabolites 104 and 106), cleavage of the urea group (108), or hydroxylation of the urea N-methyl group (109). The numeric designation of tebuthiuron metabolites used by EPA is adopted from Rutherford et al. (1995), as discussed below. Tebuthiuron was rapidly excreted primarily in the urine (50.6-85.3%) with only small amounts excreted in the feces (≈3.5%) of a 24-hour post-dosing period.

The open literature on tebuthiuron includes additional metabolism studies in mice, rats, rabbits, and dogs (Hoffman et al. 1975; Morton and Hoffman 1976) as well as cows (Rutherford et al. 1995). The studies on mice, rats, rabbits, and dogs were initially published as an abstract in Hoffman et al. (1975) followed by the full publication in Morton and Hoffman (1976). As with the above study in rats summarized by EPA, Morton and Hoffman (1976, Table 1) noted extensive urinary excretion of tebuthiuron in rats, rabbits, and dogs (85-90.4% within 24 hours post-dosing) with only minor excretion in the feces (1.1-2.4% by 96 hours post-dosing) for a total 24-hour excretion of 86.1-92.8%. A somewhat different pattern was seen in mice with only about 65.5% excreted in the urine but 30.7% excreted in the feces (for a total excretion of 96.2%) by 96 hours after dosing. Rutherford et al. (1995) do not provide details of the kinetics of tebuthiuron in cows but detected metabolites 104, 104-OH, 106, 106-OH, and 109 in cow's milk.

Morton and Hoffman (1976, Table 4, p. 763) note the *in vitro* formation of formaldehyde by rat liver preparations. Formaldehyde is not noted as a metabolite of tebuthiuron elsewhere in the literature including human health risk assessments by EPA (U.S. EPA/OPP 1994; U.S. EPA/OPP/HED 2002, 2014a).

3.1.3.2. Dermal Absorption

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

Two types of dermal exposure scenarios are considered: immersion and accidental spills. In the scenarios involving immersion, the concentration of the chemical in contact with the surface of the skin is assumed to remain constant or at least nearly so. As detailed in SERA (2014a), the calculation of absorbed dose for dermal exposure scenarios involving immersion requires an estimate of the dermal permeability coefficient (K_p) expressed in cm/hour, and the rate of absorption is assumed to be essentially constant (i.e., zero-order kinetics as discussed in Section 3.1.3.2.2). In exposure scenarios involving direct sprays or accidental spills where the compound is deposited directly on the skin, the concentration or amount of the chemical on the surface of the skin is assumed to be the limiting factor in dermal absorption. For these scenarios first-order dermal absorption rate coefficients (k_a), expressed as a proportion of the deposited dose absorbed per unit time—e.g., hour^{-1}—are used in the exposure assessment.

3.1.3.2.1. First-Order Dermal Absorption

No data are available on the dermal absorption of tebuthiuron. As noted in the two recent EPA human health risk assessments (U.S. EPA/OPP/HED 2002, 2014a), dermal absorption studies were not submitted in support of the registration of tebuthiuron (U.S. EPA/OPP/HED 2002, 2014a). As discussed in U.S. EPA/OPP/HED (2014a, p. 5), the EPA assumes 100% dermal absorption in the absence of dermal absorption data. The assumption of 100% dermal absorption is used also in the recent risk assessment of tebuthiuron prepared for the Bureau of Land Management (ENSR 2005).

In the absence of information on first-order dermal absorption rates on a pesticide, Forest Service risk assessments typically use quantitative structure activity relationships (QSAR), as detailed in SERA (2014a, Section 3.1.3.2.2). The QSAR method is based exclusively on dermal absorption data from studies in humans involving numerous chemicals. As detailed in Worksheet B03b of Attachments 1 and 2, the QSAR methods yield estimated dermal absorption rate coefficients of about 0.004 (0.002–0.009) hour^{-1} using a K_{ow} value of 63.1 and a molecular weight of 228.3 (Table 1 with values taken from U.S. EPA/OPP/HED 2014a). These properties are within the range of values on which the algorithm is based—i.e., K_{ow} values ranging from 0.0015 to 3,000,000 and molecular weights ranging from 60 to 400 g/mole.

Typically, Forest Service risk assessments defer to EPA risk assessments unless there is a compelling reason to do otherwise. As discussed further in Section 3.1.4, tebuthiuron is moderately toxic (EPA Category II) by oral exposure based on oral LD_{50} values of 447.5 mg/kg bw in male rats and 387.5 mg/kg bw in female rats (MRID 40583901). As discussed in Section 3.1.12, however, the EPA places tebuthiuron in the least toxic category (Category IV or practically nontoxic) for dermal toxicity based on a dermal LD_{50} of > 5000 mg/kg bw in rabbits (MRID 40583902). Similarly, as discussed further in Section 3.1.5, the subchronic oral NOAEL for tebuthiuron is 50 mg/kg bw/day in rats (MRID 00020662) and 25 mg/kg bw/day in dogs (MRID 00020663). As discussed in Section 3.1.12, however, the subchronic dermal NOAEL is rats is 1000 mg/kg bw/day. Taking the most direct comparison (i.e., subchronic oral and dermal NOAELs in rats), tebuthiuron appears to be at least 20 times less toxic by the dermal route of exposure, relative to the oral route of exposure [1000 mg/kg bw/day ÷ 50 mg/kg bw = 20]. Note that the subchronic oral LOAEL in rats was 125 mg/kg bw/day but a subchronic dermal LOAEL was not identified.

A previous risk assessment of tebuthiuron conducted for the Forest Service (Sassaman and Jacobs (1986) notes the lack of dermal absorption data and assumes a dermal absorption factor of 10%, apparently for a 24-hour exposure period. Sassaman and Jacobs (1986, p. 42) do not provide a detailed discussion of the 10% estimate but notes that the estimate was derived from … *occupational doses derived for phenoxy herbicides (2,4-D and 2,4,5-T).* This absorption factor corresponds to a first-order dermal absorption rate of about 0.004 $hour^{-1}$ [ln(1 - 0.1) ÷ 24 hours ≈ 0.00439 $hour^{-1}$], similar to the QSAR estimate discussed above.

The current Forest Service risk assessment uses the estimated dermal absorption rate coefficients of 0.004 (0.002 – 0.009) $hour^{-1}$ based on the QSAR method from SERA (2014a, Section 3.1.3.2.2). The acute and subchronic dermal toxicity values discussed above do not support the assumption of 100% dermal absorption. The central estimate of the rate coefficient is consistent with the estimate from Sassaman and Jacobs (1986), which was based on a different and largely subjective assessment that adds only marginal support to the approach taken in the current risk assessment.

3.1.3.2.2. Zero-Order Dermal Absorption

Exposure scenarios involving the assumption of zero-order dermal absorption require an estimate of dermal permeability (K_p) in units of cm/hour. No experimental data are available on the dermal permeability rate of tebuthiuron. In the absence of experimental data, Forest Service risk assessments generally use a QSAR algorithm developed by the EPA (U.S. EPA/ORD 1992, 2007). This approach is discussed in further detail in SERA (2014a, Section 3.1.3.2.1). As with the algorithm for estimating the first-order dermal absorption rate constant, the EPA algorithm is based on molecular weight and K_{ow} (U.S. EPA/ORD 1992, 2007). The molecular weight and K_{ow} values used for estimating the K_p are identical to those used in the estimate of the first-order dermal absorption rate constants (i.e., a K_{ow} value of 63.1 and a molecular weight of 228.3).

The EPA algorithm is derived from an analysis of 95 organic compounds with K_{ow} values ranging from about 0.0056 to 309,000 and molecular weights ranging from approximately 30 to 770 (U.S. EPA/ORD 1992, 2007). These ranges of K_{ow} values and molecular weights encompass the estimates of the corresponding values for tebuthiuron.

Details of the implementation of the algorithms are given in Worksheet B03a in the EXCEL workbooks for tebuthiuron (Attachments 1 and 2). Using the EPA algorithm results in an estimated dermal permeability (K_p) of about 0.0014 (0.00096 to 0.002) cm/hour.

3.1.3.3. Excretion

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

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

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

$$\frac{X_{Inf}}{X_1} = \frac{1}{1 - e^{-kt^*}} \quad (2)$$

Whole-body half-lives are most appropriate for estimating steady-state body burdens.

As discussed in Section 3.1.3.1, Morton and Hoffman (1976) noted whole-body excretion of 85-90.4% of orally administered tebuthiuron (as parent and metabolites) within 1 day after dosing. These data are consistent with first-order elimination rate coefficients (***k***) of about 2 day^{-1} [ln(1-0.85) ÷ 1 day **≈** 1.97328 day^{-1}] to 2.6 day^{-1}. Substituting the lower rate coefficient into Equation 3, the estimated plateau for tebuthiuron and tebuthiuron metabolites is about 1.16. In other words, over very prolonged periods of exposure, the maximum increase in the body burden of tebuthiuron should be no more than a factor of about 1.16.

3.1.4. Acute Oral Toxicity

Standard acute oral toxicity studies are typically used to determine LD_{50} values—i.e., the treatment dose estimated to be lethal to 50% of the animals. As discussed in SERA (2014a, Section 3.1.4), LD_{50} values are not used directly to derive toxicity values as part of the dose-response assessment in Forest Service risk assessments. Nonetheless, comparing the LD_{50} values for the active ingredient to the LD_{50} values for the formulations or metabolites of the active ingredient may be useful in assessing the potential impact of inerts or metabolites on potential risks. LD_{50} values as well as other measures of acute toxicity discussed in following sections are used by the U.S. EPA/OPP to categorize potential risks. U.S. EPA/OPP uses a ranking system for response ranging from Category I (most severe response) to Category IV (least severe response). Details of the EPA categorization system are detailed in SERA (2014a, Table 4) as well as the U.S. EPA/OPP (2010d) label review manual.

The acute oral toxicity data for tebuthiuron are summarized in Appendix 1, Table A1-1, and oral LD_{50} values reported in MSDSs are summarized in Appendix 1, Table A1-8. Oral LD_{50} values from registrant-submitted studies are summarized in the EPA's Reregistration Eligibility Decision (RED) document (U.S. EPA/OPP 1994) as well as the open literature study from Todd et al. (1974). The study by Todd et al. (1974) is from Eli Lilly and Company. As discussed in Section 2.2, Eli Lilly (currently Dow AgroSciences) was the initial registrant for tebuthiuron; accordingly, some of the LD_{50} values reported in Todd et al. (1974) are identical to LD_{50} values reported in U.S. EPA/OPP (1994). Definitive LD_{50} values (i.e., values reported as a discrete number) are available for mice (LD_{50} values of 528-620 mg a.i./kg bw), rats (LD_{50} values of 387-644 mg a.i./kg bw) and rabbits (an LD_{50} of 286 mg a.i./kg bw). For rats, the LD_{50} values of 447 mg a.i./kg (males) and 387 mg a.i./kg (females) reported in U.S. EPA/OPP (1994) are attributed to MRID 40583901 for which the EPA document does not provide a full reference. These LD_{50} values are below the LD_{50} of 644 mg a.i./kg bw reported in Todd et al. (1974). Other discrepancies in definitive LD_{50} values between the EPA RED and Todd et al. (1974) are insubstantial. Based on these limited data, rabbits appear to be somewhat more sensitive than either rats or mice to tebuthiuron. As discussed further in Section 3.1.91, rabbits are also more sensitive and more markedly so than rats in developmental toxicity studies.

In addition to the definitive LD_{50} values, indefinite LD_{50} values (i.e., values reported with the "greater than" designation) are reported for cats (>200 mg a.i./kg bw) and dogs (>500 mg a.i./kg bw) in U.S. EPA/OPP (1994, p. 8). Todd et al. (1974) report LD_0 values of >200 mg a.i./kg bw for cats and >500 mg a.i./kg bw for dogs. As compared to the LD_{50}, LD_0 endpoint values do not elicit mortality during animal testing. This discrepancy may be due simply to the custom of EPA to present indefinite values as LD_{50} values rather than LD_0 values.

As noted in Section 2.2, MSDSs and SDSs typically summarize standard mammalian toxicity values for formulations. A problem with both the MSDS and SDS is that they provide little experimental detail, and it is not always clear if the information applies to the formulation or the active ingredient. As summarized in Appendix 1, Table A1-8, the MSDS for Alligare Tebuthiuron 20 P reports a definitive oral LD_{50} of 644 mg a.i./kg bw. This value is identical to the rat oral LD_{50} reported in Todd et al. (1974). Todd et al. (1974) specifically note that their studies involved technical grade (>97% purity) tebuthiuron. Thus, it appears that the LD_{50} of 644 mg a.i./kg bw reported in the MSDS for Alligare Tebuthiuron 20 P applies to the technical grade material rather than the formulation.

Based on the oral LD_{50} values discussed above, the U.S. EPA/OPP (1994, p. 8) classifies tebuthiuron as Category II (the second most hazardous classification) based on reported LD_{50} values in rats and cats and as Category III based on the reported LD_{50} values in mice and dogs. As discussed above, however, the toxicity values in cats and dogs appear to be LD_0 values from the Todd et al. (1974) rather than LD_{50} values. Notwithstanding the EPA classifications, substantial differences in the toxicity of tebuthiuron to rats, mice, and rabbits are not apparent based on definitive oral LD_{50} values. The indefinite toxicity values in cats and dogs cannot be overly interpreted but suggest that these larger mammals are not more sensitive than rats, mice, and rabbits to tebuthiuron.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

As discussed in SERA (2014a, Section 3.1.5), *subchronic* and c*hronic* are somewhat general terms that refer to studies involving repeated dosing. Some repeated dose studies are designed to detect specific toxic endpoints, like reproductive and neurological effects. Except for some comments in this subsection on general signs of toxicity, these more specialized studies are discussed in subsequent subsections of this hazard identification.

The subchronic and chronic toxicity studies on tebuthiuron are summarized in Appendix 1, Table A1-2. Most of the studies relevant to the current risk assessment were submitted to the U.S. EPA/OPP in support of the registration of tebuthiuron, and the summaries of these studies are taken from the most recent human health risk assessment from EPA (U.S. EPA/OPP/HED 2014a). Some repeated dose studies are published in the open literature (i.e., Todd et al. 1974; Griffing and Todd 1974). These studies are publications from Eli Lilly and Company, an early registrant of tebuthiuron, and these publications cover studies that appear to be the same as the studies submitted to and reviewed by the EPA.

Subchronic studies are available in rats (MRID 00020662; MRID 48722705; Griffing and Todd 1974; Todd et al. 1974) and dogs (MRID 00020663), and chronic studies are available in mice (MRID 00020717), rats (MRIDs 00020714, 00098190, 40870101), and dogs (MRID 00146801). As detailed in Appendix 1, Table A1-2, the chronic studies on both mice and rats were judged to be unacceptable by EPA. While it is somewhat unusual for chronic studies to be judged unacceptable, the EPA waived the requirement for the conduct of additional chronic bioassays in rats and mice (U.S. EPA/OPP/HED 2014a, Appendix A, p. 32). As noted in Appendix 1, Table A1-2, the only issue with the chronic study in mice (MRID 00020717) was the failure to define an effect level – i.e., no effects were noted at the highest dose tested. As detailed in U.S. EPA/OPP/HED 2014a, p. 42), the study in rats was more severely flawed due to failures in the implementation of GLP (Good Laboratory Practices) guidelines.

Decreases in body weight gain are the most commonly noted signs of toxicity (MRID 00020662 in rats; MRIDs 00020663 and 00146801 in dogs). Decreased body weight gain is an extremely common and general sign of toxicity for many chemicals and does not necessarily indicate a specific mechanism of action. As discussed further in Section 3.1.9.2, a two-generation reproduction study on tebuthiuron does note a decrease in both body weight as well as food conversion efficiency, and this endpoint is used as the basis for the acute RfD on tebuthiuron (Section 3.3). Nonetheless, the EPA summaries of the standard subchronic and chronic studies in mammals do not note any effects on food conversion efficiency. As discussed in Section 3.1.2 (Mechanism of Action), subchronic and chronic exposures of rats to tebuthiuron are associated with minor changes to pancreatic cells; however, these changes are not associated with effects on glucose metabolism. Effects on the pancreas were not noted in repeated dose studies in mice or dogs.

3.1.6. Effects on Nervous System

In severely poisoned animals, virtually any chemical can cause gross signs of toxicity that might be attributed to neurotoxicity—e.g., incoordination, tremors, or convulsions. A direct neurotoxicant, however, is defined as a chemical that interferes with the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of a direct neurotoxicant distinguishes agents that act directly on the nervous system (direct neurotoxicants) from those agents that might produce neurological effects secondary to other forms of toxicity (indirect neurotoxicants).

U.S. EPA/OPP requires neurotoxicity studies for pesticides (Group E in U.S. EPA/OCSPP 2010) when standard toxicity studies or other considerations such as chemical structure suggest that concerns for effects on the nervous system are credible. This is not the case for tebuthiuron. As noted in (U.S. EPA/OPP/HED 2002, 2014a) and summarized in Appendix 1, standard acute and chronic toxicity studies on tebuthiuron provide no indication of neurotoxicity. Along with the standard registrant-submitted studies, a survey study in the open literature for neurotoxicity involving numerous pesticides found no indication that tebuthiuron is neurotoxic (Crofton 1996). Because of the failure to note signs of neurotoxicity in mammals, the U.S. EPA waived requirements for acute, subchronic, and developmental neurotoxicity studies in mammals as well as a standard study for delayed neurotoxicity using hens (U.S. EPA/OPP/HED 2002, pp. 13-14).

3.1.7. Effects on Immune System

As summarized in Appendix 1, Table A1-2, there is a standard 28-day study on tebuthiuron immunotoxicity in female rats (MRID 48722705, as summarized in U.S. EPA/OPP/HED 2014a). In this study as with several subchronic studies discussed in Section 3.1.5, the most sensitive endpoint is decreased body weight observed at a dietary concentration of 1000 ppm, corresponding to a dose of 84.9 mg a.i./kg bw/day. No inhibition of immune response was noted in rats following injections with sheep red blood cells (a measure of humoral immune response) at dietary concentrations of up to 2000 ppm, corresponding to a dose of 148 mg a.i./kg bw/day.

This study did not involve assays for cellular immune responses—i.e., assays of natural killer cell activity.

In the absence of indications of immune effects in other studies on tebuthiuron, the EPA concludes: *The overall weight of evidence suggests that the chemical does not directly target the immune system* (U.S. EPA/OPP/HED 2014a, p. 45). The EPA document, however, does not elaborate on the weight of evidence assessment. Subchronic or chronic animal bioassays typically involve morphological assessments of the major lymphoid tissues, including bone marrow, major lymph nodes, spleen and thymus (organ weights are sometimes measured as well), and blood leukocyte counts. These assessments can detect signs of inflammation or injury indicative of a direct toxic effect of the chemical on the lymphoid tissue. Changes in lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected. In this respect, it is worth noting that the immune assay did observe a decrease in absolute and relative thymus weights and a decrease in spleen weights (MRID 48722705, Appendix 1, Table A1-2). These effects, however, are not noted in other subchronic or chronic studies on tebuthiuron. As also summarized in Appendix 1, Table A1-2, another subchronic study in rats (MRID 00020662) and a subchronic study in dogs (MRID 00020663) indicate increases rather than decreases in spleen weights. Effects on the thymus are not noted in other subchronic or chronic studies. Thus, the EPA assessment regarding the weight of evidence assessment for immunotoxicity appears to be reasonable.

3.1.8. Effects on Endocrine System

The direct effects of chemicals on endocrine function are most often assessed according to mechanistic studies on estrogen, androgen, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). U.S. EPA/OPP has developed a battery of screening assays for endocrine disruption which can be found at: http://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-890-endocrine-disruptor-screening-program. In addition, the EPA has issued two lists of chemicals, including several pesticides for which endocrine screening assays are required (U.S. EPA/OPP 2009a, 2010a). Tebuthiuron is not among the listed chemicals, and U.S. EPA/OPP (2016) does not include results for tebuthiuron.

As noted in Section 3.1.2, decreased weight gain is a common sign of toxicity in mammals following exposure to tebuthiuron, and a two generation reproduction study in rats (MRID 90108, discussed further in Section 3.1.9.2) notes a decrease in body weight gain accompanied by a decrease in food conversion efficiency. Decreases in food conversion efficiency, however, are not reported in other subchronic or chronic studies in rats or other mammals. While a decrease in food conversion efficiency may suggest effects on endocrine activity (e.g., Sohlstrom et al. 1998), the single observation of decreased food conversion efficiency cannot be used as a basis to conclude that tebuthiuron is an endocrine disruptor.

Effects on endocrine function that have important public health implications could be expressed as diminished or abnormal reproductive performance. This issue is addressed specifically in Section 3.1.9.

3.1.9. Reproductive and Developmental Effects

3.1.9.1. Developmental Studies

Developmental studies are used to assess the potential of a compound to cause malformations and signs of toxicity during fetal development. These studies typically entail gavage administration of the chemical compound to pregnant rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required by the EPA for the registration of pesticides.

As summarized in Appendix 1, Table A1-3, standard developmental studies on tebuthiuron were conducted with rats (MRID 00020803/40485801) and rabbits (MRID 00020644/40776301). Details of these studies are given in EPA risk assessments (U.S. EPA/OPP/HED 2002, 2014a), and the study in rats is also summarized in Todd et al. (1974). As noted in Section 3.1.4, acute oral LD_{50} studies suggest that rabbits (LD_{50} = 286 mg a.i./kg bw) are somewhat more sensitive than rats (LD_{50} values ranging from 387 to 447 mg a.i./kg bw) to tebuthiuron. According to the developmental studies, the sensitivity of the rabbit is much greater, based on the maternal NOAEL of 10 mg a.i./kg bw/day in rabbits and the maternal NOAEL of 110 mg a.i./kg bw/day is rats. In these assays, developmental abnormalities were not observed in either species. No effects on body weight were observed in the study on rats; whereas, in rabbits, the high dose of 25 mg a.i./kg bw/day was associated with increased early resorptions and a substantial (17.3%) decrease in fetal weights in the absence of overt toxic effects in the dams, based on body weights, survival, or organ pathology.

As discussed further in Section 3.3, the U.S. EPA uses the developmental study in rabbits as the basis for the acute RfD for tebuthiuron. The increase in early fetal resorptions is a serious adverse effect in that it involves the death of the fetus. As also discussed in Section 3.3 (Dose-Severity Relationships), the proximity of the NOAEL of 10 mg a.i./kg bw/day to the LOAEL of 25 mg a.i./kg bw/day raises concerns for relatively modest exceedances of the acute RfD.

3.1.9.2. Reproduction Studies

The U.S. EPA generally requires at least one multi-generation reproduction study, usually conducted in rats (U.S. EPA/OPP 1996). Multi-generation reproduction studies typically involve dietary exposures of a group of rats referred to as the *parental generation*, generally designated as P_1 (parental) or F_0 (fetal). Male and female animals are selected from this group and mated. Exposure of the female continues through gestation and after delivery. Offspring from the parental generation, typically referred to as F_1, are then continued on dietary exposure through sexual maturity. In some studies, the F_0 generation is bred twice producing F_{1a} and F_{1b} generations. The F_1 offspring (most often F_{1a}) are mated (and then referred to as the P_2 generation) producing an F_2 generation. This is the basic design of a “2-generation” study, although variations on this design are sometimes used, and occasionally the study is carried over to a third generation. Multi-generation reproduction studies typically focus on effects on reproductive capacity—i.e., the number of young produced and their survival.

As detailed in Appendix 1, Table A1-3, U.S. EPA/OPP/HED (2014a) summarizes the results of a two-generation reproduction study in rats in which the rats were exposed to dietary concentrations of 0, 100, 200, or 400 ppm tebuthiuron. No adverse reproductive effects were noted at any dietary concentration. Based on estimated food consumption, the dietary exposure of 200 ppm was estimated to correspond to a dose of 14 mg a.i./kg bw/day, and this dose was designated as a the reproductive NOAEL based on a decrease in body weight in offspring in the 400 ppm (26 mg a.i./kg a.i./day) exposure group. The reproductive NOAEL of 14 mg a.i./kg bw/day in rats is below the developmental NOAEL of 110 mg a.i./kg bw/day in rats (MRID 00020803/40485801) but is somewhat higher than the developmental LOAEL in rabbits of 25 mg a.i./kg bw/day (MRID 00020644/40776301). As discussed in Section 3.3, the U.S. EPA/OPP/HED (2014a) uses the systemic reproductive NOAEL dose of 14 mg a.i./kg bw/day as the basis for the chronic RfD.

Prior to the risk assessment by U.S. EPA/OPP/HED (2014a), the EPA offered a different interpretation of the reproductive study in rats. The lowest exposure group of 100 ppm, corresponding to a dose of 7 mg a.i./kg bw/day was designated as the NOAEL, and the exposure group of 100 ppm (14 mg a.i./kg bw/day) was designated as a LOAEL, based on reduced body weight in F_1 females (U.S. EPA/OPP 1994, p. 12; U.S. EPA/NCEA 1988). U.S. EPA/OPP/HED (2014a) does not explicitly discuss the reclassification of the NOAEL and LOAEL doses in the reproduction study. Nonetheless, this is not an unusual situation. In the preparation of a new risk assessment, the EPA typically reassess the key studies which can lead to a reclassification of NOAELs and LOAELs. As noted in Section 3.3.2 (Chronic RfD), the current Forest Service risk assessment defers to the most recent EPA risk assessment and uses the interpretation of the reproductive study given in U.S. EPA/OPP/HED (2014a).

3.1.10. Carcinogenicity and Mutagenicity

As discussed in SERA (2014a, Section 3.1.10), three kinds of data are commonly used to assess potential carcinogenic hazard: epidemiology studies; tests for genetic toxicity, including mutagenicity; and bioassays on mammals. When applicable, quantitative estimates of carcinogenic potency are typically based on mammalian bioassays.

No epidemiology studies specific to tebuthiuron have been identified. A worker mortality study involving exposures to a large number of herbicides, including tebuthiuron, is published in the open literature (Green 1991). No association was noted between herbicide exposure and carcinogenicity or overall mortality. Again, however, this study is not specific to tebuthiuron.

Two assays of tebuthiuron for mutagenicity are published in the open literature (Rexroat et al. 1995; Venkat et al. 1995), and neither study reports signs of mutagenicity using *in vitro* test systems. The U.S. EPA requires a battery of mutagenicity studies for pesticide registration. As summarized in U.S. EPA/OPP/HED (2014a, Table A.4.6 and Table A2), these mutagenicity tests involved *in vitro* assays for bacterial reverse gene mutation, assays for unscheduled DNA synthesis and chromosome aberrations in mammals cell cultures, and an in vivo sister chromatid exchange assay in hamsters. These assays did not raise concern for mutagenic activity (U.S. EPA/OPP/HED 2014a, p. 17).

While the available epidemiology and mutagenicity studies do not raise concern for potential carcinogenicity, the status of the mammalian bioassays on tebuthiuron is problematic. The EPA has indicated that tebuthiuron is “not classifiable as to human carcinogenicity” (U.S. EPA/OPP/HED 2014a, p. 17 and p. 18). Nonetheless, as discussed in Section 3.1.5, the toxicity database on tebuthiuron is somewhat unusual in that the chronic toxicity/carcinogenicity bioassays in rats and mice are classified by the U.S. EPA/OPP/HED (2014a, pp. 33-34, Table A2) as *Unacceptable*. This classification is consistent with the previous assessment of the cancer bioassay in rats and mice by U.S. EPA/OPP/HED (2002, pp. 19-20, Section 9.1.2). As also discussed in Section 3.1.5, the EPA waived the requirements for the conduct of additional cancer bioassays in rats and mice (U.S. EPA/OPP/HED 2014a, Table A1, p. 32). Notwithstanding the classification of the rat bioassay as *Unacceptable*, the EPA appears to accept the rat bioassay as adequate for diminishing concern for carcinogenicity:

> *Despite the inadequacy of the mouse carcinogenicity study, EPA has determined that an additional mouse carcinogenicity study is not needed and that the rat chronic/carcinogenicity study will be adequate for assessing chronic risk, including cancer.*
>
> U.S. EPA/OPP/HED 2014a, p. 17

The statement that the rat bioassay is adequate for assessing carcinogenicity does not seem consistent with the EPA classification of the rat bioassay as *Unacceptable*. As summarized in Appendix 1, Table A2-2, of the current Forest Service risk assessment and detailed further in the EPA risk assessments (U.S. EPA/OPP/HED 2002, 2014a), neither the rat nor the mouse bioassay yielded any positive indication of carcinogenicity. Nonetheless, the limitations in both of the rodent bioassays reduces confidence in the qualitative assessment by EPA that tebuthiuron is "not classifiable as to human carcinogenicity" (U.S. EPA/OPP/HED 2014a, p. 17 and p. 18).

U.S. EPA/OPP/HED (2014a, p. 30) cites a report from its Hazard and Science Policy Council (U.S. EPA/OPP/HASPOC 2014) that addresses the EPA decision to waive the requirements for additional chronic bioassays in rats and mice. This document was not located at EPA web sites; however, a copy was received in response to a Freedom of Information Act (FOIA) request. This document also notes that the rat chronic study is considered unacceptable due to high mortality, the occurrence of respiratory infections, and reporting deficiencies (U.S. EPA/OPP/HASPOC 2014, p. 4).

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

The U.S. EPA/OPP requires standard studies with pesticide formulations for skin and eye irritation as well as skin sensitization (U.S. EPA/OPPTS 2015). As with acute oral toxicity, the U.S. EPA/OPP uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response) for all three groups of endpoints discussed in this subsection (e.g., U.S. EPA/OPP 2015b, p. 7-2). Assays for skin irritation and sensitization are summarized in Appendix 1, Table A1-4. Assays for eye irritation are summarized in Appendix 1, Table A1-5.

3.1.11.1. Skin Irritation

Only one study of skin irritation is summarized in EPA documents (i.e., MRID 40583902). This study indicates that tebuthiuron did not cause skin irritation in rabbits. The EPA uses the study to classify tebuthiuron as Category IV (nonirritating) for skin irritation (U.S. EPA/OPP 1994, p. 8; U.S. EPA/OPP/HED 2002, p. 3). This classification is consistent with the open literature publication by Todd et al. (1974) in which skin irritation was not observed in rabbits following a 24-hour exposure to 200 mg a.i./kg bw technical grade (>90%) tebuthiuron with or without abrasion over a 14-day post-observation period. As summarized in Appendix 1, Table A1-8, the classification of tebuthiuron as nonirritating to the skin is consistent with notations on skin irritation in the MSDSs for Spike 80DF, Alligare Tebuthiuron 20 P, and Alligare Tebuthiuron 80 WG. The MSDS for Spike 20P does not provide information on skin irritation.

3.1.11.2. Skin Sensitization

As with skin irritation, the EPA documents on tebuthiuron summarize information on a single skin irritation study in guinea pigs (the standard test species for skin sensitization studies) in which no dermal sensitization was observed (MRID 40583904 in U.S. EPA/OPP 1994, p. 8; U.S. EPA/OPP/HED 2002, p. 3). This summary is also consistent with data from the open literature publication by Todd et al. (1974) as well as notations on skin sensitization from the MSDS for Spike 80DF, Alligare Tebuthiuron 20 P, and Alligare Tebuthiuron 80 WG. Also, as with skin irritation, the MSDS for Spike 20P does not provide information on skin sensitization.

3.1.11.3. Ocular Effects

As with the dermal endpoints, only one study on eye irritation is cited in the EPA risk assessments, which provide few details other than to note slight irritation (slight conjunctival hyperemia at 1 hour after treatment) and a classification as Category IV (MRID 40583903 in U.S. EPA/OPP 1994, pp. 8-9; U.S. EPA/OPP/HED 2002, p. 3). Again, the open literature publication by Todd et al. (1974) summarizes an eye irritation study consistent with the briefer summaries in the EPA documents: slight and transient conjunctival hyperemia (redness due to increased blood flow) with no corneal involvement following the application of 71 mg of technical grade tebuthiuron (>90% purity) when assayed in rabbits. It should be noted that the EPA documents do not specifically address the presence or absence of corneal injury.

Unlike the case with the dermal endpoints, information in the MSDS does not correspond directly with the information on technical grade tebuthiuron given in Todd et al. (1974). As summarized in Table A1-8, eye irritation with corneal injury is noted in the MSDS for Spike 20P, Spike 80DF, and Alligare Tebuthiuron 80 WG. The MSDS for Alligare Tebuthiuron 20 P indicates that this formulation does not cause eye irritation. The discrepancies regarding the indication of corneal injury between the MSDS and the EPA summaries as well as the publication by Todd et al. (1974) cannot be fully resolved with the available information. Eye irritation studies are typically required for formulations but are not always summarized in EPA risk assessments, which often focus on the technical grade material. It seems plausible that the corneal damage noted in the MSDS are correct and reflect eye irritation studies on formulations that have not been identified in the available literature.

3.1.12. Systemic Toxic Effects from Dermal Exposure

Information on the dermal toxicity of tebuthiuron is summarized in Appendix 1, Table A1-6. The EPA documents summarize a single acute toxicity study in rabbits (MRID 40583902) and a 21-day subchronic toxicity study in rats (U.S. EPA/OPP 1994; U.S. EPA/OPP/HED 2014a). The only other information on dermal toxicity is an acute toxicity/dermal irritation study in the open literature publication by Todd et al. (1974).

As discussed in Section 3.1.11.1, the skin irritation study summarized in EPA documents is consistent with the information on skin irritation in the study by Todd et al. (1974). This is not the case with the data on acute dermal toxicity. The U.S. EPA/OPP (1994) indicates an acute dermal LD_{50} of >5000 mg a.i./kg bw. Based on this study, the EPA classifies tebuthiuron as Category IV for acute dermal toxicity (U.S. EPA/OPP 1994, p. 9). The paper by Todd et al.

(1974) indicates that tebuthiuron was assayed at a dose of only 200 mg a.i./kg bw. Nonetheless, it should be noted that U.S. EPA/OPP 1994 cites MRID 40583902 as the study for both the dermal irritation and acute dermal toxicity data. The discrepancy between the acute dermal toxicity study published by Todd et al. (1974) and the data reported by EPA cannot be further elaborated.

As summarized in Appendix 1, Table A1-8, the MSDS for the tebuthiuron formulations explicitly considered in the current risk assessment report dermal LD_{50} values of >2000 mg a.i./kg bw (Spike 20P and Alligare Tebuthiuron 80 WG) or >5000 mg a.i./kg bw (Spike 80DF; Alligare Tebuthiuron 20 P). These indefinite LD_{50} values do not suggest any differences in acute dermal toxicity among the formulations. The indefinite LD_{50} values probably reflect differences in the highest dose used in the formulation assays or differences in the doses used in limit tests. Both 2000 mg a.i./kg bw and 5000 mg a.i./kg bw are commonly used in limit tests (i.e., bioassays using only a single dose).

In addition to the acute dermal toxicity study, EPA documents (U.S. EPA/OPP 1994; U.S. EPA/OPP/HED 2014a) summarize the results of a standard 21-day subchronic dermal toxicity study in rats in which a dose of 1000 mg a.i./kg bw/day was associated with slight erythema and an increase in blood glucose values. The magnitude of the increase in blood glucose values is not given in the EPA documents. Since the EPA classifies 1000 mg a.i./kg bw/day as a NOAEL, a reasonable supposition is that the magnitude of the increase was not viewed by EPA as toxicologically significant.

3.1.13. Inhalation Exposure

Little information is available on the inhalation toxicity of tebuthiuron. As summarized in Appendix 1, Table A1-7, the Reregistration Eligibility Decision (RED) document on tebuthiuron cites an acute inhalation LC_{50} in rats of >3.696 mg a.i./L (MRID 00155730). Based on this study, EPA classifies tebuthiuron as Category III (*slightly toxic*) for acute inhalation toxicity (U.S. EPA/OPP 1994, p. 9 and p. 16). As summarized in Appendix 1, Table A1-8, the inhalation LC_{50} (rat, 4-hours) reported for Alligare Tebuthiuron 20 P is 3.7 mg a.i./L. While numerically similar to the LC_{50} reported in the RED, the LC_{50} reported for Alligare Tebuthiuron 20 P is definitive rather than indefinite—i.e., the LC_{50} is reported as 3.7 mg a.i./L and not >3.7 mg a.i./L. It is not clear if the definitive LD_{50} for Alligare Tebuthiuron 20 P is an error and should have been reported as >3.7 mg a.i./L, virtually identical to the LC_{50} reported in the RED and attributed to MRID 00155730. The LC_{50} for Alligare Tebuthiuron 80 WG is reported as >4.84 mg a.i./L and appears to be based on a study other than MRID 00155730. An *estimated* LC_{50} of >3 mg a.i./L is reported on the SDS for Spike 80DF; however, the basis for this estimate is not specified. The MSDS for Spike 20P does not include an inhalation LC_{50}.

As noted in the most recent EPA human health risk assessment, subchronic inhalation studies on tebuthiuron are unavailable. Accordingly, to fill this data gap, the EPA has required a 90-day subchronic inhalation study on tebuthiuron (U.S. EPA/OPP/HED 2014a, p. 5). The EPA has issued guidelines for requiring a subchronic inhalation study on a pesticide (U.S. EPA/OPP 2013a, p. 3) which cite vapor pressure as a significant criterion. As noted in the EPA human health risk assessment, vapor pressure is not likely to be a compelling factor: "*Any losses due to volatilization/sublimation are expected to be minimal due to the vapor pressure (2 x 10^{-6} mm Hg at 25 °C)*" (U.S. EPA/OPP/HED 2014a, p. 9) and references the report by Leshin (2014):

> *HED's Hazard and Science Policy Council (HASPOC) determined that a guideline 90-day inhalation study is required. (J. Leshin, TXR 0056925, May 27, 2014). No other toxicology studies are required to support the registration review of tebuthiuron.*
>
> U.S. EPA/OPP/HED 2014a, p. 7

The mention of Leshin (2014) in the above quotation references a report from the EPA's Hazard and Science Policy Council cited in the current Forest Service risk assessment as U.S. EPA/OPP/HASPOC (2014).

As discussed further in Section 3.3.4 (Surrogate RfD for Occupational Exposures), the EPA uses an uncertainty factor of 10 to account for the lack of a subchronic inhalation study in establishing the Margin of Exposure for inhalation exposure scenarios.

3.1.14. Adjuvants and Other Ingredients

3.1.14.1. Other Ingredients

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

The identities of inerts in pesticide formulations are generally considered trade secrets and need not be disclosed to the general public. Nonetheless, all inert ingredients as well as the amounts of the inerts in the formulations are disclosed to and reviewed by the U.S. EPA as part of the registration process. Some inerts are considered potentially hazardous and are identified as such on various lists developed by the federal government and state governments. Material Safety Data Sheets (MSDS) sometimes specify inerts used in pesticide formulations. U.S. EPA/OPP (2015b, p. 5-13) encourages but does not generally require expanded inert statements on product labels which specifically identify the inert ingredients in the product. One notable exception, however, involves petroleum distillates including xylene or xylene range solvents that are part of the formulation and at a concentration of ≥10%. In this case, the product label must contain the following statement: *Contains petroleum distillates, xylene or xylene range aromatic solvents* (U.S. EPA/OPP 2010d, p. 5-11). None of the product labels for the representative formulations list in Table 2 indicate that these formulations contain petroleum distillates.

Table 3 summarizes the other ingredients/inerts disclosed for the formulations of tebuthiuron explicitly covered in the current risk assessment. There are no disclosed inerts for the Alligare formulations (i.e., Alligare Tebuthiuron 20 P and Alligare 80 WG). As summarized in Table 3, the Spike formulations of tebuthiuron—i.e., Spike 20P and Spike 80DF—both contain clay. Spike DF also contains titanium dioxide. When used as a pesticide inert, both clay and titanium dioxide are categorized as List 4B inerts. This list is described by EPA as follows: *Other* *ingredients for which EPA has sufficient information to reasonably conclude that the current use pattern in pesticide products will not adversely affect public health or the environment* (U.S. EPA/OPP 2004a, p. 1). Clay is also on the FDA list of compounds that are "Generally Recognized As Safe" (GRAS) (FDA 2015). Spike 80DF also contains Silica gel which is classified as a List 4A inert. List 4A inerts are classified by EPA as Minimal Risk Inert Ingredients (U.S. EPA/OPP 2004b, p. 1).

3.1.14.2. Adjuvants

The product labels for Spike DF and Alligare Tebuthiuron 80 WG do not recommend the use of adjuvants. Similarly, the granular formulations of tebuthiuron—i.e., Spike 20P and Alligare Tebuthiuron 20 P—do not recommend the use of any adjuvants.

3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

As discussed in SERA (2014a, Sections 3.1.3.1), two types of metabolites may be considered in a risk assessment, *in vivo* metabolites and environmental metabolites. *In vivo* metabolites refer to the compounds formed within the animal after the pesticide has been absorbed. Environmental metabolites refer to compounds that may be formed in the environment by a number of different biological or chemical processes, including breakdown in soil or water or breakdown by sunlight (photolysis).

The *in vivo* metabolites of tebuthiuron are discussed in Section 3.1.3.1, and an overview of these metabolites is given in Table 4. No environmental metabolites other than the *in vivo* metabolites summarized in Table 4 are identified or discussed in the EPA risk assessments (U.S. EPA/OPP/EFED 2014a; U.S. EPA/OPP/HED 2014a). Only one publication detailing the environmental metabolites of tebuthiuron was identified in the open literature—i.e., Loh et al. 1978). Loh et al. (1978) assayed the metabolism of tebuthiuron in grass and sugarcane and identified three metabolites covered in the EPA assessments—i.e., Metabolite 104 (Compound II in Table 1 of Loh et al. 1978), Metabolite 109 (Compound III in Table 1 of Loh et al. 1978), and Metabolite 103(OH) (Compound IV in Table 1 of Loh et al. 1978). Other compounds discussed in this publication (i.e., Compounds V and VI) appear to be thermal degradation products formed during analysis of the metabolites. In terms of accounting for the metabolites of tebuthiuron, the EPA adjusts the environmental fate parameters for tebuthiuron to account for total residues—i.e., tebuthiuron and the metabolites of concern (e.g., U.S. EPA/OPP/EFED 2014a, Table 3.3, p. 24). This standard and reasonable practice in EPA risk assessments is adopted in the current Forest Service risk assessment, as discussed in Section 3.2 (Exposure Assessment).

3.1.15.2. Impurities

There is no published information regarding the impurities in technical grade tebuthiuron or any of its commercial formulations. Impurities are not discussed in the open literature, the recent risk assessments by EPA (U.S. EPA/OPP/HED 2002, 2014a), and other reviews on tebuthiuron (as specified in Section 1.1). Nonetheless, the EPA requires registrants to submit information on impurities as a condition for registration. This information is reviewed by the EPA but is not disclosed to the general public. Information on impurities is considered to be Confidential Business information (CBI) and was not obtainable for the preparation of the current Forest Service risk assessment.

The EPA Reregistration Eligibility Decision document contains the following note on impurities: *Samples must be analyzed for nitrosamine content. Additional data are required for an impurity (CBI) listed on the CSF* [Confidential Statement of Formula] (U.S. EPA/OPP 1994, p. 8), but provides no additional details. Nonetheless, all of the toxicology studies on tebuthiuron involve technical grade tebuthiuron, which is presumed to be the same as or comparable to the active ingredient in the formulations used by the Forest Service. Thus, any toxic impurities present in the formulated product are likely to be encompassed by the available toxicity studies conducted with technical grade tebuthiuron.

3.1.16. Toxicological Interactions

The toxicological interactions of tebuthiuron with other compounds in mammals are not addressed in the available literature. As discussed in 4.4.3.4.1, tebuthiuron was found to be additive in algal assays of binary combinations of tebuthiuron with other herbicides; however, this finding is not directly relevant to potential effects in humans or other mammals. As discussed further in Section 3.4.6 (Cumulative Effects), the EPA has not assessed the joint action of tebuthiuron with other pesticides based on assumptions concerning a common mechanism of action.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

The exposure assessments used in the current risk assessment are given in the accompanying EXCEL workbooks: Attachment 1 for applications of liquid formulations and Attachments 2-4 for applications of granular formulations. These workbooks contain a set of worksheets that detail each exposure scenario discussed in this risk assessment as well as summary worksheets for both workers (Worksheet E01) and members of the general public (Worksheet E02). Documentation for these worksheets is presented in SERA (2011a). All exposure assessments are conducted assuming an application rate of 0.6 lb a.i./acre (Section 2).

For both liquid and granular applications, worker exposures are modeled for backpack spray, broadcast ground spray, and aerial spray. In non-accidental scenarios involving the normal application of tebuthiuron, central estimates of exposure for workers are approximately 0.03 mg/kg bw/day for backpack applications, 0.04 mg/kg bw/day for ground broadcast applications, and 0.03 mg/kg bw/day for aerial spray. Upper prediction intervals of exposures are approximately 0.4 mg/kg bw/day for backpack applications, 0.1 mg/kg bw/day for ground broadcast applications, and 0.2 mg/kg bw/day for aerial applications.

For the general public (Worksheet E03), acute non-accidental exposure levels associated with terrestrial applications range from very low (e.g., ≈1×10^{-6} mg a.i./kg bw/day) to about 0.8 mg a.i./kg bw for liquid applications and 0.07 mg a.i./kg bw/day for granular applications. The upper bounds of exposures for both liquid and granular applications involve the consumption of contaminated vegetation. As with acute exposures, the highest longer-term exposure levels are associated with the consumption of contaminated vegetation, and the upper bound for this scenario is about 0.34 mg a.i./kg bw/day for liquid applications and 0.014 mg a.i./kg bw/day for granular applications. The differences between the estimated doses involving liquid and granular applications are based on estimated differences in their deposition on vegetation. While these differences are based on a study involving applications of liquid and granular formulations of hexazinone, the differences are supported by a study involving liquid and granular applications of tebuthiuron. The lowest exposure levels are associated with swimming in or drinking contaminated water. For the accidental exposure scenarios, the greatest exposure levels are associated with the consumption of contaminated water by a small child following an accidental spill, for which the upper bound dose is about 1.2 mg a.i./kg bw for liquid applications and 4.1 mg a.i./kg bw for granular applications.

3.2.2. Workers

3.2.2.1. General Exposures

As described in SERA (2014b), worker exposure rates used in Forest Service risk assessments are expressed in units of mg of absorbed dose per kilogram of body weight per pound of pesticide handled. Based on analyses of several different pesticides using a variety of application methods, SERA (2014b) derives exposure rates for directed foliar (backpack), boom spray (hydraulic ground spray), and aerial applications. As discussed in Section 2.3, tebuthiuron applications are intended to treat the soil rather than plant foliage. For formulations of tebuthiuron that are mixed with water prior to application (e.g., Tebuthiuron 80 WG and Spike 80DF), the worker exposure rates for foliar applications should apply reasonably well to soil applications, given that the workers are handling and applying a liquid solution of the herbicide in both foliar and ground applications.

No worker exposure studies for granular applications are covered in the SERA (2014a) report. For granular formulations applied as granules (i.e., with no mixing in water), the applicability of the worker exposure rates from SERA (2014b) to granular soil applications is less intuitive. Nonetheless, as detailed in the Forest Service risk assessment on hexazinone (SERA 2005, Section 3.2.2.1), a worker exposure study of hexazinone applied with a hand-cranked broadcast spreader yielded worker exposure rates comparable to backpack applications of liquid formulations. In addition, as summarized in Table 3 of SERA (2014b), deposition based total body worker exposure rates developed by EPA are comparable for groundboom liquid and granular applications (0.046 vs. 0.039 mg/lb handled) with open cab vehicles as well as for liquid and granular applications (0.005 vs 0.0044 mg/lb handled) with enclosed cockpit aircraft. Given the reasonable correspondence between worker exposure rates for granular and liquid applications, the current risk assessment applies the worker exposure rates from SERA (2014b) to both liquid and granular applications of tebuthiuron.

As summarized in Table 14 (p. 82) of SERA (2014b), the worker exposure rates are available for directed foliar, broadcast foliar, and aerial broadcast applications. As also discussed in SERA (2014b, Section 4.2.1), chemical-specific worker exposure rates are derived by adjusting for differences in the first-order dermal absorption rates for the reference pesticide (i.e., the pesticide used to derive the worker exposure rate) and the pesticide under consideration, in this case tebuthiuron. These adjustments are detailed in Table 5 for directed applications, Table 6 for ground broadcast applications, and Table 7 for aerial applications. As discussed in Section 3.1.3.2.1, the central estimate of the first-order dermal absorption rate coefficient is taken as 0.004 $hour^{-1}$ based on the QSAR method from SERA (2014a, Section 3.1.3.2.2). For directed soil applications (Table 5), the reference chemical is taken as triclopyr BEE, which has an estimated first-order dermal absorption rate coefficient of 0.0031 $hour^{-1}$. Thus, the worker exposure rates based on triclopyr BEE are adjusted upward by a modest factor of about 1.3 [$0.004\ hour^{-1} \div 0.0031\ hour^{-1} \approx 1.2903$]. For ground broadcast applications (Table 6) and aerial broadcast applications (Table 7), the worker exposure rates are based on studies involving 2,4-D, which has an estimated first-order dermal absorption rate coefficient of 0.00066 $hour^{-1}$. Thus, the worker exposure rates for these application methods are adjusted upward by a factor of about 6 [$0.004\ hour^{-1} \div 0.00066\ hour^{-1} \approx 6.0606$]. As discussed in SERA (2014b, Section 4.2.1), the adjustment factor for differences in dermal absorption is optional for ground broadcast and aerial applications because of the limited data supporting such an adjustment. In the case of tebuthiuron, the adjustment factor is used in the current risk assessment as a conservative , precautionary approach given the greater dermal absorption rate of tebuthiuron relative to 2,4-D and the uncertainties, discussed above, in the application of exposure rates involving liquid applications to exposure rates involving granular applications. These uncertainties are discussed further in the risk characterization for workers (Section 3.4.2).

3.2.2.2. Accidental Exposures

Generally, dermal exposure is the predominant route of exposure for pesticide applicators (Ecobichon 1998; van Hemmen 1992), and accidental dermal exposures are considered quantitatively in all Forest Service risk assessments. The two types of dermal exposures modeled in the risk assessments include direct contact with a pesticide solution and accidental spills of the pesticide onto the surface of the skin. In addition, two exposure scenarios are developed for each of the two types of dermal exposure. The estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight.

Exposure scenarios involving direct contact with solutions of tebuthiuron are characterized either by immersion of the hands in a field solution for 1 minute or wearing pesticide contaminated gloves for 1 hour. The assumption that the hands or any other part of a worker's body will be immersed in a chemical solution for a prolonged period of time may seem unreasonable; however, it is possible that the gloves or other articles of clothing worn continuously by a worker may become contaminated with pesticide. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in the solution. In both cases, the chemical concentration in contact with the skin and the resulting dermal absorption rates are essentially constant. For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. For these types of exposures, the rate of absorption is estimated based on a zero-order dermal absorption rate (K_p). Details regarding the derivation of the K_p value for tebuthiuron are provided in Section 3.1.3.2.2. The amount of the pesticide absorbed per unit time depends directly on the concentration of the chemical in solution. This concentration is highly variable depending on the application method and also on the dilution volumes, as discussed in Section 2.4.1 for foliar applications and Section 2.4.2 for bark applications. These exposure scenarios are detailed in Worksheets C02a (1-minute exposure) and C02b (60-minute exposure).

These exposure scenarios involving contaminated gloves are developed for both liquid applications (Attachment 1) and granular applications (Attachments 2-4). For liquid applications, the concentration of tebuthiuron in contaminated gloves is based on the concentrations of tebuthiuron in field solutions as detailed in Worksheet A01. For granular applications, no standard methods for estimating exposure are available. Nonetheless, granular tebuthiuron on the surface of the skin might be regarded as analogous to exposure to a neat (undiluted) solution. For such exposures, the U.S. EPA/ORD (1992) recommends using the solubility of the compound in water as an approximation of the concentration of the chemical on the surface of the skin. The apparent rationale for this approach is that the amount of the chemical on the surface of the skin will saturate the pore water of the skin and the limiting factor on the concentration in pore water will be solubility of the chemical in water. As indicated in Table 1, the water solubility of tebuthiuron is 2500 mg/L, which is equivalent to 2.5 mg/mL. This concentration is used in Worksheets C02a and C02b of Attachments 2-4.

The details of the accidental spill scenarios for workers consist of spilling a chemical solution onto the lower legs as well as spilling a chemical solution on to the hands, at least some of which adheres to the skin. The absorbed dose is then calculated as the product of the amount of chemical on the skin surface (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the chemical concentration in the liquid), the first-order absorption rate coefficient, and the duration of exposure. The first-order dermal absorption rate coefficient (k_a) is derived in Section 3.1.3.2.1. These exposure scenarios are detailed in Worksheets C03a (spill onto the hand) and C03b (spill onto the lower legs). The exposure scenario for an accidental spill is used for applications of liquid solutions as detailed in

Worksheets C01a and C01b of Attachment 1. The accidental spills onto the hands or lower legs are not applicable to granular applications and these scenarios are included in Attachments 2-4 (i.e., granular applications of tebuthiuron).

3.2.3. General Public

3.2.3.1. General Considerations

3.2.3.1.1. Likelihood and Magnitude of Exposure

The likelihood that members of the general public will be exposed to tebuthiuron in Forest Service programs appears to be highly variable, depending on the application method and where the material is applied. Tebuthiuron could be applied in or near recreational areas like campgrounds, picnic areas, and trails. Under such circumstances, it is plausible that members of the general public would be exposed to tebuthiuron following either liquid or granular applications. As discussed further in Section 3.2.3.7, the magnitude of exposures could differ substantially between liquid and granular applications.

Because of the conservative exposure assumptions used in the current risk assessment, neither the probability of exposure nor the number of individuals who might be exposed has a substantial impact on the characterization of risk presented in Section 3.4. As noted in Section 1 (Introduction) and detailed in SERA (2014a, Section 1.2.2.2), the exposure assessments developed in this risk assessment are based on *Extreme Values* rather than a single value. Extreme Value exposure assessments, as the name implies, bracket the most plausible estimate of exposure (referred to statistically as the central or maximum likelihood estimate and more generally as the typical exposure estimate) with extreme lower and upper bounds of plausible exposures.

This Extreme Value approach is essentially an elaboration on the concept of the *Most Exposed Individual* (MEI), sometime referred to as the *Maximum Exposed Individual* (MEI). As this name also implies, exposure assessments that use the MEI approach are made in an attempt to characterize the extreme but still plausible upper bound on exposure. This approach is common in exposure assessments made by U.S. EPA, other government agencies, and other organizations. In the current risk assessment and other Forest Service risk assessments, the upper bounds on exposure estimates are all based on the MEI.

In addition to this upper bound MEI value, the Extreme Value approach used in this risk assessment provides a central estimate of exposure as well as a lower bound on exposure. While not germane to the assessment of upper bound risk, it is significant that the use of the central estimate and especially the lower bound estimate is not intended to lessen concern. To the contrary, the central and lower estimates of exposure are used to assess the feasibility of mitigation—e.g., measures to limit exposure. If lower bound exposure estimates exceed a level of concern, this is strong indication that the pesticide cannot be used in a manner that will lead to acceptable risk.

3.2.3.1.2. Summary of Assessments

The exposure scenarios developed for the general public are summarized in Worksheet E03 of the EXCEL workbooks that accompany this risk assessment. As with the worker exposure scenarios, details about the assumptions and calculations used in these assessments are given in the detailed calculation worksheets in the EXCEL workbooks (Worksheets D01–D10).

For tebuthiuron, a standard set of exposure assessments used in all Forest Service risk assessments for directed and broadcast applications are considered. As summarized in Worksheet E03 of Attachments 1-4, the kinds of exposure scenarios developed for the general public include acute accidental, acute non-accidental, and longer-term or chronic exposures. The acute accidental exposure scenarios assume that an individual is exposed to the compound of concern either during or shortly after its application. Non-accidental exposures involve dermal contact with contaminated vegetation as well as the consumption of contaminated fruit, vegetation, water, or fish. The longer-term or chronic exposure scenarios parallel the acute exposure scenarios for the consumption of contaminated fruit, water, or fish. All of the non-accidental exposure scenarios are based on levels of exposure to be expected following an application of tebuthiuron at 0.6 lb a.i./acre. The upper bounds of the exposure estimates for the non-accidental scenarios involve conservative assumptions intended to reflect exposure for the MEI (*Most Exposed Individual*) as discussed in Section 3.2.3.1.1. The impact of lower or higher application rates on the risk characterization is discussed in Section 3.4.

The nature of the acute accidental exposure scenarios is intentionally extreme. The acute non-accidental exposure scenarios are intended to be conservative but plausible, meaning that it is not unreasonable to assume that the magnitude of exposures in the non-accidental exposure scenarios could occur in the routine use of tebuthiuron. This interpretation does not extend to the longer-term exposure scenarios. The longer-term exposure scenarios essentially assume that an individual will consume either contaminated vegetation, fruits, or water from a treated area every day over a prolonged period of time. However unlikely it may seem, this type of exposure cannot be ruled out completely. As discussed further in Section 3.4.3, this is an important consideration in the interpretation of hazard quotients associated with longer-term exposures to contaminated vegetation, particularly exposures involving liquid solutions of tebuthiuron.

As discussed in the following sections, a complete set of standard exposure scenarios is developed in Attachment 1 for liquid applications of tebuthiuron. For granular applications, not all of these exposure scenarios are relevant and a subset of the standard exposure scenarios is included in Attachments 2-4.

3.2.3.2. Direct Spray

Direct spray scenarios for members of the general public are modeled in a manner similar to accidental spills for workers (Section 3.2.2.2). In other words, it is assumed that the individual is sprayed with a field solution of the compound and that some amount of the compound remains on the skin and is absorbed by first-order kinetics. Two direct spray scenarios are given, one for a young child (D01a) and the other for a young woman (D01b). These exposure scenarios are relevant only to liquid applications and thus are included in Attachment 1 but excluded from Attachments 2-4.

For the young child, it is assumed that a naked child is sprayed directly during a broadcast application and that the child is completely covered with pesticide (i.e., 100% of the surface area of the body is exposed). This exposure scenario is intentionally extreme. As discussed in

Section 3.2.3.1.1, the upper limits of this exposure scenario are intended to represent the *Extreme Value* of exposure for the *Most Exposed Individual* (MEI).

The exposure scenario involving the young woman (Worksheet D01b) is somewhat less extreme, but more plausible, and assumes that the woman is accidentally sprayed over the feet and lower legs. By reason of the relationships between body size and dose-scaling, a young woman would typically be subject to a somewhat higher dose than would the standard 70 kg man. Consequently, in an effort to ensure a conservative estimate of exposure, a young woman, rather than an adult male, is used in many of the exposure assessments.

For the direct spray scenarios, assumptions are made regarding the surface area of the skin and the body weight of the individual, as detailed in Worksheet A03 of the attachments. The rationale for and sources of the specific values used in these and other exposure scenarios are provided in the documentation for WorksheetMaker (SERA 2011a) and in the methods document for preparing Forest Service risk assessments (SERA 2014a).

3.2.3.3. Dermal Exposure from Contaminated Vegetation

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

No data are available on dermal transfer rates for tebuthiuron, which is not necessarily a severe limitation in this risk assessment. As detailed in Durkin et al. (1995), dermal transfer rates are reasonably consistent for numerous pesticides, and the methods and rates derived in Durkin et al. (1995) are used as defined in Worksheet D02. Similarly, no information on dislodgeable residues for tebuthiuron has been identified, which is a somewhat greater source of uncertainty. For this exposure scenario, a default dislodgeable residue rate of 0.1 of the nominal application rate is used. This rate is based on liquid applications. For granular applications, no relevant data on dislodgeable residues in turf have been identified. Thus, this exposure scenario is not included in Attachments 2-4.

The exposure scenario assumes a contact period of 1 hour and further assumes that the chemical is not effectively removed by washing for 24 hours. Other approximations used in this exposure scenario include estimates of body weight, skin surface area, and first-order dermal absorption rates, as discussed in Section 3.2.3.2 (Direct Spray).

3.2.3.4. Contaminated Water

3.2.3.4.1. Accidental Spill

The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill of the pesticide into a small pond. The concentrations of the pesticide in the spilled solution are detailed in Section 2.4 based on application volumes. The calculation of the concentration of tebuthiuron in water following the spill is given in Worksheet B04b, and the estimate of the dose to a small child is given in Worksheet D05 of the attachments to this risk assessment. This scenario assumes that the pesticide solution is uniformly dispersed in the pond.

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

For applications of tebuthiuron as a liquid (Attachment 1), a spill volume of 100 gallons with a range of 20 to 200 gallons is used to reflect plausible spill events. These spill volumes are used in all Forest Service risk assessments involving terrestrial applications of liquid applications. The tebuthiuron concentrations in the field solution are also varied to reflect the plausible range of concentrations in field solutions—i.e., the material that might be spilled—using the same values as in the accidental exposure scenarios for workers (Section 3.2.2.2). Based on these assumptions, the estimated nominal concentration of tebuthiuron in a small pond ranges from about 0.068 to about 10.6 mg a.i./L with a central estimate of about 1.3 mg a.i./L (Attachment 1).

For granular applications (Attachments 2-4), a spill volume is not applicable. As an alternative, the amount of the pesticide spilled into the pond is taken as 40 (16-80) lbs a.i. This is a uniform assumption used by WorksheetMaker for all granular applications (SERA 2011a). Based on these spill amounts, the estimated nominal concentration of tebuthiuron in a small pond ranges from about 7.25 to about 32.6 mg a.i./L with a central estimate of about 18.1 mg a.i./L (Attachments 2-4).

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

These scenarios involve the accidental direct spray or incidental spray drift to a small pond and a small stream. The exposure scenarios involving drift are less severe but more plausible than the accidental spill scenario described in the previous section. The drift estimates are based on AgDrift (Teske et al. 2002), as detailed in SERA (2011b, Section 3.3.2). The direct spray and drift scenarios are detailed in Worksheet B04c (small pond) and Worksheet B04d (small stream).

Importantly, no distinction is made between the application of liquid and granular formulations. AgDrift does not explicitly incorporate options for the application of granular products (Teske et al. 2002), and field data do not address tebuthiuron drift following applications of granular formulations. The extent to which the general drift estimates used for liquid formulations are appropriate for granular applications is unclear. This uncertainty has little direct impact on this exposure scenario, however, because only the direct spray scenario is used quantitatively in the current risk assessment.

3.2.3.4.3. GLEAMS Modeling

The Forest Service developed a software program, Gleams-Driver, to estimate expected peak and longer-term pesticide concentrations in surface water. Gleams-Driver for conducting simulations using GLEAMS (Groundwater Loading Effects of Agricultural Management Systems), which is a field scale model developed by the USDA/ARS (Knisel and Davis 2000). The GLEAMS model has been used for many years in risk assessments by the Forest Service and other USDA agencies (SERA 2007a, 2011b).

Gleams-Driver offers the option of conducting exposure assessments using site-specific weather files from Cligen, a climate generator program developed and maintained by the USDA Agricultural Research Service (USDA/NSERL 2004). Gleams-Driver was used in the current risk assessment to model tebuthiuron concentrations in a small stream and a small pond.

As summarized in Table 8, nine locations are used in the Gleams-Driver modeling. These locations are standard sites used in Forest Service risk assessments for Gleams-Driver simulations and are intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool) (SERA 2007a). The characteristics of the fields and bodies of water used in the simulations are summarized in Table 9. For each location, simulations were conducted using clay (high runoff, low leaching potential), loam (moderate runoff and leaching potential), and sand (low runoff, high leaching potential) soil textures. For each combination of location and soil, Gleams-Driver was used to simulate pesticide losses to surface water from 100 modeled applications at a unit application rate of 1 lb a.i./acre, and each of the simulations was followed for a period of about 1½ years post application. Note that an application rate of 1 lb a.i./acre is used as a convention in all Forest Service risk assessments in order to avoid rounding limitations in GLEAMS outputs. All exposure concentrations discussed in this risk assessment are based on an application rate of 0.6 lb a.i./acre as discussed in Section 2 (Program Description).

Table 10 summarizes the chemical-specific values used in Gleams-Driver simulations. For the most part, the chemical properties used in the Gleams-Driver simulations are based on the parameters used by the Environmental Fate and Effects Division (EFED) of the U.S. EPA's Office of Pesticides Programs modeling of tebuthiuron (U.S. EPA/OPP/EFED 2014a). One difference between the EPA and GLEAMS-Driver modeling involves estimates of variability. The EPA modeling is typically based on either central estimates or upper bound (90^{th} percentile) input parameters. Following the Extreme Value approach discussed in Section 3.2.3.1.1, the input parameters for the GLEAMS-Driver modeling are based on estimates of variability either as ranges or confidence intervals. In the GLEAMS-Driver simulations, ranges are implemented as uniform distributions and central estimates with lower and upper bounds are implemented as triangular distributions (SERA 2007a). In the current risk assessment, most of the model input values are based on the environmental fate studies submitted to the U.S. EPA by registrants, standard values for GLEAMS modeling recommended by Knisel and Davis (2000), and studies from the open literature. The notes to Table 10 indicate the specific sources of the chemical properties used in the GLEAMS modeling effort. The most substantial deviations of inputs used in the current risk assessment from the modeling inputs used by U.S. EPA include estimates of the variability in soil binding (K_{oc} and K_d values) and the use of a range for the half-life of tebuthiuron in water rather than a single upper bound value used by U.S. EPA.

Table 11 summarizes the modeled concentrations of tebuthiuron in surface water by GLEAMS-Driver. Details of the GLEAMS-Driver simulations are detailed in Appendix 6 for liquid applications (i.e., Alligare Tebuthiuron 80 WG and Spike 80DF) and Appendix 7 for granular applications (i.e., Alligare Tebuthiuron 20 P and Spike 20P). As summarized in Table 11, the GLEAMS-Driver estimates for the two types of formulations are essentially identical. To some extent, this similarity is probably due to the fact that GLEAMS is not designed to assess the application of granular formulations. As in the Forest Service risk assessment on hexazinone (SERA 2005), the application of a granular formulation is mimicked by using a 1 cm layer of clay as the top soil layer for all soils. As summarized in Table 10, tebuthiuron is not highly bound to soils (i.e., K_{oc} values range from 12.2 to 152). This factor appears to account for the close similarities in the surface water concentrations for liquid and granular applications. The specific concentrations of tebuthiuron in surface water used in the exposure assessments for the current risk assessment are discussed in Section 3.2.3.4.6.

3.2.3.4.4. Other Modeling Efforts

Table 11 summarizes the results of the application of two EPA Tier 1 screening models to estimating concentrations of tebuthiuron in surfaces water (FQPA Index Reservoir Screening Tool, a.k.a. FIRST) and ground water (PRZM-GW). The inputs and outputs for these Tier 1 models is detailed in Appendix 8. Table 11 also summarizes the application of PRZM/EXAMS, a Tier 2 model, by U.S. EPA/OPP/EFED (2014a). The U.S. EPA/OPP typically models pesticide concentrations in water at the maximum labeled rate. In Table 11, the modeling results reported by U.S. EPA/OPP/EFED (2014a, Table 3.4, p. 25) are normalized to an application rate of 1 lb a.i./acre so that the results are comparable to the GLEAMS-Driver modeling discussed in the previous section. Details of the normalization are given at the end of Appendix 9 in the current risk assessment.

The results of the FIRST modeling are similar to the lower bounds of the GLEAMS-Driver modeling. The central estimates from FIRST for peak and longer-term concentrations are similar to the GLEAMS-Driver estimates for clay and loam soils. The estimates for sandy soils from GLEAMS-Driver are higher than those from FIRST by about a factor of 3. The higher concentrations for sandy soils relative to clay or loam are to be expected given the relatively low K_{oc} values for tebuthiuron. All of the product labels for tebuthiuron contain cautionary language concerning its applications to predominantly sandy soils. In addition, several studies from the open literature discuss the high leaching potential for tebuthiuron, which would be most pronounced in sandy soils (Diaz-Diaz and Loague 2001; Helbert 1990; Matallo et al. 2005; Morton et al. 1989; Negrisoli et al. 2005; Stone et al. 1993). As would be expected based on the physical process of leaching, tebuthiuron (or any other pesticide) will not typically leach in arid areas (Johnsen and Morton 1989). Nonetheless, arid areas may experience sporadic but major precipitation events which could mobilize tebuthiuron in the upper soil layers.

The more detailed Tier 2 modeling with PRZM/EXAMS yields estimated water concentration rates of 97 (55-184) ppm per lb a.i./acre. The central estimate is similar to the overall average from GLEAMS-Driver – i.e., 90.8 ppb per lb a.i./acre. The ranges from the GLEAMS-Driver modeling (6.37 to 635 ppb per lb a.i./acre), however, are much greater than those from the PRZM/EXAMS modeling. Broader ranges from the GLEAMS-Driver modeling relative to PRZM/EXAMS modeling are commonly noted in Forest Service risk assessments and appear to reflect the broader range of input values used in the GLEAMS-Driver modeling, the number and diversity of locations and soil types used in the GLEAMS-Driver modeling, and the large number of simulations conducted in the GLEAMS-Driver modeling relative to the PRZM/EXAMS modeling.

3.2.3.4.5. Monitoring Data

In terms of evaluating the surface water modeling efforts discussed in the previous sections, the most useful monitoring studies are those that associate monitored concentrations of a pesticide in water with defined applications of the pesticide—e.g., applications at a defined application rate to a well characterized field. When available, such studies can provide a strong indication of the plausibility of modeled concentrations of a pesticide in surface water. No such studies were identified for tebuthiuron.

Based on general monitoring surveys from the USGS, tebuthiuron is frequently found in surface waters but at low concentrations—i.e., 90th percentile concentrations of about 0.2 µg/L or ppb (Gilliom et al. 1999; Ryberg et al. 2010; Stone et al. 2014). Most other monitoring publications in the open literature (i.e., Bortleson and Ebbert 2000; Dalton and Frick 2008; Domagalski 1997; Kolpin et al. 1995; Tagert et al. 2014) also report generally low maximum concentrations of tebuthiuron in surface or ground water ranging from about 0.03 ppb (Bortleson and Ebbert 2000) to 2 ppb (Dalton and Frick 2008). One major exception is the report by Wade et al. (1998) of tebuthiuron in well water in North Carolina at concentrations of up to 123 ppb. Again, none of these monitoring studies involved defined applications of tebuthiuron, and these studies cannot be used to assess the quality of the modeled concentrations given in Table 11. Nonetheless, it is notable that the highest concentration from the monitoring studies is encompassed and exceeded by the concentrations of tebuthiuron in surface water estimated using GLEAMS-Driver.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

The modeled surface water concentrations of tebuthiuron used in the current risk assessment are summarized in Table 12. The concentrations are specified as water contamination rates (WCRs)—i.e., the concentrations in water expected at a normalized application rate of 1 lb a.i./acre, converted to units of ppm or mg a.i./L per lb a.i./acre. In Table 11, the summary of all of the modeling efforts, units of exposure are expressed as ppb or µg a.i./L, as a matter of convenience. In Table 12, however, ppb is converted to mg a.i./L (ppm) because mg a.i./L is the unit of measure used in the EXCEL workbooks for contaminated water exposure scenarios in both the human health and ecological risk assessments. The water contamination rates are entered in Worksheet B04Rt in the attachments to this risk assessment. The values in Worksheet B04Rt are linked to the appropriate scenario-specific worksheets in the EXCEL workbooks and are adjusted to the application rate entered in Worksheet A01—i.e., 0.6 lb a.i./acre in the workbooks released with this risk assessment. In the worksheet associated with contaminated surface water, the application rate is multiplied by the water contamination rates to estimate the expected concentrations of tebuthiuron in surface water.

As discussed previously and summarized in Table 11, the Gleams-Driver simulations of the small pond provide the highest estimates of tebuthiuron concentrations in surface water. Consequently, the Gleams-Driver simulations serve as the primary basis for the water concentrations of tebuthiuron used in the current risk assessment. As summarized in Table 11, the average modelled peak concentrations in a small pond are 185 (10.6 to 1010) µg a.i./L per lb/acre. These WCR values are rounded to two significant places and converted to mg a.i./L in

Table 12 – i.e., 0.19 (0.011 to 1.0) mg a.i./L per lb/acre. Similarly, as also summarized in Table 11, the average modelled longer-term WCR values are 90.8 (6.37 to 635) µg a.i./L per lb a.i./acre. These WCR values are rounded to two significant places and converted to mg a.i./L in Table 12—i.e., 0.091 (0.0064 to 0.64) mg a.i./L per lb a.i./acre.

As noted in 3.2.3.4.5, monitoring data on concentrations of tebuthiuron in surface water are not associated with defined applications of tebuthiuron. Thus, the monitoring data are not directly useful for assessing the quality of the modeled estimates. While the Gleams-Driver estimates are reasonably consistent with U.S. EPA/OPP modeling (Section 3.2.3.4.4), the lack of appropriate monitoring data adds uncertainty to this risk assessment. Nonetheless, the highest monitored concentration of tebuthiuron—i.e., 123 ppb or 0.123 mg a.i./L as reported by Wade et al. (1998)—is below the upper bound of the expected peak concentration of tebuthiuron based on modeling—i.e., 0.6 mg a.i./L, as summarized in Worksheet B04a of the attachments—by a factor of about 5 [0.6 mg a.i./L ÷ 0.123 mg a.i./L ≈ 4.878]. Thus, the modeled estimates of tebuthiuron in surface water appear to be protective but not unreasonably so.

As discussed in Section 2.4 (Mixing and Application Rates), label restrictions limit applications of tebuthiuron for ground water protection in areas with less than 20 inches/per year of rainfall. As summarized in Table 11, water contamination rates for ground water are 0.034 (0.0122-0.722) mg a.i./L per lb a.i./acre based on PRZM/GW modeling. These rates are encompassed by the water contamination rates used based on the GLEAMS-Driver modeling – i.e., 0.19 (0.011-1) mg a.i./L per lb a.i./acre.

3.2.3.5. Oral Exposure from Contaminated Fish

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

Three sets of exposure scenarios are presented: one set for acute exposures following an accidental spill (Worksheets D08a and D08b), one set for acute exposures based on expected peak concentrations of tebuthiuron in water (Worksheets D09c and D09d), and another set for chronic exposures based on estimates of longer-term concentrations in water (Worksheets D09a and D09b). The two worksheets for each set of scenarios are included to account for different consumption rates of caught fish among the general population and subsistence populations. Details of these exposure scenarios are provided in Section 3.2.3.5 of SERA (2014a).

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

Experimental bioconcentration factors are required by the EPA as part of the registration process. As summarized in Table 1, one bioconcentration study in bluegill sunfish was submitted to the

U.S. EPA/OPP (U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 40819501). For edible tissue (i.e., the portion of the fish that would be consumed by humans), the reported bioconcentration factor is 1.98 L/kg, which is used in the exposure assessment for humans. This approach is identical to the approach used for the consumption of fish by wildlife (Section 4.2.2.5), except that whole fish bioconcentration factors are used —i.e., 2.63 L/kg from MRID 40819501.

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

Some geographical sites managed by the Forest Service include surface water in which members of the general public might swim. The extent to which this might apply to areas treated with tebuthiuron is unclear. Nonetheless, this is an exposure assessment that is considered in most Forest Service risk assessments.

To assess the potential risks associated with swimming in contaminated water, an exposure assessment is developed for a young woman swimming in surface water for 1 hour (Worksheet D10). Conceptually and computationally, this exposure scenario is virtually identical to the contaminated gloves scenario used for workers (Section 3.2.2.2)—i.e., a portion of the body is immersed in an aqueous solution of the compound at a fixed concentration for a fixed period of time.

As in the corresponding worker exposure scenario, the 1-hour period of exposure is somewhat arbitrary given that longer periods of exposure are plausible. Nonetheless, the 1-hour period is intended as a unit exposure estimate. In other words, both the absorbed dose and consequently the risk will increase linearly with the duration of exposure, as indicated in Worksheet D10. Thus, a 2-hour exposure would lead to an HQ that is twice as high as that associated with an exposure period of 1 hour. In cases in which this or other similar exposures approach a level of concern, further consideration is given to the duration of exposure in the risk characterization (Section 3.4). For tebuthiuron, however, the HQs for this scenario are far below the level of concern—i.e., an upper bound HQ of 0.003.

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

3.2.3.7. Oral Exposure from Contaminated Vegetation

For pesticides that may be applied to vegetation, Forest Service risk assessments include standard exposure scenarios for the acute and longer-term consumption of contaminated fruit and vegetation. The applicability of these exposure scenarios to tebuthiuron may be limited. As discussed in Section 2, tebuthiuron is not labelled for the treatment of crops for human consumption. In addition, tebuthiuron is intended to be applied to soil rather than foliage. Nonetheless, incidental contamination of vegetation may occur, particularly in broadcast applications. Consequently, the standard exposure scenarios for the consumption of contaminated fruit and vegetation are included in the current risk assessment. A further discussion of the applicability of these exposure scenarios to the human health risk assessment is given in the risk characterization (Section 3.4.3).

Two sets of standard exposure scenarios are provided: one for the consumption of contaminated fruit and the other for the consumption of contaminated vegetation. These scenarios are detailed in Worksheets D03a (fruit) and D03b (vegetation) for acute exposure and Worksheets D04a (fruit) and D04b (vegetation) for chronic exposure. The key inputs for these scenarios are the initial residues on the vegetation and the amount of fruit or vegetation consumed for both acute and chronic scenarios. For chronic scenarios, additional key inputs are the half-lives of the pesticide on the fruit or vegetation as well as the period used to estimate the average concentration of the pesticide on vegetation.

In most Forest Service risk assessments, the initial concentration of the pesticide on fruit and vegetation is estimated using the empirical relationships between application rate and concentration on different types of vegetation (Fletcher et al. 1994). These residue rates are summarized in Table 13. The rates provided by Fletcher et al. (1994) are based on a reanalysis of data originally compiled by Hoerger and Kenaga (1972) and represent estimates of pesticide concentration in different types of vegetation (mg chemical/kg vegetation) at a normalized application rate of 1 lb a.i./acre. Although the human health risk assessments conducted by the EPA do not consider this exposure scenario, the residue rates recommended by Fletcher et al. (1994) are typically used by U.S. EPA/OPP in ecological risk assessments (U.S. EPA/OPPTS, 2004, p. 59; U.S. EPA/EFED 2001, p. 44). Little information exists in the literature about tebuthiuron residues on vegetation associated with defined applications. Bovey et al. (1978, Table 5, p. 236 of paper) noted peak residues of 438 mg a.i./kg on grass following a broadcast spray application of tebuthiuron at a rate of 2.24 kg a.i./ha (2 lb a.i./acre), which corresponds to a residue rate of 219 mg a.i./kg per lb a.i./acre [438 mg a.i./kg ÷ 2 lb a.i./acre]. This residue rate is close to the upper bound of 240 mg/kg grass per lb a.i./acre for short grass from EPA (Table 13).

As discussed in SERA (2014a, Section 3.2.3.7), the residue rates developed by Fletcher et al. (1994) are applicable only to applications of liquid formulations, and no systematic analyses of residues on vegetation have been identified for granular applications. Based on a study involving granular applications of hexazinone, residue rates on vegetation following a granular application are estimated as a factor of 25 below that of residues following a liquid application. In the only tebuthiuron study comparing residues following liquid and granular applications, Bovey et al. (1978, Table 5, p. 236 of paper) compare residues on grass following both liquid and granular applications of tebuthiuron. Residues in grass following granular applications were not assayed on the day of application. After about 1 month, however, the residues in grass following the granular application were a factor of about 28 below the corresponding residues on grass treated with a liquid application (i.e., 23.5 mg/kg grass ÷ 0.82 mg/kg grass ≈ 28.66). This factor is reasonably close to the factor of 25 derived from data on hexazinone. In the absence of additional data, the current risk assessment adopts the approach from SERA (2014a) and estimates residues on vegetation following granular applications as a factor of 25 below the rates used by EPA for liquid applications. The specific residue rates are given in the bottom portion of Table 13.

The half-life on vegetation used in chronic exposure scenarios is identical to the rate used in GLEAMS-Driver modeling (Table 10)—i.e., 30 days. Based on this half-life, the longer-term concentrations of the pesticide in various commodities are detailed in Worksheets B05a (fruit), B05b (broadleaf vegetation), B05c (short grass), and B05d (long grass). Only the worksheets for fruit and broadleaf vegetation are used in the human health risk assessment. All four worksheets are used in the ecological risk assessment (Section 4.2). In all cases, a maximum 90-day time-weighted average concentration is calculated for longer-term exposures. In the context of the human health risk assessment, the use of the 90-day rather than a 365-day time-weighted average is intended to reflect the harvesting of a 1-year supply of fruit and/or vegetation during a single season (i.e., about 90 days) under the assumption that degradation will not occur once the commodity is harvested—e.g., the commodities are placed in cold storage, which essentially stops the degradation of the pesticide.

As in most Forest Service risk assessments, the amount of fruit consumed per day is taken as 1.68 – 12.44 g fruit/kg bw. These values are taken from U.S. EPA/NCEA (1996, Table 9-3, p. 9-11). The value of 1.68 g fruit/kg bw is the 50th percentile value for the consumption of fruit. The lower 5th percentile is given a zero. Thus, the value of 1.68 g fruit/kg bw is used as both the lower bound and central estimate in the worksheets that accompany this risk assessment. For broadleaf vegetation, the consumption value used in the workbooks is 3.6 (0.75-10) g vegetation/kg bw. These values are taken from U.S. EPA/NCEA (1996, Table 9-4, p. 9-12) and are the 50th (5th – 95th) percentiles for the consumption of vegetables. These consumption rates are used for both acute and chronic exposures.

It should be noted that the consumption rates for fruit and vegetables from U.S. EPA/NCEA (1996) represent total consumption of these commodities from all sources. The assumption that an individual would acquire their total stock of fruits and vegetables from foraging in an area treated with tebuthiuron is probably unlikely. While this assumption may be viewed as a consideration of the Most Exposed Individual (Section 3.2.3.1.1), it is possible that the use of these consumption rates may grossly overestimate and distort the risk assessment, even for subsistence populations. Estimates of the amount of fruits and vegetables foraged from forests that are consumed by the general public or subsistence populations were not identified in the relevant literature. U.S. EPA/NCEA (1996) does provide consumption rates for home-grown fruit and vegetables. For homegrown fruit, the consumption rates are 1.07 (0168 - 11) g fruit/kg bw (U.S. EPA/NCEA 1996, Table 12-8, p. 12-11). For homegrown vegetation, the consumption rates are 1.11 (0.11 – 7.5) g vegetation/kg bw (U.S. EPA/NCEA 1996, Table 12-13, p. 12-15). Notably, the central estimate for the consumption of all fruit is higher than the corresponding estimate for homegrown fruit by a factor of about 1.6 [1.68 ÷ 1.07 ≈ 1.57]. Similarly, the central estimate for the consumption of all vegetation is higher than the corresponding estimate for homegrown vegetation by a factor of about 3.2 [3.6 ÷ 1.11 ≈ 3.243].

It is reasonable to suppose that the consumption of homegrown fruit or vegetation generally will be greater than the consumption of fruit or vegetation foraged from a forest. If this supposition has merit, the above comparisons suggest that exposure levels given in the WorksheetMaker workbooks for members of the general public may overestimate likely exposures by factors greater than 2 to 3. Again, the relevant literature does not include statistics for the longer-term consumption of foraged fruit or vegetation from forests. In addition, the more recent update of EPA's Exposure Factors Handbook (U.S. EPA/NCEA 2011) does not address the consumption of homegrown vegetation or the consumption of self-harvested fruit and vegetables by subsistence populations.

As summarized in Worksheet E03 of Attachment 1 (foliar applications), the estimated acute exposures are about 0.0071 (0.0032 – 0.11) mg a.i./kg bw for the consumption of contaminated fruit and 0.097 (0.0032-0.81) mg a.i./kg bw/day for the consumption of contaminated vegetation. The estimated longer-term exposures are 0.0030 (0.0014-0.047) mg a.i./kg bw/day for the consumption of contaminated fruit and 0.041 (0.0028-0.34) mg a.i./kg bw/day for contaminated vegetation. For granular applications, the estimated doses are summarized in Worksheets E03 of Attachments 2, 3, and 4. As discussed above, these estimated doses are a factor of 25 below the doses associated with liquid applications.

The U.S. EPA/OPP approach to dietary exposure is very different from the approach used in Forest Service risk assessments. The EPA exposure assessments are based on dietary surveys (i.e., the amounts of different commodities consumed by individuals) and tolerance limits on those commodities. In EPA's most recent human health risk assessment (U.S. EPA/OPP/HED 2014a, Table 5.4.5, pp. 22-23), the upper bound (95^{th} percentile) acute dietary dose for tebuthiuron is about 0.093 mg a.i./kg bw/day. This estimated upper bound acute dietary dose from EPA is a factor of about 9 below the upper bound of the acute dose of 0.81 mg a.i./kg bw/day estimated in Attachment 1, Worksheet D03b (foliar applications) [0.81 mg a.i./kg bw/day ÷ 0.093 mg a.i./kg bw/day ≈ 8.71]. The chronic dietary exposures estimated by EPA (U.S. EPA/OPP/HED 2014a, Table 5.4.4, pp. 22-23) range from about 0.032 to 0.1 mg a.i./kg bw/day. The upper bound of the range from EPA is a factor of about 4 below the upper bound of the longer-term exposures of about 0.34 mg a.i./kg bw/day estimated in Attachment 1, Worksheet D04b (foliar applications) [0.088184 ÷ 0.340836703 mg a.i./kg bw/day ≈ 3.87]. Given the very different methods used in the EPA risk assessment (i.e., tolerance based), compared with the current risk assessment (direct deposition based), the higher estimates in the current risk assessment are understandable.

The above discussion is not meant to suggest that the estimates of dose given in the current risk assessment are in any way validated by or preferable to the estimates from EPA. The upper bound estimates used in the current risk assessment are likely to be conservative and consistent with concern for the Most Exposed Individual (Section 3.2.3.1.1). The extent to which the upper bound estimates given in the current risk assessment may overestimate risk is discussed further in the risk characterization (Section 3.4.3).

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

Table 14 provides an overview of the dose-response assessment for human health used in this risk assessment. As with most Forest Service risk assessments, the selection of acute and chronic RfDs is based on the most recent human health risk assessment from EPA, in this case U.S. EPA/OPP/HED (2014a). As detailed in SERA (2014a, Section 3.3), RfDs are estimates of doses at which adverse effects are not anticipated. The EPA derived an acute RfD of 0.1 mg a.i./kg bw/day for women of childbearing age based on a developmental study but declined to derive an acute RfD for the general population. The EPA chronic RfD is 0.14 mg a.i./kg bw/day based on a reproduction study and is intended to be applied to all populations. While these RfDs are used in the current Forest Service risk assessment, it does not seem sensible to use an acute RfD of 0.1 mg a.i./kg bw/day and a chronic RfD of 0.14 mg a.i./kg bw/day for women of childbearing age—i.e., an acute RfD should be equal to or above the corresponding chronic RfD. For the current Forest Service risk assessment, risks to women of childbearing age are characterized with the somewhat lower acute RfD of 0.1 mg a.i./kg bw/day for both acute and chronic exposures. The LOAEL associated with the NOAEL for the acute RfD involves fetal resorptions, which amount to early fetal death. This endpoint is, of course, viewed as a serious adverse effect which has an impact on the risk characterization for exposure scenarios that exceed the acute RfD for women of childbearing age.

3.3.2. Acute RfD

The U.S. EPA/OPP sometimes derives acute RfDs for pesticides. For tebuthiuron, however, the EPA did not derive an acute RfD for the general population. The rationale for not doing so is as follows: *No appropriate endpoint attributable to a single dose was identified* (U.S. EPA/OPP (2014a, p. 18).

The EPA derived an acute RfD for tebuthiuron that is applied to women of childbearing age. This acute RfD is based on a developmental study under the assumption that the endpoint observed in the developmental study could be associated with a single dose of the tebuthiuron. As discussed in Section 3.1.9.1 and summarized in Appendix 1, Table A1-3, two developmental studies are available on tebuthiuron—i.e., a developmental study in rats that yielded a NOAEL of 110 mg a.i./kg bw/day (the highest dose tested) and a developmental study in rabbits that yielded a developmental NOAEL of 10 mg a.i./kg bw/day with a corresponding LOAEL of 25 mg a.i./kg bw/day based on decreased fetal weights and an increase in resorptions. Following standard procedure, the EPA selected the lower NOAEL from the study in rabbits (i.e., the most sensitive species based on the available data) and used an uncertainty factor of 100 (10 for species-to-species extrapolation and 10 for sensitive subgroups in the human population, i.e., 10 x 10 = 100). Thus, the acute RfD is 0.1 mg a.i./kg bw/day [10 mg a.i./kg bw/day ÷ 100] (U.S. EPA/OPP/HED 2014a, p. 18).

Because the NOAEL used in deriving the acute RfD is based on responses in female rabbits and offspring, the EPA notes that the acute RfD is applicable to women of childbearing age, designated by EPA as females between the ages of 13 to 49. This approach is maintained in the current Forest Service risk assessment. As discussed further below, the chronic RfD for the general population is 0.14 mg a.i./kg bw/day. Because this chronic RfD is almost identical to the acute RfD, the chronic RfD is used to characterize risks associated with both acute and chronic exposures to members of the general public other than women of childbearing age.

3.3.3. Chronic RfD

The U.S. EPA's Integrated Risk Information System (IRIS) derives a chronic RfD of 0.07 mg a.i./kg bw/day (U.S. EPA/NCEA 1988). This RfD is also cited in the Reregistration Eligibility Decision document for tebuthiuron (U.S. EPA/OPP 1994, p. 12). This chronic RfD is based on the two-generation reproduction study summarized in Appendix 1, Table A1-3. The earlier EPA assessments designate 7 mg a.i./kg bw/day rather than 14 mg a.i./kg bw/day as the reproductive NOAEL. As discussed in Section 3.1.9.2, the most recent EPA risk assessment (U.S. EPA/OPP/HED 2014a) designates 14 mg a.i./kg bw/day as a NOAEL and 26 mg a.i./kg bw/day as the LOAEL based on a decrease in body weight in offspring.

Following standard practice in Forest Service risk assessments, the current risk assessment defers to the most recent EPA risk assessment. As noted in Section 3.1.9.2, the U.S. EPA/OPP has access to full studies and typically reassesses the key studies which can lead to a reclassification of NOAELs and LOAELs. Consequently, the dose of 14 mg a.i./kg bw/day is accepted as the NOAEL based on information from U.S. EPA/OPP/HED (2014a). Consistent with all of the EPA risk assessments, the uncertainty factor used to derive the chronic RfD is taken as 100 (10 for species-to-species extrapolation and 10 for sensitive subgroups in the human population, i.e., 10 x 10 = 100). Thus, a chronic RfD of 0.14 mg a.i./kg bw/day is used in the current risk assessment [14 mg a.i./kg bw/day ÷ 100].

One unusual aspect of the chronic RfD for the general population (i.e., 0.14 mg a.i./kg bw/day) is that this chronic RfD is higher (albeit only modestly so) than the acute RfD for women of childbearing age (i.e., 0.1 mg a.i./kg bw/day). The most recent EPA human health risk assessment does not discuss the relationship between the acute and chronic RfDs but indicates that the chronic RfD of 0.14 mg a.i./kg bw/day is applicable to all populations (U.S. EPA/OPP/HED 2014a, p. 18). While Forest Service risk assessments generally defer to EPA risk assessments in the selection and application of RfDs, both acute and chronic, it does not seem sensible to use an acute RfD of 0.1 mg a.i./kg bw/day and a chronic RfD of 0.14 mg a.i./kg bw/day for women of childbearing age. In other words, if 0.1 mg a.i./kg bw/day is the maximum tolerable dose for a single day exposure for a woman of childbearing age, a dose of 0.14 mg a.i./kg bw/day for a prolonged period should not be viewed as tolerable for a woman of childbearing age. Thus, for women of childbearing age, the acute RfD of 0.1 mg a.i./kg bw/day is applied to both acute and longer-term exposures.

As discussed in Section 3.1.3.3, the information available on the pharmacokinetics of tebuthiuron suggests that the body burden will not alter substantially between short-term and longer-term exposures—i.e., a plateau of 1.16. This minimal increase in body burden associated with an increase if the duration of exposure is prolonged is consistent with the proximity of the acute and chronic RfDs.

3.3.4. Surrogate RfD for Occupational Exposures

Instead of deriving RfDs for occupational exposure, the EPA identifies a longer-term NOAEL from an animal study and recommends a level of concern (LOC). Often, the EPA uses the same longer-term toxicity value used to derive the chronic RfD, in which case, the recommended LOC will be identical to the uncertainty factor used to derive the chronic RfD. This, however, is not the case for tebuthiuron. The most recent EPA human health risk assessment derives separate estimates for dermal exposure (U.S. EPA/OPP/HED 2014a, Table E.1) and inhalation exposure (U.S. EPA/OPP/HED 2014a, Table E.2). The LOCs for the two routes of exposure are also different. The LOC for dermal exposures is set to 100 (i.e., identical to the uncertainty factor used to derive the acute and chronic RfDs) but the LOC for inhalation exposures is set to 1000. As discussed in Section 3.1.13, the higher LOC for inhalation exposures is due to the application of an additional uncertainty factor of 10 to account for the lack of a 90-day inhalation study on tebuthiuron.

While not related directly to the dose-response assessment, it is worth noting that the exposure component for dermal margin of exposure is based on the assumption of 100% dermal absorption. As discussed in Section 3.1.3.2.1, the current Forest Service risk assessment uses lower estimates of dermal absorption—i.e., dermal absorption rate coefficients of 0.004 (0.002–0.009) $hour^{-1}$.

The differences in EPA's approach to the risk assessment for workers and the approach used in the current Forest Service risk assessment leads to differences in the risk characterization for workers, as discussed further in Section 3.4.2.

3.3.5. Dose-Severity Relationships

Forest Service risk assessments sometimes consider dose-severity relationships to more fully characterize potential risks in exposure scenarios where the doses exceed the RfD. For tebuthiuron, this consideration is important because some of the exposure scenarios for both workers and members of the general public lead to estimated doses that substantially exceed the RfDs (Section 3.4).

As summarized in Table 15, the ratios of the LOAEL to the corresponding NOAEL are 2.5 for the acute RfD [25 mg a.i./kg bw/day ÷ 10 mg a.i./kg bw/day = 2.5] and about 1.8 for the chronic RfD [26 mg a.i./kg bw/day ÷ 14 mg a.i./kg bw/day ≈ 1.857]. While these ratios might not reflect dose-severity responses in human populations, they are the most objective basis for assessing potential concerns for exceedances in the RfDs.

While the LOAEL to NOAEL ratio for the acute RfD (2.5) is somewhat higher than the corresponding ratio for the chronic RfD (1.8), exceedances in the acute RfD raise a greater concern because of differences in the severities of the endpoints in the LOAELs associated with the acute and chronic RfDs. As summarized in Table 13 and discussed in Section 3.1.9.2, the reproductive LOAEL associated with the chronic RfD involves decreased body weights. As also summarized in Table 13 and discussed in Section 3.1.9.1, the developmental LOAEL associated with the acute RfD involves both decreased body weights and an increase in the number of resorptions. An increase in fetal resorptions is an indication of early fetal death and is viewed as an effect of substantial concern.

An additional factor to consider in dose-severity considerations is the uncertainty factor of 100 used in the derivation of all of the RfDs. A simple comparison of LOAELs to NOAELs does not consider the impact of uncertainty factors which are intended to be protective. Thus, while HQs of 2.5 for acute exposures and 1.8 for chronic exposures might be viewed with concern based on the LOAEL to NOAEL ratios, the uncertainty factor of 100 may diminish this concern if the uncertainty factor is highly protective. In other words, the uncertainty factor is intended to protect sensitive subgroups and to account for uncertainties in using data on animals to estimate toxicity values for humans. Nonetheless, the uncertainty factor and consequent RfD are not intended as precise adjustments to a human equivalent dose.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

The quantitative risk characterization in both the human health and in the ecological risk assessment is based on the hazard quotient (HQ), which is defined as the anticipated exposure divided by a toxicity value that is not likely to be associated with adverse effects. An HQ of 1 is set as the level of concern and an HQ of greater than 1 exceeds the level of concern – i.e., the estimated exposure exceeds the tolerable level of exposure. For the human health risk assessments the toxicity values are an RfD of 0.1 mg a.i./kg bw/day applicable to women of childbearing age and an RfD of 0.14 mg a.i./kg bw/day for other members of the general populations (Section 3.3.). The quantitative risk characterization for workers is provided in Worksheets E02 of the attachments to this risk assessment—i.e., Attachment 1 for liquid applications and Attachments 2-4 for granular applications. The corresponding risk characterization for members of the general public is summarized in Worksheet E04 of the attachments. All HQs are based on the anticipated application rate of 0.6 lb a.i./acre.

For workers, none of the central estimates of the HQs associated with anticipated applications of tebuthiuron exceed the level of concern; however, the upper bound estimates of the HQs exceed the level of concern for backpack applications (HQ=3) and aerial applications (HQ=1.4). While these HQs are relatively modest exceedances in the level of concern, the endpoint for women of childbearing age involves fetal resorptions—i.e., early fetal death. This, of course, is a serious adverse effect. While HQs should not be considered predictive–i.e., HQs of 1.3 to 3 might not lead to adverse effects on the fetus—the exceedances in the level of concern dictate that female workers of childbearing age should exercise extreme caution when applying tebuthiuron.

As with workers, none of the central estimates of HQs exceed the level of concern for members of the general public. Even at the upper bounds of expected exposures, none of the HQs for granular applications of tebuthiuron exceed the level of concern. This is not, however, the case for liquid applications of tebuthiuron. At the upper bounds of anticipated exposures following liquid applications, exceedances in the level of concern occur for the acute consumption of contaminated fruit (HQ=1.1), the acute consumption of contaminated broadleaf vegetation (HQ=8), and the longer-term consumption of contaminated vegetation (HQ=3). For all of these exposure scenarios, the receptor is a young woman of childbearing age. Also as with the risk characterization for workers, exceedances in the level of concern for young women should be viewed with substantial concern for potential effects on the developing fetus. While not minimizing this concern, it should be appreciated that the upper bound exposure estimates which form the basis of these HQs are extreme and should be viewed as possible but not typical or expected levels of exposure in most cases. Qualitatively, the risk characterization for the general public involving non-accidental exposures clearly suggests that granular applications raise no substantial concerns relative to those posed by liquid applications.

For both workers and members of the general public, several accidental exposure scenarios lead to HQs that exceed the level of concern. This finding is typical of most Forest Service pesticide risk assessments and reflects the extreme nature of the accidental exposure scenarios. As with virtually any pesticide, accidental exposures should be avoided. If accidental exposures occur, sensible steps should be taken to mitigate the exposure and ensure that exposed individuals receive prompt and effective medical care. As with the non-accidental exposures, women of childbearing age are the group that could be most severely impacted.

3.4.2. Workers

3.4.2.1. General Exposures

As discussed in Section 3.2.2.1, the worker exposure rates used to derive the estimates of doses for workers involved in anticipated applications of tebuthiuron are identical for both liquid and granular applications. Consequently, the HQs for workers involved in backpack, ground broadcast, and aerial applications are identical for both liquid applications (Attachment 1) and granular applications (Attachments 2-4). Based on central estimates of exposures, none of the HQs for workers exceeds the level of concern—i.e., HQs of 0.2 for backpack and broadcast aerial applications and an HQ of 0.3 for ground broadcast applications. Based on the upper bound of the prediction intervals, the HQs modestly exceed the level of concern (HQ=1) for backpack applications (HQ=3) and aerial applications (HQ=1.4) and are below the level of concern for ground broadcast applications (HQ=0.7).

Typically, HQs in the range of 1.4 to 3 would be a concern but not necessarily a substantial concern. As discussed in Section 3.3.5, however, the LOAEL associated with the dose-response assessment for women of childbearing age is a factor of 2.5 above the NOAEL used to derive the RfD for women of childbearing age and this LOAEL is associated with an increase in fetal resorptions—i.e., fetal death. Based on this relationship of the NOAEL to the LOAEL, an upper bound HQ of 3 might be viewed with substantial concern. As also discussed in Section 3.3.5, however, NOAEL to LOAEL ratios in experimental mammals are not necessarily predictive of effects that might be encountered in exceedances of the RfD, because the RfD is derived using an uncertainty factor. The presumption in the use of the uncertainty factor is that the uncertainty factor is conservative. Thus, a modest excursion above the RfD would not necessarily be associated with the same effect as seen in experimental mammals at the LOAEL. Notwithstanding these considerations, the likelihood of adverse effects in fetuses at an HQ that exceeds the level of concern (HQ=1) cannot be estimated with precision.

Given these uncertainties, the most reasonable verbal characterization of risk is that female workers of childbearing age should exercise extreme caution when applying tebuthiuron. If exposures are limited to central estimates, there is no basis for asserting that adverse effects in female workers involved in backpack or aerial applications are likely. If exposures reach upper bound estimates, however, adverse effects on offspring, perhaps including fetal mortality, could not be ruled out for backpack or aerial applications of tebuthiuron.

Qualitatively, the above risk characterization for workers is similar to that given for workers in the most recent EPA human health risk assessment which expresses concern for workers involved in both liquid and granular applications of tebuthiuron. Quantitatively, at least some of the risk characterizations given by EPA are reasonably concordant with those given in the current risk assessment. For example, the EPA derives aggregate risk indices of 0.07 to 0.16 for various aerial applications of tebuthiuron (U.S. EPA/OPP/HED 2014a, p. 28). The aggregate risk index (ARI) is essentially the reciprocal of the HQ. Thus, the ARIs of 0.7 to 0.16 correspond to HQs of about 6.25 to 14. These estimates are based on an application rate of 6 lbs a.i./acre. Adjusting to the application rate of 0.6 lb a.i./acre used in the current Forest Service risk assessment, the equivalent HQs derived by EPA correspond to 0.625 to 1.4. As discussed above and summarized in Worksheet E02 of the attachments to this risk assessment, the HQs derived in the current risk assessment range from 0.03 to 1.4. As another example, the EPA derives aggregate risk indices of 0.02 to 0.04 for a backpack worker handling 64 lbs of tebuthiuron (U.S. EPA/OPP/HED 2014a, p. 57)—i.e., 40 gallons x 1.6 lb a.i./gallon. In the current Forest Service risk assessment, the upper bound estimate of the amount handled is 8 lb a.i. because of differences in the application rates. The EPA estimated ARIs of 0.02 to 0.04 correspond to HQs of 25 to 50. Adjusting for the differences in the amounts handled, the HQs are about 3.1 to 6.25 [25 to 50 ÷ 8 lbs/64 lbs]. As indicated in Worksheet E02 of the attachments to this risk assessment, the HQs for backpack applications are estimated at 0.02 to 3.

As discussed in Section 3.3.4 (Surrogate RfD for Occupational Exposures), the EPA separately considers dermal and inhalation exposures, adds an uncertainty factor of 10 for the inhalation component, and assumes 100% dermal absorption. Given the differences in the methods used by EPA and those used in the current risk assessment, the similarities in the quantitative characterizations of risk are striking.

3.4.2.2. Accidental Exposures

The only accidental exposure scenario that leads to an exceedance in the level of concern [HQ=1] is the upper bound of the HQ for wearing contaminated gloves for 1 hour [HQ=2] during applications of tebuthiuron as a liquid (Attachment 1). The most sensible interpretation of the HQ of 2 amounts to little more than standard practice in any pesticide application—i.e., hands should be washed and gloves should be replaced as soon as possible after gloves become contaminated.

3.4.3. General Public

3.4.3.1. Non-Accidental Exposures

The HQs associated with the consumption of contaminated vegetation following liquid applications of tebuthiuron are the only HQs that exceed the level of concern (HQ=1). As summarized in Worksheet E04 of Attachment 1, exceedances in the level of concern occur only at the upper bounds of the HQs for the acute consumption of contaminated fruit (HQ=1.1), the acute consumption of contaminated broadleaf vegetation (HQ=8), and the longer-term consumption of contaminated vegetation (HQ=3). For all of these exposure scenarios, the receptor is a young woman. Consequently, as discussed in Section 3.3 (Dose-Response Assessment), all the HQs are based on the acute RfD of 0.1 mg a.i./kg bw/day. As discussed in Section 3.3.5 (Dose-Severity Relationships), exceedances in the RfD for young women are viewed with substantial concern because the LOAEL associated with the NOAEL on which the RfD is based involves fetal resorptions/early fetal deaths. While these HQs should be viewed with substantial concern, the interpretation of the HQs must also consider the uncertainties in the exposure assessment. As discussed in some detail in Section 3.2.3.7 (Oral Exposure from Contaminated Vegetation), the assumptions used in Forest Service risk assessments for this scenario are extremely conservative. As also noted in Section 3.2.3.7, the estimated doses for tebuthiuron associated with the consumption of contaminated vegetation exceed estimates from EPA by about a factor of 9 for acute exposures and a factor of about 4 for longer-term exposures. The upper bound estimates used in the current risk assessment are likely to be conservative and consistent with concern for the Most Exposed Individual (Section 3.2.3.1.1). Nonetheless, the exposure scenarios should be viewed as extreme exposures which might, in some cases, reflect exposure levels following applications of liquid solutions of tebuthiuron. Nevertheless, these exposures should not be viewed as typical or expected, in most cases.

As summarized in Worksheet E04 of Attachments 2-4, the exposure scenarios for contaminated vegetation are all below the level of concern for granular applications of tebuthiuron. The highest HQ is 0.3, the upper bound HQ for the acute consumption of contaminated vegetation by a young woman. As discussed in Section 3.2.3.7, the lesser exposures associated with granular relative to liquid applications are based on only limited but consistent information on hexazinone (SERA 2005) as well as tebuthiuron (Bovey et al. 1978). While the limitations of these data are acknowledged, it seems intuitive that granular applications would be less likely to be intercepted by nontarget vegetation.

HQs for routes of exposure other than the consumption of vegetation are below the level of concern for both liquid and granular applications of tebuthiuron. The highest of these other HQs is 0.5, the upper bound of the HQ associated with the acute consumption of contaminated water by a young child.

Qualitatively, the risk characterization for the general public involving non-accidental exposures clearly suggests that granular applications raise no substantial concerns relative to those posed by liquid applications.

The risk characterization for the general public made in the most recent EPA risk assessment is less severe than that in the current Forest Service risk assessment (U.S. EPA/OPP/HED 2014a, pp. 22=23). None of the dietary exposure assessments from EPA result in estimated doses that exceed the acute or chronic RfDs. The acute dietary assessment for females of childbearing age approaches the level of concern (i.e., an equivalent HQ of 0.93) based on the acute RfD of 0.1 mg a.i./kg bw/day. Similarly, none of the chronic assessments exceeds the level of concern (i.e., the highest equivalent HQ is 0.72 based on the chronic RfD of 0.14 mg a.i./kg bw/day. These less severe risk characterizations are due solely to the different exposure scenarios and methods used by EPA, as discussed in Section 3.2.3.7.

3.4.3.2. Accidental Exposures

For applications of tebuthiuron as a liquid, none of the central estimates of the HQs exceeds the level of concern. Three exposure scenarios exceed the level of concern at the upper bound estimates of the HQs: the direct spray of a small child (HQ=3), the consumption of contaminated water by a small child following an accidental spill (HQ=9), and the consumption of contaminated fish by subsistence populations following an accidental spill (HQ=1.6). For granular applications of tebuthiuron, the accidental direct spray scenarios are not applicable. The accidental exposures involving an accidental spill, however, lead to much higher HQs than the corresponding HQs for liquid applications. The consumption of contaminated water by a small child [HQs of 10 (2 to 29)] and the consumption of contaminated fish by subsistence populations [HQs of 3 (1.1 to 6)] exceed the level of concern across the estimated range of exposures, including the lower bounds. As discussed in Section 3.2.3.4.1, these differences in the HQs reflect differences in the accidental spill scenarios for liquid and granular applications.

3.4.4. Sensitive Subgroups

As discussed in Section 3.3 (dose-response assessment), the most sensitive subgroup for exposure to tebuthiuron appears to be pregnant women and the developing fetus. Since the acute RfD for tebuthiuron is based on a developmental study and the chronic RfD is based on a reproductive study, the sensitivity of these subgroups—i.e., pregnant women and the developing fetus—is explicitly addressed.

As discussed in Section 3.1.2, tebuthiuron may cause specific damage to the pancreas. The nature of this damage, however, does not appear to be related to effects on islets of Langerhans cells; thus, diabetics do not appear to be a specific sensitive subgroup. In the absence of additional information, it seems speculative to suggest that individuals with other diseases of the pancreas might be a particularly sensitive subgroup.

3.4.5. Connected Actions

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions as actions which occur in close association with the action of concern; in this case, the use of a pesticide (40 CFR 1508.25, https://ceq.doe.gov/nepa/regs/ceq/1508.htm). Actions are considered to be connected if they: (i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously; and (iii) Are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this assessment of tebuthiuron, “connected actions” include other management or silvicultural actions or the use of other chemicals necessary to achieve management objectives which occur in close association with the use of tebuthiuron.

As discussed in detail in Sections 3.1.14.1 and summarized in Table 3, the disclosed inert ingredients in tebuthiuron formulations do not appear to contribute substantially to the toxicity of tebuthiuron; however, not all inert ingredients have been disclosed publicly. Nonetheless, all inert ingredients are disclosed to the EPA. The EPA registration of the formulations suggests that the inerts in the formulations are not likely to cause adverse effects in the normal use of the tebuthiuron formulations.

In addition to inert ingredients, the use of adjuvants can be viewed as a connected action. As noted in Section 3.1.14.2, however, no adjuvants are recommended in the application of tebuthiuron formulations.

3.4.6. Cumulative Effects

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

The most recent EPA human health risk assessment on tebuthiuron does not determine whether other pesticides may have cumulative effects with tebuthiuron.

> *Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to tebuthiuron and any other*

> *substances and tebuthiuron does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that tebuthiuron has a common mechanism of toxicity with other substances.*
>
> U.S. EPA/OPP (2014a, pp. 26)

In the absence of a determination of a common mechanism of action with other pesticides, the U.S. EPA/OPP has not further developed a cumulative effects determination involving tebuthiuron.

As discussed in Section 2.2, tebuthiuron is an inhibitor of photosystem II, and several other herbicides are known to share this mechanism of action. This common mechanism of phytotoxicity, however, is not directly relevant to potential human health effects. As discussed in Section 3.1.2, the mechanism of action of tebuthiuron in mammals has not been characterized, and the most common signs of toxicity associated with tebuthiuron are relatively nonspecific—i.e., decreased body weight in adults and fetuses as well as fetal resorptions. In the absence of knowledge concerning a specific mechanism of action, the potential for cumulative effects associated with exposures to tebuthiuron and other agents cannot be well characterized.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

The open literature regarding the impact of tebuthiuron on terrestrial vegetation is robust. In addition, at least minimal information is available on other major groups of organisms with the exceptions of reptiles and amphibians. The key information on receptors other than terrestrial plants is taken from the most recent EPA risk assessment (U.S. EPA/OPP/EFED 2014a). Most of the studies covered in the EPA risk assessment are unpublished, and full copies or detailed summaries of most of these studies were not available for the preparation of the current risk assessment. As with most ecological risk assessments, toxicity data are available on only a few species, relative to the numerous species likely to be exposed to tebuthiuron; thus, the hazard assessment for most groups of terrestrial nontarget species should be viewed as limited and possibly incomplete.

Based on acute toxicity studies, U.S. EPA/OPP/EFED (2014a) classifies tebuthiuron as *Practically Non-toxic* to birds, honeybees, fish, and aquatic invertebrates and as *Moderately Toxic* to mammals. The EPA does not have a classification scheme for effects in plants. As would be expected, however, tebuthiuron is much more toxic to aquatic vegetation than to fish or aquatic invertebrates. The toxicity of tebuthiuron is well documented in mammals, as discussed in the human health risk assessment. The avian toxicity studies are more limited; nonetheless, the effects in birds associated with exposure to tebuthiuron are similar to those observed in mammals—i.e., decreased weight gain and reproductive effects. No data are available on the toxicity of tebuthiuron to reptiles or amphibians.

Tebuthiuron is an effective and relatively nonselective herbicide. Dicots, as a group, appear to be somewhat more sensitive than monocots, but the differences are not substantial. What is most striking is that the differences in species sensitivity within dicots and monocots appear to be greater than the overall differences between dicots and monocots in general. There is a robust and detailed open literature on the efficacy of tebuthiuron. The major use of tebuthiuron is for the control of woody vegetation, whereas grasses are typically considered nontarget species. Although tebuthiuron is toxic to grasses and other monocots, the general efficacy of tebuthiuron in promoting the growth of grasses is an indirect effect of the removal of canopy cover as a result of the toxicity of tebuthiuron to woody plants and other dicots.

The application of any effective herbicide will damage at least some vegetation, and this damage may alter the suitability (either positively or negatively) of the treated area for terrestrial and aquatic organisms in terms of habitat, microclimate, or food supply. These indirect effects (i.e., effects on the organism that are not a consequence of direct exposure to tebuthiuron) would occur with any equally effective method of vegetation management—i.e., mechanical or herbicide use. The potential for indirect effects is acknowledged but not otherwise considered in the hazard identification for nontarget species, except for the substantial body of field studies on the effects (beneficial and detrimental) of tebuthiuron to terrestrial plants. Indirect effects are considered further in the risk characterization (Section 4.4).

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

As summarized in Appendix 1 and discussed in the human health risk assessment (Section 3.1), several standard toxicity studies in experimental mammals were conducted and submitted to the EPA as part of the registration process for tebuthiuron. All of these studies, which are used in the human health risk assessment to identify the potential toxic hazards associated with exposures to tebuthiuron, can also be used to identify potential toxic effects in mammalian wildlife. In addition, there is a relatively large body of open literature publications that focuses primarily on the potential impact of tebuthiuron applications on mammals secondary to changes in vegetation (Appendix 1, Table A1-9).

While human health risk assessments typically focus on the most sensitive species as a surrogate for humans, the ecological risk assessment is concerned with differences in toxicity among species. As summarized in Appendix 1, Table A1-1, no systematic differences (e.g., correlations with body weight) in sensitivity are apparent based on acute toxicity studies. Based on definitive LD_{50} values, mice and rats appear to be about equally sensitive to tebuthiuron, with acute LD_{50} values ranging from 387 mg a.i./kg bw (female rats, MRID 40583901) to 620 mg a.i./kg bw (female mice, MRID 00226375), with no consistent differences between male and female rodents. Rabbits appear to be somewhat more sensitive than mice or rats with an acute oral LD_{50} of 286 mg a.i./kg bw (Todd et al. 1974). As discussed in Section 3.1.9.1, developmental studies also suggest that rabbits are more sensitive than rats and that the differences in sensitivity are substantial—i.e., a rabbit NOAEL of 10 mg a.i./kg bw/day versus an NOAEL in rats of 110 mg a.i./kg bw/day.

Based on acute oral toxicity studies, cats and dogs do not appear to be markedly sensitive to tebuthiuron. The data on cats and dogs come from Todd et al (1974) which reports LD_0 values (i.e., no mortality) of 200 mg a.i./kg bw/day for cats and 500 mg a.i./kg bw/day for dogs. In the Reregistration Eligibility Decision on tebuthiuron, these data are reported as indefinite LD_{50} values—i.e., LD_{50} values of >200 mg a.i./kg bw for cats and >500 mg a.i./kg bw for dogs (U.S. EPA/OPP 1994, p. 8). This discrepancy appears to reflect a convention in EPA documents to report indefinite toxicity values as LD_{50} values.

Based on subchronic and chronic toxicity studies, dogs appear to be somewhat more sensitive than rats and mice—i.e., the subchronic and chronic NOAELs in dogs are 25 mg a.i./kg bw/day (MRIDs 00020663 and 00146801) compared to NOAELs in rats above 50 mg a.i./kg bw/day (Appendix 1, Table A-2). The most sensitive endpoint for tebuthiuron, however, involves reproductive effects in rabbits (Section 3.3), and, as with most pesticides, no reproduction studies in dogs are available. Based on the acute toxicity studies discussed above, dogs do not appear to be more sensitive than rabbits to tebuthiuron.

As discussed further in Section 4.1.2.5.2, there are numerous field studies that address the effects of tebuthiuron on terrestrial plants. Several additional field studies examine the potential effects of tebuthiuron applications on mammals as secondary to changes in vegetation. These studies are summarized in Appendix 1, Table A1-9. Some of these field studies look only at changes in vegetation and suggest that tebuthiuron may have no effect on or only marginally increase habitat quality (Defazio et al. 1988; Johnson et al. 1996; Thompson et al. 1991) or the nutritional value of forage (Lopes and Stuth 1984). Changes in vegetation, specifically an increase in grasses relative to woody plants, are associated with changes in feeding patterns or feeding preferences in both rodents (McMurry et al. 1993b) and cows (Kirby and Stuth 1982; McDaniel and Balliette 1986; Scifres et al. 1983). None of these studies suggest the potential for adverse effects. The study by Scifres et al. (1983) is particularly interesting in that the study suggests that cows will preferentially feed in pastures treated with tebuthiuron relative to pastures treated with 2,4-D or picloram. The basis for this preferential feeding is unclear but does not appear to be related to changes in vegetation.

As noted above and discussed in Section 3.1.9, developmental and reproductive effects were observed in both rats and rabbits, and these endpoints serve as the basis for the dose-response assessment in both the human health risk assessment (Section 3.3) as well as the dose-response assessment for mammalian wildlife (Section 4.3.2.1.). No data are available on the impact of tebuthiuron on rabbit populations other than studies involving the prevalence of insect or helminth parasites in which no substantial effects were observed (Boggs et al. 1990a, 1990b, 1991a). In a study on woodrat populations, McMurry et al. (1993a) saw no impact on either woodrat populations or the number of reproductively active female woodrats following an application of tebuthiuron at 2 lb a.i./acre. This finding is discussed further in the risk characterization (Section 4.4.2.1.).

4.1.2.2. Birds

As summarized in Appendix 2, a standard set of toxicity studies—i.e., acute gavage studies (Appendix 2, Table 1), acute dietary studies (Appendix 2, Table 2), and reproduction studies (Appendix 2, Table 3) were submitted to the U.S. EPA/OPP in support of the registration of tebuthiuron. These are standard assays and test species usually required by the EPA. Some acute gavage studies are also summarized in the open literature (Todd et al. 1974). In addition to the studies on standard test species, data on toxicity to chickens are reported in Todd et al. (1974), including an acute gavage study summarized in Appendix 2, Table A2-1 and a subchronic feeding study summarized in Appendix 2, Table A2-3. In addition, an acute dietary toxicity in zebra finch was conducted and submitted to EPA (MRID 48928201). Based on the bibliography in U.S. EPA/OPP/EFED (2014a, p. 83), this study was conducted in 2012 and submitted to EPA by Dow AgroSciences. As with mammals, some open literature field studies are available on the indirect effects of tebuthiuron applications on bird populations (Appendix 2, Table A2-4). The number of field studies involving birds, however, is much less than the number of studies in mammals (Appendix 1, Table A1-9).

As with the acute gavage toxicity studies in mammals (Section 4.1.2.1), Todd et al. (1974) report indefinite toxicity values as $>LD_0$ values (no mortality); however, the EPA reports the indefinite toxicity values as $>LD_{50}$ values. Again, as with mammals, this difference in reporting appears to reflect the EPA convention of reporting indefinite toxicity values as $>LD_{50}$ values rather than any underlying differences in the studies reported by EPA and Todd et al. (1974). All of the studies reported by Todd et al. (1974) are summarized in EPA as MRID 00020661 and are classified by EPA as *Supplemental* rather than *Acceptable* because Todd et al. (1974) used relatively low doses (i.e., 500 mg a.i./kg bw). The only acute gavage study that is classified as *Acceptable* by EPA is MRID 00041692 in which mortality was not observed in mallards following acute gavage doses of 1000 or 2000 mg a.i./kg bw. Again following standard EPA convention, the EPA reports the results as an indefinite LD_{50} of >2000 mg a.i./kg bw. Based on this value, the

EPA classifies tebuthiuron as *Practically Nontoxic* to birds (U.S. EPA/OPP/EFED 2014a, Table 3.18, p. 40). Other than slight hypoactivity in chickens following a gavage dose of 500 mg a.i./kg bw (Todd et al. 1974, p. 463), no signs of toxicity are reported in the avian acute gavage studies.

As with the acute gavage studies, all of the acute dietary studies in mallards and quail report indefinite LC_{50} values ranging from >2500 mg a.i./kg diet (MRIDs 00041681, 00041693, and 40601001) to >5000 mg a.i./kg diet (MRID 40601001 and 40601002). While treatment-related mortality was not observed, sublethal signs of toxicity included decreased food consumption and/or decreased body weight gain. As discussed in Section 3.1.1, decreased food consumption and weight gain are also common effects observed in mammals following exposures to tebuthiuron. The study in zebra finch (MRID 48928201) yielded a definitive LC_{50} of 1465 mg a.i./kg diet, which was used by EPA to classify tebuthiuron as *Slightly Toxic* to passerines (U.S. EPA/OPP/EFED 2014a, Table 3.19, p. 42). As discussed further in Section 4.3.2.2, the zebra finch is the most sensitive species, and this study is used as the basis for the dose-response assessment in birds, based on the reported NOAEL of 497 mg a.i./kg diet.

The longer-term reproductive studies in mallards and quail consist of two early studies that yielded NOAELs of 100 mg a.i./kg diet but failed to identify a LOAEL in each species (MRIDs 00093690 and 00104243). Two more recent studies identified a LOAEL of 500 mg a.i./kg diet but failed to define a NOAEL (MRIDs 48928202 and 48928202). In mallards, the LOAEL is associated only with a decrease in hatchling body weights (MRIDs 48928202). In quail, the LOAEL is associated with a decrease in body weights in adults and hatchlings at 500 mg a.i./kg diet and more severe effects (decreases in offspring survival and egg production) at higher dietary concentrations (903 and 1550 mg a.i./kg diet). These effects in the avian reproduction studies are similar to effects seen in the mammalian reproduction study—i.e., decreased body weights in F_1 females and decreased pup weights, as discussed in Section 3.1.9.2. Todd et al. (1974) briefly describe a 30-day subchronic toxicity study in chickens in which body weights were decreased at 2500 mg a.i./kg bw but no effects were observed at 1000 mg a.i./kg diet. Based on these very limited data, Anseriformes (including mallards) might be viewed as somewhat less sensitive than Galliformes (including quail and chickens).

The available field studies that address the effect of tebuthiuron applications on bird populations do not suggest any direct adverse effects (Appendix 2, Table A2-4). Haukos and Smith (1989) suggest that changes in vegetation associated with tebuthiuron applications might have a negative impact on prairie-chickens (Galliformes) due to the loss of canopy cover. In another study on prairie chickens, however, there was a slight increase in the number of birds on treated versus untreated sites. The differences, however, do not appear to be statistically significant (Olawsky 1987, Table 1.3, p. 14). The study by Schulz et al. (1992) notes comparable increases in the species diversity of birds at sites treated with either tebuthiuron or triclopyr relative to untreated sites. Thus, the changes in species diversity are probably secondary to changes in vegetation (increases in grasses and forbs). While these field studies on birds are not as abundant or detailed as the corresponding field studies in mammals (Appendix 1, Table A1-9), they are generally consistent with the studies on mammals indicating no evidence of direct adverse effects and suggesting that any effects on vertebrate populations are most likely secondary to changes in vegetation.

4.1.2.3. Reptiles and Amphibians (Terrestrial Phase)

There is no information regarding the toxicity of tebuthiuron to reptiles or terrestrial phase amphibians (i.e., amphibians in a life-stage where they are predominantly on land) in the open literature or in the available EPA risk assessments (U.S. EPA/OPP 1994; U.S. EPA/OPP/EFED 2014a). Neither the database maintained by Pauli et al. (2000) nor the open literature include toxicity studies on the effect of tebuthiuron to reptiles or terrestrial phase amphibians. In a field study, Zavaleta (2012, p. 106-107) found no direct effect of tebuthiuron applications at a rate of 0.6 lb a.i./acre (the rate most likely to be used by the Forest Service) to pastures on the abundance or diversity of reptiles and terrestrial phase amphibians.

Risks to terrestrial phase amphibians are addressed in the most recent EPA ecological risk assessment on tebuthiuron (U.S. EPA/OPP/EFED 2014a). Following standard practice at EPA, birds are used as surrogates for Terrestrial Phase amphibians and reptiles (U.S. EPA/OPP/EFED 2014a, p. 57) in the absence of data on these groups of organisms. A concern with the use of birds as a surrogate for amphibians involves the permeability of amphibian skin to pesticides and other chemicals. While no data are available on the permeability of amphibian skin to tebuthiuron, Quaranta et al. (2009) note that the skin of the frog *Rana esculenta* is much more permeable to several pesticides than pig skin and that these differences in permeability are consistent with differences in the structure and function of amphibian skin relative to mammalian skin.

4.1.2.4. Terrestrial Invertebrates

Little information is available on the toxicity of tebuthiuron to terrestrial invertebrates. The honey bee is the standard test organism for assessing the potential effects of pesticides on terrestrial invertebrates, and the EPA typically requires an acute contact study with the technical grade pesticide for pesticides that may be applied to foliage. The most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a, p. 115) summarizes the results of a contact toxicity study in bees. In this study, no treatment related effects were seen in bees following the application of 99.1% technical grade tebuthiuron at 0, 13, 22, 36, 60, or 100 µg a.i./bee. Based on this assay, tebuthiuron is classified as *Practically Nontoxic* to bees.

Typical body weights for worker bees range from 81 to 151 mg (Winston 1987, p. 54). Taking 116 mg as an average body weight, a dose of 100 µg a.i./bee corresponds to about 860 mg a.i./kg bw [0.1 mg ÷ 0.000116 kg ≈ 862.07 mg a.i./kg bw]. This nonlethal dose in bees is higher than the definitive LD_{50} values in experimental mammals (≈ 286 to 620 mg a.i./kg bw as summarized in Appendix 1) and the upper bound of indefinite LD_{50} values for birds (up to >2000 mg a.i./kg bw as summarized in Appendix 2).

Three field studies are available regarding the impact of tebuthiuron applications on insect populations. Following an application of tebuthiuron at 0.6 lb a.i./acre, Zavaleta (2012, p. 109) observed significant increases in the abundance and diversity of insects on treated plots compared with untreated plots. Following tebuthiuron applications at rates of 0.2, 0.4, 0.6, 0.8, or 1.0 kg/ha, Doerr (1980, Table 20, p. 44) observed a significant increase in the total number of insects on fields treated at 0.2 kg/ha but not on plots treated at higher application rates. The statistical methods used by Doerr (1980, p. 11) do account for comparisons of multiple endpoints. Nonetheless, given the lack of a dose-effect relationship, the increase in insect abundance may have been incidental. There was no effect on the biomass of insects (Doerr and

Guthery 1983). Boggs et al. (1991) noted that the infestation of botfly larvae (Diptera: Cuterebridae) in small mammals was higher in pastures treated with tebuthiuron (2.2 kg a.i./ha) relative to untreated plots. This effect was probably secondary to an increase in open canopy (Boggs et al., 1991, p. 326).

4.1.2.5. Terrestrial Plants (Macrophytes)

Tebuthiuron inhibits photosynthesis, specifically at photosystem II (Tomlin 2004), the first biochemical step in the process of photosynthesis involving the extraction of electrons from water molecules by photons (e.g., Goodsell 2004; Hatzios et al. 1980). At the cellular level, blocking electron transport in photosynthesis may lead to proliferation of free-radicals which result in lipid peroxidation and the disruption of cell membranes (Fuerst and Norman 1991).

4.1.2.5.1. Toxicity Bioassays

The testing requirements for the effects of herbicides on terrestrial plants are relatively rigorous since terrestrial vegetation is the typical target group for herbicides. The testing requirements of U.S. EPA involve bioassays of several species of dicots and monocots for seedling germination and emergence (soil exposures) as well as vegetative vigor (foliar exposures). The standard toxicity studies on terrestrial plants include post-emergent assays for vegetative vigor (Appendix 3, Table A3-1) and preemergence assays for seedling emergence (Appendix 3, Table A3-2). Summaries of these studies are taken from the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a).

The bioassays used by EPA (U.S. EPA/OPP/EFED 2014a, Table 3.24, p. 46) are summarized in Table 15 and illustrated in Figure 3 of the current risk assessment. Figure 3 illustrates the species sensitivity distributions in both seedling emergence and vegetative vigor assays. The use of species sensitivity distributions is detailed in SERA (2014a, Section 4.3.5). Note that Table 15 includes both EC_{25} values and NOAELs (i.e., No Observable Adverse Effect Levels). For the purposes of discussing differences in sensitivity, EC_{25} values are used. Following standard practice in Forest Service risk assessments, as discussed further in Section 4.3.2.5, NOAEL values are used for the dose-response assessment. In both seedling emergence assays (upper part of Figure 3) and vegetative vigor assays (lower part of Figure 3), dicots are somewhat more sensitive than monocots.

In standard assays for vegetative vigor, the most sensitive dicot is sugar beet (Amaranthaceae) with an EC_{25} of 0.16 lb a.i./acre and the most sensitive monocot is ryegrass (Xanthorrhoeaceae) with an approximately 2-fold higher EC_{25} of 0.3 lb a.i./acre. Within the dicot and monocot groups, however, the variability is much greater. The least sensitive dicot is carrot (Apiaceae) with an EC_{25} of 0.52 lb a.i./acre—i.e., a factor of about 3 above the most sensitive dicot [0.52 lb a.i./acre ÷ 0.16 lb a.i./acre = 2.25]. Similarly, the least sensitive monocot is corn (Poaceae) with an EC_{25} of 2.6 lb a.i./acre–i.e., a factor of about 7 above the most sensitive monocot [2 lb a.i./acre ÷ 0.3 lb a.i./acre ≈ 6.666…].

In standard assays for seedling emergence, the most sensitive dicot is carrot (Apiaceae) with an EC_{25} of 0.018 lb a.i./acre, and the most sensitive monocot is ryegrass (Xanthorrhoeaceae) with an approximately 2-fold higher EC_{25} of 0.27 lb a.i./acre [0.27 ÷ 0.018 = 15]. The least sensitive dicot is soybean (Fabaceae) with an EC_{25} of 1.2 lb a.i./acre—i.e., a factor of about 67 above the most sensitive dicot, sugar beet [1.2 lb a.i./acre ÷ 0.018 lb a.i./acre = 66.666]. Similarly, the least sensitive monocot is corn (Poaceae) with an EC_{25} of 3.1 lb a.i./acre—i.e., a factor of about 11 above the most sensitive monocot [3.1 lb a.i./acre ÷ 0.27 lb a.i./acre ≈ 11.48]. Thus, for the standard studies on seedling emergence, the difference in sensitivity within species of dicots is greater than the difference between the most sensitive species of monocots and dicots. For variability within species of monocots (i.e., a factor of 11), the difference is nearly as great as differences between the most sensitive species of monocots and dicots (i.e., a factor of 15).

In general, seedling emergence assays yield somewhat lower toxicity values than vegetative vigor studies, which might be expected given the soil-active nature of tebuthiuron. In terms of the most sensitive species in each type of assay, the difference is substantial. As discussed above, the most sensitive species in the vegetative vigor assay is the sugar beet with an EC_{25} of 0.16 lb a.i./acre and the most sensitive species in a soil emergence assay is carrot with an EC_{25} of 0.018 lb a.i./acre, which is lower than lowest vegetative vigor assay by a factor of about 9 [0.16 lb a.i./acre ÷ 0.018 lb a.i./acre ≈ 8.888…]. The responses of carrot in the two assays, however, are somewhat unusual. The carrot is the most sensitive species in the seedling emergence assay [EC_{25} = 0.018 lb a.i./acre] but the least sensitive dicot in the vegetative vigor assay [0.52 lb a.i./acre], higher than the seedling emergence assay by a factor of nearly 30 [0.52 lb a.i./acre ÷ 0.018 lb a.i./acre ≈ 28.888…].

In addition to the standard phytotoxicity studies submitted to the EPA in support of the registration of tebuthiuron, generally comparable bioassays are published in the open literature and are summarized in Appendix 3, Table A3-3. In terms of a practical impact on the current risk assessment, a key factor in assessing the open literature studies involves the identification of the most sensitive and tolerant species. As discussed above, the most sensitive species in the standard studies is the carrot with an EC_{25} of 0.018 lb a.i./acre in pre-emergence assays. None of the open literature studies reports lower toxicity values.

The most tolerant species in the standard studies is corn, a monocot of the family Poaceae, with an EC_{25} value of 2.6 lb a.i./acre in a vegetative vigor assay and 3.1 lb a.i./acre in a seedling emergence study. Mengistu et al. (2005) reports a 50% growth inhibition value of 5.28 kg a.i./ha (≈ 4.7 lb a.i./acre) for *Kochia scoparia*. This species may be comparable to corn in tolerance to tebuthiuron but is not clearly more tolerant than corn.

One area of focus in the published bioassays not addressed in standard EPA bioassays involves resistance. As noted in Section 2.2, tebuthiuron and several other urea herbicides are classified as Group C_2 by the Herbicide Resistance Action Committee (HRAC). Group C_2 herbicides include several tebuthiuron and several other amine urea herbicides that are thought to bind in a similar manner to and inhibit photosystem II, site A (Mallory-Smith and Retzinger 2003). As discussed by Barber (2012), photosystem II is the enzyme responsible for splitting water and generating oxygen during the process of photosynthesis. Reported differences between resistant and tolerant populations range from factors of 16 for *Amaranthus retroflexus*, a species of pig weed (Oettmeier et al. 1982) to 37.7 for *Kochia scoparia*, commonly known as burningbush or fire weed (Mengistu et al. 2005). Both of these species are dicots of the Amaranthaceae family. Diaz et al. (2005) assayed differences in tebuthiuron sensitivity between two species of crabgrass (Poaceae) in sensitivity to tebuthiuron. The more tolerant species was *Digitaria nuda* with an EC_{50} of 0.82 kg a.i./ha and the more sensitive species was *Digitaria ciliaris* with an EC_{50} of 0.13

kg a.i./ha. The population of the more tolerant species, *Digitaria nuda*, was taken from an area treated previously with several herbicides. Thus, the 6-fold difference between the two species may reflect resistance rather than inherent species differences.

4.1.2.5.2. Efficacy Studies

As discussed in Section 2, the Forest Service uses tebuthiuron primarily for the control of woody vegetation. As summarized in Appendix 3, Table A3-4, many field studies document the effective use of tebuthiuron for the control of woody vegetation at application rates in the range of about 0.2 to 4.4 lb a.i./acre (i.e., ≈ 0.18 to 3.9 lb a.i./acre). Several of these field studies demonstrate an effective control of woody dicots with a beneficial effect on grasses, typically classified as nontarget species. As discussed in the previous section, however, tebuthiuron is only somewhat more toxic to dicots than to monocots, and differences in toxicity among species of both monocots and dicots exceed the differences in toxicity between dicots and monocots. While not explicitly addressed in most of the field efficacy studies, the preferential control of hardwoods and corresponding increase in grasses is probably related to the reduction in hardwood canopy cover and a concomitant increase in sunlight availability for grasses.

Notwithstanding the above, tebuthiuron is used effectively to control some species of grasses (Felker and Russell 1988; Dias et al. 2005; Meyer and Baur 1979). Furthermore, reduced cover may be observed in some species of nontarget grasses such as western wheatgrass and prairie June grass following applications of tebuthiuron (Whitson and Alley 1984; Wilson 1989). The differential efficacy of tebuthiuron on different species of grasses is not addressed in detail in the field studies but may reflect sensitivity differences among different grasses similar to the sensitivity differences among different species of monocots, as discussed in Section 4.1.2.5.1. For example, oats are about 6 times more sensitive than corn in seedling emergence assays, even though both species are members of the Poaceae family (MRID No. 48722703 as summarized in Table A3-2).

In terms of relative sensitivities, all of the field studies were conducted at application rates of at least 0.2 kg a.i./ha (≈0.18 lb a.i./acre); thus, these studies are not useful in identifying highly sensitive species. In terms of tolerant species, various species of cactus (members of the Cactaceae family) appear to be highly tolerant to tebuthiuron at application rates of up to 4.4 kg a.i./ha or about 4 lb a.i./acre (Felker and Russell 1988; Scifres et al. 1979; Whitson and Alley 1984). As noted by Wilson (1989), a lower application rate of 0.7 kg a.i./ha (≈0.62 lb a.i./acre) is beneficial to brittle prickly pear (*Opuntia fragilis*, family Cactaceae) due to damage to and subsequent reduced competition with grasses. In addition to cactus, members of the Cupressaceae family (a taxon of conifers such as juniper and some species of cedar) appear to be relatively tolerant to tebuthiuron at application rates up to 4 kg a.i./ha or about 3.6 lb a.i./acre (Britton and Sneva 1981; Engle and Stritzke 1995; Stritzke et al. 1991).

All product labels for the representative formulations covered in the current risk assessment note that tebuthiuron may be less effective when applied to soils with high levels of organic matter (>5%). As discussed by Lourencetti et al. (2012) and summarized in Table 1, tebuthiuron has a tendency to bind more strongly to soils with higher proportions of organic carbon. Consistent with the notations on the product labels, open literature publications indicate that tebuthiuron is more effective in soils with lower amounts of organic matter (Chang and Stritzke 1977;

Whisenant and Clary 1987), which is to be expected, since lower amounts of organic carbon will decrease soil binding and increase the bioavailability of tebuthiuron to plants.

4.1.2.6. Terrestrial Microorganisms

The U.S. EPA does not typically require studies on the effects of herbicides on soil microorganisms. The most recent EPA ecological risk assessment cites to registrant-submitted studies related to soil microorganisms (i.e., MRIDs 00090099 and 00090100, U.S. EPA/OPP/EFED 2014a, p. 86); however, the results from these studies are not discussed in the EPA risk assessment.

There is no indication in the open literature that tebuthiuron is likely to damage soil microorganisms at expected environmental concentrations. In a paper from the Spanish open literature, Flores Rodriguez et al. (1982, Figure 3, p. 205) note that tebuthiuron inhibits nitrogen metabolism when combined with amitrol and 2,4-D at concentrations in the 40-60 mg a.i./kg soil range. Similarly, Goodroad (1987) notes that tebuthiuron, at soil concentrations of 100 and 1000 mg a.i./kg soil, inhibits soil nitrification and nitrogen mineralization. This effect, however, is not evident at a tebuthiuron concentration of 1 mg a.i./kg soil. As noted in Table 2 of Appendices 7 and 8, however, GLEAMS-Driver modeling indicates that the expected concentrations of tebuthiuron in the top 12 inches of the soil column will not exceed 1 mg a.i./kg soil. At least some microorganisms can tolerate high concentrations of tebuthiuron (i.e., up to 1000 mg a.i./L) and use tebuthiuron as a sole carbon and nitrogen source (Mostafa and Helling 2003). This study, however, involves enrichment culturing; the study is probably not indicative of microbial responses under typical environmental conditions. Similarly, Shelton et al. (1996) note that a strain of *Streptomyces* can degrade tebuthiuron by 60-80% over a 7-day period. Again, however, this study was conducted under highly controlled conditions which are not representative of normal environmental exposures. Perhaps the most relevant study for assessing the impact of tebuthiuron on soil microorganisms is the field study by Wachocki et al. (2001) in which no effect on mycorrhizal associations in root samples or photosynthetic soil microorganisms was observed following applications of tebuthiuron at rates of 0.3, 0.5, or 0.7 lb a.i./acre.

4.1.3. Aquatic Organisms

4.1.3.1. Fish

Standard toxicity bioassays to assess the effects of tebuthiuron on fish are summarized in Appendix 4: acute studies in Table A4-1 and the chronic study in Table A4-2. Acute toxicity studies were conducted in four species of freshwater fish, including bluegill sunfish, goldfish, fathead minnow, and rainbow trout and in one saltwater species, sheepshead minnow. In addition to the acute toxicity studies, two early life-stage studies are available, one in rainbow trout and the other in fathead minnow. All of these studies were submitted to the U.S. EPA/OPP in support of the registration of tebuthiuron, and summaries of two of these studies are available in the open literature—i.e., the acute study in goldfish (Todd et al. 1974) and the early life-stage study in fathead minnow (Meyerhoff et al. 1985). In addition to these standard toxicity studies, a mesocosm study with fathead minnow is published in the open literature (Temple et al. 1991). All of the available toxicity studies on fish were conducted with technical grade tebuthiuron.

Only two acute LC_{50} values for fish are definitive—i.e., the LC_{50} of 106 mg a.i./L in bluegill sunfish and the LC_{50} of 143 mg a.i./L in rainbow trout. Both of these studies were part of the same submission to EPA (MRID 00020661), and both studies are classified as *Acceptable*. The indefinite LC_{50} values of >160 mg a.i./L in goldfish (MRID 00020661) and >140 mg a.i./L in fathead minnows (MRID 00041685) are classified as *Supplemental*. All four of these studies are used by EPA to categorize tebuthiuron as *Practically Nontoxic* to fish (U.S. EPA/OPP/EFED 2014a, Table 3.10, p. 33).

As with the repeated-dose toxicity studies in mammals (Sections 3.1.5 and 3.1.9), the early life-stage studies in fish both report decreases in growth as the primary sublethal effects. Both studies define NOAELs and LOAELs—i.e., a NOAEL of 26 mg a.i./L and a LOAEL of 52 mg a.i./L in trout (MRID 00090083) and NOAEL of 9.3 mg a.i./L and a LOAEL of 18 mg a.i./L in fathead minnows (MRID 00090084). Decreases in fry survival were observed only in the trout study and only at the highest concentration assayed—i.e., 52 mg a.i./L.

The mesocosm study by Temple et al. (1991) notes a reduction (≈18%) in biomass in fathead minnows only at the highest concentration assayed—i.e., a nominal concentration of 1000 µg a.i./L corresponding to a measured concentration of 780 µg a.i./L by Day 108 of the study. The study authors note that: *Fish biomass was not affected by the range of tebuthiuron doses used in this study* (Temple et al. 1991, p. 125). This statement indicates that the study authors did not consider the decrease in biomass at 1000 µg a.i./L to be statistically or biologically significant. Nonetheless, the decrease is substantial and is consistent qualitatively with the early life-stage study in fathead minnows (MRID 00090084). Quantitatively, however, the next lower concentration in the mesocosm study—i.e., 500 µg a.i./L (nominal) and 350 µg a.i./L (measured)—is clearly a NOAEL in terms of growth and is substantially higher than the LOAEL of 18 mg a.i./L from the early life-stage study in fathead minnows (MRID 00090084).

As discussed in Section 3.1.3.1 and summarized in Table 4, several mammalian metabolites of tebuthiuron have been identified. The metabolism of tebuthiuron in bluegill sunfish was examined by Morton and Hoffman (1976) as part of a multi-species study of metabolites derived from tebuthiuron. Unlike mammals, the only metabolite observed in bluegills was an N-demethylation at the 3-position of the urea sidechain—i.e., metabolite 104 in Table 4.

4.1.3.2. Amphibians (Aquatic Phase)

As with Terrestrial Phase amphibians, no studies on the toxicity of tebuthiuron to aquatic phase amphibians were identified in the open literature. Following standard practice at EPA, fish are used as surrogates for aquatic phase amphibians (U.S. EPA/OPP/EFED 2014a, p. 32) in the absence of data on these groups of organisms.

4.1.3.3. Aquatic Invertebrates

Standard toxicity bioassays to assess the effects of tebuthiuron on aquatic invertebrates are summarized in Appendix 5: acute studies in Table A5-1 and the chronic study in Table A5-2. A definitive acute EC_{50} is available in *Daphnia magna* (MRID 00041694) and a definitive acute LC_{50} is available in pink shrimp. For *Daphnia*, the endpoint for the EC_{50} is immobility which is functionally equivalent to mortality in larger species such as shrimp. Indefinite toxicity values are available in oyster (an EC_{50} based on shell deposition in adults and an LC_{50} for embryos) and fiddler crab (LC_{50}). The only standard chronic study is a reproduction study in *Daphnia magna* (MRID 00138700). The mesocosm study by Temple et al. (1991) may be considered a chronic study (106 days) but includes assays of only biomass in midge larvae.

Based on the LC_{50} of 62 mg a.i./L in pink shrimp, the EPA classifies tebuthiuron as *Slightly Toxic*. Based on indefinite toxicity values of >100 mg a.i./L in fiddler crab and oyster embryo and an indefinite toxicity value of >95 mg a.i./L in adult oyster, the EPA classifies tebuthiuron as *Practically Nontoxic* to these marine species (U.S. EPA/OPP/EFED 2014a, Table 3.15, p. 36). The *Practically Nontoxic* classification is also applied to *Daphnia magna* based on the acute definitive EC_{50} of 297 mg a.i./L (U.S. EPA/OPP/EFED 2014a, Table 3.12, p. 35). The standard reproduction study in Daphnia magna yielded a NOAEC of 21.8 mg a.i./L.

Midge larvae (i.e., species of Chironomidae) are used by EPA as a standard test species for benthic invertebrates (e.g., OPPTS 850.1790, Chironomid Sediment Toxicity Test). No studies on midge larvae, however, are noted in the most recent EPA risk assessment on tebuthiuron (U.S. EPA/OPP/EFED 2014a). The mesocosm study by Temple et al. (1991) does include assays for chironomid density and biomass (species not given). A statistically significant decrease (p<0.027) in chironomid density was observed at 200 µg a.i./L with an apparent NOAEC of 70 µg a.i./L. As discussed further in Section 4.1.3.4.1 (Aquatic Algae), Temple et al. (1991) also observed pronounced decreases in primary productivity at 70 µg a.i./L. As noted by the authors of this study, *depressions in chironomid density with increasing tebuthiuron concentration were due, in part, to reduced primary production and/or an algal species shift* (Temple et al. 1991, p. 125). The extent to which tebuthiuron may have directly affected chironomid density through toxicity cannot be determined.

4.1.3.4. Aquatic Plants

4.1.3.4.1. Algae

The literature on the effects of tebuthiuron on algae is substantially more robust than the literature on other groups of nontarget species addressed in this risk assessment. As summarized in Appendix 6, Table A6-1, several standard algal bioassays are summarized in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a). The open literature includes several additional bioassays, most of which involve nonstandard test species and/or atypical periods of exposure (Table A6-1) as well as microcosm studies, which are summarized in Appendix 6, Table A6-3.

Based on the standard toxicity studies in standard test species, the most sensitive species of algae identified by EPA is a marine diatom, *Skeletonema costatum*, with an EC_{50} of 50 µg a.i./L and an NOAEC of 38 µg a.i./L (U.S. EPA/OPP/EFED 2014a, Table 3.9, p. 33, MRID 41080402). The least sensitive species identified by EPA is a blue-green alga (*Anabaena flos-aquae*) with an EC_{50} of 810 µg a.i./L (U.S. EPA/OPP/EFED 2014a, p. 65, MRID 41080401).

In terms of tolerant species, the open literature is reasonably consistent with EPA. In a survey of four species of algae and six species of cyanobacteria, Peterson et al. (1994) notes that another species of *Anabaena* (i.e., *A. inaequalis*) is the most tolerant species, evidencing only a 26% decrease in growth at a concentration of 5867 µg a.i./L. Peterson et al. (1994) assayed only a single concentration; nonetheless, based on this concentration and the modest inhibition of growth, *A. inaequalis* appears to be somewhat more tolerant than *A. flos-aquae*.

Comparisons between the open literature bioassays and EPA studies involving more sensitive species are less straightforward because of differences in experimental designs—e.g., endpoints assayed and durations of exposures. As summarized in Appendix 6, Table A6-1, the EPA reports a 5-day EC_{50} of 50 µg a.i./L with a corresponding NOAEC of 13 µg a.i./L for the freshwater green alga *Selenastrum capricornutum* [a.k.a., *Pseudokirchneriella subcapita* or *Raphidocelis subcapitat*a] (MRID 00138697). These toxicity values are similar to the 96-hour EC_{50} of 102 µg a.i./L given by Hickey et al. (1991) and the NOAECs of 10 to 50 µg a.i./L reported by Adams et al. (1985), both open literature toxicity values for *Selenastrum capricornutum*. Based on the 96-hour EC_{50} of 102 µg a.i./L and a NOAEL of 100 mg a.i./L (i.e., a factor of about 1000 above the EC_{50}), Hickey et al. (1991, p. 401) suggest: *Short-term (4-h) impact on algae with these organics would generally appear inconsequential*. While this may be correct for *Selenastrum capricornutum*, the generalization may not apply to other species of algae. For example, the EPA notes a 96-hour EC_{50} of 90 µg a.i./L for a freshwater diatom, *Navicula pelliculosa* (U.S. EPA/OPP/EFED 2014a, MRID 41080403). This EC_{50} based on area under the growth curve is virtually identical to the 2.5-hour EC_{50} of 94 µg a.i./L based on a fluorometric assay of photosystem II inhibition (Magnusson et al. 2010).

Two open literature studies use assays for chlorophyll fluorescence (Jones and Kerswell 2003; Magnusson et al. 2010). Jones and Kerswell (2003) assayed the effect of a 10-hour exposure to tebuthiuron on chlorophyll activity in a symbiotic dinoflagellate in coral branches. The 10-hour EC_{50} was 175 µg a.i./L, similar to the 96-hour EC_{50} of 90 µg a.i./L for growth in *Navicula pelliculosa* (U.S. EPA/OPP/EFED 2014a, MRID 41080403, discussed above). The NOAEL for the inhibition of chlorophyll activity in the symbiotic dinoflagellate is reported as 3 µg a.i./L, which is below the lowest NOAEC identified from the standard assays submitted to EPA by a factor of about 4—i.e., NOAEC of 13 µg a.i./L in *Selenastrum capricornutum* (U.S. EPA/OPP/EFED 2014a, MRID 00138697). The study by Magnusson et al. (2010) assayed the inhibition of photosynthesis in several species of algae in an exposure period of only 2.5 hours. As summarized in Appendix 6 (Table A6-1), the EC_{50} of 94 µg a.i./L in a marine species of *Navicula* was almost identical to the standard 96-hour EC_{50} of 90 µg a.i./L in the freshwater diatom, *Navicula pelliculosa* (MRID 41080403). The LOAEC in the marine diatom (8.7 µg a.i./L), however, was substantially below the NOAEC (56 µg a.i./L) in the freshwater diatom. The study by Magnusson et al. (2010) also reports the lowest adverse effect concentration in the available assays on algae—i.e., an LOAEC of 1.1 µg a.i./L in *Nephroselmis pyriformis*. As reviewed by Ralph et al. (2007), fluorescence bioassays in algae may be viewed as highly sensitive endpoints, but the primary reservation with these assays … *is the lack of proven ecological relevance* (Ralph et al. 2007, p. 603).

As summarized in Appendix 6, Table A6-3, the microcosm studies (Day 1993; Price et al. 1989) and the mesocosm study (Temple et al. 1991) do not suggest any sensitivity to tebuthiuron that is inconsistent with the standard bioassays or other assays in the open literature. The short-term (4-hour) microcosm study by Day (1993) yields an NOAEC of 52 µg a.i./L for a mixed culture of algae that is similar to reported NOAECs in *Selenastrum capricornutum* (10-50 µg a.i./L from Adams et al. 1985), *Navicula pelliculosa* (56 µg a.i./L from MRID 41080403) and *Skeletonema costatum* (38 µg a.i./L from MRID 41080402). The much longer-term (253 days) study by Price et al. (1989) uses only a single concentration (180 µg a.i./L) and notes growth inhibition. Similarly, the longer-term (106 days) mesocosm study by Temple et al. (1991) notes an approximate NOAEC based on primary productivity of 200 to 500 µg a.i./L, levels that are substantially above several of the NOAECs from shorter-term single-species bioassays, as discussed above.

4.1.3.4.2. Aquatic Macrophytes

The available information on the toxicity of tebuthiuron to macrophytes consists of only a single standard bioassay in *Lemna gibba* (MRID 41080404) and a single high concentration exposure of *Lemna minor* (Peterson et al. 1994). As summarized in Appendix 6, Table A6-2, the 7-day EC_{50} (frond count) for *Lemna gibba* is 130 µg a.i./L with an NOAEC of 50 µg a.i./L (MRID 41080404). As discussed in the previous section, reported EC_{50} values for tolerant species of algae is are in the range of 810 µg a.i./L (*Anabaena flos-aquae*) to 5867 µg a.i./L (*A. inaequalis*). Based on this comparison, *Lemna gibba* appears to be somewhat less tolerant (i.e., more sensitive) than the most tolerant species of algae. Given the few species of algae and the single species of aquatic macrophyte on which data are available, generalizations concerning the tolerance algae relative to aquatic macrophytes are not justified.

The single exposure study by Peterson et al. (1994) notes complete inhibition of growth in *Lemna minor* at a concentration of 5867 µg a.i./L. This information adds little to the understanding of sensitivities in *Lemna* sp. other than to indicate that the complete growth inhibition at 5867 µg a.i./L in *Lemna minor* is consistent with EC_{50} of 130 µg a.i./L in *Lemna gibba*.

No data have been encountered on other major aquatic vascular macrophytes (e.g. *Potamogeton* sp., *Myriophyllum* sp. or *Vallisneria* sp.).

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

A standard set of exposure assessments for terrestrial and aquatic organisms is provided in the EXCEL workbooks for tebuthiuron. All exposure assessments are based on an application rate of 0.6 lb a.i./acre as discussed in Section 2.4. Separate workbooks are provided for liquid applications and granular applications. The workbook for liquid applications (Attachment 1) is customized to cover directed ground, broadcast ground, and aerial applications. For granular applications, separate workbooks are provided for directed ground applications (Attachment 2), ground broadcast applications (Attachment 3), aerial applications (Attachment 4).

Exposure assessments are detailed in Worksheet G01a for mammals and in Worksheet G01b for birds. For both mammals and birds, the highest exposure scenarios are associated with the consumption of contaminated vegetation. This is a common pattern for pesticides that are applied to or intended to treat vegetation. The highest exposures are associated with the consumption of contaminated short grass by a small mammal or bird. For acute exposure scenarios, the highest estimated dose for a small mammal is about 414 mg a.i./kg bw, the upper bound dose for the consumption of contaminated short grass. The comparable dose for a small bird is somewhat over 1,000 mg a.i./kg bw. For longer-term exposure scenarios, the maximum doses are also associated with the consumption of short grass—i.e., about 175 mg a.i./kg bw/day for a small mammal and 431 mg a.i./kg bw/day for a small bird.

Toxicity data are not available on terrestrial-phase amphibians and reptiles (Section 4.1.2.3); accordingly, exposure assessments for these terrestrial vertebrates are not developed.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion, and the use of contaminated irrigation water. The highest exposures for terrestrial plants are associated with direct spray and spray drift. Nonetheless, as discussed in the risk characterization, runoff and sediment losses are also significant sources of potential exposure for terrestrial plants in sites that may favor runoff, particularly sites with predominantly clay soils. Potential exposures involving the use of contaminated water for irrigation are also significant. While exposures associated with the movement of tebuthiuron on soil particles by wind do not appear to be a substantial source of exposure, the product labels for tebuthiuron provide cautionary language on this exposure route.

Exposures of aquatic plants and animals to tebuthiuron are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water.

4.2.2. Mammals and Birds

All exposure scenarios for terrestrial animals are summarized in Worksheet G01 in the EXCEL workbooks that accompany this risk assessment (Attachments 1 through 4). An overview of the mammalian and avian receptors considered in the current risk assessment is given in Table 16. These data are discussed in the subsections that follow. Because of the relationship of body weight to surface area as well as to the consumption of food and water, for any type of exposure, the dose for small animals is generally higher, in terms of mg/kg body weight, than the dose for large animals. The exposure assessment for mammals considers five nontarget mammals of varying sizes: small (20 g) and medium (400 g) sized omnivores, a 5 kg canid, a 70 kg herbivore, and a 70 kg carnivore. Four standard avian receptors are considered: a 10 g passerine, a 640 g predatory bird, a 2.4 kg piscivorous bird, and a 4 kg herbivorous bird. Because of presumed differences in diet, (i.e., the consumption of food items), all of the mammalian and avian receptors are not considered in all of the exposure scenarios (e.g., the 640 g predatory bird is not used in the exposure assessments for contaminated vegetation).

Field studies suggest that applications of tebuthiuron will alter the food items consumed by mammals and birds (Section 4.1.2.1 and 4.1.2.2). While this type of information is not available on all herbicides, all herbicides will alter the vegetation and hence the food items available to mammals and birds. The study by Scifres et al. (1983) suggests that cows will preferentially feed on pastures treated with tebuthiuron relative to pastures treated with 2,4-D or picloram. This is an unusual observation in that the preference for tebuthiuron treated sites does not appear to be related to changes in vegetation. This observation suggests that at least some mammals might prefer to feed in areas treated with tebuthiuron relative to untreated areas, which could increase the exposure of some mammals to tebuthiuron. This mechanism for a potential increase in exposure is not explicitly considered in the current Forest Service risk assessment. Nonetheless, as detailed in Section 4.2.2.3, the assumption is made that both mammals and birds feed exclusively at the treated site and that 100% of the diet is contaminated. Thus, the risk assessment implicitly considers the potential for preferential feeding at tebuthiuron treated sites.

4.2.2.1. Direct Spray

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

For this risk assessment, two direct spray or broadcast exposure assessments are conducted. The first spray scenario (Worksheet F01a) concerns the direct spray of half of the body surface of a 20 g mammal during a pesticide application. As discussed in Section 3.1.3.2, the k_a used in this risk assessment is based on quantitative structure activity relationships (QSAR) as detailed in SERA (2014a, Section 3.1.3.2.2). The second exposure assessment (Worksheet F01b) assumes complete absorption over Day 1 of exposure. This assessment is included in an effort to encompass increased exposures due to grooming.

4.2.2.2. Dermal Contact with Contaminated Vegetation

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

For tebuthiuron, as well as most pesticides applied in broadcast applications, the failure to quantify exposures associated with dermal contact adds relatively little uncertainty to the risk assessment, because the dominant route of exposure will be the consumption of contaminated vegetation, as addressed below in Section 4.2.2.3.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

In foliar applications of pesticides, the consumption of contaminated vegetation is an obvious concern. Except for the large carnivorous mammal and the predatory bird, exposure assessments for the consumption of contaminated vegetation are developed for all mammals and birds listed in Table 16.

The initial concentrations of tebuthiuron on contaminated food items are based on the U.S. EPA/OPP/EFED (2001) adaptation of the residue rates from Fletcher et al. (1994), as summarized in Table 17. The methods of estimating the peak and time-weighted average concentrations of tebuthiuron in vegetation are identical to those used in the human health risk assessment (Section 3.2.3.7). As summarized in Table 17, fruit and short grass comprise the food commodities with the lowest pesticide residue rates (fruit) and the highest pesticide residue rates (short grass). Tall grass and broadleaf forage plants are estimated to have intermediate residue rates. For each of these four types of vegetation, both acute and longer-term exposure scenarios are developed as summarized in Worksheet G01a for mammals and Worksheet G01b for birds of the attachments to this risk assessment, as noted in Section 4.2.1.

The acute and chronic exposure scenarios are based on the assumption that 100% of the diet is contaminated, which may not be realistic for some acute exposures and seems an unlikely event in chronic exposures—i.e., animals may move in and out of the treated areas over a prolonged period of time. While estimates of the proportion of the diet contaminated could be incorporated into the exposure assessment, the estimates would be an essentially arbitrary set of adjustments. The proportion of the contaminated diet is linearly related to the resulting HQs, and its impact is discussed further in the risk characterization (Section 4.4.2.1 for mammals and Section 4.4.2.2 for birds).

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

The estimates of field metabolic rates are used to calculate food consumption based on the caloric value (kcal/day dry weight) of the food items considered in this risk assessment and estimates of the water content of the various foods. Estimates of caloric content are summarized in Table 17. Most of the specific values in Table 17 are taken from Nagy (1987) and U.S. EPA/ORD (1993).

Along with the exposure scenarios for the consumption of contaminated vegetation, similar sets of exposure scenarios are provided for the consumption of small mammals by either a predatory mammal (Worksheet F10a) or a predatory bird (Worksheet F10b) and the consumption of contaminated insects by a small mammal, a larger (400 g) mammal, and a small bird (Worksheets F09a-c). The residue rates for insects are taken from the U.S. EPA/OPP (2001) adaptation of the residue rates in Fletcher et al. (1994), as summarized in Table 17.

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating tebuthiuron concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4.6). The only major differences in the exposure estimates concern the body weight of and the quantity of water consumed by the mammal or bird. Like food consumption rates, water consumption rates, which are well characterized in terrestrial vertebrates, are based on allometric relationships in mammals and birds, as summarized in Table 16. The exposure assessments for mammals and birds are detailed in Worksheets F02a-f (accidental spill), Worksheets F08a-f (peak concentrations), and Worksheets F16a-f (longer-term concentrations) in the attachments to this risk assessment.

Like food consumption, water consumption in birds and mammals varies substantially with diet, season, and many other factors; however, quantitative estimates regarding the variability of water consumption by birds and mammals are not well documented in the available literature and this variability is not considered in the exposure assessments. Nevertheless, as summarized in Table 12, the upper and lower bound estimates of tebuthiuron concentrations in surface water vary substantially (i.e., by a factor of over 90 [$1.0 \div 0.011 \approx 90.91$] for acute exposures and a factor of 100 [$0.64 \div 0.0064$] for chronic exposures). Given this degree of variability in the estimated concentrations of tebuthiuron in surface water, it is unlikely that a quantitative consideration of the variability in water consumption rates of birds and mammals would have a substantial impact on the risk characterization.

In addition and as discussed further in Section 4.4.2.1 (risk characterization for mammals) and Section 4.4.2.2 (risk characterization for birds), exposures associated with the consumption of contaminated surface water are far below the level of concern (HQ=1). For example, the highest HQ for mammals or birds is 0.009—i.e., the upper bound of the acute HQ for a small mammal consuming contaminated water. This HQ is below the level of concern by a factor of over 110 [$1 \div 0.009 \approx 111.111\ldots$]. Consequently, even extreme variations on the consumption of contaminated water by mammals or birds would have no impact on the risk characterization for these nontarget organisms.

4.2.2.5. Consumption of Contaminated Fish

In addition to the consumption of contaminated vegetation, insects, and other terrestrial prey (Section 4.2.2.3), the consumption of contaminated fish by piscivorous species is a potentially significant route of exposure to tebuthiuron. Exposure scenarios are developed for the consumption of contaminated fish after an accidental spill (Worksheets F03a-c), expected peak exposures (Worksheets F011a-c), and estimated longer-term concentrations (Worksheets F17a-c). These exposure scenarios are applied to 5 and 70 kg carnivorous mammals as well as a

2.4 kg piscivorous bird. The 70 kg carnivorous mammal is representative of a small or immature brown bear (*Ursus arctos*), a large mammals that actively feeds on fish (Reid 2006). As summarized in Table 16, the 5 kg mammal is representative of a fox, and the 2.4 kg bird is representative of a heron.

Tebuthiuron exposure levels associated with the consumption of contaminated fish depend on the tebuthiuron concentration in water and the bioconcentration factor for tebuthiuron in fish. The concentrations of tebuthiuron in water are identical to those discussed in Section 4.2.2.4. As discussed in Section 3.2.3.5, tebuthiuron does not bioconcentrate substantially in fish. As summarized in Table 2, a bioconcentration factor of 2.63 for whole fish is reported in U.S. EPA/OPP/EFED (2014a, MRID 40819501). This bioconcentration factor is used for all exposure scenarios involving the consumption of contaminated fish by mammalian or avian wildlife.

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

Estimated levels of exposure associated with broadcast terrestrial applications of tebuthiuron are detailed in Worksheet G09 of Attachments 1 through 4 (i.e., the EXCEL workbooks for tebuthiuron). In Attachment 1 (liquid applications), Worksheet G09 is a custom worksheet which includes aerial, ground broadcast (high boom and low boom), and backpack applications. The attachments for granular applications cover directed ground applications (Attachment 2), ground broadcast applications (Attachment 3), aerial applications (Attachment 4).

As discussed in Section 4.1.2.4, honeybees are typically used by the U.S. EPA as a surrogate for other terrestrial insects (e.g., U.S. EPA/OPP/EFED 2014a). Honeybee exposures are modeled in the current risk assessment as a simple physical process based on the application rate and surface area of the bee. The surface area of the honeybee (1.42 cm^2) is based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

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

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

During broadcast applications of a pesticide, it is likely that terrestrial invertebrates other than bees will be subject to direct spray. As discussed in further detail in Section 4.3.2.3 (dose-response assessment for terrestrial invertebrates), the available data on the toxicity of tebuthiuron to terrestrial invertebrates do not support the derivation of separate toxicity values for different groups of terrestrial insects.

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

As discussed in Section 4.1.2.4, data on the oral toxicity of tebuthiuron to honeybees or other species of insects are not available. Accordingly, an exposure assessment is not developed for the consumption of contaminated vegetation by terrestrial invertebrates.

4.2.3.3. Contaminated Soil

As with the oral exposure assessment for the consumption of contaminated vegetation or prey, the exposure assessment for contaminated soil is not included in the current risk assessment because appropriate and corresponding toxicity data (e.g., soil bioassays in earthworms) are not available.

4.2.4. Terrestrial Plants

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

4.2.4.1. Direct Spray

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

4.2.4.2. Off-Site Drift

Estimates of off-site drift are modeled using AgDRIFT. These estimates are summarized in Worksheets G05a and G05b of the EXCEL workbook for liquid applications of tebuthiuron (Attachments 1). These are custom worksheets that include estimates of drift for aerial, ground broadcast, and backpack applications. As with the direct spray and drift scenarios for terrestrial invertebrates (Section 4.2.3.1), the attachments for granular applications cover directed ground applications (Attachment 2), ground broadcast applications (Attachment 3), aerial applications (Attachment 4).

The drift estimates used in the current risk assessment are based on AgDRIFT (Teske et al. 2002) using Tier 1 analyses for aerial and ground broadcast applications. The term *Tier 1* is used to designate relatively generic and simple assessments which can be viewed as plausible upper limits of drift. In Worksheet G05a, aerial drift estimates are based on Tier 1 analyses using ASAE Fine to Medium drop size distributions. Tier 1 estimates of drift for ground broadcast applications are modeled using both low boom and high boom options in AgDRIFT. For both types of applications, the values are based on very fine to fine drop size distributions and the 90th percentile values from AgDRIFT. The use of small droplet sizes in Worksheet G05a is intended to generate extremely conservative estimates of drift that would not be anticipated in typical Forest Service applications.

In Worksheet G05b, aerial drift estimates are based on Tier 1 analyses using ASAE Coarse to Very Coarse droplet size distributions (VMD≈440 µm), and the ground broadcast applications are based on ASAE fine to medium coarse drop size distributions (VMD≈340 µm). The product labels for all formulations of tebuthiuron explicitly considered in this risk assessment (Table 4) specifically note that coarse droplet sizes should be used in aerial or ground applications. Thus, the drift values given in Worksheet G05b are likely to reflect estimates of drift that would be more typical of Forest Service applications than the extremely conservative estimates of drift given in Worksheet G05a.

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

The values for drift used in the current risk assessment should be regarded as generic estimates similar to the water concentrations modeled using GLEAMS (Section 3.2.3.4.3). Actual drift will vary according to a number of conditions—e.g., the topography, soils, weather, droplet size distribution, carrier, and the pesticide formulation. An additional and substantial reservation of the drift estimates apply to granular applications. As noted in Section 3.2.3.4.2, AgDrift does not explicitly incorporate options for the application of granular products (Teske et al. 2002), and the available field data do not address drift as a consequence of applying granular formulations of tebuthiuron. Thus, risks to terrestrial plants associated with granular applications of tebuthiuron are not explicitly modelled.

4.2.4.3. Runoff and Soil Mobility

Terrestrial plant exposures associated with runoff and sediment losses from the treated site to an adjacent untreated site are summarized in Worksheet G04 of the EXCEL workbooks for tebuthiuron (Attachments 1 through 4).

Any pesticide can be transported from the soil at the application site by runoff, sediment loss, or percolation. Runoff, sediment loss, and percolation are considered in estimating contamination of ambient water (Section 3.2.3.4). Only runoff and sediment loss are considered in assessing off-site soil contamination. This approach is reasonable because off-site runoff and sediment transport will contaminate the off-site soil surface and could have an impact on non-target plants. Percolation, on the other hand, represents the amount of herbicide transported below the root zone, which may affect water quality but does not affect off-site vegetation, except if the contaminated water is used for irrigation, as discussed further in Section 4.2.4.3. As with the estimates of tebuthiuron in surface water, estimates of runoff and sediment losses are modeled for clay, loam, and sand at nine sites that represent different temperatures and rainfall patterns as specified in Table 8.

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

For tebuthiuron, the results of the standard GLEAMS modeling of runoff and sediment losses are summarized in Appendix 7 for liquid applications and Appendix 8 for granular applications. Clearly, the amount of runoff and sediment loss will vary substantially with different types of climates—i.e., temperature and rainfall—as well as soils, with no runoff or sediment loss anticipated in predominantly sandy soils. The input parameters used to estimate runoff and sediment losses are identical to those used in the Gleams-Driver modeling for concentrations of tebuthiuron in surface water as discussed in Section 3.2.3.4 and summarized in Table 9 (site characteristics) and Table 10 (chemical-specific input parameters).

The runoff for tebuthiuron as a proportion of the application rate is taken as 0.05 (0.01-0.2). As detailed in Appendix 7, Table A7-1, this estimated runoff is taken as the average of values for clay and loam soils—i.e., 0.04865 (0.014808-0.1805)—rounded to one significant place. Runoff or sediment loss is not modelled for predominantly sandy soils; furthermore, for predominantly sandy soils, exposures associated with runoff will be insubstantial. As discussed further below (Section 4.2.4.5), a greater concern with applications to sandy soils is wind erosion.

4.2.4.4. Contaminated Irrigation Water

The scenario for the use of contaminated water for irrigation is standard in Forest Service risk assessments. The exposure levels associated with this scenario depend on the pesticide concentration in the ambient water used for irrigation and the amount of irrigation water used. Concentrations in ambient water are based on the peak concentrations modeled in the human health risk assessment, as discussed in Section 3.2.3.4.6 and summarized in Table 12.

The amount of irrigation used will depend on the climate, soil type, topography, and plant species under cultivation. Thus, the selection of a representative irrigation rate is somewhat problematic. In the absence of any general approach for determining and expressing the variability of irrigation rates, the application of 1 inch of irrigation water with a range of 0.25 to 2 inches is used in this risk assessment. Details of the calculations used to estimate the functional application rates based on irrigation using contaminated surface water are provided in Worksheet G06a of the EXCEL workbooks for tebuthiuron (Attachments 1 through 4).

While the labels and/or EPA documents for many herbicides specifically state that water potentially contaminated with herbicides should not be used for irrigation, no such language has been identified for tebuthiuron. Nonetheless, all of the product labels for the representative formulations of tebuthiuron explicitly considered in this risk assessment (Table 2) indicate that application should not be made to *…ditches used to transport irrigation water or potable water*. As discussed further in Section 4.4.2.5.3, this cautionary language is clearly justified.

4.2.4.5. Wind Erosion

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

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

As noted in Worksheet G06b, offsite losses are estimated to reach as much as 0.014% of the application rate. Larney et al. (1999), however, report that wind erosion of other herbicides could be associated with losses up to 1.5% of the nominal application rate following soil incorporation or 4.5% following surface application. This difference appears to be due to the much higher soil losses noted by Larney et al. (1999)—i.e., up to 56.6 metric tons/ha from a fallow field. The losses reflected in Worksheet G06b may be somewhat more realistic for forest or rangeland applications since forestry applications of herbicides are rarely made to fallow areas. As noted by Patric (1976), total soil erosion from all sources in well-managed forests is typically in the range of about 0.12-0.24 metric tons/ha/year [0.05 to 0.10 ton/acre/year], substantially below the range from 1 to 10 metric tons/ha/year used in Worksheet G06b. Thus, losses due to wind erosions following pesticide applications under forest canopies or heavily vegetated areas may be much less than the estimates used in this risk assessment.

In any event, the higher offsite losses reported by Larney et al. (1999) are comparable to exposures associated with offsite drift at distances of about 50 feet from the application site following low boom and high boom ground broadcast applications (Worksheet G05). All of the estimates for wind erosion and offsite drift are likely to vary dramatically according to site conditions and weather conditions.

The product labels for the representative formulations of tebuthiuron explicitly considered in the current risk assessment (Table 2) provide cautionary language concerning exposures associated with wind erosion. The following is taken from the Specimen Label for Alligare Tebuthiuron 80 WG:

> *Do not apply to areas where soil movement by water erosion and/or natural or mechanical means is likely. Avoid treatment or areas susceptible to wind erosion such as single grain sands or disturbed soils that are loose and powdery dry. Under these conditions, treatment should be delayed until the soil surface has been stabilized by rainfall or irrigation. Before treatment of sandy soils in areas*

subject to wind erosion, the soil surface should first be stabilized with gravel mulch or other means of preventing physical movement of surface soil.

As discussed further in Section 4.4.2.5.4, the current risk assessment does not raise substantial concerns for wind erosion relative to other routes of exposure; moreover, the open literature does not include field studies that address the issue of nontarget damage by tebuthiuron due to the wind erosion. While the most recent EPA ecological risk assessment makes general mention of wind erosion as a potential route of exposure for terrestrial animals and plants (U.S. EPA/OPP/EFED 2014a, p. 66), no incident reports on wind erosion of tebuthiuron-bearing surface soils are noted in the EPA assessment (U.S. EPA/OPP/EFED 2014a, p. 31). Nonetheless, as discussed further in Section 4.4.2.5.4, any cautionary language on a product label must be considered carefully prior to any application of any pesticide.

4.2.5. Aquatic Organisms

The concentrations of tebuthiuron in surface water used to estimate exposures for aquatic species are identical to those used in the human health risk assessment, as discussed in Section 3.2.3.4.6 and summarized in Table 12.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

All toxicity values used in the ecological risk assessment are summarized in Table 18. The derivation of each of these values is discussed in the subsections below. The available toxicity data support separate dose-response assessments in eight classes of organisms: terrestrial mammals, birds, terrestrial invertebrates (contact exposure only), terrestrial plants, fish, aquatic invertebrates, aquatic algae, and aquatic macrophytes. No dose-response assessment can be developed for reptiles or for terrestrial or aquatic phase amphibians.

Different units of exposure are used for different groups of organisms, depending on the nature of exposure and the way in which the toxicity data are expressed. To maintain consistency with the exposure assessment, which is necessary for the development of hazard quotients (HQs) in the risk characterization, all toxicity values given in Table 18 are expressed as active ingredient (a.i.).

In general, Forest Service risk assessments defer to the U.S. EPA/OPP on study selection for the most sensitive species within the groups covered in the ecological risk assessment, unless there is a compelling reason to do otherwise. The one exception is mammals. In characterizing risks to mammalian wildlife, Forest Service risk assessments generally use the NOAELs which serve as the basis for the acute and chronic RfDs from the human health risk assessment (SERA 2014a). Another difference between EPA and Forest Service risk assessments involves the endpoints used for risk characterization. For acute exposures, the EPA will often use LD_{50} or comparable definitive toxicity values (e.g., EC_{50}, EC_{25}) for risk characterization but the Forest Service prefers to use NOAEL or NOAEC values (SERA 2009).

For terrestrial mammals, the acute dose response assessment is based on the same data as the human health risk assessment (i.e., a NOAEL of 10 mg a.i./kg bw for developmental effects which is applied to both acute and chronic exposures). The acute NOAEL for birds is 180 mg a.i./kg bw, substantially higher than the corresponding NOAEL of 10 mg a.i./kg bw for mammals. The chronic NOAEL for birds (i.e., 7 mg a.i./kg bw/day) is based on a reproduction study is similar to the chronic NOAEL for mammals (NOAEL = 10 mg a.i./kg bw/day). For terrestrial invertebrates, the dose response assessment is based on a contact assay in honeybees in which a dose of 860 mg a.i./kg bw is taken as an approximate NOAEL.

Tebuthiuron is used primarily for the control of woody vegetation. In general, dicots (including woody vegetation) are somewhat more sensitive than monocots (e.g., grasses) to tebuthiuron. However, grasses may be temporarily damaged after tebuthiuron application. For exposures associated with direct sprays or drift, NOAELs for sensitive and tolerant species are 0.062 lbs/acre (sugar beet) and 2 lbs/acre (corn), respectively. With respect to soil contamination associated with runoff, the NOAEL for sensitive species (carrot) is 0.018 lbs/acre and the NOAEL for tolerant species (corn) is 2 lbs/acre.

As would be expected for an herbicide, aquatic plants are substantially more sensitive (NOAELs of 0.013 to 0.056 mg a.i./L) than either fish (NOAELs of 9.3 to 50 mg a.i./L) or aquatic invertebrates (NOAELs of 4.56 to 21.8 mg a.i./L) to tebuthiuron.

4.3.2. Terrestrial Organisms

4.3.2.1. Mammals

As discussed in Section 4.1.2.1, the available acute toxicity values suggest that rabbits are somewhat more sensitive than rats, mice, cats, and dogs. In terms of repeated dose studies, specifically developmental studies, rabbits appear to be the most sensitive species and much more sensitive than rats.

As discussed in Section 3.3, the EPA derived an acute RfD of 0.1 mg a.i./kg bw/day based on a rabbit developmental NOAEL of 10 mg a.i./kg bw/day, which is applied only to women of childbearing age. Somewhat unusually, the chronic RfD for the general population is higher than the acute RfD for women of childbearing age—i.e., 0.14 mg a.i./kg bw/day based on NOAEL of 14 mg a.i./kg bw/day from a two-generation reproduction study in rats. The magnitude of the difference between the acute and chronic RfD is insubstantial—i.e., the values are identical when rounded to one significant place.

In terms of the ecological risk assessment, endpoints associated with developmental and reproductive effects are critical in that these effects can influence population dynamics. For the current risk assessment, the NOAEL of 10 mg a.i./kg bw/day is used for both acute and chronic exposures under the assumption (typically used by EPA) that in pregnant mammals, a 1-day exposure can result in adverse fetal effects. This may be viewed as an extremely conservative/protective approach given that the developmental NOAEL for tebuthiuron in rats is 110 mg a.i./kg bw/day (MRIDs 00020803 and 40485801)—i.e., higher than the NOAEL in rabbits by a factor of 11. Nonetheless, many mammalian species may be exposed to tebuthiuron, but developmental toxicity data are available on only two species. Thus, a conservative approach seems justified. The impact of this approach is discussed further in the risk characterization for mammals (Section 4.4.2.1).

4.3.2.2. Birds

For acute exposures, U.S. EPA/OPP/EFED (2014a, Table 4.5, p. 56) uses the dietary LC_{50} of 1465 mg a.i./kg diet for zebra finch (MRID 48928201). As discussed in Section 4.1.2.2, this LC_{50} is the lowest dietary LC_{50} in avian species. All gavage LD_{50} studies are indefinite and are reported as >500 mg a.i./kg bw to >2000 mg a.i./kg bw (Appendix 2, Table A2-1). Thus, gavage LD_{50} values are not considered further for the dose-response assessment. The U.S. EPA uses dietary LC_{50} values directly for the risk characterization, calculating the risk quotient (RQ) as the ratio of the dietary LC_{50} to the expected concentration of tebuthiuron in food items. The Forest Service prefers to calculate HQs based on a NOAEL in units of mg a.i./kg bw which is then divided into the estimated consumption of tebuthiuron based on the concentration of tebuthiuron in the food item and the amount of food consumed. As summarized in Appendix 2, Table A2-2, the dietary NOAEC for zebra finch is 497 mg a.i./kg diet (MRID 48928201). Based on the feeding study in zebra finch by Salvante et al. (2007), the average food consumption for this species is about 6 g a.i./day (Fig 1D, p. 1329), and the average body weight is about 16.5 g (Figure 2, p. 1330). Thus, the food consumption factor is about 0.36 kg food per kg bw [$6/16.5 \approx 0.363636$]. This food consumption factor is similar to standard factors used in Forest Service risk assessments for quail (0.3) and mallards (0.4). Based on the food consumption factor for zebra finch, the dietary NOAEC of 497 mg a.i./kg diet corresponds to an NOAEL of about 180 mg a.i./kg bw [497 mg a.i./kg diet x 0.36 kg food per kg bw ≈ 178.92]. This NOAEL is used to characterize risks to birds following acute exposures.

For longer-term exposures, U.S. EPA/OPP/EFED (2014a, Table 4.6, p. 56) uses a dietary NOAEC of 100 mg a.i./kg diet. As summarized in Appendix 2, Table A2-3, this NOAEC is noted in reproduction studies of both mallards (MRID 00093690) and quail (MRID 00104243). For both mallards and quail, dietary concentrations (mg/kg diet) are converted to mg/kg bw/day doses using a food consumption factor of 0.07 kg food/kg bw based on reproduction studies in quail and mallards (SERA 2007b). Using this food consumption factor, the dietary NOAEC of 100 mg a.i./kg diet corresponds to 7 mg a.i./kg bw/day.

4.3.2.3. Reptiles and Amphibians (Terrestrial Phase)

Since toxicity data are not available for terrestrial-phase reptiles or amphibians (Section 4.1.2.3), a dose-response assessment cannot be derived for this group of organisms.

4.3.2.4. Terrestrial Invertebrates

If sufficient data are available, Forest Service risk assessments develop dose-response assessments involving contact and oral exposures for insects and soil exposures, typically for earthworms (SERA 2014a, Section 4.1.2.4). As discussed in Section 4.1.2.4 of the current risk assessment, however, the only toxicity data available for terrestrial invertebrates involves a single contact toxicity study in bees which yielded an acute NOAEL of 100 µg a.i./bee, equivalent to about 860 mg a.i./kg bw. Consequently, this contact NOAEL is used to estimate acute HQs for bees associated with direct spray and drift. Risks to invertebrates associated with oral or soil exposures are not characterized quantitatively. Nonetheless, field studies are used to qualitatively address risks to terrestrial invertebrates in the risk characterization (Section 4.4.2.4).

4.3.2.5. Terrestrial Plants (Macrophytes)

In terms of risk characterization for the most sensitive species, the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a, Table 4.10, p. 63) uses the EC_{25} of 0.018 lb a.i./acre for seedling emergence (carrot [dicot] from MRID 48722704) and the EC_{25} of 0.16 lb a.i./acre for vegetative vigor (sugar beet [dicot] from MRID 48722704). As summarized in Table 15 of the current risk assessment, the NOAEL values associated with the EC_{25}s used by EPA are 0.031 lb a.i./acre (seedling emergence in carrots) and 0.062 lb a.i./acre (vegetative vigor in sugar beets). Neither the sparse open literature plant bioassays (Section 4.1.2.5.1) nor the robust open literature efficacy studies (Section 4.1.2.5.2) identify toxicity values for tebuthiuron that are lower than those identified and used by EPA.

Given the lack of data in the open literature on species more sensitive than those identified in the most recent EPA risk assessment, the dose-response assessment for sensitive species would typically involve using the same studies and species used by EPA but would use the NOAELs rather than the EC_{25}. This approach is used for the vegetative vigor endpoint. As summarized in Table 15 of the current risk assessment, the EC_{25} for sugar beets is 0.16 lb a.i./acre and the corresponding NOAEL is 0.062 lb a.i./acre. Thus, for foliar exposure, the NOAEL of 0.062 lb a.i./acre is used for the risk characterization of sensitive species.

For seedling emergence, however, this approach is not used. As also summarized in Table 15, the EC_{25} for the most sensitive species (carrot) is 0.018 lb a.i./acre and the corresponding

NOAEL is 0.031 lb a.i./acre. Note that the NOAEL is higher than the EC_{25}. While the underlying raw data are not available for the conduct of the current risk assessment, this situation is not extraordinarily peculiar. The EC_{25} is estimated using a regression model while the determination of an NOAEC is based on comparisons between the exposure group and the control group. Particularly in cases where the slope of the dose-response curve is shallow, the regression estimates of the EC_{25} will be greater than the corresponding NOAEL. While the difference between the EC_{25} and the NOAEL is not substantial [0.031÷0.018≈1.72], the current Forest Service risk assessment uses the somewhat lower EC_{25} of 0.018 lb a.i./acre for the risk characterization associated with soil exposures of sensitive species.

As discussed in Section 4.1.2.5.1 and illustrated in Figure 3, monocots are somewhat less sensitive than dicots to tebuthiuron. Based on the toxicity bioassays considered by EPA and summarized in Table 15 of the current risk assessment, corn is the most tolerant species with an NOAEC of 2 lb a.i./acre in assays for both seedling emergence and vegetative vigor. Mengistu et al. (2005) reports a 50% growth inhibition value of 5.28 kg a.i./ha (≈4.7 lb a.i./acre) for *Kochia scoparia,* a dicot in the Amaranthaceae family (herbs). While Mengistu et al. (2005) do not report a NOAEL for this species, Figure 2 in the paper by Mengistu et al. (2005) indicates that the NOAEL for this species was below 2 lb a.i./acre—i.e., an EC_{25} of about 2 kg a.i./ha or ≈1.7 lb a.i./acre.

As discussed in Section 4.1.2.5.2 and summarized in Appendix 3, Table A3-4, several field studies indicate that cactus (species of the Cactaceae family) appear to be highly tolerant to tebuthiuron at application rates of up to about 4 lb a.i./acre (Felker and Russell 1988; Scifres et al. 1979; Whitson and Alley 1984). In addition, some conifers and species of cedar appear to be relatively tolerant to tebuthiuron at application rates up to 3.6 lb a.i./acre (Britton and Sneva 1981; Engle and Stritzke 1995; Stritzke et al. 1991). While these field studies suggest that some species of cactus, conifers, and cedar may be somewhat more tolerant of tebuthiuron than corn (i.e., an NOAEL of 2 lb a.i./acre as discussed above), the NOAEL in corn is based on a well-controlled and standard bioassay that was reviewed and accepted by EPA. Consequently, the NOAEC of 2 lb a.i./acre for corn is used for the risk characterization of tolerant species of terrestrial plants for both foliar and soil exposures. As discussed further in Section 4.4.2.5, tolerant species of plants do not appear to be at risk following applications of tebuthiuron. Thus, the potentially higher NOAECs for some species of plants relative to corn have no impact on the risk characterization.

4.3.2.6. Terrestrial Microorganisms

As noted in Section 4.1.2.6, the most recent EPA ecological risk assessment cites two studies on the toxicity of tebuthiuron to microorganisms but does not discuss the results of these studies or otherwise address potential risks to terrestrial microorganisms. As also noted in Section 4.1.2.6, one study in the open literature notes an inhibition of soil nitrification and nitrogen mineralization at tebuthiuron concentrations of 100 and 1000 mg a.i./kg soil but not at a concentration of 1 mg a.i./kg soil (Goodroad 1987). While a formal dose-response assessment is not developed for soil microorganisms, the study by Goodroad (1987) as well as a field study showing no adverse effects on soil microorganisms at application rates of up to 0.7 lb a.i./acre (Wachocki et al. 2001) are both used to qualitatively address potential risks to soil microorganisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish

For characterizing risks to fish, the most recent EPA ecological risk assessment for tebuthiuron uses an acute LC_{50} of 106 mg a.i./L for acute RQs (risk quotients) and a chronic NOAEC of 9.3 mg a.i./L for chronic RQs (U.S. EPA/OPP/EFED 2014a, Table 4.1, p. 48). As discussed in Section 4.1.3.1 and summarized in Appendix 4, Table 4A-1, the acute LC_{50} of 106 mg a.i./L is the lowest definitive LC_{50} in fish—i.e., the acute bioassay in bluegill sunfish from MRID 00020661. As also discussed in Section 4.1.3.1 and summarized in Appendix 4, Table 4A-2, the chronic NOAEC of 9.3 mg a.i./L is from an early life-stage study in fathead minnow reported in MRID 00090084. Both of these studies were reviewed by EPA and classified as *Acceptable*.

The open literature studies on tebuthiuron do not provide lower toxicity values for its direct effects on fish. Following standard practice in Forest Service risk assessments, the studies used by EPA are adopted for the risk characterization of sensitive species of fish. A NOAEC is not reported in the acute toxicity study. Again following standard practice in Forest Service risk assessments, the LC_{50} in bluegills could be multiplied by 0.05 to approximate an acute NOAEC of 5.3 mg a.i./L [106 mg a.i./L ÷ 20]. As discussed in the methods document for preparing Forest Service risk assessments (SERA 2014a, Section 4.3.2) this approach is based on EPA's level of concern (RQ=0.05) for acute effects in aquatic organisms based on an acute LC_{50} or EC_{50}. This approach is not adopted for tebuthiuron because the estimated acute NOAEC of 5.3 mg a.i./L for sensitive species of fish would be below the chronic NOAEC of 9.3 mg a.i./L, which is not sensible—i.e., an acute NOAEC should be greater than or equal to the chronic NOAEC. Consequently, the acute NOAEC for sensitive species of fish is taken as 9.3 mg a.i./L, equivalent to the chronic NOAEC for sensitive species of fish (SERA 2014a, p. 99, lines 49-44).

The EPA does not typically derive separate risk estimates for potentially tolerant species of fish, which is a routine practice in Forest Service risk assessments. For acute exposures, the dose response assessment is based on the 96-hour NOAEC of 50 mg a.i./L in sheepshead minnow (MRID 48722702). This NOAEC is the highest reported acute NOAEC for fish and is higher than NOAECs that could be estimated from the available acute toxicity studies (Appendix 4, Table A4-1). The chronic NOAEC for tolerant species of fish is taken as 26 mg a.i./L, the NOAEC from the early life-stage study in rainbow trout in which adverse effects were noted at the LOAEL of 52 mg a.i./L based on adult survival and growth (MRID 00090084 as summarized in Appendix 4, Table A4-2).

A reservation with the dose-response assessment for chronic effects in fish involves the mesocosm study by Temple et al. (1991). As summarized in Section 4.1.3.1 and summarized in Appendix 4, Table A4-3, Temple et al. (1991) observed a reduction in biomass of fathead minnows at a nominal concentration of 1 mg a.i./L (estimated measured concentration of 0.79 mg a.i./L by study day 108) with a NOAEL at a nominal concentration of 0.5 mg a.i./L (measured concentration of about 0.35 mg a.i./L at study day 108). As discussed further in Section 4.3.3.3, the reductions in fish biomass were associated with a reduction in invertebrate biomass which was in turn associated with a reduction in primary productivity. In addition, the authors of this study state: *Fish biomass was not affected by the range of tebuthiuron doses used in this study* (Temple et al. 1991, p. 125). While not explicitly addressed in the paper by Temple et al. (1991), the reduction of fish biomass may not have been statistically significant or the effect may have been due to a reduction in the food supply (invertebrates) for the fish. In either case, the study by Temple et al. (1991) does not make a compelling argument for a direct effect on fish. The indirect effect on fish involving reduced food supply is discussed further in the risk characterization for fish (Section 4.4.3.1).

4.3.3.2. Amphibians (Aquatic Phase)

Because of the lack of toxicity data on aquatic phase amphibians, no dose-response assessment for this group of organisms is developed. As noted in Section 4.1.3.2, the U.S. EPA uses fish as surrogates for aquatic phase amphibians and this approach is discussed further in the risk characterization (Section 4.4.2.3).

4.3.3.3. Aquatic Invertebrates

For acute exposures, the most recent EPA ecological risk assessment for tebuthiuron uses an acute EC_{50} (immobility endpoint) of 297 mg a.i./L in *Daphnia magna* (MRID 00041694) for characterizing risks to freshwater invertebrates (U.S. EPA/OPP/EFED 2014a, Table 4.2, p. 49) and an LC_{50} of 62 mg a.i./L in pink shrimp (MRID 00041684) for characterizing risks to estuarine invertebrates (U.S. EPA/OPP/EFED 2014a, Table 4.3, p. 50). Note that for small aquatic invertebrates, EC_{50} values are typically used as functional LC_{50} values.

For chronic exposures to freshwater invertebrates, the EPA uses the NOAEC of 21.8 mg a.i./L in *Daphnia magna* (MIRD 00041684). In the absence of a chronic study in estuarine invertebrates, the EPA uses the ratio of the acute LD50 to the chronic NOAEC in *Daphnia magna* to estimate a chronic NOAEC in estuarine invertebrates. For *Daphnia magna*, the ratio of the acute LC_{50} to the chronic NOAEC is about 13.6 [297 mg a.i./L ÷ 21.8 mg a.i./L ≈ 13.62385]. Using this ratio and the acute LC_{50} of 62 mg a.i./L in pink shrimp, the chronic NOAEC for pink shrimp is estimated as 4.56 mg a.i./L [62 mg a.i./L ÷ $13.6_{acute÷chronic}$ ≈ 4.5588 mg a.i./L]. This use of acute to chronic ratios is included in the National Academy of Sciences recent recommendations on the assessment of risks to threatened and endangered species (NAS 2013, p. 121, Eq. 1).

Given the few species of aquatic invertebrates on which data are available (Section 4.1.3.3) relative to the large number of species of aquatic invertebrates, Forest Service risk assessments generally identify and use data on the most sensitive and also the most tolerant species of aquatic invertebrates to characterize risks. *Daphnia magna* is the most tolerant species for which a definitive acute EC_{50} is available. As discussed in Section 4.3.3.1, Forest Service risk assessments typically approximate an acute NOAEC, if necessary, by dividing the acute EC_{50} by a factor of 20. In this case, the acute EC_{50} of 297 mg a.i./L could be used to estimate an acute NOAEC of 14.85 mg a.i./L [297 mg a.i./L ÷ 20]. As noted above, however, the chronic NOAEC in *Daphnia magna* is 21.8 mg a.i./L. As with fish (Section 4.3.3.1) and for the same rationale (SERA 2014a, p. 99, lines 49-44), the chronic NOAEC of 21.8 mg a.i./L in *Daphnia magna* is used for the risk characterization of tolerant species of aquatic invertebrates for both acute and chronic exposures.

Based on definitive LC_{50} values, pink shrimp is the most sensitive species of aquatic invertebrate. As discussed above, the chronic NOAEC of 4.56 mg a.i./L developed by EPA is adopted without modification. As with tolerant species, the acute LC_{50} of 62 mg a.i./L would typically be divided by 20 to estimate an acute NOAEC of 3.1 mg a.i./L [62 mg a.i./L ÷ 20]. As with the similarly estimated acute NOAEC for *Daphnia magna* (discussed above), the estimated acute NOAEC is below the estimated chronic NOAEC. Consequently, the estimated chronic NOAEC of 4.56 mg a.i./L is used for the risk characterization of sensitive species of aquatic invertebrates for both acute and chronic exposures.

With the exception of the chronic NOAEC for *Daphnia magna*, all of the toxicity values for aquatic invertebrates are estimates/extrapolations rather than experimental values. As discussed further in Section 4.4.3.4, the reliance on estimates rather than experimental values diminishes confidence in the risk characterization for this group of organisms.

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

For the risk characterization of non-vascular aquatic plants, the most recent EPA ecological risk assessment uses data on a marine diatom, *Skeletonema costatum*, from MRID 41080402 which reports a 96-hour EC_{50} of 0.05 mg a.i./L and an 96-hour NOAEC of 0.038 mg a.i./L (U.S. EPA/OPP/EFED 2014a, Table 4.4, p. 52, and Table 4.11, p. 66). Following standard methods in EPA risk assessments, the EC_{50} is used to characterize risks to non-listed species and the NOAEC is used to characterize risks to listed species (i.e., threatened or endangered species).

The selection of *Skeletonema costatum* from MRID 41080402 rather than *Selenastrum capricornutum* from MRID 00138697 might seem somewhat unusual. As summarized in Appendix 6 (Table A6-1) as well as in Table 3.16 of U.S. EPA/OPP/EFED (2014a, p. 38), the EC_{50} is 0.05 mg a.i./L for both species of algae; however, the NOAEC for *Selenastrum capricornutum* is 0.013 mg a.i./L, which is lower than the corresponding NOAEC for *Skeletonema costatum* by a factor of about 3 [0.038 mg a.i./L ÷ 0.013 mg a.i./L ≈ 2.923]. Both studies are classified by EPA as *Supplemental* (U.S. EPA/OPP/EFED (2014a, Table 3.16, p. 38). Nonetheless, Table 3.16 from the EPA risk assessment has the following note on the study in *Selenastrum capricornutum*: *Results could not be verified since raw data were not provided*. In other words, because the EPA did not have the raw data on *Selenastrum capricornutum*, the EPA's confidence in this study appears to have been diminished relative to the study on *Skeletonema costatum*.

While Forest Service risk assessments typically defer to EPA in terms of study selection, the study on *Selenastrum capricornutum*, which yields a somewhat lower NOAEC than the study selected by EPA, is published in the peer reviewed open literature—i.e., Meyerhoff et al. 1985 in Environmental Toxicology and Chemistry. In addition, as noted above, this study was reviewed by EPA and was classified similarly to the unpublished registrant study on *Skeletonema costatum*—i.e., *Supplemental*. While the lack of raw data is an understandable reservation on the part of EPA, Forest Service risk assessments consider and use data from the open literature that appear credible. In terms of the NOAEC, the 0.013 mg a.i./L NOAEC reported by Meyerhoff et al. (1985) is supported by the less detailed study by Adams et al. (1985). While the study by Adams et al. (1985) does not report definitive EC_{50} values, this study does report NOAECs in the range of 0.01 to 0.05 mg a.i./L, depending on endpoint and duration of exposure. Consequently, the NOAEC of 0.013 mg a.i./L from the study by Meyerhoff et al. (1985) is used in the current risk assessment to characterize risks associated with sensitive species of algae.

For tolerant species of algae, the NOAEC of 0.056 mg a.i./L (with a corresponding EC_{50} of 0.09 mg a.i./L) in *Navicula pelliculosa* is used for risk characterization. As summarized in Appendix 6 (Table A6-1) and discussed in Section 4.1.3.4.1, *Anabaena* species appear to be the most tolerant species based on EC_{50} values; however, the NOAEC in *Navicula pelliculosa* is the highest well-defined NOAEC. The much higher concentration of 5.867 mg a.i./L from the study by Peterson et al. (1994) caused only a 20% inhibition in the growth of *Anabaena inaequalis*. Nonetheless, Peterson et al. (1994) note that this decrease was statistically significant with respect to controls and thus 5.867 mg a.i./L is clearly a LOAEC rather than a NOAEC.

Another issue with the dose-response assessment for algae involves the open literature studies by Jones and Kerswell (2003) and Magnusson et al. (2010). As discussed in Section 4.1.3.4.1 and summarized in Appendix 6 (Table A6-1), these studies report short-term (2.5 to 10 hour) EC_{50} values for the inhibition of photosynthesis based on bioassays of fluorescence that are comparable to EC_{50} values for cell counts in algae from standard bioassays. Nevertheless, the fluorescence assays also report NOAECs and LOAELs that are much lower than the NOAECs reported in the standard bioassays. While the lower NOAECs and LOAECs from the fluorescence-based bioassays are internally consistent, these results are not used in the dose-response assessment. As noted in Section 4.1.3.4.1, fluorescence-based bioassays may be viewed as extremely sensitive; however, the direct ecological relevance of these endpoints is not clear (e.g., Ralph et al. 2007).

Other open literature studies involving microcosms or mesocosms (i.e., Day 1993; Price et al. 1989; Temple et al. 1991) do not provide NOAEC values that are below the standard toxicity studies reviewed by EPA.

4.3.3.4.2. Aquatic Macrophytes

For the risk characterization of vascular aquatic plants, the most recent EPA ecological risk assessment uses a standard registrant study in duckweed (MRID 41080404) which reports a 7-day EC_{50} of 0.13 mg a.i./L and a 7-day NOAEC of 0.05 mg a.i./L (U.S. EPA/OPP/EFED 2014a, Table 4.4, p. 52, and Table 4.11, p. 66). Following standard methods in EPA risk assessments, the EC_{50} is used to characterize risks to non-listed species and the NOAEC is used to characterize risks to listed species (i.e., threatened or endangered species).

The study on duckweed used by EPA is the only study that defines a NOAEC in aquatic macrophytes. While the EPA uses the EC_{50} for non-listed species, the Forest Service prefers to characterize risks to all organisms using an NOAEC, regardless of the status of the species as threatened or endangered. Consequently, the NOAEC of 0.05 mg a.i./L is used in the current risk assessment. In the absence of data on the sensitivity of other species of aquatic macrophytes to tebuthiuron, the NOAEC of 0.05 mg a.i./L is applied to tolerant species. As discussed in the previous section, the NOAEC of 0.05 mg a.i./L is close to the NOAEC of 0.056 mg a.i./L in tolerant species of algae. The NOAEC for tebuthiuron in sensitive species of aquatic macrophytes is treated as a data gap.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

While tebuthiuron is an effective herbicide for the control of woody vegetation, it is not selective, and the sensitivities of dicots and monocots to tebuthiuron overlap substantially. Consequently, tebuthiuron can adversely affect sensitive species of monocots as well as woody vegetation and other dicots. Nonetheless, the HQs for impacts on nontarget vegetation are not remarkably high. The highest HQ for sensitive species of vegetation is 10, which is associated with direct spray. For runoff scenarios, the upper bound HQ for sensitive species of vegetation is 7. If water contaminated with tebuthiuron is used for irrigation, the upper bound HQ for sensitive species of vegetation is 4. For all exposure scenarios, including direct spray, the HQs for tolerant species of vegetation are below the level of concern. The impact of tebuthiuron on vegetation, both target and nontarget, is documented in numerous field studies. The relatively modest HQs for tebuthiuron are due primarily to the relatively low application rates proposed by the Forest Service. Although the maximum application rate for tebuthiuron is 6 lb a.i./acre, the Forest Service will typically use an application of no more than 0.6 lb a.i./acre. For nontarget plants, the HQs are linearly related to the application rate. If higher application rates are needed at some sites, the EXCEL attachments to this risk assessment can be used to refine the risk characterization.

The most substantial nontarget impact of tebuthiuron applications made near surface water will involve effects on algae. Direct effects on fish and invertebrates are unlikely. The available toxicity data in algae indicate that differences in their sensitivity to tebuthiuron are much less than differences in the sensitivity of terrestrial macrophytes. Based on estimated peak concentrations in surface water, adverse effects in algae may be anticipated at the upper bounds of acute exposure for both sensitive and tolerant species and at the central and upper bound estimates of acute exposure for sensitive species. Over prolonged periods after tebuthiuron applications at a rate of 0.6 lb a.i./acre, adverse effects could be apparent at the upper bounds of exposure for both sensitive and tolerant species of algae. In practical terms, the most important factor in refining the risk characterization involves site-specific conditions. For instance, at sites or in regions where water contamination might be minimal due to weather or the distance of surface water from the application site, risks to algae could be minimal.

The risk characterization for both mammals and birds differs depending on the type of formulation applied. Applications of granular formulations will lead to lower concentrations of tebuthiuron in vegetation, the major route of exposure for mammals and birds. Following applications of granular formulations, risks to mammals and birds are minimal. Following applications of liquid formulations, risks to sensitive species of mammals and birds could substantially exceed the level of concern. The risk characterization for mammals is based on rabbits, the group of mammals apparently most sensitive to tebuthiuron. The available data indicate that rodents are much less sensitive than rabbits to tebuthiuron and are not likely to be adversely affected. The sensitivities of other groups of mammals to tebuthiuron are unknown.

The data on the toxicity of tebuthiuron to terrestrial invertebrates is sparse—i.e., limited to a single bioassay in honeybees and some field observations. Based on these data, effects on terrestrial invertebrates appear to be unlikely. No data are available on the toxicity of tebuthiuron to reptiles or amphibians (terrestrial or aquatic phase). Thus, no risk characterization for these groups of organisms is developed.

While the risk characterization for tebuthiuron focuses on the potential for direct toxic effects, there is also a potential for indirect effects in virtually all groups of nontarget organisms. The best documented indirect effect of tebuthiuron involves terrestrial vegetation. Consistent with the labelled uses of tebuthiuron, several efficacy studies involving application rates in the range of those proposed by the Forest Service (i.e., 0.6 lb a.i./acre) indicate that tebuthiuron will reduce canopy cover (woody vegetation) and encourage the growth of grasses. Alterations in vegetation following the application of any effective herbicide, including tebuthiuron, could also cumulatively impact animals. These alterations in vegetation may be beneficial to some species and detrimental to others; moreover, the magnitude of secondary effects is likely to vary over time. The potential for cumulative impacts on animals is documented in field studies but to a much lesser extent than impacts on nontarget vegetation. If algae are adversely affected by tebuthiuron, cumulative impacts on aquatic invertebrates and fish could be detrimental due to a decrease in available food.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

The quantitative risk characterization for mammals is summarized in Worksheets G02a of the EXCEL workbooks for liquid formulations (Attachment 1) and granular formulations (Attachments 2-4). As with the human health risk assessment (Section 3.4.3.1), the predominant route of exposure involves the consumption of contaminated vegetation, and the HQs are much greater for liquid applications (i.e., water dispersible granules or dry flowable formulations mixed with water) than for granular applications of pellet formulations. The substantial differences in the HQs between liquid and granular applications are due solely to the much higher estimates of tebuthiuron on contaminated vegetation after the application of liquid formulations relative to granular formulations (Section 3.2.3.7 and Table 14). These differences are apparent in risk assessments of other herbicides that may be applied either as liquids or granules (e.g., SERA 2005).

4.4.2.1.1. Liquid Applications (non-accidental scenarios)

For liquid applications (Attachment 1, Worksheet G02a), the central estimates of acute exposure for a small (20 g) mammal exceed the level of concern (HQ=1) for the consumption of broadleaf vegetation (HQ=5), tall grasses (HQ=4), and short grasses (HQ=9). At the upper bounds of exposure, the acute HQs exceed the level of concern for small through large (70 kg) mammals for the consumption of broadleaf vegetation (HQs of 3 to 23), tall grasses (HQs of 2 to 19), and short grasses (HQs of 5 to 41). In addition, the upper bound acute HQ for the consumption of contaminated fruit exceeds the level of a concern for a small mammal (HQ=3).

The chronic HQs for the consumption of contaminated vegetation also exceed the level of concern following liquid applications. The central estimates of chronic exposure for a small mammal exceed the level of concern for the consumption of broadleaf vegetation (HQ=1.9), tall grasses (HQ=1.5), and short grasses (HQ=4). At the upper bounds of exposure, the chronic HQs reach or exceed the level of concern for small through large mammals for the consumption of broadleaf vegetation (HQs of 1.3 to 10), tall grasses (HQs of 1 to 8), and short grasses (HQs of 2 to 17). As with acute exposures, the upper bound acute HQ for the consumption of contaminated fruit exceeds the level of a concern for a small mammal (HQ=1.5).

Because of differences in methodology between Forest Service and EPA risk assessments (SERA 2009) and differences in exposure assumptions, direct quantitative comparisons to the most recent EPA ecological risk assessment are not straightforward. For example, the highest mammalian RQ from EPA is 1.6 with a level of concern of 0.1 at an application rate of 6 lb a.i./acre. Correcting for the difference in application rate (6 lb a.i./acre for EPA and 0.6 lb a.i./acre for the current risk assessment), the RQ of 1.6 corresponds directly to an acute HQ of 1.6 [(1.6÷0.1)÷(6÷0.6)]. As noted above, the highest acute HQ derived in the current risk assessment is 41. The reason for this difference is that the EPA characterizes risk with acute LD_{50} values of about 300 to 850 mg a.i./kg bw (U.S. EPA/OPP/EFED 2014a, Table 4.7, p. 58), while the current Forest Service risk assessment uses a developmental NOAEL of 10 mg a.i./kg bw (Section 4.3.2.1). Correcting for this difference, the RQ of 1.6 from EPA corresponds to HQs of 48 to 136 [1.6 x (300 to 850 mg a.i./kg bw ÷ 10 mg a.i./kg bw)]. Despite these quantitative differences, the qualitative characterization of risk for mammals given in the current Forest Service risk assessment is essentially identical to that given by EPA. Acute and chronic risks to mammals of all size groups exceed the level of concern for liquid applications (U.S. EPA/OPP/EFED 2014a, Table 1, p. 3).

The HQs for mammals are based on the assumption that 100% of the diet is contaminated (SERA 2014a, Section 4.2.2.3). This assumption may be unrealistic for some acute exposures and will probably be a rare event in terms of chronic exposures, at least for larger mammals (i.e., larger animals may move in and out of the treated areas). While the potential for a limited consumption of contaminated vegetation is not considered quantitatively in the current risk assessment, this consideration could be justified at least for some species in site-specific applications of tebuthiuron.

A major reservation with the severe risk characterization for mammalian wildlife involves the substantial differences in the toxicity of tebuthiuron to different groups of mammals. As discussed in Section 4.3.2.1 and summarized in Table 14, the dose-response assessment for mammals is based on a NOAEL for development effects in rabbits (Order Lagomorpha), specifically the NOAEL of 10 mg a.i./kg bw/day and a LOAEL for fetal resorptions of 25 mg a.i./kg bw/day (MRIDs: 00020644, 40776301). Based on the relationship of the NOAEL to the LOAEL, adverse effects in sensitive species of mammals would be expected at an HQ of 2.5—i.e., the ratio of the LOAEL to the NOAEL. In rats (Order Rodentia), however, no developmental effects were noted at doses up to 110 mg a.i./kg bw/day (MRIDs 00020803 and 40485801). If the sensitivity of rats is typical of other species of rodents, no adverse effects would be anticipated in rodents at HQs of up to 11—i.e., the NOAEL in rats divided by the NOAEL for rabbits. Given that the study in rats does not define an adverse effect level, the actual dose associated with reproductive effects in rodents is indeterminate.

Because data on developmental effects (the most sensitive endpoint) are available in only two studies, each involving a different order of mammals, it is not clear that all or most species of rodents would be less sensitive to tebuthiuron than all or most species of lagomorphs. The relative sensitivity of other orders of mammals (e.g., carnivores, deer and other species of

Artiodactyla, insectivores, etc.) as compared to rodents and lagomorphs is not known. Given the large number of mammalian orders and their respective species, it is reasonable to select the more sensitive species of the two species for which data are available for risk characterization. Nonetheless, it seems equally justifiable to note that some species, particularly some mammalian species of rodents, may be more tolerant than rabbits and that high HQs would not necessarily apply to these more tolerant species.

The practical importance of differences in sensitivity among different groups of mammals is suggested by the field study by McMurry et al. (1993a). As discussed in Section 4.1.2.1 and summarized in Appendix 1 (Table A1-9), McMurry et al. (1993a) found no substantial changes in woodrat populations following applications of tebuthiuron at an application rate of 2.2 kg a.i./ha or about 2 lb a.i./acre. Assuming that the woodrat is a member of a relatively tolerant group of mammals (i.e., rodents), the lack of a direct effect of tebuthiuron on woodrat populations is consistent with the high NOAEL of 110 mg a.i./kg bw/day in the developmental study in rats.

As noted in Section 4.4.1, the application of any effective herbicide will change the composition of the vegetation in the treated area, which may be beneficial to some species and detrimental to others. As also discussed in Section 4.1.2.1 and summarized in Appendix 1 (Table A1-9), several field studies assess the impact or potential impact of tebuthiuron applications to mammals due to changes in vegetation. These studies do not suggest any systematic negative effects. Even within the same order of mammals (in this case rodents), studies on populations of small mammals following tebuthiuron treatments note no substantial or consistently detrimental effects (Boggs et al. 1990a,b; Johnson et al. 1996; Olson et al. 1994; Zavaleta 2012). For example, Johnson et al. (1996) observed an increase in grasshopper mice but a decrease in deer mice following applications of tebuthiuron at rates of about 0.36 to 0.9 lb a.i./acre. Neither effect, however, was dose-related. Thus, while changes in vegetation may impact different species of mammals, the impacts do not appear to be consistently negative, and similar impacts might be expected following any attempt to alter the composition of vegetation using any effective herbicide or other vegetation management method.

4.4.2.1.2. Granular Applications (non-accidental scenarios)

The risk characterization for mammals following granular applications of tebuthiuron is simple. Even at the upper bounds of exposure, only one of the non-accidental acute exposure scenarios exceeds the level of concern—i.e., the upper bound of the acute HQ for a small mammal consuming short grass is 1.7. Since small mammals do not exclusively consume short grass, this minor exceedance in the level of concern is probably inconsequential.

As with the risk characterization for liquid applications, the risk characterization given in the current Forest Service risk assessment is similar to the risk characterization given by EPA. No chronic risks are anticipated, and acute risks are limited to small and medium sized mammals (U.S. EPA/OPP/EFED 2014a, Table 2, p. 4).

4.4.2.1.3. Accidental Exposures

The accidental exposure scenarios for applications of tebuthiuron lead to HQs that are generally below those for non-accidental exposures associated with liquid applications (Section 4.4.2.1.1). This is not an unusual pattern. Most of the accidental exposure scenarios of concern in the

Forest Service risk assessments involve an accidental spill into surface water. For many pesticides applied to vegetation, the exposures of mammals to the pesticide in contaminated vegetation exceed the exposures associated with a spill into water.

For liquid applications, the only scenario leading to the exceedance in the level of concern (HQ=1) involves the direct spray of a small mammal assuming 100% absorption—i.e., HQs = 1.5 (0.7-3). As discussed in Section 4.2.2.1, the assumption of 100% absorption is extreme and is included in an effort to encompass increased exposures due to grooming.

For granular applications, the only accidental scenarios that exceed the level of concern (at least at the upper bounds) are for a canid—i.e., HQs = 0.2 (0.008-2) and a large carnivore consuming contaminated fish—i.e., HQs = 0.1 (0.006-1.6).

4.4.2.2. Birds

The quantitative risk characterization for birds is summarized in Worksheets G02b of the EXCEL workbooks for liquid formulations (Attachment 1) and granular formulations (Attachments 2-4). As with mammals and for the same reasons (Section 4.4.2.1), the HQs are much greater for liquid applications than for granular applications.

4.4.2.2.1. Liquid Applications (non-accidental scenarios)

For acute exposures following liquid applications (Attachment 1, Worksheet G02b), the central estimates of the HQs for a small (10 g) bird exceed the level of concern (HQ=1) only modestly for the consumption of short grass (HQ=1.2). At the upper bounds of exposure, the acute HQs exceed the level of concern for a small bird for the consumption of broadleaf vegetation (HQ=3), tall grasses (HQ=3), and short grass (HQ=6).

Unlike the case for mammals in which the acute and chronic HQs are based on the same toxicity value (10 mg a.i./kg bw as discussed in Section 4.3.2.1), the HQs for chronic exposure scenarios involving birds are based on a much lower toxicity value (7 mg a.i./kg bw/day) than the toxicity value used for acute exposures (180 mg a.i./kg bw) (Section 4.3.2.2). Consequently, the chronic HQs for birds are much higher than the corresponding acute HQs. For the consumption of short grass, the HQs for a small bird exceed the level of concern across the range of exposures—i.e., HQs = 14 (1.4 to 62). The HQs for a small bird also exceed the level of concern (HQ=1) at the central and upper bounds for the consumption of fruit [HQs = 1.3 (0.2 to 5)], broadleaf foliage [HQs = 7 (0.7 to 35)], and tall grass [HQs = 5 (0.5 to 28)]. Some HQs also exceed the level of concern for a large (4 kg) bird—i.e., the HQs for the consumption of broadleaf vegetation (upper bound HQ of 4), tall grass (upper bound HQ of 3), and short grass [HQs = 1.5 (0.2 to 7)].

Also, as with mammals, this risk characterization for birds is qualitatively similar to that in the most recent EPA risk assessment which notes acute risks to small birds and chronic risks to small and larger birds (U.S. EPA/OPP/EFED 2014a, Table 1, p. 3).

Reservations with the risk characterization for birds parallel the factors noted for mammals (Section 4.4.2.1.1). These factors include the assumption that 100% of the diet is contaminated and uncertainties in the applicability of toxicity data on zebra finch (the most sensitive species and the species used for the dose-response assessment) to other species or groups of birds (Section 4.3.2.2).

As discussed in Section 4.1.2.2 and summarized in Appendix 2 (Table A2-4), the available field studies suggest that tebuthiuron may impact bird habitat but these studies cannot be used to infer the likelihood of direct toxic effects on birds.

4.4.2.2.2. Granular Applications (non-accidental scenarios)

As with mammals (Section 4.4.2.1), HQs for birds associated with granular applications of tebuthiuron are much lower than HQs associated with liquid applications. No acute HQs exceed the level of concern (HQ=1). The highest acute HQ is 0.2, the upper bound HQ for a small (10 g) bird consuming contaminated short grass. Some chronic HQs exceed the level of concern only at the upper bounds of exposures—i.e., upper bound HQs for a small birds following the consumption of broadleaf foliage (HQ=1.4), tall grass (HQ=1.1), and short grass (HQ=2). As summarized in Table 18, the chronic NOAEL for birds (7 mg a.i./kg bw/day) is much lower than the acute NOAEL (180 mg a.i./kg bw/day) and this relationship is the primary factor in the higher HQs for chronic relative to acute exposures.

A meaningful comparison of the risk characterization for birds in the current risk assessment to the most recent ecological risk assessment from EPA cannot be made. The EPA did not derive RQs (risk quotients) for birds following granular applications of tebuthiuron (U.S. EPA/OPP/EFED 2014a, Table 2, p. 4). Instead, the EPA noted potential risks to birds that would directly consume granules as a sole food source (U.S. EPA/OPP/EFED 2014a, p. 27).

4.4.2.2.3. Accidental Exposures

All of the accidental exposure scenarios for birds used in Forest Service risk assessments involve contaminated water associated with an accidental spill. None of these exposure scenarios lead to HQs that exceed the level of concern (HQ=1). The highest HQ is 0.1, the upper bound HQ for a piscivorous bird consuming contaminated fish (Attachments 2-4, Worksheet G02b).

4.4.2.3. Reptiles and Amphibians (Terrestrial Phase)

No explicit or quantitative risk characterization is developed for reptiles or terrestrial-phase amphibians because the available toxicity data do not support a dose-response assessment (Section 4.3.2.3). As discussed in Section 4.1.2.3, the U.S. EPA/OPP/EFED typically uses data on birds as a surrogate for reptiles and terrestrial phase amphibians. Given the limited data available on birds, uncertainties in species-to-species and particularly class-to-class extrapolation, as well as other concerns relating to absorption, as discussed in Section 4.1.2.3, obvious reservations are apparent in relying on the risk characterization for birds as a reasonable surrogate for a risk characterization in terrestrial phase reptiles and amphibians.

4.4.2.4. Terrestrial Invertebrates

As discussed in Section 4.1.2.4, little information is available on the toxicity of tebuthiuron to terrestrial invertebrates—i.e., a single contact NOAEC of about 860 mg a.i./kg bw. Based on this toxicity value, the direct spray of a honeybee with tebuthiuron leads to an HQ of 0.05—i.e., below the level of concern by a factor of 20 (Worksheet G09 in the attachments to this risk assessment).

As also discussed in Section 4.1.2.4, the apparently low risks to terrestrial invertebrates are supported by field studies, particularly the study by Doerr (1980) which notes a significant increase in the total number of insects on fields treated at 0.2 kg a.i./ha and no significant effect on terrestrial insects at concentrations of up to 1.0 kg a.i./ha (≈0.892 lb a.i./acre). In addition, the field study by Zavaleta (2012, p. 109) notes significant increases in the abundance and diversity of insects on plots treated with tebuthiuron at a rate of 0.6 lb a.i./acre—i.e., the application rate used in this Forest Service risk assessment.

Although the information on the effects of tebuthiuron on insects is modest, the available information does not suggest that tebuthiuron applications are likely to be hazardous to terrestrial insects. This risk characterization is essentially identical to that given in the most recent EPA ecological risk assessment for both liquid and granular applications—i.e., *low likelihood of risk* (U.S. EPA/OPP/EFED 2014a, Table 1, p. 3 and Table 2, p. 4).

4.4.2.5. Terrestrial Plants

4.4.2.5.1. Direct Spray and Spray Drift

The HQs for sensitive and tolerant species of terrestrial plants are summarized in Worksheet G05a (fine droplet sizes) and Worksheet G05b (course droplet sizes) of Attachment 1 (i.e., the EXCEL workbook for liquid applications). The worksheets are customized to reflect four sets of values for drift: aerial application, ground high-boom broadcast application, ground low-boom broadcast application, and backpack application. As detailed in Section 4.2.4.2, all estimates of drift are based on AgDRIFT (Teske et al. 2002). As detailed in Section 4.3.2.5 and summarized in Table 18, all HQs are based on NOAECs from studies on vegetative vigor (foliar applications)—i.e., an NOAEC of 0.018 lb a.i./acre for a sensitive species of dicot (sugar beet) and a NOAEL of 2 lb a.i./acre for a tolerant species of monocot (corn). As illustrated in Figure 3 (bottom graph), there is substantial overlap in the sensitivity of dicots and monocots in assays of vegetative vigor. Thus, sensitive species of monocots could be impacted in a manner similar to sensitive species of dicots. As also illustrated in Figure 3, however, the variability in sensitivities of dicots seems somewhat less than that of monocots. Based on this pattern, the HQs for tolerant species would probably apply primarily to tolerant species of monocots rather than tolerant species of dicots.

If sensitive species of dicots or monocots are directly sprayed with tebuthiuron at the application rate of 0.6 lb a.i./acre, the impact will be severe (HQ=10), and damage to the vegetation will be apparent. Following a direct spray, the HQ for tolerant species (i.e., most likely monocots) is 0.3 (below the level of concern by a factor of about 3), and tolerant species of monocots are not likely to show signs of damage. This risk characterization is relatively unambiguous and supported by numerous field studies (Appendix 3, Table A3-4).

Based on estimates of drift using AgDRIFT, risks to sensitive species remain above the level of concern downwind from the application site for distances of up to about 100 feet for fine droplets and about 50 feet (course droplets) downwind following aerial application. For other application methods, HQs are at or below the level of concern at distances of 25 feet downwind of the application site.

To put it simply, directed or broadcast ground spray applications are not likely to damage nontarget vegetation at distances of 25 feet or more from the application site, based on the Tier 1 estimates of drift used in the current risk assessment. Aerial applications of tebuthiuron could impact sensitive species of vegetation at distances of close to 100 feet downwind using fine droplets or about 50 feet using course droplets. As detailed in the documentation for WorksheetMaker (SERA 2011a, Section 3.2.2), many application-specific factors may impact drift, and these factors can be reflected in elaborated AgDrift modeling.

Note that estimates of tebuthiuron drift are not included in the EXCEL workbooks for granular applications (Attachments 2-4). As noted in Section 4.2.4.2, AgDrift does not explicitly incorporate options for the application of granular products (Teske et al. 2002); furthermore, the available information does not include field data involving tebuthiuron drift associated with the application of granular formulations.

4.4.2.5.2. Soil Exposures by Runoff

Risks to nontarget vegetation associated with runoff and sediment losses to a field adjacent to the treated site are estimated in Worksheet G04 of the attachments to this risk assessment. For soil exposures, the toxicity values are based on seedling emergence assays. As summarized in Table 18 and discussed in Section 4.3.2.5, HQs are calculated using an EC_{25} of 0.018 lb a.i./acre for a sensitive species of dicot (carrot) and an NOAEC of 2 lb a.i./acre for a tolerant species of dicot (corn). As illustrated in Figure 3 (upper graph), dicots are only modestly more sensitive than monocots, except for the very low toxicity value in carrots. Thus, for sensitive species, the risk characterization clearly applies to sensitive species of dicots, but may be less relevant to sensitive species of monocots. The exposure estimates are based on runoff and sediment losses from GLEAMS-Driver, as discussed in Section 4.2.4.3.

For tolerant species of plants, including tolerant species of both monocots and dicots, the upper bound HQs are below the level of concern—i.e., an HQ of 0.06—by about a factor of 17 [1÷0.06 ≈ 16.666…]. For tolerant species of terrestrial plants, the risk characterization is unequivocal. No adverse effects are anticipated.

For sensitive species of plants (i.e., primarily sensitive dicots), the HQs are 1.7 (0.3 to 7). These relatively modest HQs reflect both the relatively low application rate proposed by the Forest Service—i.e., 0.6 lb a.i./acre, compared with the maximum labelled rate of 6 lb a.i./acre—as well as the limited runoff potential for tebuthiuron.

As with most exposure scenarios, the HQs are linearly related to application rate. If higher application rates are used, risks to sensitive species of terrestrial plants would increase. Given the very low HQs for tolerant species, however, risks would not be apparent even at the maximum application rate of 6 lb a.i./acre.

4.4.2.5.3. Contaminated Irrigation Water

The HQs for nontarget plants associated with using tebuthiuron contaminated surface water for irrigation are summarized in Worksheet G06a of the attachments to this risk assessment. As with runoff, the HQs for tolerant species are substantially below the level of concern—i.e., HQs = 0.01 (0.0002 to 0.1). For sensitive species, the HQs exceed the level of concern only at the upper bounds of exposure—i.e., HQs = 0.4 (0.006 to 4).

The key variables in this exposure scenario are the expected concentrations in ambient water (Section 3.2.3.4.6.1) and the amount of irrigation water applied, which is assumed to be 1 inch as a central estimate with a range of 0.25 inch to 2 inches. Taking into account reasonable variations that might be made in the exposure scenario, there is little basis for asserting that tolerant species of plants will be at risk even from higher rates of irrigation. Risks to sensitive species of plants, however, could be substantial at the upper bounds of exposures.

Also, as with the estimates of risks from runoff (Section 4.4.2.5.2), the exposure components of the HQs are based on the Gleams-Driver simulations. Consequently, the upper bound risks will be most commonly associated with site conditions, including high rates of rainfall and soils conducive to runoff and/or percolation losses. As with the assessment of risks due to runoff, Table 1 of Appendix 7 (liquid applications) and Appendix 8 (granular applications) could be consulted in any consideration of the consequences of potential risks to sensitive species of nontarget vegetation in regional-specific applications. The use of GLEAMS-Driver for site-specific applications could be justified.

4.4.2.5.4. Wind Erosion

Risks to nontarget vegetation associated with wind erosion of contaminated soils are summarized in Worksheet G06b of the attachments to this risk assessment. Based on the assumptions typically used in Forest Service risk assessments (Section 4.2.4.5), risks associated with this exposure scenario are far below the level of concern for both tolerant species [HQs = 0.00002 (0.000004 to 0.00004)] and sensitive species [HQs = 0.0007 (0.0001 to 0.001)]. Note that at the upper bound of the HQs, the risks to sensitive species are below the level of concern by a factor of 1000.

As detailed in Section 4.2.4.5, substantial uncertainties are associated with this exposure scenario, and the expected loss rates for soil are intended to represent forestry applications. Much higher loss rates could occur if tebuthiuron were to be applied inadvertently to fallow soil. In this respect and as discussed in Section 4.2.4.5, the cautionary commentaries on the product labels for tebuthiuron are worth noting and repeating:

> *Do not apply to areas where soil movement by water erosion and/or natural or mechanical means is likely. Avoid treatment or areas susceptible to wind erosion such as single grain sands or disturbed soils that are loose and powdery dry. Under these conditions, treatment should be delayed until the soil surface has been stabilized by rainfall or irrigation. Before treatment of sandy soils in areas subject to wind erosion, the soil surface should first be stabilized with gravel mulch or other means of preventing physical movement of surface soil.*
>
> Specimen Label for Alligare Tebuthiuron 80 WG

While it does not seem likely that the Forest Service would apply tebuthiuron to areas with a high potential for the wind erosion of soil, the cautionary language on the product labels for tebuthiuron should be considered in any site-specific application of this herbicide.

4.4.2.6. Terrestrial Microorganisms

As also noted in Section 4.1.2.6, little information is available on the toxicity of tebuthiuron to terrestrial microorganisms, but this information suggests little basis for concern. Goodroad (1987) observed inhibition of soil nitrification and nitrogen mineralization at tebuthiuron concentrations of 100 and 1000 mg a.i./kg soil but not at a concentration of 1 mg a.i./kg soil. As summarized in Appendices 7 and 8, the maximum concentrations of tebuthiuron in the top 12 inches of soil are estimated at less than 0.5 mg a.i./kg soil at an application rate of 1 lb a.i./acre. Adjusting for the application rate of 0.6 lb a.i./acre proposed by the Forest Service, the maximum concentration in the top 12 inches of soil would be less than 0.3 mg a.i./kg soil. Consistent with this assessment that risks to soil microorganisms appear to be low, the field study by Wachocki et al. (2001) reports no adverse effects on soil microorganisms at application rates of up to 0.7 lb a.i./acre.

As with virtually every group of organisms covered in the current risk assessment, the relatively benign qualitative risk characterization for tebuthiuron must be tempered by limitations in the available data in terms of endpoints assayed and species tested, relative to the large number of species of terrestrial microorganisms that could be exposed to tebuthiuron.

4.4.3. Aquatic Organisms

The risk characterization for aquatic organisms is summarized in Worksheet G03 of the attachments that accompany this risk assessment. As would be expected for a herbicide, aquatic plants are the aquatic organisms at highest risk and effects on aquatic plants may lead to indirect effects on fish and invertebrates due to food reduction, habitat modification, and the potential for oxygen depletion in the event of an accidental spill.

4.4.3.1. Fish

The risk characterization for fish is relatively simple. None of the HQs for anticipated levels of exposure approaches the level of concern (HQ=1) for acute exposures (maximum HQ of 0.06) or longer-term exposures (maximum HQ of 0.04). This risk characterization for fish is qualitatively identical to that given in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a, Table 4.1, p. 48).

For accidental exposures, the upper bounds of the HQ modestly exceed the level of concern for liquid applications (HQ=1.1) and exceed the level of concern at the central estimate and upper bound of HQs for granular applications [HQs = 2 (0.8-4)]. For the accidental spill scenario involving liquid applications, the upper bound HQ of 1.1 is associated with a peak concentration in water of about 10.6 mg a.i./L. This value is only slightly above the NOAEC of 9.3 mg a.i./L for sensitive species of fish (Table 18) and is below the lowest definitive LC_{50} for fish (106 mg a.i./L from MRID 00020661) by a factor of 10 [106 mg a.i./L ÷ 10.6 mg a.i./L]. Thus, there is no basis for asserting that fish are likely to be adversely affected. For the accidental spill scenario involving granular applications, the upper bound HQ of 4 is associated with a concentration of about 36.3 mg a.i./L. This concentration is above the NOAEC for fish by about a factor of 4 [36.3 mg a.i./L ÷ 9.3 mg a.i./L ≈ 3.90] but is below the lowest LC_{50} by a factor of about 3 [106 mg a.i./L ÷ 36.3 mg a.i./L ≈ 2.92]. Thus, there may be a modest potential for adverse effects in fish following spills involving granular applications.

As discussed in Section 4.3.3.1 (dose-response assessment for fish), a minor reservation with the risk characterization for fish involves the mesocosm study by Temple et al. (1991) in which reductions in fish biomass were noted at a tebuthiuron concentration in water of about 0.79 to 1 mg a.i./L over a 108-day exposure period. This decrease in fish biomass was accompanied by a decrease in invertebrate biomass (Section 4.1.3.3) and primary productivity by algae (Section 4.3.3.4.1). While the study design used by Temple et al. (1991) cannot be used to rule out a direct effect on fish as opposed to an indirect effect on food supply (i.e., a separate group of fish given supplemental feeding was not used in the study), the study authors conclude that the decrease in fish biomass was not associated with direct toxic effect of tebuthiuron to fish. Nonetheless, the mesocosm study by Temple et al. (1991) does illustrate the potential for cumulative impacts on fish due to a reduction in primary productivity in algae (a direct effect) and the consequent reduction in invertebrate food supply for fish (an indirect effect).

4.4.3.2. Amphibians (Aquatic Phase)

As discussed in Section 4.3.3.2, no dose-response assessment can be developed for aquatic phase amphibians. The EPA uses data on fish as a surrogate for aquatic phase amphibians and concludes that risks to this group of organisms are not likely (U.S. EPA/OPP/EFED 2014a, Table 1.1, p. 10).

4.4.3.4. Aquatic Invertebrates

As summarized in Table 18, the toxicity values used for aquatic invertebrates are only modestly lower (about a factor of 2) than those used for the risk characterization for fish. Consequently, the risk characterization for aquatic invertebrates is essentially identical to the risk characterization for fish. As with fish, none of the HQs for anticipated levels of exposure approaches the level of concern (HQ=1) for acute exposures (maximum HQ of 0.1) or longer-term exposures (maximum HQ of 0.08). This risk characterization for aquatic invertebrates is qualitatively identical to that given in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2014a, Table 4.2, p. 49).

For accidental exposures, the upper bounds of the HQ modestly exceed the level of concern for liquid applications (HQ=2) and exceed the level of concern across the range of HQs for granular applications [HQs = 4 (1.6-8)]. As with fish, the HQs for accidental exposures are of minimal concern in liquid applications; nevertheless, adverse effects in some species of aquatic invertebrates could not be ruled-out in granular applications.

Lastly, and also similar to the risk characterization for fish, there is the potential for indirect effects on aquatic invertebrates. As discussed in the following section, tebuthiuron applications could have adverse effects on algae. As illustrated in the mesocosm study by Temple et al. (1991), substantial decreases in algal populations could lead to a reduced food supply for aquatic invertebrates and a consequent decline in the population of aquatic invertebrates. Based on the longer-term HQs for algae (Section 4.4.3.4.1), these adverse indirect effects on aquatic invertebrates could persist for a prolonged period. The HQs for algae are sufficiently high that considerations of lower but still effective application rates would not substantially impact the risk characterization of this potential indirect effect. As discussed in Section 3.2.3.4.3, a large number of site specific factors will impact the concentrations of tebuthiuron over time. In any specific application of tebuthiuron in which effects on aquatic invertebrates would be major concern, site-specific modeling should be considered.

4.4.3.4. Aquatic Plants

4.4.3.4.1. Algae

Although there is no basis for asserting that direct effects of tebuthiuron on fish or aquatic invertebrates are likely, direct effects on both sensitive and tolerant species of algae are plausible and in some cases reasonably certain.

For acute exposures, the HQs are 9 (0.5 to 46) for sensitive algal species and 2 (0.1 to 11) for tolerant species. For longer-term exposures, the HQs are 4 (0.3 to 30) for sensitive species and 1 (0.07 to 7) for tolerant species. Given the magnitude of these exceedances, the NOAECs are less relevant than the EC_{50} values in terms of characterizing the likelihood of adverse effects. As discussed in SERA (2009), the ratios of the exposures to EC_{50} values discussed below are essentially equivalent to the use of RQs (risk quotients) by EPA.

As discussed in Section 4.3.3.4.1, the EC_{50} values encompass a relatively narrow range—i.e., 0.05 mg a.i./L for sensitive species and 0.09 for tolerant species. As summarized in Worksheet G03 of the attachments to this risk assessment, the estimated peak concentrations in water are 0.114 (0.0066 to 0.6) mg a.i./L. Thus, at the upper bound of exposures, concentrations in water exceed the EC_{50} by a factor of 12 for sensitive species [0.6 mg a.i./L ÷ 0.05 mg a.i./L] and a factor of nearly 7 for tolerant species [0.6 mg a.i./L ÷ 0.09 mg a.i./L ≈ 6.667]. At the central estimate of exposure, concentrations in water exceed the EC_{50} by a factor of about 2 for sensitive species [0.114 mg a.i./L ÷ 0.05 mg a.i./L ≈ 2.28] and a factor of about 1.3 for tolerant species [0.114 mg a.i./L ÷ 0.09 mg a.i./L ≈ 1.267]. At the lower bounds of exposure, however, the EC_{50} values are not exceeded and the ratios of exposure to the EC_{50}s are about 0.1. Qualitatively, these values clearly indicate that adverse effects would be readily observable in algae at the central estimates and upper bounds of exposure but might not be observed at the lower bounds of exposures.

The risk characterization in the most recent EPA risk assessment is reasonably consistent with the above risk characterization for algae in which an RQ of 18 is derived for an application rate of 4 lb a.i./acre (U.S. EPA/OPP/EFED 2014a, Table 3, p. 6,). Adjusted for an application rate of 0.6 lb a.i./acre, this RQs corresponds to 2.7 [(18 ÷ 4) x 0.6]. This RQ is similar to the central estimate of the equivalent value (i.e., exposure ÷ EC_{50}) derived for sensitive species of algae in the current risk assessment—i.e., 2.28 [0.114 mg a.i./L ÷ 0.05 mg a.i./L].

As also summarized in Worksheet G03 of the attachments to this risk assessment, the estimated longer-term concentrations in water are estimated at about 0.0546 (0.00384 to 0.384) mg a.i./L. At the upper bounds of the estimated exposures, the EC_{50} is exceeded by a factor of about 7 [0.384 mg a.i./L ÷ 0.05 mg a.i./L ≈ 6.667] for sensitive species and about 4 for tolerant species [0.384 mg a.i./L ÷ 0.09 mg a.i./L ≈ 4.267]. Over prolonged periods of tebuthiuron applications at a rate of 0.6 lb a.i./acre, adverse effects could be apparent at the upper bounds of exposure.

For accidental exposures, the HQs are 105 (5 to 815) for sensitive species and 24 (1.2 to 189) for tolerant species. These HQs require little explanation or interpretation. In the event of a substantial accidental spill, adverse effects on sensitive and tolerant species of algae are virtually certain.

In practical terms, the most important factor in refining the risk characterization for algae involves site-specific conditions. As discussed in detail in Section 3.2.3.4 and summarized in Table 11, the estimated concentration in water will vary substantially with site-specific factors, especially soil type and rainfall. As detailed in SERA (2011b), the utility for developing EXCEL workbooks such as those used as attachments to the current risk assessment is designed to allow for site-specific modeling to be incorporated into a regional or site-specific assessment. For tebuthiuron, this effort would be clearly justified. At sites or in regions where water contamination might be minimal due to weather, the location of surface water with respect to the application site, or other factors, risks to algae could be minimal. In the absence of a site-specific assessment, however, the current generic (i.e., non-site-specific) risk assessment justifies extreme caution when applying tebuthiuron near surface water. This cautionary language is consistent with language on product labels for the representative formulations of tebuthiuron considered explicitly in the current risk assessment (Table 2). For example, the Specimen Label for Tebuthiuron 20 P contains the following language: *Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.* In terms of potential effects on algae, this language is clearly justified.

4.4.3.4.2. Macrophytes

As discussed in Section 4.3.3.4.2, toxicity data on aquatic macrophytes are limited to a single bioassay on duckweed, specifically *Lemna gibba*, a monocot. The NOAEC for this species is 0.05 mg a.i./L, similar to the NOAEC of 0.056 mg a.i./L for tolerant species of algae (Section 4.4.3.4.1). Given the similarities in these NOAELs, the risk characterization for tolerant species of aquatic macrophytes is virtually identical to that for tolerant species of the algae. Based on acute HQs of 2 (0.1 to 12) and longer-term HQs of 1.1 (0.08-4), adverse effects on tolerant species of aquatic macrophytes could be evident at the central and upper bounds of acute exposures and at the upper bounds of longer-term exposures. As with the risk characterization for algae, the levels of exposure will depend on site-specific considerations. Consequently, refinements in the exposure assessment for aquatic macrophytes would be justified in applications of tebuthiuron that are near surface water.

In the absence of additional toxicity data, it seems reasonable to assume that some species of aquatic macrophytes may be more sensitive than duckweed to tebuthiuron and that sensitive species of aquatic macrophytes would be more severely impacted than duckweed. Again, however, whether or not adverse effects would be observed will depend on site-specific considerations.

5. REFERENCES

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

FOIA	**Documents associated with FOIA requests.**
FS	**Input from the Forest Service.**
PrRev	**References added during peer review.**
SET00	**Papers from preliminary scoping.**
SET01	**Initial TOXLINE search.**
SET02	**Initial supplemental search.**
SET03	**Supplemental papers on secondary effects in mammals.**
SET04	**Supplemental papers on terrestrial and aquatic plants.**
SET05	**Methods papers for algal bioassays.**
Std	**Standard references used in most Forest Service risk assessments.**

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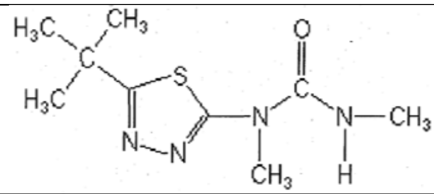
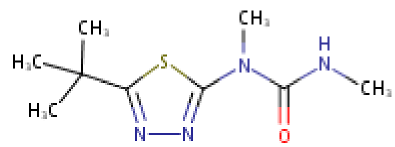
Table 1: Chemical and Physical Properties

Item	Value	Reference[1]
	Identifiers	
Common name:	Tebuthiuron	
CAS Name	N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N,N'-dimethylurea	ChemIDplus 2015; Tomlin 2004; U.S. EPA/OPP/HED 2014a
CAS No.	34014-18-1	Tomlin 2004
Chemical Group	Herbicide Urea carbamate	U.S. EPA/OPP/HED 2014a
Development Codes	EL-103 (Lilly)	Tomlin 2004
EC (European Community) No.	251-793-7	Tomlin 2004
IUPAC Name	1-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1,3-dimethylurea	Tomlin 2004
Molecular formula	$C_9H_{16}N_4OS$	Tomlin 2004
Mechanistic group		
EPA PC Code	105501	U.S. EPA/OPP/HED 2014a
Smiles Code without stereochemistry	`CNC(=O)N(C)c1nnc(s1)C(C)(C)C`	Tomlin 2004
Structure		U.S. EPA/OPP/EFED 2014a
		ChemIDplus 2015
Resistance Classification	WSSA 7, HRAC C_2	Retzinger and Mallory-Smith 1997; Tomlin 2004
	Chemical Properties(1)	
a.i. to a.e. conversion	N/A	
Henry's Law Constant	$3.0x10^{-5}$ Pa m^3 mol^{-1}	Tomlin 2004
Hydrolysis	No degradation at 10 and 100 ppm over 64 days at pH 3,6, and 9.	U.S. EPA/OPP/EFED 2014a, MRID 00020779
	DT_{50}: >64 days at pH 3, 6, and 9	Tomlin 2004
K_{ow}	≈66.1 [logP=1.82 @ 20°C]	Tomlin 2004
	≈61.7 [log P = 1.79]	ChemIDplus 2015
	≈63.1 [logP=1.8 @ 25°C and pH 7] *This value is used in the current risk assessment.	U.S. EPA/OPP/HED 2014a
Molecular weight (g/mole)	228.3 *This value is used in the current risk assessment.	Tomlin 2004; U.S. EPA/OPP/HED 2014a
	228.318	ChemIDplus. 2015
Melting point	162.85 °C	Tomlin 2004
	161 ºC at 760 mm Hg	U.S. EPA/OPP/HED 2014a
pK_a	1.2	Weber 1980
Vapor pressure	0.04 mPa at 25 °C	Tomlin 2004
	2x10-6 mm Hg at 25°C [≈0.2666 mPa]	U.S. EPA/OPP/HED 2014a
Water solubility	2,570 mg/l at 20 °C	Tomlin 2004
	2,500 mg/L *This value is used in the current risk assessment.	U.S. EPA/OPP/EFED 2014a; U.S. EPA/OPP/HED 2014a; Knisel and Davis 2000

<table>
<tr><th>Item</th><th>Value</th><th>Reference[1]</th></tr>
<tr><td></td><td>Environmental Properties</td><td></td></tr>
<tr><td>Aqueous photolysis</td><td>Stable</td><td>U.S. EPA/OPP/EFED 2014a, MRID 41305101</td></tr>
<tr><td>Aqueous photolysis</td><td>No degradation at pH 5 over 33 days.</td><td>U.S. EPA/OPP/EFED 2014a, MRID 41328001</td></tr>
<tr><td>Aqueous aerobic metabolic half-life</td><td>683 days</td><td>U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 41372501</td></tr>
<tr><td></td><td>PRZM/EXAMS input: 2050 days
3x estimated based on a single aerobic aquatic half-life for total residues</td><td>U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 41372501</td></tr>
<tr><td></td><td>95.2% parent compound after 4 weeks.</td><td>U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 41372501</td></tr>
<tr><td>Aqueous Anaerobic metabolism (benthic)</td><td>Stable
After 365 days, 93.7% of parent remained.</td><td>U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 41913101</td></tr>
<tr><td>Bioconcentration in fish (BCF)</td><td>Bluegill, 5 ppm
Edible tissue: 1.98
Whole fish: 2.63</td><td>U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 40819501</td></tr>
<tr><td>Field dissipation</td><td>Deepest soil penetration: 60-72 inches
Half-lives of 81 days (Florida), 495 days (California), and 385 days (Nebraska).</td><td>U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 43318101</td></tr>
<tr><td></td><td>Half-life of about 433 day (k=0.0016) in Arizona rangeland.</td><td>Emmerich et al. 1984</td></tr>
<tr><td></td><td>Half-life of about 10 months.</td><td>Helbert 1990</td></tr>
<tr><td>Foliar washoff fraction</td><td>0.9</td><td>Knisel and Davis 2000</td></tr>
<tr><td>Foliar half-life</td><td>30 days</td><td>Knisel and Davis 2000</td></tr>
<tr><td>K_{ads} and K_{oc}</td><td><table>
<tr><th>Soil</th><th>K_{ads}</th><th>K_{oc}</th></tr>
<tr><td>Sand</td><td>0.11</td><td>38</td></tr>
<tr><td>Sandy loam</td><td>0.62</td><td>716</td></tr>
<tr><td>Loam</td><td>0.82</td><td>75</td></tr>
<tr><td>Loam</td><td>1.82</td><td>152</td></tr>
</table>Appears to have typo with Koc value of 716 for sandy loam.</td><td>U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 40768401</td></tr>
<tr><td>K_{ads}</td><td>0.11, 0.62, 0.82, and 1.82 mL/g.
Average = 0.84 mL/g.</td><td>U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 40768401</td></tr>
<tr><td>K_{oc}</td><td>PRZM/EXAMS Input: 85.2 (mg/L?)
Note: Unit given by EPA is a typo. Correct unit is mL/g or L/kg.</td><td>U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 40768401</td></tr>
<tr><td></td><td>39 (12.2 to 84.1) [five different soils at various depths, see Table 2 of paper]</td><td>Koskinen et al 1996</td></tr>
<tr><td></td><td><table>
<tr><th>Soil</th><th>K_{ads}</th><th>K_{oc}</th></tr>
<tr><td>Clay</td><td>0.7102</td><td>54.63</td></tr>
<tr><td>Clay- with sugar cane vinasse</td><td>0.6407</td><td>45.76</td></tr>
<tr><td>Sand</td><td>0.5513</td><td>45.94</td></tr>
<tr><td>Sand-with sugar cane vinasse</td><td>0.6683</td><td>51.41</td></tr>
</table></td><td>Lourencetti et al. 2012</td></tr>
<tr><td></td><td>80 (mL/g)</td><td>Knisel and Davis 2000</td></tr>
<tr><td>Sediment half-life</td><td>Not available</td><td></td></tr>
<tr><td>Soil half-life (NOS)</td><td>360 days</td><td>Knisel and Davis 2000</td></tr>
</table>

Item	Value	Reference[1]
Soil metabolic half-life, aerobic	PRZM/EXAMS Input: 270.6 days 3x single soil metabolism for total residues. Note and discuss discrepancy with summaries below. This appears to be a typo. Use longer half-life below for modelling.	U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 41328001
	1062 days *Used in current risk assessment.	U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 41328001
	35.4 months [≈1062 days]	U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 41328001
Soil metabolic half-life, anaerobic	Little (4.7%) degradation over 60 day period.	U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 41328002
Soil, dissipation half-life	20 days (following application rate of 1.0 kg a.i./ha)	Cerdeira et al. 2007
	55 to 128 days (sugarcane)	Lourencetti et al. 2012
Soil photodegradation	Half-life: 39.7 days.	U.S. EPA/OPP/EFED 2014a, MRID 41050201
Ground water monitoring	15 feet (180 inches) leaching to water table. Persistent above limit of detection for 4 years.	U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 42390901

[1] There a many sources of information on some standard values – e.g., molecular weight. In general, only two sources as cited for each value. More than two sources are cited only to highlight apparent discrepancies.

See Section 2.2.2 for discussion.

Table 2: Representative Formulations of Tebuthiuron

Source: www.Greeenbook.net unless otherwise specified.

Formulation, Form Supplier, EPA Registration Number EPA Label Information	Composition/ Characteristics[1]	Application Information, Methods and Rates
Tebuthiuron 80 WG, water dispersible granules, Alligare, 81927-37 Active - Conditionally Registered (April 21, 2009). Most recent EPA label: May 2, 2011	80% w/w a.i., 20% inerts. No inerts specified on MSDS.	Maximum Application Rates Sandy soils or shallow water table: 2 lb a.i./acre once every 3 years. Other sites: 4 lb a.i./acre once every 3 years. Total Vegetation Control: 4 lb a.i./acre once per year, no more than 6 lb a.i. per acre in any 3 year period. Spot applications up to 6 lb a.i./acre. Use Restrictions for Groundwater Protection Ground Broadcast or Banded Surface/Soil Applications. Spray Volume: ≥ 5 gallons/acre Maximum Application Rate: 1 lb a.i./acre in areas with <20 inches of precipitation/year. 2 lb a.i./acre in areas with >20 inches of precipitation/year. Aerial Applications (soil surface). Fixed wing or helicopter for most sites. Helicopter only for rights-of way. Instructions similar to applications with special note to use large droplets (NOS). Do not apply in areas with shallow (<5 feet) water table [3]. Not for sale, distribution, or use in Nassau and Suffolk Counties in New York State. Not registered in Florida.
Spike 80DF, dry flowable Dow AgroSciences, 62719-107 Active: Registered (June 4, 1989). Most recent EPA label July 22, 2013. Transferred from Dow Elanco on December 4, 1989.	80% w/w a.i., 20% inerts. Inerts specified on MSDS Silica gel Kaolin (Clay) Titanium dioxide	Rates, mixing, and limitations identical to Tebuthiuron 80 WG. Not for sale, distribution, or use in Nassau and Suffolk Counties in New York State. Not registered in the state of Florida.
Tebuthiuron 20 P, pellets, Alligare, 81927-41. Active. Most recent EPA label dated Nov. 3, 2009.	20% w/w a.i., 80% inerts. No inerts specified on MSDS.	Rates and limitations identical to Tebuthiuron 80 WG. Pellet formulation. No mixing with water prior to application. Not for sale, distribution, or use in Nassau and Suffolk counties in New York State. In Broward, Collier, Dad, Hendry, Lee, Monroe, and Palm Beach Counties of Florida, Alligare Tebuthiuron 20 P may be applied only in accordance with supplemental labeling.
Spike 20P, pellets Dow AgroSciences, 62719-121 Active: Reregistered (June 30, 1997). Most recent EPA label: Dec. 14, 2006. Transferred from Dow Elanco on December 4, 1989.	20% w/w a.i., 80% inerts [2]. Inerts specified on MSDS: Clay	Rates and limitations identical to Tebuthiuron 80 WG. Pellet formulation. No mixing with water prior to application. Not for safe, distribution, or use in Nassau and Suffolk Counties in New York State. Use Restrictions In the State of Florida in Broward, Collier, Dade, Hendry, Lee, Monroe, and Palm Beach Counties of Florida, Spike 20P may be applied only in accordance with supplemental labeling.

[1] The % inerts is taken from product label. See Table 3 for additional details on inerts from SDSs/MSDSs.
[2] SDS/MSDS taken from http://www.msdsonline.com/.
[3] Several similar restrictions to prevent ground water contamination. See product labels.

Table 3: Disclosed Inerts in Representative Formulations

Sources: Material Safety Data Sheets from www.greenbook.net unless otherwise specified.

Formulation (Supplier, % a.i./inerts) [1]	Inert[2]	CAS No.	% w/w from MSDS
Spike 20P [3] Dow AgroSciences 20% a.i./80% inerts	Clay	1332-58-7	20%
Spike 80DF Dow AgroSciences 80% a.i./20% inerts	Silica gel	112926-00-8	3%
	Kaolin (Clay)	1332-58-7	≥0.3 - ≤6.9%
	Titanium dioxide	13463-67-7	0.1%
	Not otherwise specified	N/A	≥10 - ≤16.6%
Alligare Tebuthiuron 80 WG, 20% inerts	No inerts disclosed on label or MSDS.	N/A	20%
Alligare Tebuthiuron 20 P	No inerts disclosed on label or MSDS.	N/A	80%

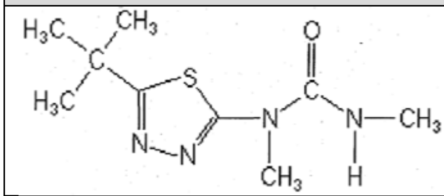
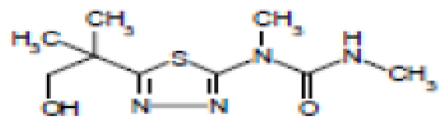
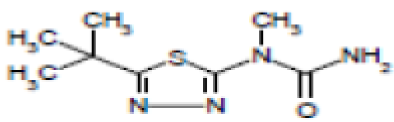
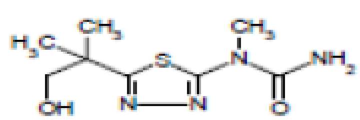
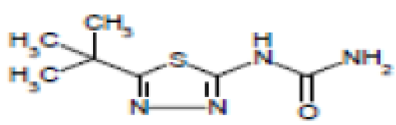
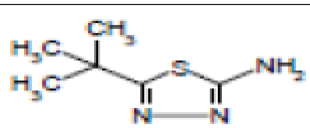
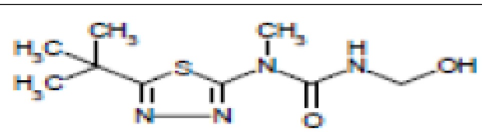
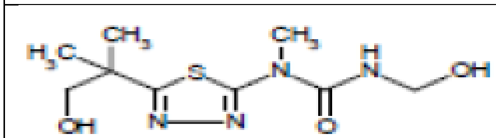
[1] See Table 2 for additional details on applications.

[2] Chemical names as indicated on MSDS with synonyms in parentheses. Material Safety Data Sheets from www.greenbook.net unless otherwise specified.

[3] SDS/MSDS taken from http://www.msdsonline.com/.

See Section 2.2 for initial discussion.

Table 4: Tebuthiuron and Metabolites of Concern

Structure	Chemical Name	Metabolite Code [1]
	Tebuthiuron N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-z-yl]-N,N-dimethylurea	N/A
	N-[5-(2-hydroxy-1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N,N’-dimethylurea	103 (OH)
	N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N-methylurea	104
	N-[5-(2-hydrozy-1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N-methylurea Major metabolite with 109-OH	104 (OH)
	N-[50(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl] urea	106
	2-dimethylethyl-5-amino-1,3,4-thiadiazole	108
	N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]N’-hydroxymethyl-N-methylurea	109
	N-[5-(2-hydroxy-1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]N’-hydroxymethyl-N-methylurea Major metabolite with 104-OH	109 (OH)

[1] Metabolite codes adopted from Rutherford et al. 1995.

Sources: U.S. EPA/OPP/EFED 2014a, Appendix B.
U.S. EPA/OPP/HED 2014a, Figure A, p. 48

Table 5: Directed Applications, Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	Triclopyr BEE	Section 3.2.1	2
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.0031	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.01	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.002	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.06	SERA 2014b, Table 14	7
Subject Chemical	Tebuthiuron		8
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.004	Section 3.1.3.2.1	9
$ka_P \div ka_{Ref}$	1.2903226		10
Occupational Exposure Rates for Reference Chemical			11
Central Estimate	0.0129032	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.0025806	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.0774194	SERA 2014b, Eq. 22	14

See Section 3.2.1. for discussion.

Documentation for Table: The above table implements the adjustment of worker exposure rates based dermal absorption rates. The table uses MS Word "fields" rather than macros.

- Determine the first-order dermal absorption rate coefficient for the chemical under review. See SERA 2014a, Section 3.1.3.2.2.
- Select the reference chemical. See SERA 2014b, Section 4.1.6.1.
- Fill in the information on the reference chemical in the upper section of the above table.
- Fill in the first-order dermal absorption rate coefficient for the chemical under review in the Value column of Row 9 in the above table.
- Update the estimated values for ration of the k_a values and the occupational exposure rates for the chemical under review – i.e., the green shaded cells in the above table. The simplest way to update these fields is to select each of the 4 green shaded cells (one at a time and in order), press the right mouse button, and select 'Update field'.

See Section 3.2.2.1 for discussion.

Table 6: Ground Broadcast Applications, Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.1	2
First-order dermal absorption rate coefficient for reference chemical ($hour^{-1}$) [ka_{Ref}]	0.00066	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.0001	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.00004	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.0002	SERA 2014b, Table 14	7
Subject Chemical	Tebuthiuron		8
First-order dermal absorption rate coefficient for subject chemical ($hour^{-1}$) [ka_P]	0.004	Section 3.1.3.2.1	9
$ka_P \div ka_{Ref}$	6.06060606		10
Occupational Exposure Rates for Reference Chemical			11
Central Estimate	0.00060606	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.00024242	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.00121212	SERA 2014b, Eq. 22	14

See Section 3.2.1. for discussion.

Documentation for Table: The above table implements the adjustment of worker exposure rates based dermal absorption rates. The table uses MS Word "fields" rather than macros.

- Determine the first-order dermal absorption rate coefficient for the chemical under review. See SERA 2014a, Section 3.1.3.2.2.
- Select the reference chemical. See SERA 2014b, Section 4.1.6.1.
- Fill in the information on the reference chemical in the upper section of the above table.
- Fill in the first-order dermal absorption rate coefficient for the chemical under review in the Value column of Row 9 in the above table.
- Update the estimated values for ration of the k_a values and the occupational exposure rates for the chemical under review – i.e., the green shaded cells in the above table. The simplest way to update these fields is to select each of the 4 green shaded cells (one at a time and in order), press the right mouse button, and select 'Update field'.

See Section 3.2.2.1 for discussion.

Table 7: Aerial Broadcast Applications, Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.1	2
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.00066	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.00002	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.000006	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	.00007	SERA 2014b, Table 14	7
Subject Chemical	Tebuthiuron		8
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.004	Section 3.1.3.2.1	9
$ka_P \div ka_{Ref}$	6.06060606		10
Occupational Exposure Rates for Reference Chemical			11
Central Estimate	0.00012121	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.00003636	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.00042424	SERA 2014b, Eq. 22	14

See Section 3.2.1. for discussion.

Documentation for Table: The above table implements the adjustment of worker exposure rates based dermal absorption rates. The table uses MS Word "fields" rather than macros.

- Determine the first-order dermal absorption rate coefficient for the chemical under review. See SERA 2014a, Section 3.1.3.2.2.
- Select the reference chemical. See SERA 2014b, Section 4.1.6.1.
- Fill in the information on the reference chemical in the upper section of the above table.
- Fill in the first-order dermal absorption rate coefficient for the chemical under review in the Value column of Row 9 in the above table.
- Update the estimated values for ration of the k_a values and the occupational exposure rates for the chemical under review – i.e., the green shaded cells in the above table. The simplest way to update these fields is to select each of the 4 green shaded cells (one at a time and in order), press the right mouse button, and select 'Update field'.

See Section 3.2.2.1 for discussion.

Table 8: Precipitation, Temperature and Classifications for Standard Test Sites

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

[1] Based on composite estimation in WEPP using a latitude of 47.94 N and a longitude of -124.54 W.

See Section 3.2.3.4.3 for discussion.

Table 9: Input Parameters for Fields and Waterbodies Used in Gleams-Driver Modeling

Field Characteristics	Description	Pond Characteristics	Description
Type of site and surface (FOREST)	Field (0)	Surface area	1 acre
Treated and total field areas	10 acres	Drainage area:	10 acres
Field width	660 feet	Initial Depth	2 meters
Slope	0.1 (loam and clay) 0.05 (sand)	Minimum Depth	1 meter
Depth of root zone	36 inches	Maximum Depth	3 meters
Cover factor	0.15	Relative Sediment Depth	0.01
Type of clay	Mixed		
Surface cover	No surface depressions		

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

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

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

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

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

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

See Section 3.2.3.4.3 for discussion.

Table 10: Chemical parameters used in Gleams-Driver modeling

Parameter	Values	Note/Reference
Half-lives (days)		
Aquatic Sediment	2050	Note 1
Foliar	30	Knisel and Davis 2000
Soil	1062	Note 2
Water	683 to 2050	Note 3
Soil $K_{o/c}$, mL/g	85.2 (12.2 to 152)	Note 4
Sediment K_d, mL/g	0.84 (0.11 to 1.82)	Note 5
Water Solubility, mg/L	2500	Note 6
Foliar wash-off fraction	0.9	Knisel and Davis 2000
Fraction applied to foliage	0.5	Standard assumption
Depth of Soil Incorporation	1 cm	Standard assumption
Irrigation after application	none	N/A
Initial Application Date	March 20	Note 7

Notes

Number	Text
1	Little degradation after 1 year (U.S. EPA/OPP/EFED 2014a, Appendix A, MRID 41372501). Use upper bound of rate for aqueous aerobic metabolism (see Note 3).
2	U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 41328001.
3	The lower bound is the estimate from the study. The upper bound is about 3x the central value and this was used by EPA in the PRZM/EXAMS modeling (U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 41372501). Note that the values correspond to half-lives of about 1.9 to 5.6 years.
4	The central estimate is the Koc used by EPA in PRZM/EXAMS modeling (U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 41372501). This is close to value of 80 mL/g from Knisel and Davis 2000. The lower bound is the lowest Koc reported in Koskinen et al. (1996). The upper bound is from MRID 40768401.
5	U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 40768401. Average (lowest-highest) values.
6	Value taken from U.S. EPA/OPP/EFED (2014a), U.S. EPA/OPP/HED (2014a), and Knisel and Davis (2000).
7	Based on the label recommendation: "For optimum results, applications should be made prior to the resumption of active seasonal growth in the spring or before expected seasonal rainfall." As noted by U.S. EPA/OPP/EFED (2014a, p. 6), the application timing for tebuthiuron can be highly variable. For a persistence pesticide, the application date will not be a sensitive parameter.

See Section 3.2.3.4.3 for discussion.

Table 11: Summary of Modeled Concentrations in Surface Water

Scenario/Source	Peak Concentrations (ppb or µg/L per lb/acre)		Long-Term Average Concentrations (ppb or µg/L per lb/acre)	
Direct Spray and Spray Drift				
Pond, Direct Spray (Section 3.2.3.4.2) [1]	112		N/A	
Pond, drift at 25 feet (Section 3.2.3.4.2) [1]	25 (Aerial) 12 (Ground boom) 3.9 (Backpack)		N/A	
Stream, Direct Spray (Section 3.2.3.4.2) [2]	91		N/A	
Stream, drift at 25 feet (Section 3.2.3.4.2) [2]	20 (Aerial) 9.5 (Ground boom) 3.2 (Backpack)		N/A	
Liquid Formulation (Appendix 7)				
Pond, Section 3.2.3.4.4, Appendix 7, Tables 7 and 8	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	119 (32 - 540)	Clay	67.5 (19.1 - 266)
	Loam	115 (0.024 - 850)	Loam	50.5 (0.004 - 500)
	Sand	317 (0.0027 - 1640)	Sand	155 (0.0011 - 1140)
	Ave.	185 (10.6-1010)	Ave.	90.8 (6.37-635)
Stream, Section 3.2.3.4.4, Tables 5 and 6	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	78.2 (64 - 231)	Clay	1.15 (0.28 - 6.9)
	Loam	14.5 (0.06 - 81)	Loam	1.7 (0.00025 - 7.6)
	Sand	43.2 (0.005 - 151)	Sand	3.22(2.4×10^{-5} - 10.2)
Granular Formulation (Appendix 8)				
Pond, Section 3.2.3.4.4	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	115 (33 - 510)	Clay	66.3 (20.7 - 261)
	Loam	110 (0.05 - 760)	Loam	51.5 (0.014 - 370)
	Sand	320 (0.0028 - 1550)	Sand	159 (0.0015 - 1100)
Stream, Section 3.2.3.4.4	**Soil**	**Conc.**	**Soil**	**Conc.**
	Clay	78.3 (62 - 232)	Clay	1.15 (0.27 - 6.9)
	Loam	14.3 (0.18 - 70)	Loam	1.65 (0.0005 - 7.4)
	Sand	40.3 (0.005 - 138)	Sand	3.13 (2.4×10^{-5} - 9.6)
EPA Tier 1 Models				
FIRST (Reservoir model), Appendix 9	90.9 (19.8-102)		51 (2.5-68)	
PRZM-GW (Ground water) , Appendix 9	34 (12.2-722)		N/A	
EPA PRZM/EXAMS Tier 2[3]			97 (55-184)	

[1] See Attachment 1, Worksheet B04c. Values normalized by dividing by the application rate of 0.6 lb a.i./acre.
[2] See Attachment 1, Worksheet B04d. Values normalized by dividing by the application rate of 0.6 lb a.i./acre.
[3] Data from U.S. EPA/OPP/EFED (2014a), Table 3.4, p. 25. Conversion to Water Contamination Rates summarized at the end of Appendix 9.

See Section 3.2.3.4.3 for initial discussion.

Table 12: Concentrations in surface water used in this risk assessment

Estimate	Peak WCR[1] (mg a.i./L per lb a.i./acre)	Longer-term WCR[1] (mg a.i./L per lb a.i./acre)
Central	0.19	0.091
Lower	0.011	0.0064
Upper	1.0	0.64

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

See Section 3.2.3.4.6 for discussion

Table 13: Estimated residues in food items in mg/kg wet weight per lb/acre applied

Broadcast Liquid Applications

Food Item	Central [1]	Lower [2]	Upper [1]
Short grass	85	30	240
Tall grass	36	12	110
Broadleaf/forage plants and small insects	45	15	135
Fruits, pods, seeds, and large insects	7	3.2	15

Broadcast Granular Applications [3]

Food Item	Central [1]	Lower [2]	Upper [1]
Short grass	3.4	1.2	9.6
Tall grass	1.44	0.48	4.4
Broadleaf/forage plants and small insects	1.8	0.6	5.4
Fruits, pods, seeds, and large insects	0.28	0.13	0.6

[1] From Fletcher et al. (1997) and U.S. EPA/EFED 2001, p. 44.
[2] Central values × (Central Value ÷ Upper Value).
[3] Based on estimates from granular applications of hexazinone (SERA 2005).

See Section 3.2.3.7 for discussion.

Table 14: Summary of toxicity values used in human health risk assessment

Acute – single exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2014a, Table 4.5.4, p. 18
Study	MRIDs: 00020644, 40776301, developmental study
NOAEL Dose	10 mg a.i./kg bw/day
LOAEL Dose	25 mg a.i./kg bw/day
LOAEL Endpoint(s)	Decreased fetal body weights in F_1 females (17.3%) and increased resorptions.
Species, sex	Rabbits, female
Uncertainty Factor/MOE	100
Acute RfD	0.1 mg a.i./kg bw/day
Target population	Females of childbearing age (13 to 49 years of age)[1]

[1] No Acute RfD derived for members of the general population. Acute RfD not derived for general population because … *No appropriate endpoint attributable to a single dose was identified* (U.S. EPA/OPP/HED 2014a).

Chronic – lifetime exposure [2]

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2014a, Table 4.5.4, p. 18
Study	MRID: 00090108, 2-generation reproduction study
NOAEL Dose	14 mg a.i./kg bw/day
LOAEL Dose	26 mg a.i./kg bw/day
LOAEL Endpoint(s)	Decreased body weights in F_1 females (13%) as well as pup weight in F_1 and F_2 generation (5-8%).
Species, sex	Rats, females
Uncertainty Factor/MOE	100
Chronic RfD	0.14 mg a.i./kg bw/day
Target population	General population

[2] This toxicity value and MOE is also used for incidental short-term exposures (1-30 days).

See Section 3.3 for discussion

Table 15: Terrestrial Plants: Species Sensitivity Distributions

	Seedling Emergence[3]		
Group/Species	**EC_{25}**	**Relative Sensitivity[1]**	**NOAEL**
Monocots	**lb a.i./acre**	**(i-0.5)÷N**	**lb a.i./acre**
Ryegrass	0.27	0.125	0.25
Onion	0.46	0.375	0.25
Oat	0.52	0.625	0.5
Corn	3.1	0.875	2.0
Dicots			
Carrot	0.018	0.083	0.031
Sugar beet	0.2	0.250	0.12
Cabbage	0.23	0.417	0.12
Tomato	0.26	0.583	0.062
Cucumber	0.33	0.750	0.12
Soybean	1.2	0.917	1.0
	Vegetative Vigor [4]		
Group/Species	**EC_{25}**	**Relative Sensitivity[1]**	**NOAEL**
Monocots	**lb a.i./acre**	**(i-0.5)÷N**	**lb a.i./acre**
Ryegrass	0.3	0.3	0.12
Onion	0.57	0.57	0.25
Oat	0.93	0.93	0.5
Corn	2.6	2.6	2.0
Dicots[1]			
Sugar beet	0.16	0.1	0.062
Cucumber	0.28	0.3	0.12
Cabbage	0.32	0.5	0.12
Tomato	0.43	0.7	0.25
Carrot	0.52	0.9	0.5
Soybean[2]	N/A	N/A	0.12

[1] Relative sensitivities based on EC_{25} values and are calculated as the i^{th} value minus 0.5 divided by the number of species for what data are available.
[2] EC_{25} values for soybean could not be calculated. Soybeans not used in the calculation of relative sensitivities for dicots.
[3] MRID 48722703 for seedling emergence summarized in Appendix 3, Table A3-3.
[4] MRID 48722704 for vegetative vigor summarized in Appendix 3, Table A3-1.

Data Source: U.S. EPA/OPP/EFED 2014a, Table 3.24, p. 46.
See Sections 4.1.2.5.1 and 4.3.2.5 for discussion.

Table 16: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

MAMMALS [1]

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption
Small mammal	Mice	20	$2.514\ W^{0.507}$ [Eq 3-48]	$0.099\ W^{0.9}$ [Eq 3-17]
Larger mammal	Squirrels	400	$2.514\ W^{0.507}$ [Eq 3-48]	$0.099\ W^{0.9}$ [Eq 3-17]
Canid	Fox	5,000	$0.6167\ W^{0.862}$ [Eq 3-47]	$0.099\ W^{0.9}$ [Eq 3-17]
Large Herbivorous Mammal	Deer	70,000	$1.518\ W^{0.73}$ [Eq 3-46]	$0.099\ W^{0.9}$ [Eq 3-17]
Large Carnivorous Mammal	Bear	70,000	$0.6167\ W^{0.862}$ [Eq 3-47]	$0.099\ W^{0.9}$ [Eq 3-17]

BIRDS [2]

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption
Small bird	Passerines	10	$2.123\ W^{0.749}$ [Eq 3-36]	$0.059\ W^{0.67}$ [Eq 3-15]
Predatory bird	Owls	640	$1.146\ W^{0.749}$ [Eq 3-37]	$0.059\ W^{0.67}$ [Eq 3-15]
Piscivorous bird	Herons	2,400	$1.916\ W^{0.704}$ [Eq 3-38]	$0.059\ W^{0.67}$ [Eq 3-15]
Large herbivorous bird	Geese	4,000	$1.146\ W^{0.749}$ [Eq 3-37]	$0.059\ W^{0.67}$ [Eq 3-15]

INVERTEBRATES [3]

Animal	Representative Species	W[4]	Food Consumption[5]
Honey bee [7]	*Apis mellifera*	0.000116	≈2 (1.2 to 4)[6]
Herbivorous Insects	Various	Not used	1.3 (0.6 to 2.2)

[1] Sources: Reid 2006; U.S. EPA/ORD 1993.
[2] Sources: Sibley 2000; Dunning 1993; U.S. EPA/ORD 1993.
[3] Sources: Humphrey and Dykes 2008; Reichle et al. 1973; Winston 1987
[4] Body weight in grams.
[5] For vertebrates, based on allometric relationships estimating field metabolic rates in kcal/day for rodents (omnivores), herbivores, and non-herbivores. For mammals and birds, the estimates are based on Nagy (1987) as adapted by U.S. EPA/ORD (1993). The equation numbers refer to U.S. EPA/ORD (1993). See the following table for estimates of caloric content of food items. For herbivorous insects, consumption estimates are based on fractions of body weight (g food consumed/g bw) from the references in Note 3.
[6] For honeybees, food consumption based on activity and caloric requirements. Used only when estimates of concentrations in nectar and/or pollen can be made, which is not the case in the current risk assessment.
[7] A surface area of 1.42 cm2 is used for the direct spray scenario of the honey bee. This value is based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

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

Table 17: Diets: Metabolizable Energy of Various Food Commodities

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

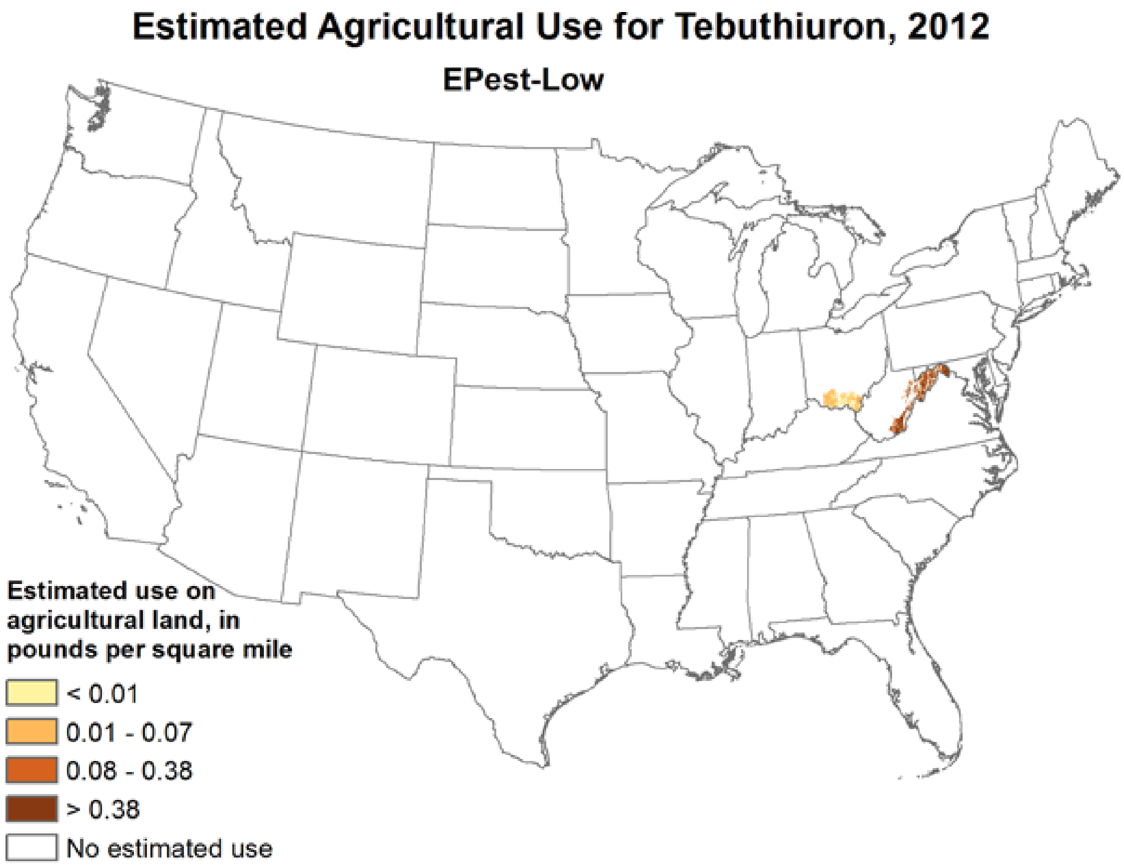
[1] Metabolizable energy. Unless otherwise specified, the values are taken from U.S. EPA/ORD (1993), Table 3-1, p. 3-5 as adopted from Nagy 1987.
[2] From U.S. EPA/ORD (1993), Table 4-2, p. 4-14 unless otherwise specified.
[3] Based on a gross caloric value of 2.2 kcal/g bw (U.S. EPA/ORD 1993, Table 4-2). An assimilation factor for mammals eating fruit not identified. Use estimate for birds (see below).
[4] Based on a gross caloric value of 2.2 kcal/g bw (U.S. EPA/ORD 1993, Table 4-2) and an assimilation factor for the consumption of fruit by birds of 51% [2.2 kcal/g bw x 0.51 ≈ 1.1 kcal/g bw]
[5] Based on a gross caloric value of 4.2 kcal/g bw for dicot leaves (U.S. EPA/ORD 1993, Table 4-2). For birds, the value is corrected by an assimilation factor for the consumption leaves by birds of 47% [4.2 kcal/g bw x 0.47 = 1.974 kcal/g bw]

See Sections 4.2.2.3 for discussion.

Table 18: Summary of toxicity values used in ecological risk assessment

Group/Duration	Organism	Endpoint	Toxicity Value (a.i.)	Reference
Terrestrial Animals				
Acute				
	Mammals	Developmental NOAEL, rabbits	10 mg/kg bw	Section 4.3.2.1.
	Birds	Acute dietary NOAEL, finch	180 mg/kg bw	Section 4.3.2.2.
	Honey Bee (contact)	Acute contact assay	860 mg/kg bw	Section 4.3.2.4.
Longer-term				
	Mammals	Use acute value.	10 mg/kg bw	Section 4.3.2.1
	Bird	Reproductive NOAEL, finch	7 mg/kg bw/day	Section 4.3.2.2.
Terrestrial Plants				
Soil	Sensitive	Dicot, carrot, EC_{25}	0.018 lb/acre	Section 4.3.2.5
	Tolerant	Monocot, Corn, NOAEC	2.0 lb/acre	
Foliar	Sensitive	Dicots, sugar beet, NOAEC	0.062 lb/acre	Section 4.3.2.5
	Tolerant	Monocot, Corn, NOAEC	2.0 lb/acre	
Aquatic Animals				
Acute				
Amphibians	Sensitive	No data	N/A	Section 4.3.3.2
	Tolerant	No data	N/A	
Fish	Sensitive	Fathead minnow chronic NOAEC	9.3 mg/L	Section 4.3.3.1
	Tolerant	NOAEC, Sheepshead minnow	50 mg/L	
Invertebrates	Sensitive	Pink shrimp, use chronic	4.56 mg/L	Section 4.3.3.3
	Tolerant	*Daphnia magna*, use chronic	21.8 mg/L	
Longer-term				
Amphibians	Sensitive	No data	N/A	Section 4.3.3.2
	Tolerant	No data	N/A	
Fish	Sensitive	Fathead minnow, NOAEC	9.3 mg/L	Section 4.3.3.1
	Tolerant	Rainbow trout, NOAEC	26 mg/L	
Invertebrates	Sensitive	Acute-to-chronic ratio method based on daphnid chronic.	4.56 mg/L	Section 4.3.3.3
	Tolerant	*Daphnia magna*, NOAEC	21.8 mg/L	
Aquatic Plants				
Algae	Sensitive	*S. capricornutum*, NOAEC	0.013 mg/L	Section 4.3.3.4.1
	Tolerant	*N. pelliculosa*, NOAEC	0.056 mg/L	Section 4.3.3.4.1
Macrophytes	Sensitive	Not determined	N/A	Section 4.3.3.4.2
	Tolerant	*Lemna gibba*, NOAEC	0.05 mg/L	Section 4.3.3.4.2

See Section 4.3.1 for initial discussion.
See the sections specified in the last column for details.



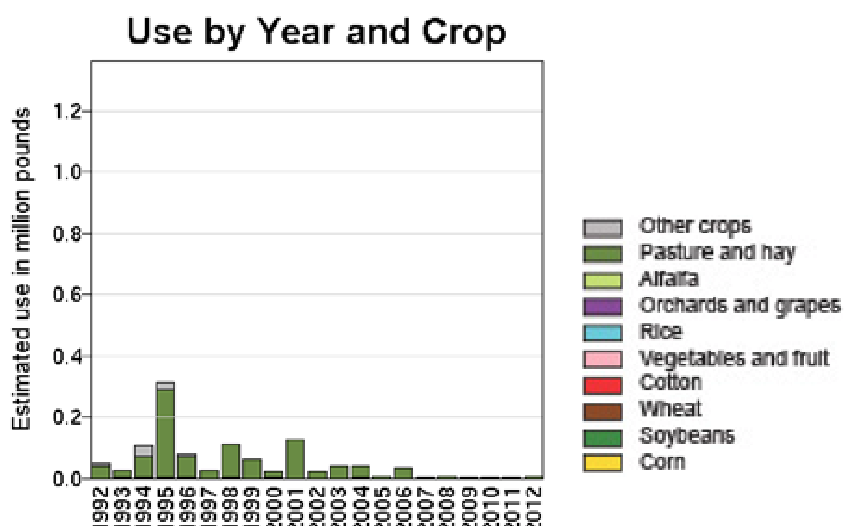
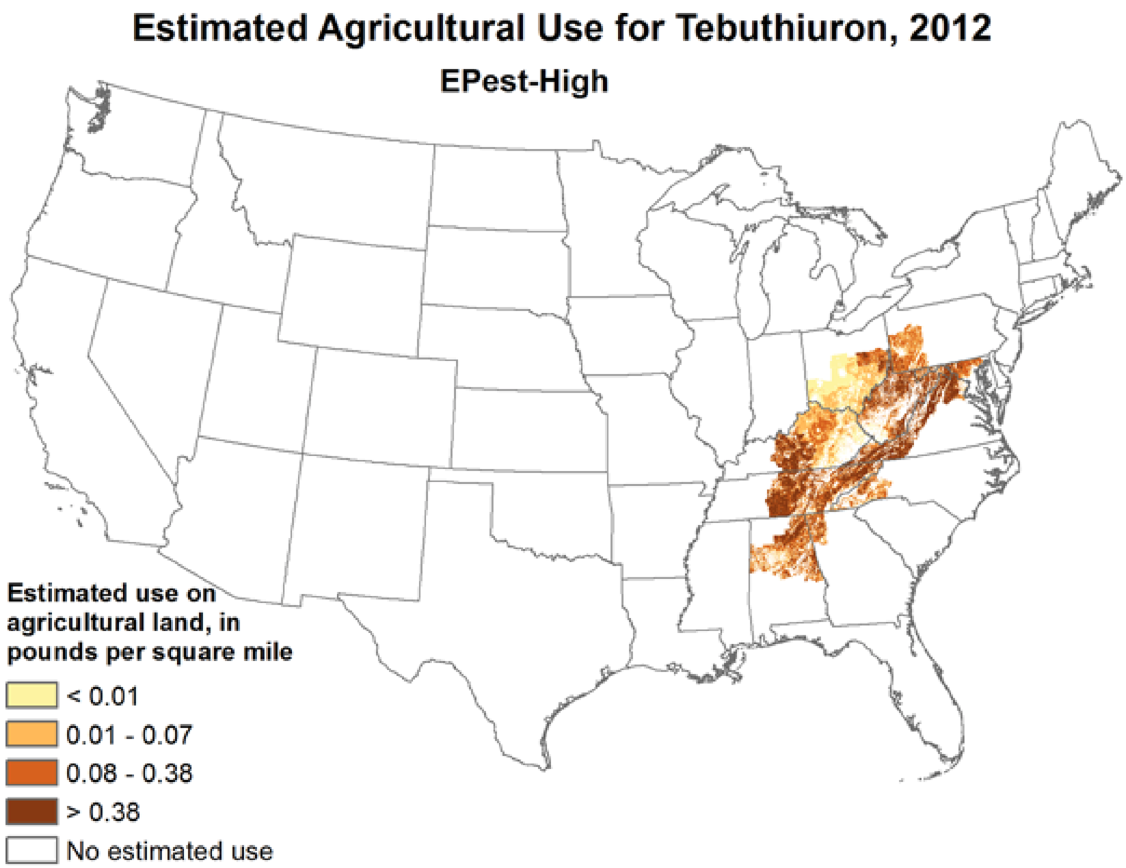


Figure 1: Lower Bound Estimated Agricultural Use of Tebuthiuron for 2012

Source: USGS(2015)
See Section 2.5 for discussion.



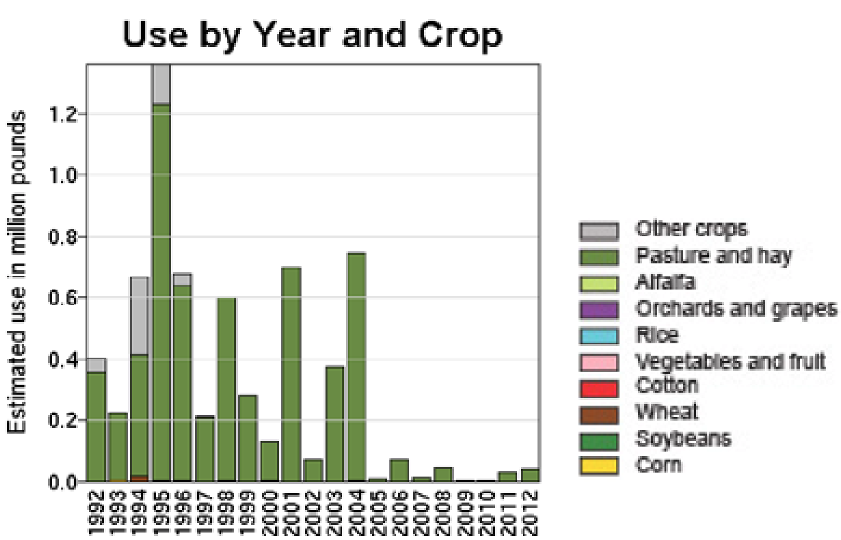


Figure 2: Upper Bound Estimated Agricultural Use of Tebuthiuron for 2012

Source: USGS(2015)
See Section 2.5 for discussion.

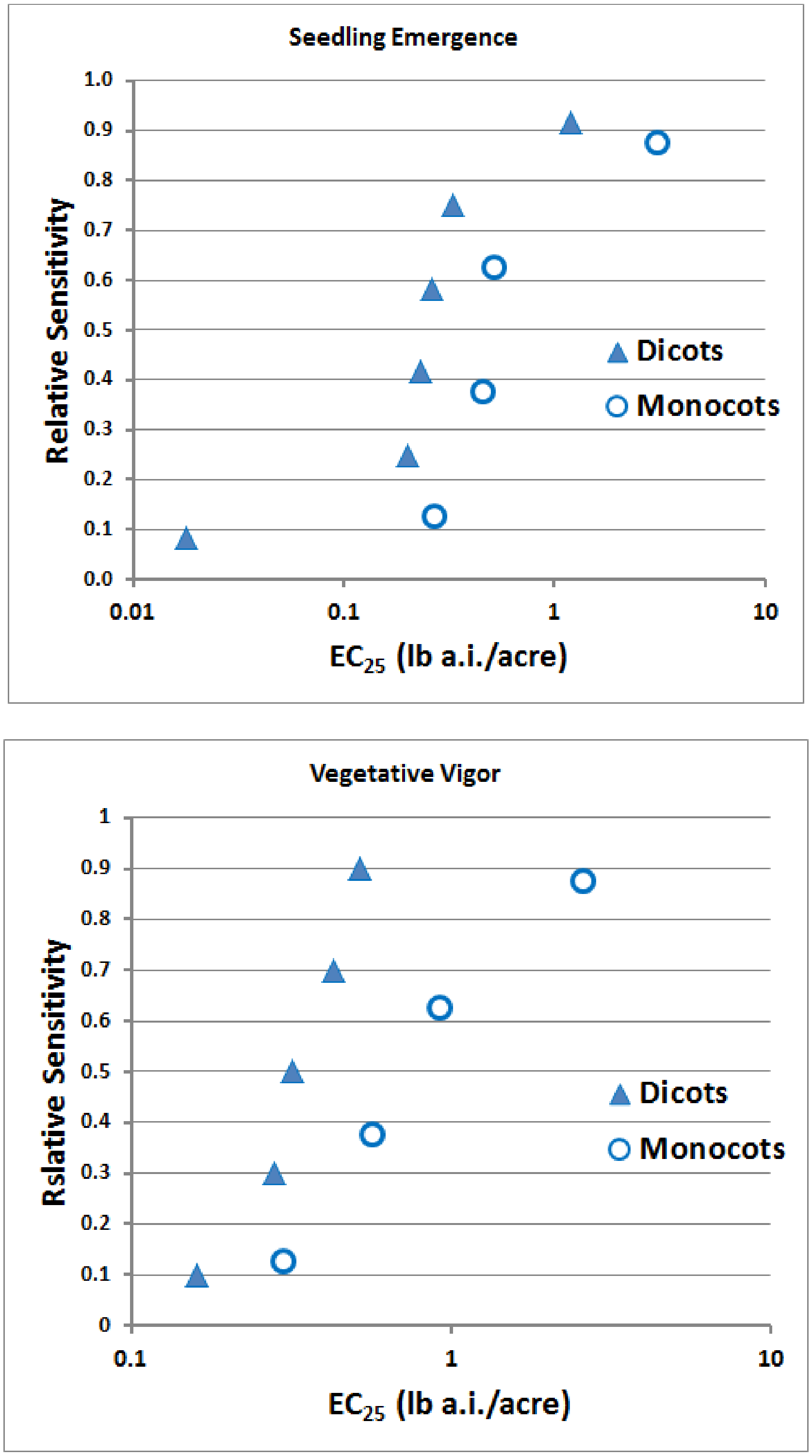


Figure 3: Terrestrial Plants: Species Sensitivity Distributions

See Sections 4.1.2.5.1 and 4.3.2.5 for discussion.
See Table 15 for data and species used.

Appendix 1: Toxicity to mammals.

Note: Summaries of registrant studies taken with little or no modification from the EPA RED (U.S. EPA/OPP 1994) or the EPA risk assessment for registration review (U.S. EPA/OPP/HED 2014a) unless otherwise specified.
Units of dietary exposures are given in the units used in the citations, typically mg a.i./kg diet or the equivalent ppm.
All values designate tebuthiuron in units of a.i. unless otherwise specified.

Table A1-1: Acute Oral Toxicity

Species	Compound (Purity)	Response	Reference
Gavage			
Cat (NOS), males and females	Tebuthiuron (NOS)	LD_{50}: >200 mg/kg Toxicity category II	U.S. EPA/OPP 1994 (RED) MRID 00226375
Cat (NOS)	Tebuthiuron (>97%)	LD_0: >200 mg/kg (no mortality)	Todd et al. 1974
Dog(NOS), males and females	Tebuthiuron (NOS)	LD_{50}: >500 mg/kg Toxicity category III	U.S. EPA/OPP 1994 (RED) MRID not specified
Dog (NOS)	Tebuthiuron (>97%)	LD_0 >500 mg/kg (no mortality)	Todd et al. 1974
Mouse (NOS), males and females	Tebuthiuron (NOS)	LD_{50} = 528 mg/kg (males) LD_{50} = 620 mg/kg (females) LD_{50} = 574 mg/kg (average) Toxicity category III	U.S. EPA/OPP 1994 (RED) MRID 00226375
Mouse (NOS)	Tebuthiuron (>97%)	LD_{50} = 579±11 mg/kg	Todd et al. 1974
Rabbit (NOS), males and females	Tebuthiuron (NOS)	LD_{50} = 286±30 mg/kg Toxicity category II	U.S. EPA/OPP 1994 (RED)
Rabbit (NOS)	Tebuthiuron (>97%)	LD_{50} = 286 mg/kg	Todd et al. 1974
Rat (NOS), males and females	Tebuthiuron (NOS)	LD_{50} = 447 mg/kg (males) LD_{50} = 387 mg/kg (females) LD_{50} = 417 mg/kg (average) Toxicity category II	U.S. EPA/OPP 1994 (RED) MRID 40583901
Rat (NOS)	Tebuthiuron (>97%)	LD_{50}: 644±27 mg/kg bw	Todd et al. 1974
Rats, Long-Evans, ≈60 days old	Tebuthiuron (>90%), doses of 125 to 500 mg/kg bw (NOS) Assayed for neurotoxicity on maze after 30 minutes to 2 hours (NOS)	No signs of neurotoxicity. `Working Note: This is survey study of several triazoles. No detailed discussion of tebuthiuron.`	Crofton 1996

Note: The study by Todd et al. (1974) appears to be identical to MRID 00226375 with minor discrepancies.

Table A1-2: Subchronic and Chronic Toxicity Studies

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
		Subchronic Studies	
Rats, Sprague-Dawley, 105-146 g, 40 per group	Tebuthiuron (>97%), 0 or 2500 mg/kg diet for 14 days with 16 day recovery period.	Reduced body weight gain during but not following treatment. Pancreatic acinar cells displayed vacuolization and decrease in zymogen granules during treatment. Changes rapidly reversed during recovery period. Pathology attributed to interference in protein synthesis.	Griffing and Todd 1974 Also summarized in Todd et al. 1974.
Rat, Haerlan, males and females	0, 20, 50, or 125 mg/kg/day in diet for 90 days	**NOAEL =** 50 mg/kg/day, based on increased relative liver, kidney, prostate, spleen and gonad weights in high dose-dose males and females **LOAEL** = 125 mg/kg/day based on decreased body weight (25-28%) and an increase in slight vacuolization of the pancreatic acinar cells in high-dose males and females.	U.S. EPA/OPP/HED 2014a MRID 00020662 (1972) CORE –minimum data **Acceptable/Guideline**
Rats, Wistar (28-35 days, 74-156 g), 10 males and 10 females per dose group	Tebuthiuron (>97%), 0, 400, 1000, and 2500 mg/kg diet, 3 months	No overt signs of toxicity. No changes in blood chemistry. 2500 ppm: Decreased body weights and food consumption in week 1. Diffuse vacuolization of pancreatic acinar cells.	Todd et al. 1974 Note: This study appears to be identical to MRID 00020662.
Dog, beagle, male and female, 13-23 months-old, 7-12.2 kg	Tebuthiuron (purity not specified) in gelatin capsules 0, 12.5, 25, or 50 mg/kg/day for 90 days	No mortality. Anorexia noted especially in high-dose males and females leading to weight loss. No effects observed on hematology or urinalysis. Clinical chemistry findings in 2000 ppm females included increased BUN (blood urea nitrogen) and increasing levels of ALP (alkaline phosphatase), up to 4-fold over the control group. Females at 1000 ppm had increased relative thyroid and spleen weights. **NOAEL** = 25 mg/kg/day **LOAEL** = 50 mg/kg/day based on significant decreases in body weight and increased ALP activity.	U.S. EPA/OPP/HED 2014a; U.S. EPA/Office of Drinking Water 1987 (Draft Health Advisory) MRID 00020663 (1972) **Acceptable/Guideline** Also summarized in Todd et al. 1974. See Table 2 of paper for clinical chemistries.

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
		Immunotoxicity	
Rats, Female, Crl:WI (Han), 10 per dose	Tebuthiuron (99.8 %) Dietary Conc.: 0, 400, 1000, or 2000 ppm Dose Equivalence: 0, 33.8, 84.9, and 148 mg/kg/day. Duration: 29 days Injection of sheep red blood cells (SRBC) on Day 24. Cyclophosphamide (i.p. as positive control	1000 and 2000 ppm: Decreases in body weight, body weight gain, and food consumption throughout study. 2000 ppm: Decreases in absolute and relative thymus weights; statistically significant increased relative liver weights; and statistically significant decreased in absolute kidney and spleen weights in this group. **Systemic LOAEL**: 1000 ppm (84.9 mg/kg bw) based on decreased body weight. **Systemic NOAEL**: 400 ppm (33.8 mg/kg bw) based on decreased body weight. No evidence for immunotoxicity based on anti-SRBC Immunoglobulin M levels. Natural Killer (NK) cells activity not evaluated.	U.S. EPA/OPP/HED 2014a MRID 48722705
		Chronic Studies	
Dog, beagle	0, 12.5, 25, or 50 mg/kg/day for one year.	No mortality, no treatment-related effects on absolute body weights for females or food consumption for male and females; no treatment-related ophthalmological lesions, changes in urinalysis parameters, or microscopic lesions, and gross necropsy was unremarkable **NOAEL** = 25 mg/kg/day **LOAEL** = 50 mg/kg/day based on clinical signs (anorexia, emesis, and diarrhea, decreased body weight (-12.5%), increased ALT (4-5 fold), AP (3-fold) in males only, significantly increased ($p \leq 0.05$) absolute liver weights in high-dose males and females, significant ($p \leq 0.05$) differences in organ weights relative to final body weight included increased liver weights in males and females, increased relative kidney weights (females only), and increased relative thyroid weights (males only).	U.S. EPA/OPP/HED 2002 and 2014a MRID 00146801 (1985) **Acceptable/Guideline**

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Mice, Harlan ICR, 80/sex/dose	Tebuthiuron (>97% a.i.) in pelleted diet for 2 years Dietary concentrations: 400, 800, or 1600 ppm (equivalent to 0, 60, 120, or 240 mg/kg/day, based on the default food factor of 0.15) Duration: 2 years	No treatment-related effects on mortality, clinical signs, hematology, or clinical chemistry, organ weights, or gross or microscopic pathology **NOAEL** = 240 mg/kg/day **LOAEL** for systemic toxicity not established.	U.S. EPA/OPP/HED 2014a MRID 00020717 (1986) **Unacceptable/Guideline** Dosing was not considered adequate based on the absence of systemic effects (U.S. EPA/OPP/HED 2014a). See p. 42 of the EPA document for details.
Rat, Wistar, males and females, 40/sex/group	Dietary concentrations: 400, 800, or 1600 ppm (equivalent to 0, 20, 40, or 80 mg/kg/day, based on the default food factor o 0.05) Duration: 2 years	No treatment-related effects on mortality, clinical signs, or clinical pathology in males or females at any dose of test material. No NOAEL may be established for this study as several major deficiencies were identified. 25% or fewer animals were living at study termination in all groups. Additionally, respiratory infections were prevalent among the controls and treated groups confounding the study results.	U.S. EPA/OPP/HED 2014a MRID Nos. 00020714 (1976) 00098190 (1981) 40870101 (1988) **Unacceptable/Guideline** *The evidence suggests that this study does not comply with GLP procedures* (U.S. EPA/OPP/HED 2014a). See p. 42 of the EPA document for details.

See Section 3.1.5 for discussion.

Table A1-3: Reproductive and Developmental Studies

Species	Exposure	Response	MRID(s), (Year), Classification
Developmental			
Rats, Harlan, 25 presumed pregnant	Tebuthiuron (purity not specified) in the diet: <u>Nominal dietary concentrations</u>: 0, 600, 1200, or 1800 ppm <u>Doses to animals</u>: 0, 37, 72, or 110 mg/kg bw/day on days 6-15 of gestation	No treatment related-effects on body weight, body weight gain or food consumption were observed. There were no clinical signs of toxicity, and all dams survived to terminal sacrifice, with no treatment related lesions observed at necropsy. Pancreatic tissue appeared normal, as evaluated by gross and microscopic examination. **Maternal NOAEL** = 110 mg/kg bw/day No effects observed on pregnancy rate, number of corpora lutea/dam, number of implantation sites/dam, pre- or post-implantation losses, number of fetuses/litter, fetal body weights, or fetal sex ratios, compared with controls. No dead fetuses were observed. No treatment-related abnormalities were found in any fetus. D**evelopmental NOAEL** = 110 mg/kg/day U.S. EPA/OPP/HED 2014a, p. 38, notes the following: *test article concentrations in the diets were not measured; therefore, it may be possible that the doses to the animals were different from nominal*.	U.S. EPA/OPP/HED 2014a MRID Nos. 00020803 (1972) 40485801 (1972) **Acceptable/Guideline** Also summarized in Tood et al. 1974.
Rabbit, presumed pregnant Dutch belted, 15/group	Tebuthiuron (96.5% a.i.) by gavage 0, 10, or 25 mg/kg/day on gestation days 6-18	No treatment related-effects on body weight, body weight gain or food consumption were observed. There were no clinical signs of toxicity, and all dams survived to terminal sacrifice, with no treatment related lesions observed at necropsy. Total early resorptions and the percentage of litters with early resorptions were increased in the high-dose group. **<u>Maternal</u>** **NOAEL** = 10 mg/kg/day **LOAEL** = 25 mg/kg/day based on increased resorptions at the high-dose. No effects observed on pregnancy rate, number of corpora lutea/dam, number of implantation sites/dam, or dams/litter. Mean fetal body weight was decreased at 25 mg/kg/day (17.3%), and total early resorptions and the percentage of litters with early resorptions was observed in the high-dose group. Also, in the range-finding study, an increase in early resorptions was observed at doses ≥25 mg/kg/day. **<u>Developmental</u>** **NOAEL** = 10 mg/kg/day **LOAEL** = 25 mg/kg/day based on significantly decreased fetal weights (F_1 females) and an increase in resorptions.	U.S. EPA/OPP/HED 2014a MRID Nos. 00020644 (1975) 40776301 (1988) **Acceptable/Guideline** Basis for Acute RfD in U.S. EPA/OPP/HED 2014a (p. 5) and U.S. EPA/OPP/HED (2002, p. 22).

Species	Exposure	Response	MRID(s), (Year), Classification
Reproduction			
Rat, Wistar, 25 males and 25 females	Tebuthiuron (98.0% a.i.) in the diet for two generations (98 days for F_0 and 124 days for F_1 rats) Dietary concentrations: 0, 100, 200, or 400 ppm Dietary dose levels: 6-7, 13-14, or 26-28 mg/kg/day (respectively for F_0 and F_1 males) 7-8, 14-15, or 30-31 (respectively for F_0 and F_1 females average over premating period only)	No treatment related deaths, clinical signs of toxicity, gross lesions, or microscopic lesions observed in adults of either generation. **Parental NOAEL** = 200 ppm or 14 mg/kg/day **LOAEL** = 400 ppm or 30 mg/kg/day based on decreased body weights in F_1 females and decrease in food efficiency (13%). **Reproductive NOAEL** = 400 ppm or 26 mg/kg/day. No effects were observed on reproductive parameters as measured by sperm morphology, fertility index for females, and the number of litters produced. LOAEL not established. **Offspring NOAEL** = 200 ppm or 14 mg/kg/day **Offspring LOAEL** = 400 ppm or 26 mg/kg/day based on decreased pup body weights on post-natal day 21 in the F_1 and F_2 generation (5-8%).	U.S. EPA/OPP/HED 2014a MRID 00090108 (1981) **Acceptable/Guideline** Basis for Chronic RfD in U.S. EPA/OPP/HED 2014a (p. 5) and U.S. EPA/OPP/HED (2002, p. 22). Special Note: The IRIS entry for tebuthiuron (U.S. EPA/NCEA 1988) as well as the RED (U.S. EPA/OPP 1994, p. 10-11) designates 7 mg/kg bw/day as a NOAEL and 14 mg/kg bw/day as a LOAEL. See Section 3.1.9.2 for discussion.

Table A1-4: Skin Irritation and Sensitization Studies

Species	Exposure	Response	Reference
Skin Irritation			
Rabbits, New Zealand albino, 2-3-month-old. 3 per sex per group	Tebuthiuron (>90%), 200 mg/kg bw with or without abrasion. 24 hour exposure, 14 day observation period.	One rabbit died following development of diarrhea and emaciation. No signs of skin irritation.	Todd et al. 1974
Rabbit (NOS)	Tebuthiuron (NOS)	No dermal irritation observed Toxicity category IV	U.S. EPA/OPP 1994 (RED) MRID 40583902
Skin Sensitization			
Guinea pig (NOS)	Tebuthiuron (NOS)	No dermal sensitization observed	U.S. EPA/OPP 1994 (RED) MRID 40583904 Similar observation in Todd et al. 1974.

Table A1-5: Eye Irritation Studies

Species	Exposure	Response	Reference
Rabbit (NOS)	Tebuthiuron (NOS)	Slight conjunctival hyperemia at 1 hour post treatment Toxicity category IV	U.S. EPA/OPP 1994 (RED) MRID 40583903
Rabbits, New Zealand albino, 2-3-month-old.	Tebuthiuron (>90%), 71 mg (0.1 mL) into one eye with the other eye serving as control.	No irritation of the cornea or iris. Slight transient hyperemia of conjunctiva. All eyes normal by Day 7 after treatment.	Todd et al. 1974 `Note: This is probably identical to MRID 40583903.`

Table A1-6: Acute and Repeated Dose Dermal Toxicity

Species	Exposure	Response	Reference
Acute			
Rabbits, New Zealand albino, 2-3-month-old. 3 per sex per group	Tebuthiuron (>90%), 200 mg/kg bw with or without abrasion. 24 hour exposure, 14 day observation period.	One rabbit died following development of diarrhea and emaciation. **`Working Note: See observations for dermal irritation in Table A1-4.`**	Todd et al. 1974 **`Working Note: This information is clearly not the basis for the EPA data summarized below.`**
Rabbit (NOS), males and females	Tebuthiuron (NOS)	LD_{50} >5000 mg/kg Toxicity category IV **`Working Note: This MRID number is also cited for the dermal skin irritation study in Table A1-4.`**	U.S. EPA/OPP 1994 (RED) MRID 40583902
Repeated Dose			
Rat (NOS)	0 or 1000 mg/kg/day, 6 hours/day for 21 days [Details of duration from U.S. EPA/OPP 1994, p. 9]	**NOAEL** = 1000 mg/kg/day … slight erythema which cleared by 7 days, and increased blood glucose values [Details of observations from U.S. EPA/OPP 1994, p. 9]	U.S. EPA/OPP/HED 2014a MRID Nos. 00149733 (1985) 00160796 (1986) **Acceptable/Guideline**

Table A1-7: Inhalation Toxicity

Species	Exposure	Response	Reference
Acute			
Rat (NOS), males and females	Tebuthiuron (NOS)	LD_{50} >3.696 mg/L Toxicity category III	U.S. EPA/OPP 1994 (RED) MRID 00155730
Subchronic			
None available		**Working Note: EPA is requiring a subchronic inhalation study. …** *The Hazard and Science Policy Council, (HASPOC) determined that a guideline 90-day inhalation study is required for this route of exposure.*	U.S. EPA/OPP/ HED 2014a, p. 5.

Table A1-8: MSDS Mammalian Effects Summary of Selected Formulations

	Spike 20P	Spike 80DF	Alligare Tebuthiuron 20 P	Alligare Tebuthiuron 80 WG
% a.i.	20%	80%	20%	80%
Oral LD_{50} (mg/kg bw)	>2000	>400 (estimated)	644	488
Dermal LD_{50} (mg/kg bw)	>2000	>5000	>5000	>2000
Inhalation LC_{50} (mg/L x 4 hours)	N.S.	>3 (estimated)	3.7	>4.84
Skin irritation	N.S.	Not likely	Non-irritating	Non-irritating
Eye Irritation	Slight with corneal injury.	Slight with corneal injury.	Non-irritating	Irritation with corneal injury.
Skin Sensitization	N.S.	No	No	No

Source: Material Safety Datasheets (MSDSs) from www.greenbook.net or https://www.msdsonline.com.

Table A1-9: Field Studies

Application[1]	Observations	Reference
Aerial application at 2.0 kg/ha [≈1.8 lb a.i./acre] for brush control on 32.4-ha pasture sites. With or without prescribed burning. Stillwater, Oklahoma Note: Formulation and type of formulation not specified.	No significant impact on abundance or prevalence of cottontail rabbits infected with *Obeliscoides cuniculi*, a parasitic helminth stomach worm ($p>0.23$, Table 1, p. 149).	Boggs et al. 1990a and 1990b
Aerial application at 2.0 kg/ha [≈1.8 lb a.i./acre] for brush control on 32.4-ha pasture sites. With or without prescribed burning. Stillwater, Oklahoma Note: Formulation and type of formulation not specified.	Assay for populations of five species of nematodes and two species of cestodes. No effect on prevalence of rabbits with parasites. Prevalence of *Mosgovoy pectinata americana* (cestode) was less on treated sites vs. control sites.	Boggs et al. 1990b
Aerial application at 2.2 kg/ha [≈2 lb a.i./acre] for brush control on 32.4-ha pasture sites. With or without prescribed burning. Stillwater, Oklahoma Note: Formulation and type of formulation not specified.	Assay for populations of *Cuterebra* sp. (Diptera, botfly larvae) in 10 species of small mammals. No effects of treatments on prevalence of infestations. Differences noted between burned and unburned sites as well as between tebuthiuron and triclopyr.	Boggs et al. 1991a
Pellet formulations (Graslan)aerial application at 3.0 kg/ha [≈2.7 lb a.i./acre] to 17 or 11.2 ha sites. Georgia	Assay for quality of deer habitat. No significant differences in total forage biomass. Significant increase in grasses. No apparent or consistent impact on deer habitat. `Working Note: Authors suggest that rates in excess of 3.1 kg/ha may be detrimental to deer habit but no deer population surveys were conducted.`	Defazio et al. 1988

Application[1]	Observations	Reference
Pellet formulations (NOS) at rates of 0.4, 0.7, and 1.0 kg ai/ha (≈0.36, 0.62, and 0.89 lb a.i./acre) to 5.2 ha plots (sagebrush) Wyoming	Increase in habitat quality for small mammals. Based on population estimates of mammals (species of mice, squirrel, vole as well as prairie dog), increases were noted in grasshopper mouse (not dose-related) and two species of ground squirrel (dose-related). Decreases in deer mice (not dose-related). Results in other species not significant. [Table 6 of paper] Based on animal captures, a significant increase in Montane vole at the highest application rate. [Table 7 of paper] No consistent impact on diversity indices for small mammals [Table 8 of paper]	Johnson et al. 1996
Aerial application of pellet formulation (20%, NOS) at 2.2 kg/ha to 1.5 and 2.5 ha pastures. Also mechanical treatments and untreated pastures.	Cows: Less consumption of woody vegetation on tebuthiuron treated pastures. Higher consumption of grasses on tebuthiuron treated pastures. No clear indication if this represents a food preference or simply beneficial changes in the forage materials.	Kirby and Stuth 1982
Aerial application of pellet formulation (20%, NOS) at 2.2 kg/ha to 1.5 and 2.5 ha pastures. Also mechanical treatments and untreated pastures.	Goats: Grasses predominated on tebuthiuron treated pastures. Increased consumption of vines on tebuthiuron treated pastures but not significantly different from mechanical treatment (Table 2). Diets on tebuthiuron treated pastures of higher nutritional value.	Lopes and Stuth 1984
Ground application of pellet formulation (20%, NOS) at 0.6 kg/ha to pastures.	Cows: Increases in grasses preferred by cattle on tebuthiuron treated pastures in second and third growing seasons. Preferential feeding on treated pastures clearly secondary to changes in vegetation.	McDaniel and Balliette 1986
Aerial application at 2.2 kg/ha [≈2 lb a.i./acre] for brush control on 32.4-ha pasture sites. With or without prescribed burning. Stillwater, Oklahoma Note: Formulation and type of formulation not specified.	Assay of eastern woodrat populations. No substantial change in populations between tebuthiuron treated and control sites. Increase in the mean density of nests on tebuthiuron (5.7 ± 1.2) relative to control sites (0.43 ± 0.15). Lack of correlation between populations and nest site densities not determined. No apparent impact on number of reproductively active females.	McMurry et al. 1993a
See McMurry 1993a above.	Detailed study of rat diets in treated and untreated areas. In general, forb and browse diet classes were used in accordance with availability - i.e. eastern woodrats are opportunistic feeders.	McMurry et al. 1993b

Application[1]	Observations	Reference
Applications of 0.31, 0.67, or 0.94 lbs a.i./acre to 10 acre plots dominated by sagebrush. Note: Application method not specified. Wyoming	Increase in ground squirrel populations (marginally dose-related). Slight decrease in white-footed deer mice only at highest application rate. Grasshopper mice found only in treated plots but decreasing trend with increasing application rate in these plots. Working Note: Only small numbers of mammals but overall effect appears to be beneficial to small mammals. See Table 3 of paper.	Olson et al. 1994
Hand-spreader application of pelleted formulation (20% NOS) at 0, 1, or 2 kg./ha to 4x4 m subplots.	Cows: Grazing preference to plots treated with tebuthiuron relative to plots treated by spray with 2,4-D (1 kg/ha) or picloram (1 kg/ha) in first growing season. The preference for tebuthiuron treated plots does not seem associated with differences in grass maturity or weed control. **Working Note: This appears to be the only clear indication of a preference for tebuthiuron treatment in terms of food consumption.**	Scifres et al. 1983
Aerial application of granular formulation (Graslan, 20% a.i.) at 2.3 kg a.i./ha (≈2 lbs a.i./acre) Oklahoma	Decrease in overstory cover and increase in forbs. Treatment suppressed more desirable forbs but increase in grasses. Working Note: Authors suggest (reasonably) that impact would be beneficial to deer but not data on deer populations are presented.	Thompson et al. 1991
Application rate of 0.6 kg/ha to 532 acres of land dominated by shinnery oak	Little impact on abundance of small mammals.	Zavaleta 2012

[1]All application rates in a.i. unless otherwise specified.

Appendix 2: Toxicity to birds

Table A2-1: Acute Oral/Gavage Toxicity to Birds

Species	Exposure	Response	Reference[1]
Mallard duck, *Anas platyrhynchos*, 9-months-old	Tebuthiuron (98% a.i.) by gavage. Nominal concentrations: 0, 1000, or 2000 mg a.i./kg bw. 14 day observation period.	No mortality observed in treated birds or controls throughout the test. Signs of toxicity included anorexia and low appetite in females; also observed were hypoactivity and lethargy, however, by day 2 birds were no longer hypoactive or lethargic 14-day LD_{50} >2000 mg a.i./kg bw *Practically nontoxic* Results of bodyweights taken on days 3, 7, and 14 not reported	U.S. EPA/OPP/EFED 2014 MRID No. 00041692 **Acceptable**
Mallard duck, *Anas platyrhynchos*, 1-year-old	Tebuthiuron (98% a.i.) by gavage. Nominal concentration: Limit dose 500 mg a.i./kg bw 14 day observation period.	No mortality and no signs of toxicity observed throughout the study; behavior, appearance, and appetite remained normal throughout the course of the study, and birds gained weight. 14-day LD_{50} >500 mg a.i./kg bw Test concentration too low (not as high as 2000 mg a.i./kg bw) to make a firm toxicity classification.	U.S. EPA/OPP/EFED 2014 MRID No. 00020661 **Supplemental**(study does not report age of birds, individual body weight, or mean food consumption, and does not establish a definite LD_{50})
Duck (NOS)	Tebuthiuron (>97%)	LD_0: >500 mg/kg bw (no mortality	Todd et al. 1974
Northern bobwhite quail, *Colinus virginianus*	Tebuthiuron (98% a.i.) Nominal concentration: Limit dose 500 mg a.i./kg bw. 14 day observation period.	No mortality observed throughout the study; behavior, appearance, and appetite remained normal throughout the course of the study, and birds gained weight. 14-day LD_{50} >500 mg a.i./kg bw Test concentration too low (not as high as 2000 mg a.i./kg bw) to make a firm toxicity classification.	U.S. EPA/OPP/EFED 2014 MRID No. 00020661 **Supplemental** (study does not report age of birds, individual body weight, or mean food consumption, and does not establish a definite LD_{50})
Quail (NOS)	Tebuthiuron (>97%)	LD_0: >500 mg/kg bw (no mortality	Todd et al. 1974

Species	Exposure	Response	Reference[1]
Domestic chicken, *White Rock Cross*,	Tebuthiuron (NOS) by gavage for 14 days Nominal concentration: Limit dose 500 mg a.i./kg bw (1st study) and Limit dose 500 mg a.i./kg bw (2nd study)	1st study: no mortality, slight hypoactivity and mild anorexia observed 24 hours post-treatment, which resolved thereafter; all birds gained weight during the test period 2nd study: no mortality, all chickens appeared normal and gained weight throughout the test period. 14-day LD_{50} >500 mg a.i./kg bw Test concentration too low (not as high as 2000 mg a.i./kg bw) to make a firm toxicity classification	U.S. EPA/OPP/EFED 2014 MRID No. 00020661 **Supplemental**(study does not report age of birds, individual body weight, or mean food consumption, and does not establish a definite LD_{50})
Chicken (NOS)	Tebuthiuron (>97%)	LD_0: >500 mg/kg bw (no mortality	Todd et al. 1974

Table A2-2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference[1]
Mallard duck, *Anas platyrhynchos*, 7-day-old, 10/test level	Tebuthiuron (98% a.i.) in the diet for 8 days Nominal concentrations: 0, 400, 1000, or 2500 mg a.i./kg diet	No mortality up to and at 2500 mg a.i./kg diet (highest concentration tested); no adverse effects on behavior, appearance, or posture of treated chicks, relative to controls. Additional data (MRID 00041693) on food consumption and body weight gain indicates a significant reduction in food consumption in all treatment groups, compared with controls, from day 0 to 5, with no significant effect on body weight gain. 8-day LC_{50} >2500 mg a.i./kg diet Test concentration too low (not as high as 5000 mg a.i./kg diet) to make a firm toxicity classification	U.S. EPA/OPP/EFED 2014 MRID Nos. 00041680 and 00041693 **Supplemental** (test concentrations below 5000 mg a.i./kg diet)

Species	Exposure	Response	Reference[1]
Northern bobwhite quail, *Colinus virginianus*, 7-days-old, 10/test level	Tebuthiuron (98% a.i.) in the diet for 8 days Nominal concentrations: 0, 400, 1000, or 2500 mg a.i./kg diet	No mortality up to and at 2500 mg a.i./kg diet (highest concentration tested); no adverse effects on behavior, appearance, or posture of treated chicks, relative to controls; no apparent reluctance to eat the compound-containing diet. Additional data (MRID 00041693) on food consumption and body weight gain indicates a significant reduction in food consumption in all treatment groups, compared with controls, from day 0 to 5; however, there was no significant reduction in body weight gain between treated and control groups. 8-day LC_{50} >2500 mg a.i./kg diet Test concentration too low (not as high as 5000 mg a.i./kg bw) to make a firm toxicity classification	U.S. EPA/OPP/EFED 2014 MRID Nos. 00041681 and 00041693 **Supplemental** (test concentrations below 5000 mg a.i./kg diet)
Northern bobwhite quail, *Colinus virginianus*, 11-days-old, 10/test level	Tebuthiuron (99.1% a.i.) in the diet for 8 days Nominal concentrations: 0, 600, 1200, 2500 or 5000 mg a.i./kg diet Mean-measured: 0 (<LOQ), 636, 1210, 2573, or 5113 mg a.i./kg diet	No significant mortality or behavioral signs of toxicity observed throughout the study; birds in the two highest dose groups (2573, and 5113 mg a.i./kg diet) gained significantly less weight, relative to controls during 5-day treatment phase; however mean body weight gain values were not significantly different from controls during 3-day basal diet phase. Mean food consumption among treated birds was not significantly different from that of control group. 8-day LC_{50} >5133 mg a.i./kg diet *Practically nontoxic* Two birds (one in 1210 mg a.i./kg diet group and one in 5113 mg a.i./kg diet group, likely due to stress from handling)	U.S. EPA/OPP/EFED 2014 MRID No. 40601001 **Acceptable**

Appendix 2: Toxicity to birds *(continued)*

Species	Exposure	Response	Reference[1]
Mallard duck, *Anas platyrhynchos*, 4-day-old, 10/test level	Tebuthiuron (99.1% a.i.) in the diet for 8 days Nominal concentrations: 0, 600, 1200, 2500 or 5000 mg a.i./kg diet Mean-measured: 0 (<LOQ), 583, 1176, 2578, or 5093 mg a.i./kg diet	No significant mortality or behavioral signs of toxicity observed throughout the study; no significant differences in mean body weight at 583 mg a.i./kg diet, compared with controls during the 5-day treatment phase; however, birds exposed to >1176 mg a.i./kg diet gained significantly less weight than control. No significant effects on mean body weight gains were observed during the 3-day basal diet phase. 8-day LC_{50} >5093 mg a.i./kg diet *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID No. 40601002 **Acceptable**
Zebra finch, *Taeniopygia guttata*, 5- to 7-months-old	Tebuthiuron (99.8% a.i.) in the diet for 8 days Nominal concentrations: 0, 562, 1000, 1780, 3160, or 5620mg a.i./kg diet Mean-measured: 0 (<LOQ), 497, 895, 1590, 2870, and 5380mg a.i./kg diet	Treatment-related food consumption observed at ≥895 mg a.i./kg diet during exposure period (days 0-5); post-exposure food consumption was comparable to controls. Clinical signs of toxicity included ruffled appearance, wing droop, lethargy, loss of coordination, prostrate posture, and loss of righting reflex, which increased in frequency with increasing dose and duration. LC_{50} = 1465 mg a.i./kg diet 95% CI = 1145 – 1883 mg a.i./kg diet *Slightly toxic* Estimated NOAEL dose [2]: 497 mg a.i./kg diet x 0.36 ≈ 180 mg/kg bw	U.S. EPA/OPP/EFED 2014 MRID No. 48928201 **Acceptable**

[1] As indicated in a previous Forest Service risk assessment for which both body weights and food consumption rates in acute dietary studies were available for quail and mallards (SERA 2007b), approximate food consumption rates in acute dietary studies are about 0.4 kg food/kg bw for mallards and 0.3 kg food/kg bw for quail. These food consumption rates are from standard studies using very young birds.

[2] Food consumption factor for zebra finch taken as 0.36 from Salvante et al. 2007. Average food consumption of about 6 g/day (Fig 1D, p. 1329) and average body weight of about 16.5 g (Figure 2, p. 1330). 6/16.5 ≈ 0.363636364.

Table A2-3: Reproductive and Subchronic Toxicity to Birds

Species	Exposure	Response	Reference[1]
Reproduction			
Mallard ducks, *Anas Platyrhynchos*, 5-months-old	Tebuthiuron (96.4% a.i.) in the diet for 22 weeks Nominal concentrations: 0, 20 or 100 mg a.i./kg diet Mean-measured: *not significantly different from nominal concentrations*	No treatment-related mortality, signs of toxicity, or effects on body weight or food consumption. No significant reduction in the numbers of eggs laid, eggs cracked, viable embryos, live 3-week embryos, normal hatchlings, 14-day-old survivors, or egg thickness. A statistically significant but not dose related decrease in 14-day survivors was observed in the 20 mg a.i./kg diet group. **NOAEC** = 100 mg a.i./kg diet (highest concentration tested) [7 mg/kg bw/day [1]] **LOAEC** >100 mg a.i./kg diet	U.S. EPA/OPP/EFED 2014 MRID No. 00093690 **Acceptable**
Northern bobwhite quail, *Colinus virginianus*, 6-months-old	Tebuthiuron (96.4% a.i.) in the diet for 22 weeks Nominal concentrations: 0, 20 or 100 mg a.i./kg diet Mean-measured: *not significantly different from nominal concentrations*	No treatment-related mortality, signs of toxicity, or effects on body weight or food consumption. No significant reduction in the numbers of eggs laid, eggs cracked, viable embryos, live 3-week embryos, normal hatchlings, 14-day-old survivors, or egg thickness. **NOAEC** = 100 mg a.i./kg diet (highest concentration tested) [7 mg/kg bw/day [1]] **LOAEC** >100 mg a.i./kg diet	U.S. EPA/OPP/EFED 2014 MRID No. 00104243 **Acceptable**
Mallard ducks, *Anas Platyrhynchos*, 22-weeks-old, males and females, 16 pairs/test level	Tebuthiuron (99.8% a.i.) in the diet for 20 weeks Nominal concentrations: 0, 500, 900, or 1500 mg a.i./kg diet Mean-measured: <50 (<LOQ,), 500, 903, or 1550 mg a.i./kg diet	No treatment-related mortality, signs of toxicity, or effects on body weight or food consumption at any dietary level. Statistically significant (p<0.5) dose-dependent decrease in hatching body weight and eggshell thickness at 1550 mg a.i./kg diet, compared with controls. Statistically significant (p<0.5) decrease in egg production at all dietary concentrations. **NOAEC** <500 mg a.i./kg diet (highest concentration tested) **LOAEC** =500 mg a.i./kg diet	U.S. EPA/OPP/EFED 2014 MRID No. 48928202 **Supplemental** (due to significant decrease in egg production (eggs laid/pen) at all dietary levels.

Species	Exposure	Response	Reference[1]
Northern bobwhite quail, *Colinus virginianus*, 36-weeks-old males and females, 16 pairs/test level	Tebuthiuron (99.8% a.i.) in the diet for 20 weeks Nominal concentrations: 0, 500, 900, or 1500 mg a.i./kg diet Mean-measured: <50 (<LOQ,), 500, 903, or 1550 mg a.i./kg diet	No treatment-related mortality; there was a dose-related significant ($p<0.05$) decrease in adult male body weight gain at all dietary levels, compared with controls; a significant ($p<0.05$) decrease in adult female body weight was observed at 1550 mg a.i/kg diet, relative to controls ($p<0.01$); there were no statistically significant treatment-related effects on food consumption at any test level. A significant, dose-dependent decrease in offspring body weights, relative to controls, was observed at 903 and 1550 mg a.i./kg diet for hatchlings and at 1550 mg a.i./kg diet (p<o.01)for 14-day survivor weight ($p<0.5$). There were no treatment-related effects on reproductive performance in the 500 mg a.i./kg diet group; however, dose-dependent effects on offspring survival were observed. At 903 and 1550 mg a.i./kg diet, offspring survival was reduced by 4-7%; and egg production was decreased by 23% from average at 1550 mg a.i./kg diet. **NOAEC** <500 mg a.i./kg diet (highest concentration tested) **LOAEC** =500 mg a.i./kg diet	U.S. EPA/OPP/EFED 2014 MRID No. 48928202 **Supplemental** (due to significant effects on male weight gain at all test levels)
Other subchronic			
Chickens, White Cornish, 10 per sex per dose	Tebuthiuron (>90%). Dietary concentrations of 0, 400, 1000, or 2500 ppm Duration: 1 month	No effects at two lower concentrations. 2500 ppm: Decreases in food consumption and body weight gain (Table 5 of paper). No organ pathology at any dose.	Todd et al. 1974

[1] Dietary concentrations (mg/kg diet) converted to mg/kg bw doses using food consumption rates of 0.07 kg food/kg bw for reproduction studies in quail and mallards taken from SERA (2007b).

Table A2-4: Field Studies

Application	Observations	Reference
Applications of 0.56 kg/ha (0.5 lb a.i./acre) to 2,331 ha area of grazing rangeland with shinnery oak and sagebrush. Compared to a comparable untreated area. Texas	Study population: female lesser prairie-chickens (*Tympanuchus pallidicinctus*). Based on a total of 10 nesting females at both treated and untreated sites, a significant difference ($p<0.05$) in the number of females nesting at untreated sites (n=8) relative to treated sites. Authors state that reduction in vertical screening cover (i.e., canopy) may have a negative impact on the birds.	Haukos and Smith 1989
Plots that had been previously treated at 0.5 lb a.i./acre, area with shinnery oak and sagebrush. Comparison to comparable untreated areas. New Mexico	Study population: female lesser prairie-chickens (*Tympanuchus pallidicinctus*). Slight increase in numbers of birds on treated vs. untreated areas in both winter and summer but these differences are not statistically significant (Table 1.3, p. 14). Differences in predominant foods consumed: Foliage and flowers in treated area, shinnery oak acorns in untreated areas.	Olawsky 1987
Aerial applications (formulation not specified) to 32.4 ha pastures for brush control, primarily oaks. Two control and treated pastures. Oklahoma	Study of diverse species (n=35) of birds. Greater number and diversity of birds on treated sites in both years of study (Table 1 of paper) except for tufted titmouse during study Year 1 (year 5 after applications). Effects of tebuthiuron similar to that of triclopyr – i.e., effects on bird populations probably secondary to changes in vegetation rather than specific herbicide. Decrease in deciduous plants with increase in grass and forbs.	Schulz et al. 1992

Appendix 3: Toxicity to Terrestrial Plants

Table A3-1: Vegetative Vigor

Species	Exposure	Response	Reference
Monocots Corn, Zea mays (Poaceae) Oat, Avena sativa, (Poaceae) Onion, Allium cepa (Liliaceae) Ryegrass, Lolium perenne (Xanthorrhoeaceae)	Spike 20 P Application rate: 0.0078 to 4 lb a.i./acre 21 day observation period	Corn (Fresh weight) NOAEC = 2 lb a.i./acre EC05 = 1.8 lb a.i./acre EC25 = 2.6 lb a.i./acre **Least sensitive monocot** Oats (Shoot length) NOAEC = 0.5 lb a.i./acre EC05 = 0.16 lb a.i./acre EC25 = 0.93 lb a.i./acre Onion (Fresh weight) NOAEC = 0.25 lb a.i./acre EC05 = 0.16 lb a.i./acre EC25 = 0.93 lb a.i./acre Ryegrass (fresh weight) NOAEC = 0.12 lb a.i./acre EC05 = 0.30 lb a.i./acre EC25 = 0.30 lb a.i./acre **Most sensitive monocot** Significant effects on plant fresh weight and shoot weight. Survival was significantly affected in onion and oat.	U.S. EPA/OPP/EFED 2014 MRID 48722704 Supplemental See Table 3.24 in EPA document for toxicity values and Appendix G, p. 117 for study description.
Dicots Carrot, *Daucus carota* (Apiaceae) Cucumber, *Cucumis sativus* (Cucurbitaceae) Cabbage, *Brassicacea oleracea* (Brassicaceae) Soybean, *Glycine max* (Fabaceae) Sugar beet, *Beta vulgaris* (Amaranthaceae) Tomato, Lycopersicon esculentum (Solanaceae)	Spike 20 P (a.i. tebuthiuron) Application rate: 0.002 to 2 or 4 lbs a.i./acre depending on species 21 day observation period	Carrot (Fresh weight) NOAEC = 0.5 lb a.i./acre EC05 = 0.3 lb a.i./acre EC25 = 0.52 lb a.i./acre **Least sensitive dicot** Cucumber (Fresh weight) NOAEC = 0.12 lb a.i./acre EC05 = 0.097 lb a.i./acre EC25 = 0.28 lb a.i./acre Cabbage (Fresh weight) NOAEC = 0.12 lb a.i./acre EC05 = 0.18 lb a.i./acre EC25 = 0.32 lb a.i./acre *Continued on next page*	U.S. EPA/OPP/EFED 2014 MRID 48722704 Supplemental See Table 3.24 in EPA document for toxicity values and Appendix G, p. 117 for study description.

Species	Exposure	Response	Reference
Continuation of U.S. EPA/OPP/EFED 2014 MRID 48722704		Soybean: NOAEC values only Fresh weight: 0.12 lb a.i./acre Shoot length: 0.5 lb a.i./acre Survival: 2 lb a.i./acre Sugar beet (fresh weight) NOAEC = 0.062 lb a.i./acre EC05 = 0.053 lb a.i./acre EC25 = 0.16 lb a.i./acre **Most sensitive dicot** Tomato (fresh weight) NOAEC = 0.25 lb a.i./acre EC05 = 0.25 lb a.i./acre EC25 = 0.43 lb a.i./acre Significant effects on plant fresh weight and shoot weight. Survival was significantly affected in sugar beet.	

Table A3-2: Seedling Emergence

Species	Exposure	Response	Reference [1]
Monocots			
Corn, *Zea mays* (Poaceae) Wheat, *Triticum aestivum* (Poaceae) Sorghum, *Sorghum bicolor* (Poaceae) Rice, *Orya sativa* (Poaceae)	Tebuthiuron, technical grade Application rate: 0.04, 0.08, 0.16, 0.32, 0.64, or 1.28 lb a.i./acre 21 day observation period.	No interference with seedling emergence in any species tested Wheat severely injured 3 weeks after exposure to 0.08 lb a.i./acre and seedlings killed at highest dose (1.28 lb a.i./acre) Corn determined to be intermediate in susceptibility, injured 50% or more at highest level tested. **Most sensitive species**: wheat (based on fresh weight) **NOAEC** = 0.04 lb a.i./acre **21-day EC_{25}** = 0.07 lb a.i./acre	U.S. EPA/OPP/EFED 2014 MRID 41066901 **Acceptable**
Corn, *Zea mays* (Poaceae) Oat, *Avena sativa,* (Poaceae) Onion, *Allium cepa* (Liliaceae) Ryegrass, *Lolium perenne* (Xanthorrhoeaceae)	Spike 20 P Application rate: 0.0078 to 4 lb a.i./acre 21 day observation period	Corn (Shoot length) NOAEC = 2 lb a.i./acre EC_{05} = 1.8 lb a.i./acre EC_{25} = 3.1 lb a.i./acre **Least sensitive monocot** Oats (Fresh weight) NOAEC = 0.5 lb a.i./acre EC_{05} = 0.27 lb a.i./acre EC_{25} = 0.52 lb a.i./acre Onion (Fresh weight) NOAEC = 0.25 lb a.i./acre EC_{05} = 0.23 lb a.i./acre EC_{25} = 0.46 lb a.i./acre Ryegrass (Fresh weight) NOAEC = 0.25 lb a.i./acre EC_{05} = 0.12 lb a.i./acre EC_{25} = 0.27 lb a.i./acre **Most sensitive monocot** Compound-related phytotoxic effects observed in all test species.	U.S. EPA/OPP/EFED 2014 MRID 48722703 **Supplemental** See Table 3.24 in EPA document for toxicity values and Appendix G, p. 117 for study description.

Appendix 3 Toxicity to Terrestrial Plants (*continued*)

Species	Exposure	Response	Reference [1]
Dicots			
Cabbage, *Brassicacea oleracea* (Brassicaceae) Cotton, *Gossypium hirsutum* (Malvaceae) Cucumber, *Cucumis sativus* (Cucurbitaceae) Radish, *Raphanus sativus* (Brassicaceae) Soybean, *Glycine max*(Fabaceae) Sunflower, *Helianthus annuus* (Asteraceae)	Tebuthiuron, technical grade Application rate: 0.02, 0.04, 0.08, 0.16, 0.32, or 0.64 lb a.i./acre for 21 days	No interference with seedling emergence in any species tested Radish determined to be extremely sensitive to 0.08 lb a.i./acre application rate 1 week after emergence Radish, cucumber, and cabbage severely injured 3 weeks after exposure to 0.08 lb a.i./acre and seedlings killed at highest dose (1.28 lb a.i./acre) Rice, cotton, and sunflower determined to be intermediate in susceptibility, injured 50% or more at highest level tested. **Most sensitive species**: cabbage (based on fresh weight) **NOAEC** = 0.02 lb a.i./acre **21-day EC_{25}** = 0.03 lb a.i./acre	U.S. EPA/OPP/EFED 2014 MRID 41066901 **Acceptable**
Carrot, *Daucus carota* (Apiaceae) Cucumber, *Cucumis sativus* (Cucurbitaceae) Cabbage, *Brassicacea oleracea* (Brassicaceae) Soybean, *Glycine max* (Fabaceae) Sugar beet, *Beta vulgaris* (Amaranthaceae) Tomato, *Lycopersicon esculentum* (Solanaceae)	Spike 20 P (a.i. tebuthiuron) Application rate: 0.002 to 2 or 4 lbs a.i./acre depending on species 21 day observation period	Carrot (Fresh weight) NOAEC = 0.031 lb a.i./acre EC_{05} = 0.0032 lb a.i./acre EC_{25} = 0.018 lb a.i./acre **Most sensitive dicot.** Cucumber (Fresh weight) NOAEC = 0.12 lb a.i./acre EC_{05} = 0.13 lb a.i./acre EC_{25} = 0.33 lb a.i./acre Cabbage (Fresh weight) NOAEC = 0.12 lb a.i./acre EC_{05} = 0.14 lb a.i./acre EC_{25} = 0.23 lb a.i./acre Soybean: NOAEC = 1.0 lb a.i./acre EC_{05} = 0.79 lb a.i./acre EC_{25} = 1.2 lb a.i./acre **Least sensitive dicot.** Sugar beet (fresh weight) NOAEC = 0.12 lb a.i./acre EC_{05} = 0.11 lb a.i./acre EC_{25} = 0.20 lb a.i./acre Tomato (fresh weight) NOAEC = 0.062 lb a.i./acre EC_{05} = 0.13 lb a.i./acre EC_{25} = 0.26 lb a.i./acre Significant effects on plant fresh weight and shoot weight. Survival was significantly affected in sugar beet.	U.S. EPA/OPP/EFED 2014 MRID 48722704 **Supplemental** See Table 3.24 in EPA document for toxicity values and Appendix G, p. 117 for study description.

Table A3-3: Other Toxicity Studies

Species	Exposure	Response	Reference
Dicots			
Soybeans (Fabaceae), soil exposures	Tebuthiuron (NOS). Soil exposures Two soils: Eufaula sand: 0.3% OM Hector loam: 4.8% OM	50% inhibition of growth (GR_{50}) Eufaula sand: 0.21 ppm (w/w) Hector loam: 1.03 ppm (w/w) See Table 3	Chang and Stritzke 1977
Catclaw mimosa (Fabaceae)	Tebuthiuron, 10% granular formulation. Equivalent application rates: 0.0175 to 6.72 kg/ha (see Table 2)	100% mortality at rates of 0.07 lb a.i./acre or higher. Time to mortality of 21 to 34 days. 10% mortality at 0.0175 kg/ha, 35 days to mortality. 80% mortality at 0.035 kg/ha, 43 days to mortality See Table 2 of paper	Creager 1992
Kochia scoparia, a.k.a. *Bassia scoparia* Amaranthaceae	Tebuthiuron (NOS) Equivalent application rates of about 0.3 to 9.6 kg/ha (Figure 2)	GR_{50}s: Tolerant Strain: 5.28 kg/ha. Sensitive Strain: 0.14 kg/ha Resistance Ratio: 37.7	Mengistu et al. 2005
Amaranthus retroflexus Amaranthaceae Isolated chloroplasts	Tebuthiuron (NOS) Working Note: Resistance resides in chloroplasts.	50% Inhibition of photosynthetic ferricyanide reduction: Tolerant Strain: ≈0.000016 µMol Sensitive Strain: 0.000001 µMol Resistance Ratio: 16 Note: Paper gives values as negative logs (base 10) of the concentrations.	Oettmeier et al. 1982
Monocots			
Kleingrass (M), *Panicum coloratum* (Poaceae) Greenhouse assay	Tebuthiuron (80% a.i., NOS) Application rates: 0, 0.14, 0.28, 0.56, 1.12 and 2.24 kg/ha. Preemergence and early postemergence. Observations to 2 months	1 month Significant visual injury at all application rates in pre-emergent or early post-emergent applications (Table 1 and 2) 2 months Pre-emergent assay: Significant visual injury at rates of 0.28 kg/ha and above after 2 months (Table 2). NOAEC: 0.14 kg/ha. Post-emergent assay: Significant but lesser injury at 1.12 kg/ha and higher. NOAEC. 0.56 kg/ha.	Bovey et al. 1979
Kleingrass (Poaceae) and six other species of forage crops.	Tebuthiuron (80% a.i., NOS) Application rates: 0, 0.56, 1.12 and 2.24 kg/ha. Mature plants Observations at 2 months	Injury to Kleingrass and other species at 0.56 kg/ha and higher. Least effect on sideoats grama (*Bouteloua curtipendula*, Poaceae) with no clear dose-response. Statistical significance not reported.	Bovey et al. 1979

Species	Exposure	Response	Reference
Corn (Poaceae) soil exposures	Tebuthiuron (NOS). Soil exposures Two soils: Eufaula sand: 0.3% OM Hector loam: 4.8% OM	50% inhibition of growth (GR_{50}) Eufaula sand: 0.48 ppm (w/w) Hector loam: 4.1 ppm (w/w) See Table 3	Chang and Stritzke 1977
Crabgrasses (Poaceae): *Digitaria nuda* and *Digitaria ciliaris*.	Tebuthiuron (NOS) Equivalent application rates: 0, 0.25, 0.5, 1.0, and 2.0 kg/ha. Greenhouse assay	GR_{50}s: *Digitaria nuda*: 0.82 kg/ha. *Digitaria ciliaris*: 0.13 kg/ha Resistance Ratio: 6.3 Working Note: The *D. ciliaris* population had no known prior exposure to herbicide. The *D. nuda* population taken from sugarcane field with prior exposure to triazine herbicides.	Diaz et al. 2005
Crested wheatgrass (*Agropyron cristatum*), seedlings Poaceae	Tebuthiuron, 40% a.i. granular formulation	GR_{50}s: 0.04 ppm in low OC soil 0.12 ppm in intermediate OC soil 0.2 ppm in high OC soil.	Whisenant and Clary 1987

Table A3-4: Efficacy Studies

Target Species (Group[1], Family)	Crop (Nontarget)	Application Rate[2]	Observations [No report of nontarget/crop damage unless otherwise stated.][3]	Reference[4]
Sand shinnery oak (D, Fagaceae)	Grasses	0.2 to 1 kg/ha	Decrease in oak cover and increase in grasses. Increased protein content of grasses with increasing application rate in first but not second year after application (Table 2)	Biondini et al. 1986
Woolly Croton (D, Euphorbiaceae) and Bitter Sneezeweed (D, Asteraceae)	Grasses	0.28, 0.56, and 1.1 kg/ha	Reduction in woolly croton but not bitter sneezeweed. Increase in grass cover in year 2 (Tables 3) but not year 1 (Table 2)	Bovey and Meyer 1990
Western Juniper (Cupressaceae), shrubs and sagebrush (D)	N.S.	2 or 4 kg/ha	Little impact on juniper at 2 kg/ha and only 22% mortality at 4 kg/ha. Substantial mortality in shrubs and sagebrush. Damage to several grasses.	Britton and Sneva 1981
St John's wort (*Hypericum perforatum*) [Hypericaceae]	N.S.	0.8 – 6.4 kg/ha	Ineffective.	Campbell et al. 1991
Woody species	Grasses	3 kg/ha	Substantial decreases in trees and shrubs with increase in grasses during summer (Table 2).	Defazio et al. 1988

Target Species (Group[1], Family)	Crop (Nontarget)	Applic-ation Rate[2]	Observations [No report of nontarget/crop damage unless otherwise stated.][3]	Reference[4]
Various broadleaf and grassy weeds	Dallisgrass (M)	0.6, 0.8, 1.1, 2.2, and 4.4 kg/ha	No nontarget damage at rates up to 1.1 kg/ha. Maximum seedling density at 1.1 kg/ha. Significant increases in nontarget seedling density. Most effective applications were pre-emergent.	Evers 1981
Grasses (M) and forbs (D)	*Opuntia* sp. (D, Cactaceae), prickly pear	4 kg/ha	No damage to nontarget species (cactus). Substantial reduction in grasses and forbs.	Felker and Russell 1988
Crabgrass (M, Poaceae) *Digitaria nuda* (tolerant population) and *Digitaria ciliaris* (sensitive population).	Sugar cane (M, Poaceae)	1 kg/ha	Effective control *Digitaria ciliaris* (100% at 21 DAT) Less effective control *Digitaria nuda* (77% at 21 DAT) No remarks on adverse effects in sugarcane.	Dias et al. 2005
Several species of brush (D)		0.84 kg/ha	Tarbush, *Flourensia cernua*: 100% effective Fourwing saltbush (*Atriplex canescens*): 100% effective Littleleaf sumac, *Rhus microphylla*. Graythorn, *Condalia spathulata*: Ineffective (0% control) See Table 4 for other species responses. Note that all are dicots.	Emmerich et al. 1984
Eastern redcedar (*Juniperus virginiana*, Cupressaceae), oaks, and various brush species		2.2 kg/ha	Ineffective alone for cedar control but more effective with burning so long as tebuthiuron is applied in the same year as burning.	Engle and Stritzke 1995
Creosotebush (*Larrea tridentate*) and other species of brush	Grasses	0.4 kg/ha	Over 5-year post-application period, excellent control of shrubs and substantial increase in grass cover (Table 3). No effect on perennial forbs but an increase in annual forbs (Table 5).	Gibbens et al. 1987
	Buffelgrass (*Cenchrus ciliaris*) (M)	0.6, 1.1, 2.2, 3.3, and 4.4 kg/ha	Damage to buffelgrass at rates of 2.2 kg/ha or higher. Recovery of populations by larger surviving plants.	Hamilton and Scifres 1983
Brush, Site preparation	Loblolly pine	1.5 lb/acre	Significant decrease in brush height at 1 of 2 sites. No significant effects on cover or number of trees or shrubs. No significant damage to pine based on survival and growth (Table 4).	Haywood 1993

Target Species (Group[1], Family)	Crop (Nontarget)	Application Rate[2]	Observations [No report of nontarget/crop damage unless otherwise stated.][3]	Reference[4]
Shrubs (D)	Grasses (bush muhly and bristlegrass.	0.2 to ≈3 hg/ha	Damage to shrubs at all rates. Most sensitive species: *Zinnia acerosa*, 100% control at 0.27 gl/ha (Table 1). Least sensitive species, Honey mesquite, effective control (81-99%) at about 1.5 kg/ha and higher. Increase in grass cover.	Herbel et al. 1985
Broadleaf and grass weeds		2-4 lb a.i./acre	Effective long-term control of both annual grasses and broadleaf weeds.	Lade et al. 1974
Melaleuca (*Melaleuca quinquenervia* (D, Myrtaceae)	Grasses	11.2 kg/ha	Effective (>80%) control of Melaleuca. Secondary note on damage to grasses. Not well described.	Laroche 1998
Broadleaf weeds (D)	Bermudagrass (M)	0.25, 0.5, and 1.0 kg/ha	Dose-related decrease in broadleaf weeds with corresponding increases in Bermudagrass. Sprays somewhat more effective than pellets (Table 3).	Mayeux 1989
Sagebrush (*Artemisia tridentata*) (D)	Grasses	0.6 to 1.1 kg/ha	Effective control of sagebrush. Significant increase in grasses in 2nd and third year after application.	McDaniel and Balliette 1986
Smutgrass (*Sporobolus poiretii*) (M), broadleaf weeds (D)	Other grasses including Bermuda-grass (M)	1.1 and 2.2 kg/ha	Effective reduction in smutgrass and broadleaf weeds particularly at 2.2 kg/ha (Table 3). Increase in nontarget grasses (Table 4). Some applications damaged Bermudagrass (Table 6.)	Meyer and Baur 1979
Woody plants and herbs (D)		1.12 kg/ha	Effective control of most species except blue vervain (*Verbena hastata*).	Meyer and Bovey 1990
Yankeeweed (*Eupatorium compositifolium*), woolly croton (*Croton capitatus*), and partridge pea (*Chamaecrista fasciculata*) (D)	Grasses	0.28, 0.56, and 1.1 kg/ha	Effective control of wooly croton and partridge pea at application rates of 0.56 and 1.1 kg/ha but not at 0.28 kg/ha at 4 months but not 1 month. Ineffective control of Yankeeweed (Table 1). Inconsistent impact on grasses (Table 2). Decrease in some grasses at 2 months after treatment (data not presented).	Meyer and Bovey 1991
Shrubs	Grasses	0.6 and 1.1 kg/ha	Decrease in shrub cover and increase in grass cover. Some detrimental effect on grasses with 40% as opposed to 20% pellet formulations. No substantial impact on forb cover.	Murray 1988

Appendix 3 Toxicity to Terrestrial Plants (*continued*)

Target Species (Group[1], Family)	**Crop (Nontarget)**	**Applic-ation Rate[2]**	**Observations [No report of nontarget/crop damage unless otherwise stated.][3]**	**Reference[4]**
Shrubs and trees		2 kg/ha	Decrease in canopy cover but not completely effective due to high OM and clay content of soil.	Nolte and Fick 1992
Shrubs	Grasses	0.3 to 0.5 lb/acre	Decrease in sagebrush cover and increase in grasses in treated sites. See Appendix 1, Table A1-9 for indirect effects in mammals.	Olson et al. 1994
Shrub (*Dichapetalum cymosum*) (D)		0.03 – 1.2 g/m^2 [3-12 kg/ha]	Only transient (1 year) control at higher application rates. `Working Note: This is an apparently tolerant target species but the study involves a South African plant and the response cannot be characterized as an NOAEL.`	Phillips et al. 1993
Oaks, mixed hardwoods		2.2 kg/ha	Substantial reduction in canopy cover with prescribed burning (Table 2)	Scifres 1987
Various species of brush		1.12 to 4.4 kg/ha	Good control of several brush species at rates of 2.2 kg/ha and higher. Ineffective control, however, of several other species (lime pricklyash, Texas persimmon, prlcklypear, and tasajlllo).	Scifres et al. 1979
Broom Snakeweed (*Xanthocephalum sarothrae*) (D)	Grasses	0.25 to 1 lb/acre	Damage to buffalograss *(Buchloe dactyloides*) (M, Poaceae)	Sosebee et al. 1981
Oaks and other tree species, brush (D)		2.2 kg/ha	Generally effective control of trees and brush. Ineffective control, however, of eastern redcedar (*Juniperus virginiana*, Cupressaceae).	Stritzke et al. 1991
Broad-leaved paperbark tree (*Melaleuca quinquenervia*).,		4.5 to 13.4 hg/ha	Control of melaleuca seedlings at 4.5 kg/ha. Complete mortality at 13.4 kg/ha after 23 weeks. Pellet formulations less effective than WP formulations (Table 1). Tree mortality (100%) at 24 weeks at 11.2 kg/ha for both pellet and WP formulations. Only partial mortality at 4.5 kg/ha (Table 3).	Stocker and Sanders 1997
Hogpotato (*Hoffmannseggia glauca*) (D)	Cotton (D), grain, and wheat (M).	1,1, 2.2 or 3.4 kg/ha	Relatively effective control of hogpotato at 2 sites but not clearly dose-related. Transient control at one site (Table 3). Significant and dose-related damage to all three nontarget crops (Table 5).	Westerman et al. 1993

Target Species (Group[1], Family)	**Crop (Nontarget)**	**Applic-ation Rate[2]**	**Observations [No report of nontarget/crop damage unless otherwise stated.][3]**	**Reference[4]**
Sagebrush, *Artemisia* sp. (D)	Grasses	0.6 to 1.1 kg/ha	Adequate control of big sagebrush (*Artemisia tridentata*). Incomplete control of silver sagebrush (*Artemisia cana*). Other dicots (blue grama and plains pricklypear) not damaged at highest application rates Most grasses tolerant. Western wheatgrass and prairie junegrass cover reduced at one site.	Whitson and Alley 1984
Sand sagebrush (*Artemisia filifolia*) and Brittle prickly pear (*Opuntia fragilis*) (D, Cactaceae)	Grasses	0.4, 0.5, 0.6, and 0.7 kg/ha	Effective against sagebrush at 0.6 and 0.7 kg/ha. Ineffective against prickly pear. Increase in prickly pear at 0.6 and 0.7 kg/ha due to less competition from grasses. Visible damage to grasses [data not given in paper.]	Wilson 1989

[1] (M) – monocot; (D) – dicot
[2] All applications in units of a.i. unless otherwise specified.
[3] Table designations in the response column refer to tables from the paper given in the reference column.
[4] Does not include spot treatments of individual target plants with no information on nontarget impacts (e.g., Bing and Corell 1979; Bruce et al. 1997; Meyer and Bovey 1988; Miller 19898; Petersen and Ueckert 1992).

Appendix 4: Toxicity to fish.

Table A4-1: Acute Toxicity

Species	Exposure	Response	Reference
Freshwater			
Bluegill sunfish, *Lepomis macrochirus*, 10/test level	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 1, 10, 50, 87, 120, or 160 mg a.i./L	96-hour LC_{50} =106 mg a.i./L 95% CI = 87 - 120 mg a.i./L *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00020661 **Acceptable**
Goldfish, *Carassius auratus*, 10/replicate, up to 6 replicates, depending on which test was performed	Tebuthiuron (>97%) Nominal concentrations: 0, 5, 10, 20, 40, 80, or 160 mg a.i./L (**without solvent)** Nominal concentrations: 0, 6.23, 12.5, 25, 50, or 100 mg a.i./L (**with solvent)** Nominal concentrations: 0.33, 0.67, or 1.33 ml/L (**solvent alone)** **Solvent not specified**	Only one mortality observed throughout the tests. 96-hour LC_{50} >160 mg a.i./L *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00020661 **Supplemental** (*several departures from guideline protocols)* Appears to be identical to open literature publication by Todd et al. 1974.
Fathead minnow, P*imephales promelas*,10/test level	Tebuthiuron (98% a.i.); tebuthiuron (80% wettable powder); or tebuthiuron (20% pelleted formulation) Nominal concentrations: 0, 70, 90. 110, 140, or 180 mg a.i./L	Sublethal effects, exploratory behavior and hypoactivity, observed at ≥140 mg a.i./L Fish exposed to 70, 90, or 110 mg a.i./L appeared normal with the exception of less aggressive feeding activity, compared with controls. 96-hour LC_{50} >180 mg a.i./L (for TGAI and formulations) *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00041685 **Supplemental** (*study deviates from recommended protocol and presents inadequate reporting of the data)*
Rainbow trout, *Oncorhynchus mykiss*, 10/test level	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 1, 10, 50, 87, 120, or 160 mg a.i./L	96-hour LC_{50} =143 mg a.i./L 95% CI = 118 – 224 mg a.i./L *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00020661 **Acceptable**
Estuarine/ Marine			
Sheepshead minnow, *Cyprinodon variegates*	Tebuthiuron (NOS) Nominal concentrations: 0, 6.3, 13, 25, 50, or 100 mg a.i./L under static renewal conditions Mean-measured: <0.42, 6.5, 13, 25, 50 or 98 mg a.i./L	No mortality observed. 96-hour LC_{50} >98 mg a.i./L NOAEC = 50 mg a.i./L (based on sublethal effects – loss of equilibrium – observed at 98 mg a.i./L) *Practically nontoxic up to the exposure levels tested*	U.S. EPA/OPP/EFED 2014 MRID 48722702 **Acceptable**

Table A4-2: Chronic toxicity

Species	Exposure	Response	Reference
Rainbow trout, *Oncorhynchus Mykiss*, 50 eyed embryos/treatment, two replicates	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 3.1, 6.2, 12.5, 25, or 50 mg a.i./L for 45 days Mean-measured: 0, 3.1, 6.3, 12.5, 25, or 52 mg a.i./L 45 day exposure period. Embryo/larva assay	Hatching = 100% in replicate aquaria; statistically and biologically significant reduction of larvae survival observed only at the highest test concentration at days 30 and 45; behavior and feeding response in treated larvae groups considered normal, compared with controls; significantly reduced length of larvae exposed to the highest test concentration observed at days 30 and 45, which correlated well with average weight of control larvae. **NOAEC** = 26 mg a.i./L (based on significant reduction in survival and size of larvae at 52 mg a.i./L – highest test concentration) **LOAEC** = 52 mg a.i./L (based on adult survival and length)	U.S. EPA/OPP/EFED 2014 MRID 00090083 **Acceptable**
Fathead minnow, *Pimephales promelas*, 50 embryos/treatment, two replicates	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 5, 10, 20, 40, or 80 mg a.i./L for 33 days under flow-through conditions Mean-measured: 0, 4.7, 9.3, 18, 38, or 76 mg a.i./L 33 day exposure period. Embryo/larva assay	No significant effects on hatching or survival at concentrations as high as76 mg a.i./L; statistically significant reduction in length of larvae in the 18, 38, and 76 mg a.i./L groups. **NOAEC** = 9.3 mg a.i./L (length) **LOAEC** = 18 mg a.i./L	U.S. EPA/OPP/EFED 2014 MRID 00090084 **Acceptable** Also published in Meyerhoff et al. 1985.

Table A4-3: Mesocosm Studies

Species	Exposure	Response	Reference
Fathead minnow, *Pimephales promelas*. In outdoor 2,846 L water from local pond and 6 cm topsoil mesocosms with naturally developing algal and invertebrate communities.	Tebuthiuron (97.5% purity) Nominal Conc.: 0 (control), 10, 70, 200, 500, and 1000 µg/L. 3 replicated for control and 200 µg/L concentration. No replicates for other levels. 30-day pre-treatment period for algae and invertebrates. Fish add one day prior to treatment. Tebuthiuron analyses on treatment days - 1, 1, 3, 7, 14, 34, 64, and 108. Metabolites not assayed. Observations on fish on days 3, 7, 14, 41, 56, 116.	Based on the data in Tables 5 and 7 of paper, no concentration response is apparent for concentrations of 10, 70, 200, and 500 µg/L. Also based on data in Table 5 of paper, a decrease in fish biomass is apparent at 1,000 µg/L (53.79 g fish/mesocosm) relative to controls (65.44 g fish/ mesocosm). `Working Note: Authors state that fish biomass was not affected by treatment (p. 125, bottom of page). Cannot directly assess whether decrease at 1000 µg/L was statistically significant.` Concentrations of tebuthiuron: Reductions to nominal concentrations noted (Table 2 of paper). For the nominal concentration of 1000 µg/L, concentrations were reduced to 790 µg/L by Day 108. NOAEL (biomass): 500 µg/L (nominal), 350 µg/L (measured per Table 2 of study). Note: Results for midge larvae in Appendix 5, Table A5-3 and results for algae summarized in Appendix 6, Table A6-3	Temple et al. 1991

Appendix 5: Toxicity to aquatic invertebrates

Table A5-1: Acute Toxicity

Species	Exposure	Response	Reference
Freshwater			
Water flea, *Daphnia magna*, 10-hours-old, 1st instar, 9, 10, 11/test vessel.	Tebuthiuron (99.2% a.i.) Nominal concentrations: 0, 225, 300 or 400 mg a.i./L	48-hour EC_{50} = 297 mg a.i./L 95% CI = 279 - 316 mg a.i./L *Practically nontoxic* Working Note: This EC_{50} is given in ECOTOX (http://cfpub.epa.gov/ecotox/report.cfm?type=long&record_number=2104850) but an NOAEC is not reported in ECOTOX or in the EPA risk assessment.	U.S. EPA/OPP/EFED 2014 MRID 00041694 **Acceptable**
Estuarine/Marine			
Eastern oyster, *Crassostrea virginica*, shell deposition.	Tebuthiuron (NOS) Nominal concentrations: 0, 6.3, 13, 25, 50, or 100 mg a.i./L Mean-measured: <LOD, 6.5, 14, 26, 50, or 95 mg a.i./L	96-hour EC_{50} >95 mg a.i/L based on shell deposition *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 48722701 **Acceptable**
Eastern oyster, *Crassostrea virginica*, embryos, three replicates per level, 27,000 ± 1350 embryos/replicate	Tebuthiuron (NOS) Nominal concentrations: 0, 32, 56, 100, 180, or 320 mg a.i./L	100% mortality observed at highest test concentration (320 mg a.i./L); embryos at all other test concentrations were normal at test termination, 48-hour **definite** LC_{50} not calculated 48-hour **estimated** LC_{50} >180 and <320 mg a.i./L *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00041684 **Acceptable**
Fiddler crab, *Uca pugilator*	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 10, 32, 100, 180, or 320 mg a.i./L	96-hour LC_{50} >320 mg a.i/L *Practically nontoxic*	U.S. EPA/OPP/EFED 2014 MRID 00041684 **Supplemental**
Pink shrimp, *Penaeus duorarum*	Tebuthiuron (98% a.i.) Nominal concentrations: 0, 10, 32, 100, 180, or 320 mg a.i./L	96-hour LC_{50} = 62 mg a.i./L 95% CI = 39 – 90 mg a.i./L *Slightly toxic to pink shrimp* Working Note: This EC_{50} is given in ECOTOX (http://cfpub.epa.gov/ecotox/report.cfm?type=long&record_number=2113047) but an NOAEC is not reported in ECOTOX or in the EPA risk assessment.	U.S. EPA/OPP/EFED 2014 MRID 00041684 **Acceptable**

Table A5-2: Chronic toxicity

Species	Exposure	Response	Reference
Water flea, *Daphnia magna*, <24-hours 1st instar, 10 replicates/treatment level; 7 replicates with one daphnia each used for fecundity; 3 replicates of five daphnia each used for survival data	Tebuthiuron (97.4% a.i.) Nominal concentrations: 0, 5.63, 11.25, 22.5, 45, or 90 mg a.i./L under static renewal conditions in 21-day full life cycle study Mean-measured: 0, 5.47, 11, 21.8, 44.2, or 90.2 mg a.i./L	No significant mortality occurred at any test concentrations; at 44.2 and 90.2 mg a.i./L there was a significant reduction in daphnia length as well as the number of broods per reproducing adult and number of offspring per adult, compared with controls; at 90.2 mg a.i./L, daphnia required significantly longer time to release their first brood. **NOAEC** = 21.8 mg a.i./L (based on significant differences in growth, fecundity, time of first brood release, and young per adult) **LOAEC** = 44.2 mg a.i./L	U.S. EPA/OPP/EFED 2014 MRID 00138700 **Acceptable** Also published in Meyerhoff et al. 1985.

Table A5-3: Mesocosm Studies

Species	Exposure	Response	Reference
Invertebrate communities in mesocosm with algae and fish. Only Midge larvae assayed quantitatively.	Tebuthiuron (97.5% purity) Nominal Conc.: 0 (control), 10, 70, 200, 500, and 1000 µg/L. 3 replicated for control and 200 µg/L concentration. No replicates for other levels. 30-day pre-treatment period for algae and invertebrates. Invertebrates (midge larvae only) assayed on treatment days -3, 7, 64, 106.	Midge larvae: Decrease in density and biomass with increasing concentrations. Authors do not estimate a NOAEC. Based on data from Table 5 of paper, no effects are apparent at 10 or 70 µg/L (nominal). Increase in biomass at 70 µg/L (not clear if this is significant). Clear decrease in larval density at 200 µg/L (p=0.027). Apparent NOAEC: 70 µg/L LOAEC: 200 µg/L Working Note: Decrease midge larvae biomass may have been secondary to decrease in primary production.	Temple et al. 1991

Appendix 6: Toxicity to Aquatic Plants

Table A6-1: Algae

Species	Exposure	Response	Reference
Freshwater green alga, *Selenastrum capricornutum*	Tebuthiuron (98% a.i.) Nominal concentrations: 0 (negative control), 5, 10, 15, 20, 40, 80, 160, or 320 µg/L under static conditions for 14 days. Mean-measured concentrations: 0 (control; LOD <0.5, µg/L), 5, 10, 13, 16, 33, 79, 168, or 338 µg a.i./L Duration: 14 days	After 5 days, the percent inhibition in biomass, relative to controls, ranged from 0% - 83% **NOAEC** = 13 µg a.i./L **5-day EC_{50}** = 50 µg a.i./L (based on biomass). Working Note: Meyerhoff et al. (1985) give an EC_{50} of 307 µg/L . The NOAEC is reported as 16 µg/L (nominal).	U.S. EPA/OPP/EFED 2014a MRID 00138697 **Supplemental** (does not satisfy guideline requirement for Tier II algal toxicity study with freshwater green algae) Also published in Meyerhoff et al. 1985.
Freshwater green alga, *Selenastrum capricornutum*	Tebuthiuron (99% purity) Nominal Concentrations: Observation period: 96 hours Endpoint: microplate assay (i.e., cell counts)	96 h-EC_{50}: 102 (49-134) µg/L	Hickey et al. 1991
Freshwater green alga, *Selenastrum capricornutum*	Tebuthiuron (99% purity) 4-hour exposure Endpoints: ATP assay at 4-hours and cell count assay at 96 hours.	NOAEC: 100 mg/L Working Note: This seems somewhat remarkable, suggesting that transient high exposures will have no effect. Results not given in a table. See discussion on bottom of p. 395	Hickey et al. 1991
Freshwater green alga, *Selenastrum capricornutum*	Tebuthiuron (NOS) Nominal Concentrations: 0, 5, 10, 50, 100, and 500 µg/L 1 to 7 day periods of observation. Duration: 7 days	Estimated NOAEC values of 10 or 50 µg/L depending on endpoint duration of exposure. See Table 5 of paper. LOAECs: 50 or 100 µg/L	Adams et al. 1985
Symbiotic dinoflagellate in coral branches	Tebuthiuron (NOS) 10-hour exposure Concentrations: ≈0.02 to 1,000 µg/L (Figure 1) Endpoint: Reduction in effective quantum yield of chloroplasts using fluorometry.	10 h-EC_{50}: 175±7 µg/L LOAEC: 10 µg/L NOAEC: 3 µg/L See Figure 1 and text, p. 153 of paper.	Jones and Kerswell 2003 See Schreiber and Berry 1977 for methods.

Appendix 6: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Freshwater blue-green *algae*, *Anabaena flos-aquae*	Tebuthiuron (99.08% a.i.) Nominal concentrations: 0 (negative control), 0.31, 0.62, 1.25, 2.5, 5, or 10 mg a.i./L for 7 days. Mean-measured concentrations: <0.012 (<LOD), 0.31, 0.62, 1.32, 2.62, 5.49, or 11.05 mg a.i./L. Duration: 96 hours	Percent inhibition in yield based on cell density, relative to controls, was the most sensitive endpoint **NOAEC** <0.31 mg a.i./L **EC_{05}** =0.03 mg a.i./L **96-hour EC_{50}** = 0.81 mg a.i./L (cell density) 95% CI = 0.59 – 1.12 mg a.i/L	U.S. EPA/OPP/EFED 2014a MRID 41080401 **Supplemental** (does not satisfy guideline requirement for Tier II algal toxicity study with freshwater blue-green algae)
Freshwater diatom, *Navicula pelliculosa*	Tebuthiuron (NOS.) Nominal concentrations0 (negative control), 0.005, 0.01, 0.05, 0.1, 0.2, 0.4, or 0.8 mg a.i./L for 7 days. Mean-measured concentrations: <0.005 (<LOD), 0.0012, 0.011, 0.056, 0.11, 0.22, 0.46, or 0.89 mg a.i./L	Significant reduction in yield at the four highest test concentrations, relative to controls, was the most sensitive endpoint. **NOAEC** = 0.056 mg a.i./L **96-hour EC_{50}** = 0.09 mg a.i./L for area under the growth curve.	U.S. EPA/OPP/EFED 2014a MRID 41080403 **Supplemental** (does not satisfy guideline requirement for Tier II algal toxicity study with freshwater diatom)
Marine diatom, *Navicula* sp.	Tebuthiuron (NOS) Endpoint: Inhibition of photosystem II using fluorometry. Exposure period: 150 minutes (2.5 hours).	EC_{50}: 94 µg/L LOAEC: 8.7 µg/L `Working Note: Very short-term exposure. Note similarity of this short-term EC50 with the above 96-h EC50. Contrast with S. capricornutum.`	Magnusson et al. 2010
Phaeodactylum tricornutuma, diatom	Tebuthiuron (NOS) Endpoint: Inhibition of photosystem II using fluorometry. Exposure period: 150 minutes (2.5 hours).	EC_{50}: 51.4 µg/L LOAEC: 8.7 µg/L	Magnusson et al. 2010
Cylindrotheca closterium, marine diatom	Tebuthiuron (NOS) Endpoint: Inhibition of photosystem II using fluorometry. Exposure period: 150 minutes (2.5 hours).	EC_{50}: 76.9 µg a.i./L LOAEC: 8.7 µg a.i./L	Magnusson et al. 2010
Nephroselmis pyriformis, marine green algae.	Tebuthiuron (NOS) Endpoint: Inhibition of photosystem II using fluorometry. Exposure period: 150 minutes (2.5 hours).	EC_{50}: 11.9 µg/L LOAEC: 1.1 µg/L	Magnusson et al. 2010

Species	Exposure	Response	Reference
Marine diatom, *Skeletonema costatum*	Tebuthiuron (99.08% a.i.) Nominal concentrations: 0 (negative control), 0.002, 0.01, 0.02, 0.04, 0.08, 0.16, or 0.32 mg a.i./L under static conditions for 7 days. Mean-measured concentrations: 0.0018, 0.0092, 0.018, 0.038, 0.076, 0.16, and 0.3 mg a.i./L	Percent inhibition yield was the most sensitive endpoint. **NOAEC** = 0.038 mg a.i./L (based on significant reductions in three highest test levels, relative to controls) **96-hr EC_{50}** = 0.05 mg a.i./L (for yield)	U.S. EPA/OPP/EFED 2014a MRID 41080402 **Supplemental** (three replicates/treatment level were used; EPA requires four replicates/level)
4 species of algae, 6 species of cyanobactiera	Tebuthiuron (NOS), 5.867 mg/L Duration: 22 hours Note: Studied the phytotoxicity of the expected environmental concentrations (EEC).	26% to 100% reduction of growth. Statistically significant reductions for all organisms. Most tolerant species: *Anabaena inaequalis* with 26% inhibition. `Working Note: Given the high concentration assayed (5,867 µg/L) these results are consistent with the rest of the literature.`	Peterson et al. 1994

Table A6-2: Macrophytes

Species	Exposure	Response	Reference
Duckweed, *Lemna gibba*	Tebuthiuron (99.08% a.i.) Mean-measured concentrations: <0.005 (<LOD), 0.005, 0.0096, 0.049, 0.091, 0.19, 0.38, or 0.78 mg a.i./L for 14 days	Yield in frond dry weight was the most sensitive endpoint. 7-Day (frond count) **NOAEC** = 0.05 mg a.i./L **EC_{50}** = 0.13 mg a.i./L 95% CI = 0.06-0.26 mg a.i./L 14-Day (frond weight) **NOAEC** = 0.091 mg a.i./L **EC_{50}** = 0.126 mg a.i./L	U.S. EPA/OPP/EFED 2014a MRID 41080404 **Supplemental** (does not satisfy guideline requirement for Tier II aquatic vascular plant toxicity study)
Duckweed, *Lemna minor*	Tebuthiuron (NOS), 5.867 mg/L Duration: 7 days	100% inhibition of growth. As with algal assay (Table A6-1), the results are consistent with other study (MRID 41080404 above).	Peterson et al. 1994

Table A6-3: Microcosm/Mesocosm Studies

Species	Exposure	Response	Reference
Naturally occurring periphyton communities, Primarily filamentous cyanophytes, green algae and diatoms (microcosms)	Tebuthiuron, 80% WP formulation (NOS) Nominal Concentrations: 0, 52, 137, 247, and 427 µg/L Duration: 20 minutes to 4 hours (p. 127).	NOAEC: 52 µg/L LOAEC: 137 µg/L	Day 1993
11 species of green algae. At total of 129 control microcosms and 111 treated microcosms	Tebuthiuron (97.4% TGAI) Single conc.: 180 µg/L Duration: range from 25 days to 253 days (including a 21 day acclimation period). 66 cultures treated before maximum growth (Treatment 1 in paper) 45 cultures treated after maximum growth (Treatment 2 in paper)	Treatment 1: Significant inhibition only in *Bracteacoccus minor*. Total packed cell volumes were reduced in Treatment 1 (substantial) and Treatment 2 (modest). See Table 2. Significant decreases in chlorophyll (Treatment 1 only. See Table 3).	Price et al. 1989
Naturally developing algal communities in mesocosms with fish and aquatic invertebrates.	Tebuthiuron (97.5% purity) Nominal Conc.: 0 (control), 10, 70, 200, 500, and 1000 µg/L. 3 replicated for control and 200 µg/L concentration. No replicates for other levels. 30-day pre-treatment period for algae and invertebrates. Primary production assayed on treatment days -9, -7, -1, 1, 2, 3, 5, 7, 11, 14, 35, 42, 57, 64, 106.	Primary Production: Decrease with increasing concentration. Based on data from Table 4 of paper, differences from controls (n=3) do not appear to be significant until DAT 11. Clear concentration response relationship at DAT 42, 57, and 64. No significant differences between controls (n=3) and replicates of 200 µg/L (n=3). The apparent NOAEC on Day 11 is 200 µg/L. Over all durations, the apparent NOAEC is 200-500 µg/L (authors' conclusions on p. 122).	Temple et al. 1991

Appendix 7: Gleams-Driver Modeling, Liquid formulations

Table A7-1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0136 (0 - 0.076)	0 (0 - 0.00296)	0 (0 - 0)
Dry and Temperate Location	0.0119 (0.00025 - 0.056)	1.68E-05 (0 - 0.00262)	0 (0 - 0)
Dry and Cold Location	0.0296 (0.0059 - 0.077)	0 (0 - 0.00182)	0 (0 - 0)
Average Rainfall and Warm Location	0.098 (0.038 - 0.172)	0.0041 (0.00046 - 0.0206)	0 (0 - 8.50E-10)
Average Rainfall and Temperate Location	0.096 (0.043 - 0.184)	0.0033 (0.000064 - 0.0201)	0 (0 - 0)
Average Rainfall and Cool Location	0.168 (0.056 - 0.264)	0.0091 (0.00058 - 0.0294)	0 (0 - 0)
Wet and Warm Location	0.139 (0.0284 - 0.32)	0.0086 (0.000152 - 0.041)	0 (0 - 6.00E-09)
Wet and Temperate Location	0.153 (0.057 - 0.288)	0.0079 (0.00036 - 0.035)	0 (0 - 0)
Wet and Cool Location	0.129 (0.0265 - 0.222)	0.0057 (0.000198 - 0.0275)	0 (0 - 0)
Average of Central Values:	0.093	0.0043	0
25th Percentile:	0.0296	1.68E-05	0
Maximum:	0.32	0.041	6.00E-09
Summary:	0.093 (0.0296 - 0.32)	0.0043 (1.68E-05 - 0.041)	0 (0 - 6.00E-09)

NOTE: Average of values for clay and loam: 0.04865 (0.014808-0.1805). Round to one significant digit for risk assessment 0.05 (0.01-0.2). See Section 4.2.4.3 for discussion.

Table A7-2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.43 (0.42 - 0.43)	0.4 (0.4 - 0.41)	0.4 (0.38 - 0.41)
Dry and Temperate Location	0.45 (0.44 - 0.45)	0.42 (0.4 - 0.43)	0.42 (0.33 - 0.42)
Dry and Cold Location	0.47 (0.47 - 0.47)	0.44 (0.44 - 0.44)	0.44 (0.42 - 0.44)
Average Rainfall and Warm Location	0.39 (0.34 - 0.41)	0.34 (0.25 - 0.39)	0.249 (0.224 - 0.33)
Average Rainfall and Temperate Location	0.41 (0.289 - 0.43)	0.34 (0.238 - 0.41)	0.246 (0.223 - 0.34)
Average Rainfall and Cool Location	0.4 (0.293 - 0.43)	0.35 (0.239 - 0.4)	0.253 (0.223 - 0.32)
Wet and Warm Location	0.264 (0.238 - 0.33)	0.227 (0.223 - 0.264)	0.223 (0.223 - 0.224)
Wet and Temperate Location	0.26 (0.229 - 0.32)	0.228 (0.222 - 0.256)	0.223 (0.221 - 0.224)
Wet and Cool Location	0.29 (0.239 - 0.36)	0.234 (0.223 - 0.277)	0.223 (0.223 - 0.224)
Average of Central Values:	0.37	0.33	0.297
25th Percentile:	0.29	0.234	0.223
Maximum:	0.47	0.44	0.44
Summary:	0.37 (0.29 - 0.47)	0.33 (0.234 - 0.44)	0.297 (0.223 - 0.44)

Table A7-3: Concentration in Top 36 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.142 (0.14 - 0.144)	0.134 (0.132 - 0.135)	0.134 (0.132 - 0.135)
Dry and Temperate Location	0.15 (0.148 - 0.151)	0.141 (0.14 - 0.142)	0.141 (0.14 - 0.142)
Dry and Cold Location	0.157 (0.156 - 0.158)	0.148 (0.147 - 0.148)	0.148 (0.147 - 0.148)
Average Rainfall and Warm Location	0.138 (0.13 - 0.141)	0.132 (0.128 - 0.133)	0.126 (0.088 - 0.132)
Average Rainfall and Temperate Location	0.146 (0.139 - 0.148)	0.14 (0.127 - 0.141)	0.131 (0.089 - 0.14)
Average Rainfall and Cool Location	0.146 (0.14 - 0.151)	0.143 (0.131 - 0.144)	0.136 (0.081 - 0.143)
Wet and Warm Location	0.131 (0.095 - 0.14)	0.112 (0.075 - 0.131)	0.076 (0.074 - 0.094)
Wet and Temperate Location	0.136 (0.103 - 0.147)	0.118 (0.075 - 0.136)	0.075 (0.074 - 0.087)
Wet and Cool Location	0.147 (0.097 - 0.151)	0.128 (0.077 - 0.143)	0.077 (0.074 - 0.097)
Average of Central Values:	0.144	0.133	0.116
25th Percentile:	0.138	0.128	0.077
Maximum:	0.158	0.148	0.148
Summary:	0.144 (0.138 - 0.158)	0.133 (0.128 - 0.148)	0.116 (0.077 - 0.148)

Table A7-4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	18 (8 - 30)	18 (4 - 36)	18 (8 - 36)
Dry and Temperate Location	24 (12 - 36)	24 (8 - 36)	36 (8 - 36)
Dry and Cold Location	30 (24 - 36)	30 (18 - 36)	36 (24 - 36)
Average Rainfall and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average of Central Values:	32	32	34
25th Percentile:	30	30	36
Maximum:	36	36	36
Summary:	32 (30 - 36)	32 (30 - 36)	34 (36 - 36)

Table A7-5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	29.6 (0 - 116)	0 (0 - 7.3)	0 (0 - 0.7)
Dry and Temperate Location	21.4 (0.9 - 119)	0.06 (0 - 6.7)	0 (0 - 17.6)
Dry and Cold Location	64 (13.2 - 162)	0.000024 (0 - 6.8)	0.005 (0 - 18.6)
Average Rainfall and Warm Location	77 (19 - 140)	10.3 (2.35 - 64)	67 (18.2 - 125)
Average Rainfall and Temperate Location	66 (22.7 - 154)	8.7 (1.26 - 80)	63 (26.5 - 122)
Average Rainfall and Cool Location	121 (48 - 231)	16.8 (4.2 - 81)	66 (28.5 - 127)
Wet and Warm Location	104 (36 - 189)	31 (17.8 - 60)	59 (42 - 113)
Wet and Temperate Location	116 (60 - 209)	30.8 (17 - 54)	65 (44 - 117)
Wet and Cool Location	105 (54 - 184)	33 (25.3 - 58)	69 (49 - 151)
Average of Central Values:	78.2	14.5	43.2
25th Percentile:	64	0.06	0.005
Maximum:	231	81	151
Summary:	78.2 (64 - 231)	14.5 (0.06 - 81)	43.2 (0.005 - 151)

Table A7-6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.14 (0 - 0.5)	0 (0 - 0.024)	0 (0 - 0.002)
Dry and Temperate Location	0.12 (0.004 - 0.4)	0.00025 (0 - 0.019)	0 (0 - 0.23)
Dry and Cold Location	0.28 (0.07 - 0.6)	1.2E-07 (0 - 0.019)	0.000024 (0 - 0.22)
Average Rainfall and Warm Location	0.6 (0.3 - 0.9)	0.16 (0.018 - 2.26)	2.56 (0.6 - 6.4)
Average Rainfall and Temperate Location	0.5 (0.3 - 1.88)	0.27 (0.02 - 4.3)	3.6 (0.7 - 9)
Average Rainfall and Cool Location	0.8 (0.5 - 2.42)	0.5 (0.08 - 6.1)	4.8 (1.49 - 10.2)
Wet and Warm Location	2.41 (0.6 - 6.7)	4.6 (2.29 - 7.3)	6.1 (4.4 - 8.1)
Wet and Temperate Location	2.43 (0.8 - 6)	4.3 (2.05 - 7.2)	5.8 (4.4 - 8.8)
Wet and Cool Location	3.11 (1.11 - 6.9)	5.5 (3.7 - 7.6)	6.1 (4.9 - 8)
Average of Central Values:	1.15	1.7	3.22
25th Percentile:	0.28	0.00025	2.40E-05
Maximum:	6.9	7.6	10.2
Summary:	1.15 (0.28 - 6.9)	1.7 (0.00025 - 7.6)	3.22 (2.40E-05 - 10.2)

Table A7-7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	15.2 (0 - 88)	0 (0 - 3.6)	0 (0 - 0.3)
Dry and Temperate Location	12.8 (0.27 - 62)	0.024 (0 - 3.4)	0 (0 - 23.1)
Dry and Cold Location	32 (6.2 - 87)	0.000013 (0 - 2.02)	0.0027 (0 - 28.5)
Average Rainfall and Warm Location	120 (63 - 225)	38 (4.8 - 440)	510 (86 - 1200)
Average Rainfall and Temperate Location	113 (62 - 285)	39 (3.5 - 590)	530 (108 - 1500)
Average Rainfall and Cool Location	206 (116 - 350)	69 (13.8 - 790)	650 (207 - 1640)
Wet and Warm Location	204 (71 - 540)	370 (156 - 850)	600 (340 - 1080)
Wet and Temperate Location	184 (71 - 360)	221 (102 - 390)	259 (122 - 680)
Wet and Cool Location	183 (58 - 390)	301 (148 - 470)	302 (115 - 560)
Average of Central Values:	119	115	317
25th Percentile:	32	0.024	0.0027
Maximum:	540	850	1640
Summary:	119 (32 - 540)	115 (0.024 - 850)	317 (0.0027 - 1640)

Table A7-8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	8.8 (0 - 60)	0 (0 - 2.52)	0 (0 - 0.19)
Dry and Temperate Location	8 (0.24 - 37)	0.004 (0 - 2.6)	0 (0 - 19.7)
Dry and Cold Location	19.1 (4.9 - 52)	0.000006 (0 - 1.11)	0.0011 (0 - 8.4)
Average Rainfall and Warm Location	85 (34 - 180)	16.3 (2.52 - 193)	245 (29 - 700)
Average Rainfall and Temperate Location	90 (48 - 179)	17.6 (1.87 - 340)	267 (26.8 - 920)
Average Rainfall and Cool Location	157 (88 - 266)	31.2 (5.2 - 400)	304 (83 - 1140)
Wet and Warm Location	94 (30.7 - 244)	160 (69 - 500)	272 (144 - 600)
Wet and Temperate Location	92 (32 - 168)	109 (51 - 211)	123 (45 - 287)
Wet and Cool Location	54 (16.5 - 220)	120 (69 - 276)	180 (47 - 316)
Average of Central Values:	67.5	50.5	155
25th Percentile:	19.1	0.004	0.0011
Maximum:	266	500	1140
Summary:	67.5 (19.1 - 266)	50.5 (0.004 - 500)	155 (0.0011 - 1140)

Appendix 8: Gleams-Driver Modeling, Granular formulations

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.0137 (0 - 0.069)	0 (0 - 0.0042)	0 (0 - 1.14E-05)
Dry and Temperate Location	0.0129 (0.000236 - 0.058)	0.000043 (0 - 0.0056)	0 (0 - 0.000071)
Dry and Cold Location	0.0302 (0.0054 - 0.078)	0 (0 - 0.00178)	0 (0 - 0)
Average Rainfall and Warm Location	0.096 (0.042 - 0.21)	0.0044 (0.00043 - 0.0229)	0.00005 (0 - 0.00182)
Average Rainfall and Temperate Location	0.096 (0.033 - 0.205)	0.00304 (0.000146 - 0.0261)	7.40E-06 (0 - 0.00121)
Average Rainfall and Cool Location	0.168 (0.074 - 0.262)	0.0086 (0.00065 - 0.0245)	1.90E-06 (0 - 0.00037)
Wet and Warm Location	0.138 (0.039 - 0.34)	0.0127 (0.00039 - 0.053)	0.00032 (5.20E-07 - 0.0055)
Wet and Temperate Location	0.147 (0.04 - 0.272)	0.0075 (0.000213 - 0.033)	0.000033 (8.30E-10 - 0.00266)
Wet and Cool Location	0.132 (0.071 - 0.252)	0.0064 (0.000207 - 0.0254)	8.20E-06 (0 - 0.00143)
Average of Central Values:	0.093	0.0047	4.70E-05
25th Percentile:	0.0302	4.30E-05	0
Maximum:	0.34	0.053	0.0055
Summary:	0.093 (0.0302 - 0.34)	0.0047 (4.30E-05 - 0.053)	4.70E-05 (0 - 0.0055)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.43 (0.42 - 0.43)	0.42 (0.4 - 0.43)	0.42 (0.4 - 0.43)
Dry and Temperate Location	0.45 (0.44 - 0.45)	0.43 (0.41 - 0.45)	0.43 (0.34 - 0.45)
Dry and Cold Location	0.47 (0.47 - 0.47)	0.46 (0.44 - 0.47)	0.46 (0.42 - 0.47)
Average Rainfall and Warm Location	0.39 (0.32 - 0.42)	0.33 (0.262 - 0.38)	0.268 (0.239 - 0.36)
Average Rainfall and Temperate Location	0.4 (0.3 - 0.43)	0.35 (0.271 - 0.39)	0.266 (0.237 - 0.32)
Average Rainfall and Cool Location	0.4 (0.32 - 0.43)	0.35 (0.266 - 0.4)	0.274 (0.239 - 0.36)
Wet and Warm Location	0.271 (0.238 - 0.33)	0.245 (0.236 - 0.269)	0.239 (0.233 - 0.24)
Wet and Temperate Location	0.261 (0.226 - 0.307)	0.242 (0.229 - 0.272)	0.239 (0.229 - 0.24)
Wet and Cool Location	0.297 (0.244 - 0.36)	0.254 (0.239 - 0.3)	0.239 (0.239 - 0.242)
Average of Central Values:	0.37	0.34	0.315
25th Percentile:	0.297	0.254	0.239
Maximum:	0.47	0.47	0.47
Summary:	0.37 (0.297 - 0.47)	0.34 (0.254 - 0.47)	0.315 (0.239 - 0.47)

Table A8-3: Concentration in Top 36 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.142 (0.14 - 0.144)	0.139 (0.135 - 0.143)	0.139 (0.137 - 0.143)
Dry and Temperate Location	0.15 (0.148 - 0.151)	0.145 (0.143 - 0.149)	0.145 (0.142 - 0.149)
Dry and Cold Location	0.157 (0.156 - 0.158)	0.153 (0.15 - 0.156)	0.153 (0.149 - 0.156)
Average Rainfall and Warm Location	0.138 (0.13 - 0.141)	0.134 (0.127 - 0.135)	0.128 (0.084 - 0.135)
Average Rainfall and Temperate Location	0.146 (0.139 - 0.148)	0.141 (0.135 - 0.142)	0.132 (0.09 - 0.141)
Average Rainfall and Cool Location	0.146 (0.14 - 0.15)	0.144 (0.135 - 0.145)	0.137 (0.087 - 0.145)
Wet and Warm Location	0.134 (0.107 - 0.141)	0.115 (0.08 - 0.131)	0.08 (0.079 - 0.095)
Wet and Temperate Location	0.136 (0.094 - 0.145)	0.113 (0.085 - 0.137)	0.08 (0.078 - 0.096)
Wet and Cool Location	0.147 (0.126 - 0.151)	0.13 (0.08 - 0.144)	0.083 (0.08 - 0.105)
Average of Central Values:	0.144	0.135	0.12
25th Percentile:	0.138	0.13	0.083
Maximum:	0.158	0.156	0.156
Summary:	0.144 (0.138 - 0.158)	0.135 (0.13 - 0.156)	0.12 (0.083 - 0.156)

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

Site	Clay	Loam	Sand
Dry and Warm Location	18 (8 - 30)	18.5 (6.83 - 36)	18.5 (6.83 - 36)
Dry and Temperate Location	24 (12 - 36)	24.3 (12.7 - 36)	36 (12.7 - 36)
Dry and Cold Location	30 (24 - 36)	30.2 (24.3 - 36)	36 (24.3 - 36)
Average Rainfall and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average of Central Values:	32	32.1	34.1
25th Percentile:	30	30.2	36
Maximum:	36	36	36
Summary:	32 (30 - 36)	32.1 (30.2 - 36)	34.1 (36 - 36)

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

Site	Clay	Loam	Sand
Dry and Warm Location	28.3 (0 - 113)	0 (0 - 9.8)	0 (0 - 0.6)
Dry and Temperate Location	23.7 (0.8 - 111)	0.18 (0 - 8.2)	0 (0 - 47)
Dry and Cold Location	62 (12 - 185)	0.00014 (0 - 7.2)	0.005 (0 - 2.44)
Average Rainfall and Warm Location	74 (25.8 - 155)	11.8 (1.94 - 47)	60 (22.9 - 136)
Average Rainfall and Temperate Location	71 (24.1 - 187)	8 (1.35 - 58)	66 (23.5 - 129)
Average Rainfall and Cool Location	119 (58 - 232)	17.8 (4.1 - 64)	67 (20.5 - 138)
Wet and Warm Location	106 (30.7 - 201)	29.1 (15.8 - 51)	58 (36 - 113)
Wet and Temperate Location	114 (57 - 211)	29.8 (16.4 - 49)	53 (35 - 117)
Wet and Cool Location	107 (51 - 194)	32 (21.9 - 70)	59 (42 - 116)
Average of Central Values:	78.3	14.3	40.3
25th Percentile:	62	0.18	0.005
Maximum:	232	70	138
Summary:	78.3 (62 - 232)	14.3 (0.18 - 70)	40.3 (0.005 - 138)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.14 (0 - 0.6)	0 (0 - 0.03)	0 (0 - 0.0017)
Dry and Temperate Location	0.12 (0.003 - 0.4)	0.0005 (0 - 0.03)	0 (0 - 0.4)
Dry and Cold Location	0.27 (0.05 - 0.7)	7.0E-07 (0 - 0.02)	0.000024 (0 - 0.016)
Average Rainfall and Warm Location	0.6 (0.28 - 1.01)	0.23 (0.024 - 2.18)	2.54 (0.6 - 6.1)
Average Rainfall and Temperate Location	0.6 (0.3 - 1.57)	0.21 (0.021 - 3.9)	3.9 (0.6 - 7.8)
Average Rainfall and Cool Location	0.8 (0.5 - 2.05)	0.6 (0.08 - 5.3)	4.7 (1 - 9.6)
Wet and Warm Location	2.17 (0.6 - 6.5)	4.2 (2.33 - 6.4)	6 (4.5 - 8.2)
Wet and Temperate Location	2.75 (1.01 - 5.7)	4.2 (1.96 - 7.4)	5.3 (4.2 - 7.6)
Wet and Cool Location	2.89 (1.05 - 6.9)	5.4 (2.64 - 7.4)	5.7 (4.6 - 7.5)
Average of Central Values:	1.15	1.65	3.13
25th Percentile:	0.27	0.0005	2.40E-05
Maximum:	6.9	7.4	9.6
Summary:	1.15 (0.27 - 6.9)	1.65 (0.0005 - 7.4)	3.13 (2.40E-05 - 9.6)

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

Site	Clay	Loam	Sand
Dry and Warm Location	15.3 (0 - 79)	0 (0 - 4.9)	0 (0 - 0.29)
Dry and Temperate Location	13.9 (0.26 - 62)	0.05 (0 - 6.4)	0 (0 - 52)
Dry and Cold Location	33 (5.6 - 87)	0.00008 (0 - 2.05)	0.0028 (0 - 1.74)
Average Rainfall and Warm Location	120 (71 - 268)	45 (6 - 390)	510 (111 - 1320)
Average Rainfall and Temperate Location	115 (79 - 253)	34 (3.4 - 520)	580 (95 - 1360)
Average Rainfall and Cool Location	197 (118 - 330)	85 (16.2 - 760)	660 (114 - 1550)
Wet and Warm Location	189 (74 - 510)	330 (146 - 650)	610 (286 - 1050)
Wet and Temperate Location	189 (97 - 400)	223 (87 - 440)	211 (106 - 670)
Wet and Cool Location	164 (63 - 360)	273 (144 - 420)	305 (114 - 490)
Average of Central Values:	115	110	320
25th Percentile:	33	0.05	0.0028
Maximum:	510	760	1550
Summary:	115 (33 - 510)	110 (0.05 - 760)	320 (0.0028 - 1550)

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

Site	Clay	Loam	Sand
Dry and Warm Location	9.4 (0 - 57)	0 (0 - 3.4)	0 (0 - 0.1)
Dry and Temperate Location	8.7 (0.23 - 39)	0.014 (0 - 4.1)	0 (0 - 10.5)
Dry and Cold Location	20.7 (3.9 - 53)	0.00004 (0 - 1.13)	0.0015 (0 - 1.05)
Average Rainfall and Warm Location	84 (43 - 202)	19.2 (2.74 - 227)	252 (38 - 840)
Average Rainfall and Temperate Location	90 (57 - 204)	15.6 (1.4 - 220)	306 (26 - 900)
Average Rainfall and Cool Location	152 (90 - 261)	37 (5.8 - 370)	330 (39 - 1100)
Wet and Warm Location	84 (29.6 - 250)	160 (66 - 330)	253 (120 - 510)
Wet and Temperate Location	96 (45 - 209)	116 (44 - 223)	108 (42 - 254)
Wet and Cool Location	52 (17.8 - 165)	116 (56 - 227)	185 (51 - 284)
Average of Central Values:	66.3	51.5	159
25th Percentile:	20.7	0.014	0.0015
Maximum:	261	370	1100
Summary:	66.3 (20.7 - 261)	51.5 (0.014 - 370)	159 (0.0015 - 1100)

Appendix 9: EPA Surface Models

Inputs used for Tier 1 models

Input	Central	Lower Bound Run	Upper Bound Run
Application rate (lb a.i./acre)	1	1	1
Proportion of Area Treated	1	1	1
K_{oc}	85.2 [1]	152[2]	12.2[3]
Soil aerobic half-time [6]	1062	1062	1062
Wetted in	No	No	No
Drift/Application Efficiency	0%/100% [D]	0%/100% [D]	0%/100% [D]
Incorporation depth (cm)	0	0	0
Water Solubility (mg/L)	2500	2500	2500
Aerobic aquatic half-life (days)[4]	2050	2050	2050
Proportion of Area Treated	1	1	1
FIRST Output (µg/L)	**Peak**	**Annual Average**	
Central Estimate	90.993	51.410	
Lower Bound	19.884	2.494	
Upper Bound	102.459	68.050	
PRZM-GW Output (µg/L)	**Peak**		
Central Estimate	34		
Lower Bound	12.2		
Upper Bound	722		

[1] Koc used in U.S. EPA/OPP/EFED 2014a, Table 3.3, for PRZM/EXAMS modelling. Close to value of 80 mL/g from Knisel and Davis 2000.
[2] Koc for loam of 152 from MRID 40768401.
[3] Lower bound from Koskinen et al. 1996
[4] PRZM/EXAMS input from U.S. EPA/OPP/EFED 2014a, Table 3.3, MRID 41372501.
[5] Stable. U.S. EPA/OPP/EFED 2014a, MRID 41305101.
[6] U.S. EPA/OPP/EFED 2014a, Table 3.2, MRID 41328001.

FIRST Output Files

```
CENTRAL ESTIMATE (Central Estimate of Koc)
   RUN No.   1 FOR Tebuthiuron      ON   None          * INPUT VALUES *
   --------------------------------------------------------------------
    RATE (#/AC)   No.APPS &   SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
     ONE(MULT)    INTERVAL    Koc   (PPM )   (%DRIFT)     AREA    (IN)
   --------------------------------------------------------------------
  1.000(  1.000)   1   1      85.2 2500.0   GRANUL( 0.0) 100.0   0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   --------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   --------------------------------------------------------------------
   1062.00        2           0.00    0.00-    0.00  ******    2050.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
```

```
   --------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION             CONCENTRATION
   --------------------------------------------------------------------
             90.933                      51.410


UPPER BOUND (Lower Bound of Koc)
   RUN No.   2 FOR Tebuthiuron      ON   None          * INPUT VALUES *
   --------------------------------------------------------------------
    RATE (#/AC)   No.APPS &   SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
     ONE(MULT)    INTERVAL    Koc   (PPM )   (%DRIFT)     AREA    (IN)
   --------------------------------------------------------------------
  1.000(  1.000)   1   1      12.2 2500.0   GRANUL( 0.0) 100.0   0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   --------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   --------------------------------------------------------------------
   1062.00        2          N/A      0.00-    0.00   ******   2050.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
   --------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION             CONCENTRATION
   --------------------------------------------------------------------
            102.459                      68.050


LOWER BOUND (Upper Bound of Koc)
   RUN No.   3 FOR Tebuthiuron      ON   None          * INPUT VALUES *
   --------------------------------------------------------------------
   RATE (#/AC)   No.APPS &   SOIL  SOLUBIL   APPL TYPE  %CROPPED INCORP
    ONE(MULT)    INTERVAL     Kd   (PPM )    (%DRIFT)     AREA    (IN)
   --------------------------------------------------------------------
  1.000(  1.000)   1   1     152.0 2500.0   GRANUL( 0.0) 100.0     0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   --------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   --------------------------------------------------------------------
   1062.00        2          N/A      0.00-    0.00   ******   2050.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
   --------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION             CONCENTRATION
   --------------------------------------------------------------------
             19.884                       2.494
```

SciGrow version 2.3 Output files
CENTRAL ESTIMATE (Central Estimate of Koc)

```
   SciGrow version 2.3
    chemical:Tebuthiuron
    time is  1/14/2016  16: 1:36
    ------------------------------------------------------------------------
     Application      Number of       Total Use    Koc      Soil Aerobic
     rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
    ------------------------------------------------------------------------
         1.000           1.0           1.000      8.52E+01     1062.0
    ------------------------------------------------------------------------
    groundwater screening cond (ppb) =   3.40E+01
    ************************************************************************
```

LOWER BOUND (Upper Bound of Koc)

```
   SciGrow version 2.3
    chemical:Tebuthiuron
    time is  1/14/2016  16: 2:26
    ------------------------------------------------------------------------
     Application      Number of       Total Use    Koc      Soil Aerobic
     rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
    ------------------------------------------------------------------------
         1.000           1.0           1.000      1.52E+02     1062.0
    ------------------------------------------------------------------------
    groundwater screening cond (ppb) =   1.22E+01
    ************************************************************************
```

UPPER BOUND (Lower Bound of Koc)

```
   SciGrow version 2.3
    chemical:Tebuthiuron
    time is  1/14/2016  16: 3: 3
    ------------------------------------------------------------------------
     Application      Number of       Total Use    Koc      Soil Aerobic
     rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
    ------------------------------------------------------------------------
         1.000           1.0           1.000      1.22E+01     1062.0
    ------------------------------------------------------------------------
    groundwater screening cond (ppb) =   7.22E+02
    ************************************************************************
```

Summary of EPA PRZM/EXAMS modelling from U.S. EPA/OPP/EFED 2014a, , Table 3.4, p. 25. Conversion to Water Contamination Rates summarized in Appendix 9.

Tier II PRZM/EXAMS Scenario	Ap. Method	ppb at 6 lb a.i./acre	ppb at 4 lb a.i./acre	WCR at 6 lb a.i./acre	WCR at 5 lb a.i./acre
TXalfalfaOP	Aerial	1109.0	736.3	184.83	184.08
	Ground	1018.0	679.0	169.67	169.75
	Granular	997.3	664.9	166.22	166.23
MNalfalfaOP	Aerial	558.6	372.7	93.10	93.18
	Ground	376.0	251.0	62.67	62.75
	Granular	330.8	220.8	55.13	55.20
NCalfalfaOP	Aerial	604.0	403.0	100.67	100.75
	Ground	453.1	301.5	75.52	75.38
	Granular	414.7	276.8	69.12	69.20
PAalfalfaOP	Aerial	693.9	462.9	115.65	115.73
	Ground	534.8	355.9	89.13	88.98
	Granular	494.8	329.9	82.47	82.48
CAalfalfa_WirrigOP	Aerial	498.9	332.0	83.15	83.00
	Ground	367.9	245.0	61.32	61.25
	Granular	335.0	223.0	55.83	55.75
				Average	97.60
				Min	55.13
				Max	184.83