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Bifenthrin:
Human Health and Ecological Risk Assessment
Final Report

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
a.k.a.	also known as
a.s.	active substance
APHIS	Animal and Plant Health Inspection Service
ARI	Aggregate Risk Index
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BMDXX	benchmark dose associated with a XX% response
BMDLXX	lower bound of benchmark dose associated with a XX% response
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
DEM	diethyl maleate (synergist)
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
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
FMC	FMC Corporation (original registrant for bifenthrin)
g	gram
GLP	Good Laboratory Practices
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
hpf	hours post-fertilization
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
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
LR_{50}	50% lethal response [EFSA/European term]
m	meter
M	male
MAPK	mitogen-activated protein kinase (signaling pathway)
MATC	maximum acceptable tolerance concentration
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
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
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
N.R.	not reported
OC	organic carbon
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
Pa	Pascal
PBO	piperonyl butoxide (P450 inhibitor)
PBPK	physiologically-based kinetic

ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
TFP-acid	trifluoro-1-propenyl)-2,2-dimethyl-cyclopropane carboxylic acid
TGIA	Technical grade active ingredient
TPP	triphenyl phosphate (synergist)
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)
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

Bifenthrin is a pyrethroid insecticide and miticide that modifies voltage-gated ion channels, disrupting the normal function of nerve cells. The Forest Service will use bifenthrin primarily in the control of bark beetles as an alternative to carbaryl. Other uses under consideration include the control of leaf beetles and some coleopteran borers (e.g., the gold spotted oak borer and polyphagous shot hole borer). In addition to coleopteran pest control, some bifenthrin formulations are labeled for the control of termites, and the Forest Service is considering the use of bifenthrin for termite control in some regions. Application methods for controlling leaf beetles involve relatively standard ground broadcast applications in which the leaves of the tree are treated directly. Applications for preventing bark beetle infestations involve directed applications by high-pressure spray to a section of the tree trunk. For forestry applications, the maximum single and maximum seasonal application rate is taken as 0.2 lb a.i./acre; accordingly, the application rate of 0.2 lb a.i./acre is used in all exposure scenarios developed in the current risk assessment.

Bifenthrin shares a common mechanism of action with other pyrethroids and with pyrethrins. If other pyrethroids or pyrethrins are used in Forest Service programs or projects along with bifenthrin, the risks posed by the other pyrethroids or pyrethrins should be considered quantitatively under the assumption of dose addition—i.e., the HQs should be added. The WorksheetMaker program used in the development of Forest Service risk assessments has a utility for conducting such assessments.

In both the human health and ecological risk assessments, the quantitative expression of the risk characterization is the hazard quotient (HQ), the ratio of the anticipated dose or exposure to the RfD (human health) or no-observed-effect level or concentration (ecological effects) using 1 as the level of concern—i.e., an HQ of < 1 is below the level of concern.

None of the central estimates for general exposures of workers results in HQs that exceed the level of concern (HQ=1); however, upper bound exposures for foliar applications are in the range of 4 to 11. In addition, the accidental exposure scenarios for wearing contaminated gloves for 1 hour result in HQs of 4 for foliar applications and an HQ of 3 for bark applications. A reasonable interpretation of the HQs is that most workers who exercise reasonable care in the application of bifenthrin should not be at risk of adverse effects; however, workers who do not follow prudent handling practices could be at risk of effects that might lead to overt signs of neurotoxicity. Wearing contaminated gloves could be a major source of excessive exposure to bifenthrin.

Except for upper bound HQs associated with the consumption of contaminated vegetation following foliar applications, members of the general public do not appear to be at risk. The scenario for the consumption of contaminated vegetation does lead to upper bound HQs of 9 for acute exposures and 3 for long-term exposures. These are extreme exposure scenarios that should not be viewed as typical or expected, in most cases. Based on EPA exposure assessments, typical uses of bifenthrin in agricultural applications lead to exposures that are far below the level of concern.

Nontarget organisms at greatest risk are the invertebrates, both terrestrial and aquatic. At the anticipated application rate of 0.2 lb a.i./acre, adverse effects are virtually certain in sensitive species of phytophagous insects. Bifenthrin will be applied to and will contaminate terrestrial vegetation; consequently, sensitive species of phytophagous insects that consume the contaminated vegetation will likely be killed. This risk characterization pertains to virtually any effective insecticide applied to vegetation. Based on toxicity data in the honeybee, sensitive species of flying insects could be harmed by direct spray or drift. Similarly, sensitive species of aquatic invertebrates will be adversely affected by foliar or bark applications of bifenthrin to areas near surface water, unless effective measures are taken to limit the contamination of surface water from drift, runoff, percolation, and sediment losses. This severe risk characterization is limited to sensitive species of invertebrates. There is little basis for asserting that tolerant species or populations of both terrestrial and aquatic invertebrates will be adversely affected by applications of bifenthrin. Based on the available data, however, generalizations concerning sensitivity or tolerance to bifenthrin cannot be made at the level of taxonomic orders.

Vertebrates are generally less sensitive than invertebrates to bifenthrin. Nonetheless, foliar applications of bifenthrin at a rate of 0.2 lb a.i./acre could result in exposure levels for some terrestrial mammals and birds that substantially exceed the level of concern. In all cases, risks to mammals (HQs up to 45) and birds (HQ up to 22) are associated with the consumption of contaminated vegetation, and risks are greatest for smaller animals consuming contaminated grasses or food items with bifenthrin concentrations comparable to those associated with contaminated grasses. For fish, exceedances in the level of concern are limited to longer-term exposures in sensitive species (HQs up to 5).

Risks to vertebrates following bark applications of 0.2 lb a.i./acre are less than those associated with foliar applications. Specifically, hazard quotients in mammals (highest HQ=4), birds (highest HQ=2) and sensitive species of fish (highest HQ=3) are a concern but are substantially less than HQs associated with foliar applications.

The risk characterization for bifenthrin focuses on the potential for direct toxic effects. Nonetheless, there is a potential for secondary effects in virtually all groups of nontarget organisms. Terrestrial applications of any effective insecticide, including bifenthrin, are likely to alter insect and other invertebrate populations within the treatment area. This alteration could have secondary effects on terrestrial or aquatic animals and plants, including changes in food availability, predation, and habitat quality. These secondary effects may be beneficial to some species and detrimental to others; moreover, the magnitude of secondary effects is likely to vary over time.

1. INTRODUCTION

1.1. Chemical Specific Information

This document provides human health and ecological risk assessments addressing the consequences of using bifenthrin for the control of insect pests in Forest Service programs. As detailed further in Section 2.2, bifenthrin is an insecticide used to control a broad spectrum of insects that may damage vegetation. The Forest Service has evaluated the use of bifenthrin for the control of insect pests (e.g., Fettig et al. 2006, 2013; McCullough et al. 1998) but has not developed a full risk assessment on bifenthrin.

The available literature on bifenthrin is robust and includes numerous studies submitted to regulatory agencies in both the United States and Europe in support of the registration of bifenthrin. The registrant studies are classified as Confidential Business Information (CBI) and are not publically available. For the conduct of the current risk assessment, full copies of these registrant submitted studies have not been available. As summarized in Table 1, however, recent and detailed reviews of registrant studies submitted to the U.S. EPA are available. Specifically, U.S. EPA/OPP/HED (2007a, 2010a, 2011a, 2012a) provides a detailed summary of registrant studies relevant to human health effects and U.S. EPA/OPP/EFED (2012a) provides an extensive summary of registrant studies relevant to ecological effects. The European regulatory literature on bifenthrin is well-covered in EFSA (2011), FAO (2012), and (WHO 2012). In addition to these reviews, a large number of cleared reviews and data evaluation records are available from U.S. EPA (http://iaspub.epa.gov/apex/pesticides). These studies are designated in Section 5 (references) as ClRev. While these cleared reviews were obtained for the conduct of the current risk assessment, most of the DERs are from the late 1980s. It appears that the EPA has reevaluated at least some of the studies and the summaries of the studies in the recent EPA risk assessments are not consistent with the older DERs. This is not uncommon since the EPA will often review and revise the assessment of studies in the conduct of a new risk assessment. Consequently, the current Forest Service risk assessment uses the summaries in the newer EPA risk assessments rather than the older cleared reviews. Specific examples of discrepancies between the older DERs and the more recent EPA documents, which might be a source of confusion, are discussed in the current risk assessment as needed.

As also summarized in Table 1, several additional reviews on bifenthrin are available in the open literature. Except as otherwise specified, these reviews are used only to supplement the literature searches on bifenthrin.

The U.S. EPA registration review program for pesticides operates on a 15-year cycle. The registration review for bifenthrin is underway but is not scheduled for completion until 2016 (U.S. EPA/OPP 2011a, p. 9). While preliminary assessments supporting the registration review of bifenthrin are available (U.S. EPA/OPP/EFED 2010a,b; U.S. EPA/OPP/HED 2010a, 2011a), it is likely that additional studies will be submitted to the U.S. EPA/OPP as part of the registration review.

The open literature on bifenthrin is also substantial. For example, a search of TOXLINE in May 2015, using bifenthrin and synonyms as key words, identified approximately 1400 citations. An

initial screen of the open literature is summarized in Table 2, which includes the open literature studies that are most relevant to the human health and ecological risk assessments.

Most of the primary literature relating to potential human health effects is focused on mechanistic studies involving neurotoxicity. As discussed in U.S. EPA/OPP/HED (2010a, 2011a), pesticide testing requirements now include assays for estrogenic effects and immunotoxicity. It is not clear, however, that such studies have been conducted and sent to U.S. EPA/OPP. As noted in Table 2, several studies relating to the estrogenic and immunotoxic effects of bifenthrin have been identified in the open literature, and these studies will be covered in some detail. In terms of a quantitative impact on the human health risk assessment, the dermal absorption study by Hughes and Edwards (2010) is extremely relevant. Hughes and Edwards (2010) report limited dermal absorption (5% per day in *in vitro* systems) relative to dermal absorption estimate of 25% per day cited in U.S. EPA/OPP/HED (2010a, 2011a). A preliminary application of the QSAR methods for estimating dermal absorption in Forest Service risk assessments yields estimates of about 10% (2.2% to 45%). These estimates of dermal absorption are discussed further in Section 3.1.3.2.

Few studies have been identified on the effects of bifenthrin in humans (Lebailly et al. 1998; Srivastava et al. 2005). While these studies are covered in the risk assessment, these studies do not impact the risk assessment quantitatively. Additional analyses are available on worker exposures to bifenthrin when applied as a termiticide (Dong 1995; U.S. EPA/OPP/HED 1992a).

As would be expected with an insecticide, the literature on ecological effects is dominated by studies on both terrestrial and aquatic invertebrates (Table 2). In combination with the registrant submitted studies on invertebrates, risks to both terrestrial and aquatic invertebrates can be well characterized. A robust literature on the efficacy of bifenthrin is available (e.g., Liesch and Williamson 2010; Lowe et al. 1994; McCullough and Smitley 1995; McCullough et al. 1998; Miller 1997; Negron and Clarke 1995; Peterson 2012a,b; Wiltz et al. 2009; Womac et al. 1994). For the most part, efficacy studies are not reviewed in detail in the current risk assessment except when the studies provide information of the differences in the toxicity of bifenthrin to nontarget and target organisms.

The toxicity data on fish are limited. The U.S. EPA/OPP states that an acceptable long-term study of bifenthrin in fish has not been identified. The EPA has taken the unusual approach of basing the risk assessment for longer-term exposures in fish on a tefluthrin study in fathead minnows with a NOAEC of 0.004 µg/L (U.S. EPA/OPP/EFED 2012a, Appendix J). In the open literature, Jin et al. (2009, 2010, 2013b) conducted early life-stage studies on Zebrafish, and the Jin et al. (2009) study is classified as acceptable to OPP (U.S. EPA/OPP/EFED 2012a, Appendix G, p. 13). OPP's rationale for not using the data from Jin et al. (2009, 2010) and the potential impact of the data from Jin et al. (2013b) is discussed further in Section 4.1.3.1 (hazard identification for fish) and Section 4.3.3.1 (dose-response assessment for fish). While the dose-response assessment in fish is important, the risk assessment in aquatic species is driven by aquatic invertebrates for which the chronic NOAEC identified by U.S. EPA/OPP/EFED (2012a, p. 138) is 0.0013 µg/L [*Daphnia magna* from MRID 41156501].

As also summarized in Table 2, several studies are available on different chiral forms of bifenthrin. While this literature is reviewed, differences in the [R] and [S] enantiomers of bifenthrin are not a major factor in the risk assessment. Technical grade bifenthrin is a mixture of both cis-isomers (97%) and trans-isomers (3%) which includes both [R] and [S] enantiomers. Most of the toxicity data are based on this mixture (i.e., technical grade bifenthrin), and the exposure assessments will also be based on this mixture. This approach is essentially identical to the approach taken by U.S. EPA/OPP/EFED (2012a) and appears to be the only approach supported by the available data.

The open literature on bifenthrin does impact the quantitative assessment of bifenthrin residues on vegetation. U.S. EPA/OPP/EFED (2012a, p. 117) cites a standard *default* foliar half-life of 35 days from Willis and McDowell (1987) as well as a *pyrethroid class* foliar half-life of 8.3 days. As summarized in Table 2, several studies on persistence of bifenthrin on vegetation are available in the open literature. U.S. EPA/OPP/EFED (2012a, Appendix G) classifies the study by Mukherjee et al. (2010) as "not acceptable" and the study by Papadopoulou-Mourkidou et al. (1989) as "acceptable." The studies by Chauhan et al. (2012) and You et al. (2013) have been published since the most recent EPA risk assessment. The use of these studies in the current risk assessment are detailed further in Section 3.2.3.4.3 (GLEAMS-Driver modeling) and Section 3.2.3.7 (Oral Exposure from Contaminated Vegetation).

1.2. General Information

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

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

As noted in Section 1.1, studies submitted by registrants in support of the registration of bifenthrin 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 with the design, conduct and reporting of studies submitted to the U.S. EPA for pesticide registration are minor. 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://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm. 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.

Despite the real and legitimate concerns with risk assessments based largely on registrant-submitted studies, data quality and data integrity are not substantial concerns. The major limitation of risk assessments based substantially on registrant-submitted studies involves the nature and diversity of the available studies. The studies 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 bifenthrin is noted in various parts of this risk assessment as appropriate. Overall and as discussed in Section 1.1, the open literature on bifenthrin is robust and this literature is used quantitatively in the current risk assessment as needed and as appropriate.

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.

Some of the calculations, however, 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 is the ratio of the estimated exposure to a toxicity value, typically a no adverse effect level or concentration (i.e., NOAEL or NOAEC). Both the rationale for the calculations and the interpretation of the hazard quotients are contained in this risk assessment document.

2. PROGRAM DESCRIPTION

2.1. Overview

Bifenthrin is a neurotoxic pyrethroid insecticide and miticide. Structurally, bifenthrin consists of a mixture of various three dimensional (i.e., isomeric and enantiomeric) configurations. While there are differences in the biological activity of the isomeric and enantiomeric configurations, this does not substantially complicate the risk assessment because most toxicity studies are conducted on technical grade bifenthrin – i.e., a mixture of the isomeric and enantiomeric configurations – and technical grade bifenthrin is the mixture of concern in the current risk assessment.

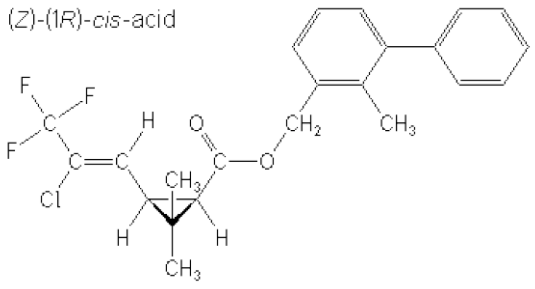
The Forest Service will use bifenthrin primarily in the control of bark beetles as an alternative to carbaryl. Other uses under consideration include the control of leaf beetles and some coleopteran borers (e.g., the gold spotted oak borer and polyphagous shot hole borer). In addition to coleopteran pests, some bifenthrin formulations are labeled for the control of termites (Order: Blattodea) and bifenthrin is being considered for termite control in some regions.

Application methods for controlling leaf beetles involve relatively standard ground broadcast application methods in which the leaves of the tree are treated directly. Applications for preventing bark beetle infestations involve directed applications by high-pressure spray to a section of the tree trunk. Applications for the control of termites would also involve directed applications (e.g., around building perimeters or fencing) but would use low pressure rather than high pressure sprays.

The maximum labelled application rate for bifenthrin is 2 lbs a.i./acre. These high application rates do not appear to be relevant to forestry applications. For forestry applications, the maximum single and maximum seasonal application rate is taken as 0.2 lb a.i./acre and the application rate of 0.2 lb a.i./acre is used in all exposure scenarios developed in the current risk assessment. The use of lower application rates is discussed in the sections on risk characterization – i.e., Section 3.4 for human health and Section 4.4 for ecological effects. Based on the available data on the uses of bifenthrin, it appears that forestry uses are far below agricultural uses. This use pattern is common in pesticides and reflects the larger areas of crop cultivation relative to forestry management.

2.2. Chemical Description and Commercial Formulations

Bifenthrin (a.k.a. biphenthrin) is the common name for 2-Methylbiphenyl-3-ylmethyl-(Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate:



While bifenthrin is not a particularly large molecule (i.e., MW=422.9), it is structurally complex in that it can take both *cis* and *trans* isomeric configurations as well as both [R] and [S] enantiomer configurations, with [R] (right-handed) and [S] (left-handed) referring to the three-dimensional configuration of the molecule. Bifenthrin has two chiral carbons (i.e., carbons with four different substituents) leading to somewhat complex nomenclature. The above figure illustrates the 1 R cis-isomer, which accounts for about 98% of technical grade bifenthrin and is generally abbreviated as the Z 1 R/S cis-enantiomer. In the interest of brevity, the terms [R] or [S] cis enantiomer is used to designate this enantiomer unless a fuller designation is required.

One potentially confusing aspect of the nomenclature of enantiomers involves the (+) and (-) designation which is used in some of the open literature publications. Enantiomers with a (+) designation rotate polarized light to the right and those with a (-) designation rotate polarized light to the left. These optical properties do not necessarily correspond to the [S] and [R] three dimensional configurations. For bifenthrin, the [S] enantiomer rotates polarize light to the left (-) and the [R] enantiomer rotates polarized light to the right (+) (Liu et al. 2005c, p. 131). The (+) and (-) designations are only used in the appendices of the current risk assessment and only when these designations are used in the original publications. This approach is taken to allow clearer review of the appendices in terms of comparison to the source documents. The [R] and [S] three dimensional designations are used consistently in the main body of this risk assessment.

In general, the cis-isomers of pyrethroids are more potent than trans-isomers (U.S. EPA/OPP/HED 2012a). Studies are available on differences in the biological activity and biodegradation of the isomeric and enantiomeric forms of bifenthrin (Liu et al. 2005a,b, 2008a,b; 2009; Lu 2013; Wang et al. 2007; Yang et al. 2009; Zhao et al. 2009), and these studies are discussed specifically in the appropriate subsections of this risk assessment. From a practical perspective, however, the toxicity studies used quantitatively in the current risk assessment were conducted using technical grade bifenthrin—i.e., a mixture of the *cis* and *trans* isomer and [R] and [S] enantiomers. As discussed in the U.S. EPA guidance for the conduct of risk assessments on chemical mixtures (U.S. EPA/ORD 2000, Section 2.5.1), data on technical grade bifenthrin is essentially equivalent to the mixture of concern in the current Forest Service risk assessment. Given the modest literature on biological activity of the isomeric and enantiomeric forms of bifenthrin, relative to the extensive literature on technical grade bifenthrin (Table 1 and Table 2), the mixture of concern approach is preferable and the only practical approach to the current risk assessment on bifenthrin.

Bifenthrin is a pyrethroid insecticide and miticide, a class of synthetic insecticides that mimic pyrethrins – i.e., a class of naturally occurring insecticides found in *Chrysanthemum* species (von Stackelberg 2012). As discussed further in Section 3.1.2 (Mechanism of Action), pyrethroids are neurotoxins that interfere with the normal regulation of ions in nerve tissue by modifying the voltage-gated ion channels (Cao et al. 2011b) Structurally, bifenthrin is classified as a Type I pyrethroid in that it does not contain a cyano (CN) group. In terms of overt mammalian toxicity, Type I pyrethroids are characterized by body tremors, salivation, and increased sensitivity to stimuli (Schleier and Peterson 2011; Soderlund et al. 2002; Wolansky et al. 2007; Yang et al. 2009a). In terms of the potential for the development of resistance in insect populations, bifenthrin along with other pyrethroids and pyrethrins is placed in Class 3A (sodium channel modulators) (IRAC 2013).

Selected chemical and physical properties of bifenthrin are summarized in Table 3. The dominant characteristics of bifenthrin are lipophilicity and persistence. Bifenthrin will partition strongly from water to lipid materials—i.e., an octanol-water partition coefficient of over 1 million. As a corollary, bifenthrin has a strong tendency to bind to soil (K_d values in the range of about 1000 to 5000) and to bioconcentrate in fish (BCFs up to about 9000). Also related to the high lipophilicity, bifenthrin is relatively insoluble in water. As summarized in Table 3, reported water solubilities for bifenthrin range from about 0.000014 mg/L (i.e., 14 parts per trillion) to 0.1 mg/L (100 parts per billion). The rationale for the widely discrepant estimates of water solubility is not completely clear. The most fully documented value for water solubility is the lowest value from the review by Laskowski (2002) which is in turn linked to a report from FMC Corporation (MRID 132518). As discussed further below, FMC Corporation is the original developer of bifenthrin.

In terms of persistence, bifenthrin is stable to aqueous photolysis, abiotic hydrolysis, and anaerobic soil metabolism and is relatively non-volatile. In environmental fate/dissipation studies in ponds, no substantial degradation/dissipation was noted over observation periods of up to 1 year. The major route of degradation of bifenthrin is aerobic soil metabolism with soil degradation/dissipation half-lives of about 100 to over 300 days (Table 3).

Bifenthrin was initially developed by FMC Corporation, whose corporate headquarters are currently located in Philadelphia, PA (http://www.fmc.com/). The initial patent for bifenthrin was granted to John F. Engel, a member of FMC Corporation on Dec. 9, 1980. Bifenthrin is currently off-patent, and there were 432 active product labels and 62 Special Local Needs labels for bifenthrin as of 2012 (U.S. EPA/OPP/EFED 2012a). As of July 2014, 632 active formulations are listed on PAN Pesticides Database - Pesticide Products (Kegley 2014).

As discussed further in Section 2.5 (Use Statistics), most formulations of bifenthrin are labelled for agricultural uses including the control of insect pests on corn, soybeans, wheat, cotton, rice, grapes, and various other fruits and vegetables (U.S. EPA/OPP/EFED 2012a, p. 48). Although none of the Forest Service applications of bifenthrin will involve crop treatment, crop treatments may be conducted on some Forest Service lands by individuals or organizations with permission from the Forest Service to use Forest Service lands for the cultivation of crops. All such agricultural applications are subject to U.S. EPA/OPP regulatory constraints (e.g., tolerance limits) and exposures associated with agricultural applications are not explicitly considered in Forest Service risk assessments. As discussed further in Section 3.4.3 (Risk Characterization for the General Public), dietary exposures to pesticides associated with agricultural applications of pesticides are below, and often far below, the exposure assessments developed for forestry applications of pesticides.

Aerial applications of bifenthrin are allowed only in agricultural applications (U.S. EPA/OPP/EFED 2012a, p. 100). While agricultural applications are not explicitly covered in the current Forest Service risk assessment, the workbooks that accompany this risk assessment do include aerial applications in the event that Forest Service cooperators would elect to use aerial applications on agricultural crops.

In the tasking of the current risk assessment, the Forest Service has not designated the most likely formulations to be used or the target insects for bifenthrin applications in Forest Service programs. As summarized in Table 2, there are several Forest Service or related forestry publications on the use of bifenthrin. Based on these publications, the most likely use of bifenthrin in Forest Service programs involves the control of bark beetles on various conifers. Specifically, bifenthrin can be used as an alternative to carbaryl for the control of bark beetles (Monture Creek Land Management, Inc. 2014; Montana DNRC 2014). The use of carbaryl for the control of bark and leaf beetles is covered in the Forest Service risk assessment on carbaryl (SERA 2009a). Based on publications involving USDA Forest Service personnel (Ball et al. 2012; Burke et al. 2012; Fettig et al. 2006) as well as the Nebraska Forest Service personnel (Hartell et al. 2009), Onyx formulations of bifenthrin have been explicitly evaluated for this use. In addition to bark beetles, bifenthrin is recommended for the control of various leaf beetles including the elm leaf beetle (*Xanthogaleruca luteola*, Cranshaw 2014) and the *Viburnum* leaf beetle (*Pyrrhalta viburni*, Hartell et al. 2009). As discussed in SERA (2009a), carbaryl is also used to control leaf beetles, and the Forest Service may be considering bifenthrin as an alternative to carbaryl. Lastly, the Forest Service has indicated that bifenthrin is being considered for the control of the gold spotted oak borer (*Agrilus coxalis*) as well as the polyphagous shot hole borer (*Euwallacea fornicatus*). These coleopteran pests would be treated in a manner similar to that used for the control of bark beetles (Bakke 2014). In addition to the control of bark beetles and leaf beetles, the Forest Service has evaluated the use of bifenthrin for the control of termites using a 7.9% Talstar formulation (Peterson 2012a) or a Biflex formulation (Wagner 2003).

Based on the above considerations, representative formulations of bifenthrin explicitly covered in the current risk assessment are summarized in Table 4. These formulations include Onyx Insecticide, Biflex SFR Termiticide/Insecticide, Talstar GC Flowable, and Talstar One Multi-insecticide. All formulations are supplied by FMC Corporation, the original developer of bifenthrin.

The list of formulations in Table 4 is not intended to be exclusive. Other formulations of bifenthrin are available commercially, and new formulations of bifenthrin may become available at some point in the future. The Forest Service may elect to use other formulations of bifenthrin registered for applications relevant to forestry. If other formulations are used in Forest Service programs, however, attempts should be made to identify information on the inerts in the formulations as well as the toxicity of the formulations to ensure that the formulation under consideration is comparable to the formulations explicitly designated in Table 4.

2.3. Application Methods

The application methods most likely to be used for bifenthrin vary according to the target pest. As discussed in Section 2.2, it appears that the primary uses of bifenthrin in Forest Service programs will involve the control of leaf beetles and bark beetles. Bifenthrin may also be used in termite control. Application methods for controlling leaf beetles involve relatively standard ground broadcast application methods in which the leaves of the tree are treated directly. Applications for preventing bark beetle infestations involve directed applications by high-pressure spray to a section of the tree trunk. Applications for the control of termites would also involve directed applications (e.g., around building perimeters or fencing) but would use low pressure rather than high pressure sprays.

Different application methods will involve different estimates of the amount of pesticide 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).

2.3.1. Leaf Beetles

For leaf beetles, bifenthrin formulations are applied to trees by standard broadcast foliar application methods. As noted in Section 2.2, bifenthrin is labelled for aerial application only at agricultural sites. While aerial applications are included in the EXCEL workbook for leaf beetle control (Attachment 1), they would not be conducted as part of Forest Service programs (i.e., forestry and related uses) and are not explicitly considered in the risk characterizations given in the current Forest Service risk assessment.

Forestry applications for leaf beetle control might involve backpack directed foliar applications; however, these types of applications would probably be limited to small trees. Ground applications to larger trees will use high pressure hoses. For the current risk assessment, these high-pressure applications are assessed as hydraulic sprays using spray equipment mounted on tractors or trucks.

2.3.2. Bark Beetles

Bifenthrin treatment to prevent bark beetle damage to trees is made prior to beetle flight and infestation of the host trees. Bifenthrin is applied to the tree trunk (rather than the leaves) from the base of the tree—i.e., ground level—and upward until the tree diameter is less than 5 inches. For protections against the elm bark beetle, all bark surfaces including trunk, limbs, and twigs must be treated. Most Forest Service applications will involve a high-pressure sprayer, which can typically be used to apply bifenthrin formulations up to a height of 30-35 feet from the ground. If the target application height needs to exceed 30-35 feet, the applicator must use a bucket-lift to allow treatment of the higher areas of the tree. This is a labor and material intensive application method. As with carbaryl (SERA 2009a), it is anticipated that bark beetle control will be used primarily for preventive treatment to high-value trees, such as those in a campground or trees of high genetic or other intrinsic value. The significant practical difference between carbaryl and bifenthrin is that carbaryl may provide protection for up to 2 years whereas bifenthrin needs to be applied annually (Bakke 2014; Fettig et al. 2006).

2.3.3. Termite Control (Soil Applications)

Bifenthrin formulations labelled for termite control (e.g., Biflex Termiticide and Insecticide) encompass both subterranean and wood-infesting termites. Most pesticide applications for termite control focus on subterranean (soil-dwelling) termites (Lewis et al. 2014), and soil treatments appear to be the focus of Forest Service programs to evaluate different options for termite control (Wagner 2003).

It appears that applications of bifenthrin for the control of termites are more localized relative to applications for the control of bark beetles and leaf beetles. In this respect, termite applications are encompassed by the current risk assessment. Because termite applications will often involve the use of less bifenthrin per unit area, applications of bifenthrin for the control of termites may pose lower risks than bifenthrin applications to control leaf or bark beetles.

Developing elaborate exposure scenarios for termite control will require detailed information about the sites to be treated and the specific types of applications to be made. The most recent EPA risk assessment for bifenthrin (U.S. EPA/OPP/EFED 2012a) does not include elaborate exposure scenarios for termite control. The current Forest Service risk assessment addresses applications for termite control qualitatively.

2.4. Mixing and Application Rates

2.4.1. Leaf Beetles

For leaf beetles, bifenthrin formulations are applied to trees by standard directed or broadcast foliar application methods. As summarized in Table 4, all of the representative formulations of bifenthrin are labeled for foliar applications; however, restrictions on application rates differ.

The Onyx and Biflex formulations (both of which contain 23.4% a.i. and petroleum distillates) are labeled for maximum single application rates 0.2 lb a.i./acre, and maximum seasonal application rates are not specified on the product labels.

Talstar GC Flowable (which contains 7.9% a.i. and propylene glycol but not petroleum distillates) is labelled explicitly for a maximum single application rate of 0.1 lb a.i./acre and a maximum seasonal application rate of 0.2 lb a.i./acre (p. 3 of the product label under General Applications Instructions). Under mixing directions for ornamental applications, however, the product label specifies application rates of up to 1.0 fluid ounce of formulation per 1000 ft^2. As summarized in Table 4, this corresponds to an application rate of 0.227 lb a.i./acre. [0.666 lb a.i./gallon = 0.666 lb a.i./128 fl. oz. ≈ 0.00521 lb/oz.; 0.00521 lb/oz./1000 ft2 x 43,560 ft^2/acre ≈ 0.22695 lb a.i./acre] While 0.227 lb a.i./acre rounds to 0.2 lb a.i./acre, the former value is 13% greater than the latter value, and this difference in application rates could impact the qualitative interpretation of risk assessment for some species.

As with the Talstar GC Flowable formulation, Talstar One Multi-insecticide contains 7.9% a.i. and propylene glycol. The product label for Talstar One Multi-insecticide does not explicitly state maximum single or seasonal application rates in units of lb a.i./acre. As with the product label for Talstar GC Flowable, however, the product label for Talstar One Multi-insecticide specifies a maximum single application rate of 1 fluid ounce per1000 ft^2. As noted above, this corresponds to 0.227 lb a.i./acre.

As detailed in U.S. EPA/OPP/EFED (2012a, Appendix M, p. 2), maximum application rates of over 2 lbs a.i./acre are permitted in some areas for some agricultural commodities. These high application rates are not relevant to forestry applications. At this time, it appears that Onyx and Biflex are formulations most likely to be used in Forest Service programs, and the maximum single and maximum seasonal application rate is taken as 0.2 lb a.i./acre.

In addition to application rates, application volumes, meaning the number of gallons of pesticide solution applied per acre, have an impact on the estimates of potential risk. The extent to which a formulation of bifenthrin is diluted prior to application primarily influences dermal and direct spray scenarios, both of which depend on 'field dilution' (i.e., the concentration of bifenthrin in the applied spray). In all cases, the higher the concentration of pesticide (i.e., equivalent to the

lower dilution of the herbicide), the greater is the risk. As summarized in Table 4, the recommended application volume for the Onyx formulation is 100 gallons/acre for ground broadcast applications to trees. The product label notes that low or high volume applications may be used, but specific values for applications to trees are not given. Application volumes of 87 to 440 gallons/acre are specified for applications to turf. In the absence of additional information, the application volumes used in the current risk assessment are taken as 100 (80 to 400) gallons per acre.

2.4.2. Bark Beetles

As summarized in Table 4, the Onyx and Biflex product labels provide clear and specific application rates for bark beetle control in terms of the amount of bifenthrin per tree. For preventative applications, rates of 0.0025 lb a.i./tree to 0.02 lb a.i./tree are recommended for *Dendroctonus* species of bark beetle, and somewhat higher rates of 0.015 to 0.07 lb a.i./tree are recommended for other types of beetles—e.g., ambrosia beetles, elm bark beetles and emerald ash borers. The Forest Service will typically use the highest labelled rate for the control of the gold spotted oak borer. The amounts applied to a particular tree will be dependent on the size of the tree and roughness of the tree bark (Bakke 2014). Notwithstanding the recommended treatment rates, the product labels for Onyx and Biflex product labels indicate that the maximum application rate of 0.2 lb a.i./acre cannot be exceeded in bark applications.

As noted by Ball et al. (2012), the lb a.i./acre restriction in application rates will typically limit the application of bifenthrin to 10 to 20 trees per acre. Based on the labelled rates of 0.0025 lb a.i./tree to 0.03 lb a.i./tree, a somewhat broader range of trees per acre can be derived. The treatment of infested trees at the upper bound treatment rate/tree would limit the treatment to about 7 trees/acre [0.2 lb a.i./acre ÷ 0.03 lb a.i./tree ≈ 6.66 trees/acre]. Based on the lower bound of the per tree rates for preventative treatments, about 80 trees/acre might be treated [0.2 lb a.i./acre ÷ 0.0025 lb a.i./tree = 80 trees/acre]. Ambiguities in the number of trees per acre that might be treated has no practical impact on the current risk assessment because all exposure assessments are based on the maximum labelled rate of 0.2 lb a.i./acre.

Dilution volumes of 6.4 to 12.8 fluid ounces per 100 gallons are specified on the product label for Onyx [EPA Reg. No. 279-3177]. This formulation contains 2 lb a.i./gallon or 0.015625 lb a.i./fluid ounce [2 lb ÷ 120 fl. oz/gallon] which corresponds to 0.1 to 0.2 lb per 100 gallons or 0.001 to 0.002 lb/gallon. In Worksheet A01, this range of concentrations is achieved by using dilution volumes of 66 (50-100) gallons per acre under the assumption of the application rate of 0.2 lb a.i./acre.

Another factor that must be considered in the assessment of bifenthrin applications to tree bark is the proportion of bifenthrin that is actually applied to the tree bark relative to the proportion that misses the tree (through splashing or misapplication) during application. When bifenthrin is applied directly to tree bark, it is readily absorbed by the bark, and this is the basis for the efficacy of the treatment. While risks to nontarget insects or other organisms in close contact with the tree bark are plausible, risks to other organisms will be minimal, as discussed further in Section 4.4. Because of the nature of the application method, however, some bifenthrin will be applied to surrounding vegetation or soil. Very little quantitative information is available on application efficiency. Hoy (1980) reports that a good applicator can apply 90% of a pesticide solution to the tree bark during a bark treatment. A more recent study by Fettig et al. (2007)

suggests that an application efficiency of 80% may approximate worst-case application efficiency.

For this risk assessment, the unit exposures are based on the assumption that the typical application efficiency is 90% and that the functional offsite application rate is 10% of the nominal application rate.

2.5. Use Statistics

Forest Service risk assessments attempt to characterize the use of an herbicide or other pesticide in Forest Service programs relative to the use of the herbicide or other pesticide in agricultural applications. 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). While this dated information is not clearly relevant to the current use of pesticides by the Forest Service, recorded uses of bifenthrin are limited to Region 5 (Pacific Southwest) and involve very small quantities—i.e., <0.3 lbs a.i. in 2003 and <0.13 lbs a.i. in 2004.

Information on the agricultural use of pesticides is compiled by the U.S. Geological Survey (USGS) (http://water.usgs.gov/nawqa/pnsp/usage/maps/). The agricultural use of bifenthrin in 2001 is estimated by the USGS (2013) to range from about 600,000 lbs (Figure 1) to somewhat over 800,000 lbs (Figure 2). The greatest use of bifenthrin is in the north central to central United States running from North Dakota to Oklahoma and eastwards to Michigan and Georgia. Based on use data by crop (also summarized in Figure 1 and Figure 2), bifenthrin is currently used primarily on soybeans, corn, wheat, and cotton. The temporal pattern in the use of bifenthrin is noteworthy with a substantial increase in use from a maximum of about 0.2 million pounds in 2007 to somewhat over 0.8 million pounds in 2011.

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 about 290,027.15 lbs of bifenthrin was used in California (CDPR 2015, p. 214). The major non-agricultural uses appear to be applications to Christmas trees (4.3 lbs), landscape maintenance (2103.53 lbs), applications to nursery soil (17.46 lbs), applications associated with public health (5.48 lbs) or regulatory pest control (75.75 lbs), and rights-of-way management (32.36 lbs). The total of these uses (2,238.88 lbs) accounts for only about 0.77% of the total bifenthrin use in California in 2013 [2,238.88 lbs ÷ 290,027.15 lbs ≈ 0.007719553].

Based on the use statistics from California, agricultural uses of bifenthrin are much greater than uses related to forestry or other non-agricultural applications. This is a common pattern in pesticides that reflects, in part, the larger areas of crop cultivation relative to forestry management—i.e., about 613 million acres for agriculture (http://www.epa.gov/agriculture/ag101/landuse.html) relative to 193 million acres of forests managed by the Forest Service (http://www.fs.fed.us/documents/USFS_An_Overview_0106MJS.pdf) and the more intensive use of pesticides in agriculture relative to forestry.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

Bifenthrin is a Type 1 pyrethroid insecticide that interferes with the normal activity of nerve cells by disrupting the function of sodium and calcium ion channels. Numerous mechanistic studies are available in the open literature documenting the neurotoxic action of bifenthrin. These studies clearly indicate that in mammals, the [S] enantiomer of the cis-isomer is more potent than the corresponding [R] enantiomer. In addition to the studies in the open literature, a reasonably complete set of standard toxicity studies were submitted to the U.S. EPA in support of the registration of bifenthrin.

U.S. EPA's Office of Pesticide Programs (U.S. EPA/OPP) classifies potential acute hazards, based on several standard tests, ranging from the most hazardous (Category I) to the least hazardous (Category IV). U.S. EPA/OPP reviewed the acute toxicity data on bifenthrin and classified it as Category II (moderately toxic) based on acute oral toxicity and Category III based on acute dermal and inhalation toxicity. Bifenthrin is not a skin or eye irritant (Category IV). In addition, the EPA does not consider bifenthrin to be a skin sensitizer.

Acute, subchronic, and chronic toxicity studies indicate that neurotoxicity is the most sensitive endpoint from all routes of exposure to bifenthrin. The most sensitive endpoint involving neurotoxicity—i.e., the endpoint observed at the lowest dose—is decreased activity. As with other Type 1 pyrethroids, tremors are characteristic of bifenthrin poisoning. Bifenthrin is not a reproductive or developmental toxicant. While there is some evidence that bifenthrin may induce tumors, the data are not compelling, and the U.S. EPA has elected not to quantify risks that might be associated with potential carcinogenicity. While some studies suggest that bifenthrin may have an impact on immune and endocrine systems, these effects appear to occur at doses higher than those associated with neurotoxicity.

3.1.2. Mechanism of Action

Bifenthrin is a pyrethroid, which is a class of man-made insecticides structurally similar to pyrethrins, a group of naturally occurring insecticides. The primary site of action for both pyrethrins and pyrethroids is the voltage-gated membrane sodium channel of nerve cells (e.g., Cao et al. 2011a). The basic function of nerve cells involves repeated polarization and depolarization associated with neural activation or firing. These processes are controlled by channels that allow for the influx of ions into nerve cells. Both pyrethroids and pyrethrins inhibit the closing of sodium channels and thus disrupt normal nerve function (ATSDR 2003). Bifenthrin also interferes with the function of calcium ion channels (Cao et al. 2011b ; Cao et al. 2014).

Based on chemical structure, pyrethroids are classified either as Type I pyrethroids (compounds with no cyano group) or Type II pyrethroids (compounds with a cyano group). As illustrated in Section 2.2, bifenthrin does not contain a cyano group (i.e., a carbon-nitrogen triple bond) and is classified as a Type I pyrethroid. Type I and Type II pyrethroids differ in signs of neurotoxicity. Type I pyrethroids typically induce fine tremors, increased body temperatures, and coma. Type II pyrethoids induce involuntary movements, salivation, enhanced responses to stimuli, and

coarse body tremors (ATSDR 2003; Soderlund et al. 2002; Verschoyle and Aldridge 1980). As with other Type I pyrethroids, the most common gross signs of bifenthrin toxicity are decreased motor activity and tremors (Scollon et al. 2011; Wolansky et al. 2006, 2007). The recent paper by Yang and Li (2015) on rat cerebral cortical neurons suggests that bifenthrin may affect sodium channels in both the open and closed configurations, thereby displaying a combination of both Type I and Type II activity. In addition to interfering with normal nerve cell function, as discussed further in Section 3.1.6, some studies suggest that bifenthrin may also lead to nerve cell degeneration (Nandi et al. 2006) and an inhibition of neurite formation (Tran et al. 2006).

General signs of oxidative stress after exposure to bifenthrin were observed in both *in vivo* studies (Dar et al. 2013; Jin et al. 2014) and *in vitro* studies (Lu et al. 2011; Skandrani et al. 2006). Oxidative stress is a general metabolic imbalance causing an increase in reactive oxidant compounds and a decrease in antioxidant compounds which leads to cellular and organ level damage. Oxidative stress is a common manifestation of general toxicity seen with many pesticides as well as other toxic agents (Abdollahi et al. 2004). As reviewed by Jin et al. (2014), compounds causing oxidative stress responses are often associated with adverse effects on immune function. The effects of bifenthrin on immune function, however, appear to be associated with inflammatory responses rather than immune suppression (Section 3.1.7).

As summarized in Appendix 1, Table 3, there are several available *in vitro* studies that attempt to characterize the mechanism of action of bifenthrin, including the importance of cis- and trans-isomers and [R] and [S] enantiomers. A series of studies using resolved or separated [S] and [R] enantiomers clearly indicate that the [S] enantiomer is more potent than the [R] enantiomer based on endpoints associated with cytotoxicity and endocrine function (Liu et al. 2008b; Liu et al. 2009; Liu et al. 2011a; Lu et al. 2011; Wang et al. 2007; Zhao et al. 2010, 2014). The effects of bifenthrin on endocrine function are discussed further in Section 3.1.8.

3.1.3. Pharmacokinetics and Metabolism

3.1.3.1. General Considerations

Most of the metabolism studies on bifenthrin were submitted to the U.S. EPA/OPP in support of registration. These studies are reviewed in several risk assessments from U.S. EPA/OPP/HED (2007b, 2010a, 2011a, 2012a) as well as the California EPA (Dong 1995) and the Food and Agriculture Organization of WHO (FAO 2009, 2012). As with other pyrethroids (ATSDR 2003), bifenthrin is metabolized by the liver primarily via hydroxylation by the cytochrome P450 enzyme system and ester hydrolysis involving both plasma and liver carboxylesterases. Based on studies of several pyrethroids using human liver microsomes, Yang et al. (2009a) notes that bifenthrin induces and is metabolized by the CYP3A4 isozyme of cytochrome P450. Scollon et al. (2005) also notes the metabolism of bifenthrin by cytochrome P450 in preparations of rat liver microsomes. Mammals have several types of carboxylesterases (e.g., Hosokawa 2008). Of these, bifenthrin has been shown to be metabolized by HCE1 (Nishi et al. 2006) and HCE2 (Yang et al. 2005).

The U.S. EPA (2007) and Knaak et al. (2012) are involved in the development of a generalizable physiologically-based pharmacokinetic (PBPK) model for pyrethroids; however, a PBPK model for bifenthrin was not identified in the available literature. Nonetheless, as discussed in U.S. EPA/OPP/HED (2012a, p. 23), a PBPK model for deltamethrin developed by EPA indicates that

levels of deltamethrin in the brains of young rats may be higher than doses in adult rats subjected to comparable exposures by a factor of about 3.8. As discussed further in Section 3.3 (dose-response assessment), the EPA applied the results of this model to bifenthrin by assuming that generally juveniles are more sensitive than adults to pyrethroid exposure.

3.1.3.2. Absorption

Most of the occupational exposure scenarios and some 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. Hence, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which bifenthrin is likely to be absorbed from the skin surface.

As discussed further in Section 3.2, two types of dermal exposure scenarios are considered: immersion and accidental spills. As detailed in SERA (2014a), the calculation of absorbed dose for dermal exposure scenarios involving immersion or prolonged contact with chemical solutions uses Fick's first law and requires an estimate of the zero-order permeability coefficient (K_p) expressed in cm/hour. In exposure scenarios like direct sprays or accidental spills involving deposition of the compound onto the skin's surface, first-order dermal absorption rates (k_a), expressed as a proportion of the deposited dose that is absorbed per unit time, are used in the exposure assessment—e.g., $hour^{-1}$.

3.1.3.2.1. First-Order Dermal Absorption

Estimates of the dermal absorption of bifenthrin are highly variable. The most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2012a, pp. 69-70) briefly summarizes several studies of dermal absorption in rats. DERs or cleared reviews of the dermal absorption studies are not available. In one study (MRID 001630-72), the percent absorption at 10 hours post-exposure was 55.8%, 54.1%, and 37.5% at doses of 49.2, 514 and 5253 µg/rat. The lower absorption rate at the highest dose is consistent with the saturation of dermal absorption at high skin loading rates, as discussed by Kissel (2010). In another study (MRID 412842-02), only 5.11% of the applied dose (not specified in the EPA summary) was absorbed after 24 hours. In a recent *in vitro* study using rat and human skin, Hughes and Edwards (2010) noted absorption rates of 1.6% for rat skin preparations (Table 3 of paper) and 1% for human skin preparations (Table 6 of paper) over a 24-hour period.

The U.S. EPA/OPP/HED (2012a) does not derive a dermal absorption factor for bifenthrin. As discussed further in Section 3.1.12 (systemic effects from dermal absorption), the Agency elected to use a subchronic dermal toxicity study in rats for characterizing risks to humans following dermal absorption. Specifically, as discussed further in Section 3.3 (dose-response assessment), the EPA based a dose-response assessment for dermal exposure on a dose of 96.3 mg/kg bw and based the corresponding dose-response assessment for oral exposure on a dose of 3.1 mg/kg bw (U.S. EPA/OPP/HED 2012a, p. 34), which is functionally equivalent to a dermal absorption factor of about 0.032 [3.1 mg/kg bw ÷ 96.3 mg/kg bw ≈ 0.03219]. As summarized in an earlier EPA risk assessment, the Agency had derived a dermal absorption factor of 25% for pyrethroids based on a weight of evidence determination (U.S. EPA/OPP/HED 2007a, p. 30). The 25% factor is similar to the absorption factor of 17.9% used in an occupation exposure assessment by the California Department of Pesticide Regulation (Dong 1995, p.6). Although

Dong (1995) does not discuss the derivation of the estimated absorption factor, it is referenced to an unpublished study in rats submitted to the California Department of Pesticide Regulation. The ATSDR review of pyrethroids does not include information on the dermal absorption of bifenthrin; however, it notes a maximum dermal absorption rate for permethrin of 46% in rats ATSDR (2003).

In the absence of information on first-order dermal absorption rates, quantitative structure activity relationships (QSAR) are used to estimate these rates (SERA 2014a, Section 3.1.3.2.2, Equation 3). The QSAR method is based exclusively on dermal absorption data from studies in humans. As detailed in Worksheet B03b of attachments to this risk assessment, the QSAR methods yield an estimated dermal absorption rate of about 0.0042 (0.00092-0.019) $hour^{-1}$, equivalent to about 0.10 (0.022-0.46) day^{-1}. These estimates are based on a K_{ow} value of 3,000,000 and a molecular weight of 422.9 for bifenthrin. These properties are at, or modestly above, 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.

In general, experimental data are given preference over QSAR estimates in selecting kinetic or toxicological inputs. For bifenthrin, however, the relevant dermal absorption studies or cleared reviews of these studies were not available for review in the conduct of the current risk assessment. In addition, U.S. EPA/OPP/HED (2012a) uses the chronic dermal toxicity study on bifenthrin, discussed further in Section 3.1.12, as the basis for risk characterization of dermal exposures. As noted above, this approach is functionally equivalent to adopting a dermal absorption factor of 0.032 day^{-1}. The central estimate QSAR method discussed above—i.e., 0.10 day^{-1} – is only a factor of about 3 higher than the functional dermal absorption factor used by EPA [0.10 day^{-1} ÷ 0.032 day^{-1} = 3.125]. To maintain consistency with EPA, the estimates from the QSAR algorithm are adjusted downward by a factor of 3.125—i.e., 0.032 (0.007 to 0.015) day^{-1} [0.10 (0.022-0.46) day^{-1} ÷ 3.125]. In the workbooks that accompany this risk assessment, these rates are expressed in units of $hour^{-1}$ – i.e., 0.0042 (0.00092-0.019) $hour^{-1}$ ÷ 3.125 ≈ 0.0013 (0.00029 – 0.0061) $hour^{-1}$.

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 bifenthrin. 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 3,000,000 [Log Kow≈6.48] and a molecular weight of 422.9). 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).

The range of molecular weight values encompasses the estimates of the corresponding values for bifenthrin; nonetheless, the K_{ow} for bifenthrin substantially exceeds the range of values on which the EPA algorithm is based. The high K_{ow} for bifenthrin adds uncertainty to the estimates of the

K_p. As detailed in Worksheet B03a of the EXCEL workbooks for bifenthrin, the EPA algorithm results in an estimated dermal permeability (K_p) of about 0.18 (0.053-0.60) cm/hour. As discussed by Flynn (1990, Table 2) and reiterated in U.S. EPA/ORD (1992, Table 5-5), a reasonable approximation for the K_p for high molecular weight compounds (MW>150) with a high lipid solubility (log K_{ow}>3.5) is about 0.032 cm/hour [log K_p=-1.5]. This K_p is above the upper bound K_p estimated by the EPA algorithm by a factor of 18.25 [0.60 cm/hour ÷ 0.032 = 18.75]. In order to account for the likely overestimate of the upper bound K_p based on the EPA algorithm, the K_p values from Worksheet B03a are adjusted downward by a factor of 18.25 and rounded to two significant figures. Thus, the K_p values used for bifenthrin are 0.0096 (0.0028-0.032) 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). As discussed in Section 3.3 (dose-response assessment), these considerations are particularly important for bifenthrin because the most recent EPA human health risk assessment uses the acute RfD for characterizing risks associated with longer-term exposures.

Under the assumption of first-order elimination, the first-order elimination rate coefficient (***k***) is inversely related to the half-life (***T*****$_{50}$**) [***k*** = ln(2) ÷ ***T*****$_{50}$**]. If a chemical with a first-order elimination rate constant of ***k*** is administered multiple times at a fixed time interval (***t****) between doses, the body burden after the ***N*****th** dose (***X*****$_{N\ Dose}$**) relative to the body burden immediately following the first dose (***X*****$_{1\ Dose}$**) is:

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

As the number of doses (***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 (***X*****$_{Inf}$**) can be calculated as:

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

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

U.S. EPA/OPP/HED (2012a, pp. 67-69) summarizes several standard metabolism studies on bifenthrin which estimate half-lives of about 3 days in plasma and much longer half-lives of about 20-40 days in ovaries, liver, kidneys and sciatic nerve tissue (MRID 001630-71). For estimates of total body burden using the plateau principle, whole-body half-times are preferable. Although the EPA reviews of the metabolism studies do not provide estimates of whole-body half-lives, U.S. EPA/OPP/HED (2012a, p. 20) notes that 70% of bifenthrin and metabolites was excreted in the feces and about 19% of bifenthrin and metabolites were excreted in the urine within 48 hours. Taking 0.11 as the proportion of bifenthrin retained in the body [1 – (0.70 + 0.19)], the whole-body excretion coefficient can be estimated at about 1.1 day^{-1} [-ln(0.11) ÷ 2

days ≈ 1.10364 day^{-1}]. Substituting this rate coefficient into the above equation for the plateau principle, the estimated plateau for bifenthrin and bifenthrin metabolites is about 1.5. In other words, over very prolonged periods of exposure, the maximum increase in the body burden of bifenthrin should be no more than a factor of about 1.5.

The application of the plateau principal to bifenthrin may be viewed as tenuous in that the whole-body elimination of bifenthrin most likely follows multi-compartment rather than simple first-order kinetics. Nonetheless and as discussed further in Section 3.3 (dose-response assessment), this application of the plateau principle is generally supportive of the approach taken in U.S. EPA/OPP/HED (2012a) of applying the acute RfD to both acute and chronic exposures.

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. LD_{50} values are not used directly to derive toxicity values as part of the dose-response assessment in Forest Service risk assessments. 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 responses ranging from Category I (most severe response) to Category IV (least severe response). Details of the EPA system of categorization are detailed in SERA (2014a, Table 4) as well as in U.S. EPA/OPP (2010a), the label review manual.

Acute oral LD_{50} values for bifenthrin are summarized in Appendix 1, Table 1. In the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2012a), bifenthrin is classified as Category II for acute oral toxicity. The classification is based on acute oral LD_{50} values for technical grade bifenthrin of 70.1 mg/kg bw in male rats and 53.8 mg/kg bw in female rats (MRID 00132519). As summarized in Appendix 1, Table 1, several other acute oral LD_{50} values in rats are available, all of which are somewhat higher than the acute oral LD_{50} value used by EPA. As summarized in WHO (2012), somewhat lower LD_{50} values are available in mice—i.e., 43.5 mg/kg bw in males and 42.5 mg/kg bw in females. Based on the EPA classification system noted above, these LD_{50} values could be used to classify bifenthrin as Category I for acute oral toxicity. This classification, however, has no direct impact on the current risk assessment, and the differences in the sensitivity of rats and mice to bifenthrin are insubstantial.

As summarized in Appendix 1, Table 2, the U.S. EPA conducted and published a series of studies on the acute neurotoxicity of bifenthrin in rats (Scollon et al. 2011; Wolansky et al. 2006, 2007). As discussed further in Section 3.3, these studies are central to the current risk assessment, particularly the study by Wolansky et al. (2007), because U.S. EPA/OPP/HED (2012a) uses acute neurotoxicity to characterize risks associated with both acute and longer – term exposures to bifenthrin. The study by Wolansky et al. (2006, 2007) involves acute dosing of rats with technical grade bifenthrin (89%) consisting primarily (>99%) of the [R] enantiomer. Rats were gavaged with bifenthrin at single doses ranging from 0.1 to 26 mg/kg bw, and neurotoxicity was assessed using both a figure-eight maze to assess motor activity and a standard functional observational battery to assess behavioral changes (e.g., McDaniel and Moser 1993; Moser 2011). Based on benchmark dose estimates (e.g., Setzer and Kimmel 2003) of EC_{30} values (the dose associated with a 30% decrement in function), a decrease in motor activity was a somewhat more sensitive endpoint (ED_{30} = 4.6 mg/kg bw) than the assessment based on the functional observational battery (ED_{30} = 5.5 mg/kg bw). As discussed further in Section 3.3, the

EPA modified the analysis of the decrement in motor function as the basis for the dose-response assessment on bifenthrin U.S. EPA/OPP/HED (2012a).

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 bifenthrin are summarized in Appendix 1, Table A1-2. Most of the subchronic and chronic toxicity studies are unpublished studies submitted to the U.S. EPA/OPP in support of the registration of bifenthrin. These studies include standard 90-day oral studies in rats (MRID 00141199) and dogs (MRID 00141200), a subchronic neurotoxicity study in rats (MRID 44862103) as well as standard chronic toxicity studies in dogs (MRID 00163065), rats (MRID 00157226), and mice (MRID 00157227). Summaries of these studies are taken from reviews and risk assessments from EPA and other sources (Table 1), as specified in Appendix 1, Table 2. In addition to the relatively standardized registrant-submitted studies, studies published in the open literature are available for repeated doses after gavage dosing of rats (Dar et al. 2013), dietary exposures in mice (Jin et al. 2014), and intraperitoneal dosing of mice (Nieradko-Iwanicka et al. 2015).

As would be expected for a Type 1 pyrethroid, the registrant-submitted studies consistently note signs of neurotoxicity, particularly tremors. As discussed further in Section 3.1.9, tremors and other signs of neurotoxicity are also noted in repeated dosing studies designed to assay for developmental and reproductive effects. As discussed further in Section 3.3, most of the LOAELs for neurotoxicity occur over a relatively narrow range of about 4 to 7 mg/kg bw. The only exception is the chronic study in mice for which the LOAEL is 25.6 mg/kg bw/day in male mice and 32.7 mg/kg bw/day in female mice. As specified in Appendix 1 (Table A1-4), this difference does not appear to be an artifact of dose spacing, given that the NOAEL for neurotoxicity in mice is 6.7 mg/kg bw/day for males and 8.8 mg/kg bw/day for females. Thus, the NOAELs in mice are comparable to the LOAELs for rats and dogs (i.e., 4-7 mg/kg bw/day), suggesting that mice are at least somewhat less sensitive than rats and dogs to chronic exposures to bifenthrin.

The supposition that mice may be less sensitive than rats and dogs to bifenthrin is at least peripherally supported by the open literature. In the Nieradko-Iwanicka et al. (2015) study, mice were given intraperitoneal injections of 0, 4, or 8 mg/kg bw/day bifenthrin (99% purity) for 28 days. Based on a passive avoidance assay as an index of memory retention, significant decrements in memory were noted on Day 2 of dosing but not on Days 7, 14, and 28 of dosing. Similarly, a significant and dose-related decrement in locomotor activity was noted on Day 1 of dosing; however, only sporadic decrements not related to dose were noted on Day 28 of dosing (see Figures 1 and 4 in the paper by Nieradko-Iwanicka et al. 2015). The bifenthrin study by Jin et al. (2014) does not report neurotoxicity in mice as a result of dietary exposures to 10 or 20 mg/kg diet for 21-days. As discussed further in Section 3.1.7, the Jin et al. (2014) study is focused primarily on immunological effects. Nonetheless, it seems that signs of neurotoxicity

would have been reported had they occurred, and there is no reference to tremors or other signs of neurotoxicity in the mice.

3.1.6. Effects on Nervous System

As discussed in ATSDR (2003), bifenthrin and many other pyrethroids and pyrethrins are clearly neurotoxic. As discussed in Section 3.1.2, the mechanism of neurotoxicity is understood relatively well. As discussed in Sections 3.1.4 and 3.1.5, neurotoxicity is the most sensitive endpoint for acute and chronic exposures to bifenthrin. As noted by the U.S. EPA:

> *There are no residual uncertainties with regard to evidence of neurotoxicity for bifenthrin. Like other pyrethroids, bifenthrin causes toxicity from interaction with sodium channels leading to clinical signs of neurotoxicity. These effects are adequately assessed by the available guideline and non-guideline studies. Bifenthrin is a Type I pyrethroid and tremors were consistently observed throughout its toxicology database. Neurotoxicity was consistently observed throughout the database in a dose-dependent manner in most of the studies conducted.*
>
> U.S. EPA/OPP/HED 2012a, p. 29.

The above summary of the evidence for neurotoxicity is consistent with all of the available reviews and risk assessments on bifenthrin (Table 1) and further elaboration on neurotoxicity in the hazard identification is unnecessary. As discussed further in the dose-response assessment (Section 3.3), neurotoxicity is the endpoint used for the development of the RfD for bifenthrin.

3.1.7. Effects on Immune System

There are various methods for assessing the effects of chemical exposure on immune responses, including assays of antibody-antigen reactions, changes in the activity of specific types of lymphoid cells, and assessments of changes in the susceptibility of exposed animals to resist infection from pathogens or proliferation of tumor cells. Typical subchronic or chronic animal bioassays 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 morphology of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected.

In reviewing the standard registrant-submitted studies on the toxicology of bifenthrin, the EPA noted no evidence for immunotoxicity:

> *The toxicology database for bifenthrin does not show any evidence of treatment-related effects on the immune system, and the overall weight-of-evidence suggests that this chemical does not directly target the immune system. Therefore, the Agency does not believe that conducting a functional immunotoxicity study will result in a lower POD* [Point of Departure] *than that currently in use for overall risk assessment, and additional safety factors are not needed to account for a lack of this study.*
>
> U.S. EPA/OPP/HED 2012a, p. 7

Nonetheless, as also noted in U.S. EPA/OPP/HED (2012a, p. 6), recent changes to pesticide regulations (40 CFR § 158) now require immunotoxicity assays as a condition for pesticide registration, and it seems likely that an immunotoxicity study will be required during the registration review of bifenthrin. Notably, the position taken in the most recent EPA risk assessment, as quoted above, differs from the EPA's assessment in the scoping documents for the registration review of bifenthrin of the need for an additional uncertainty factor to address the potential immunotoxicity of bifenthrin (U.S. EPA/OPP/HED 2010a, 2011a, p. 17). In these scoping documents, the EPA notes that a 10X uncertainty factor might be used to address the data deficiency on immunotoxicity. As discussed in Section 1.1, the U.S. EPA/OPP will complete the registration review of bifenthrin in 2016. When this review is completed, the Agency's position on the potential immunotoxicity of bifenthrin may be clarified.

The open literature provides no clear information that bifenthrin will cause immune suppression; however, there is some indication of immune stimulation or inflammation. In rats given gavage doses of 0.5 mg/kg bw/day for 3 weeks, Akhtar et al. (1996) note significant decreases in serum T3 and T4 but also a stimulation of the thyroid stimulating hormone. This study from the Pakistan literature used a 10% EC Talstar formulation purchased in the UK. The *in vitro* study by Hoffman et al. (2006) notes a stimulation of T-cell response at concentrations of about 0.042 mg/L, which is also indicative of an inflammatory response. While these effects suggest the potential for bifenthrin to induce inflammatory immune responses, the EPA found no relationship between exposures to pyrethroids (including bifenthrin) and the development of asthma or other allergic responses (U.S. EPA/OPP 2009).

The only suggestion of a potential suppression of immune function in an *in vivo* study is the decrease in spleen and thymus weights noted by Jin et al. (2014) following dietary exposures of 4-week old mice to bifenthrin at a concentration of 20 mg/kg chow. These effects, however, were not seen by these investigators in 7-week old mice subjected to the same exposure. In addition, as discussed above, changes in spleen and thyroid weights are not noted in the standard registrant-submitted studies. In an *in vitro* study using macrophage cells, Zhao et al. (2010) noted decreases in macrophage viability at concentrations of 0.0042 mg/L for both the [S] and [R] enantiomers of bifenthrin. In the absence of other supporting data, however, this observation may simply be a sign of cytotoxicity rather than a specific effect on immune function.

3.1.8. Effects on Endocrine System

Assessments of the direct effects of chemicals on endocrine function are most often based on mechanistic studies on estrogen, androgen, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). In addition, inferences concerning the potential for endocrine disruption can sometimes be made from responses seen in standard toxicity tests—i.e., changes in the structure of major endocrine glands (i.e., the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis) or changes in growth rates. Effects on organs associated with endocrine function may be secondary to other toxic effects. Thus, in the absence of information on specific endocrine mechanisms, pathological changes in endocrine tissues do not necessarily indicate a direct effect on endocrine function.

As summarized in Appendix 1, Table A1-3, several *in vitro* studies in the open literature assess the potential of bifenthrin to interfere with endocrine function (Liu et al. 2011a,b; Wang et al. 2007; Zhao et al. 2010, 2014). All of these studies involve purified (1RS)-cis-bifenthrin (95.5 to 99.5%) from which the [R] and [S] enantiomers were isolated and assayed separately. In all assays, the [S] enantiomer was more potent than the [R] enantiomer, and various signs of endocrine effects are noted. In addition to these *in vitro* studies on mammalian cells, studies in fish also note a potential for bifenthrin to interfere with normal endocrine function (Brander et al. 2012; Riar et al. 2013; Schlenk et al. 2012; Wang et al. 2007). The studies in fish are summarized in Appendix 6 and discussed further in Section 4.1.3.1.

Only one *in vivo* mammalian study, conducted by Jin et al. (2013a), assays the effects of bifenthrin on endocrine function. Jin et al. (2013a) administered either [S] or [R] cis-bifenthrin to female mice at a dose of 15 mg/kg bw/day for 21 days either before or during pregnancy. A significant reduction in the transcription of genes associated with testosterone production was observed in male offspring from female mice dosed with [S] enantiomer during but not before pregnancy. Nonetheless, no statistically significant decreases in testicular testosterone were observed in 6-week old male offspring of female mice dosed either before or during pregnancy with either enantiomer (Jin et al. 2013a, Figure 5).

The most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2012a) does not specifically address the potential impact of bifenthrin on endocrine function. The scoping documents for the registration review of bifenthrin note that bifenthrin was selected for testing in a battery of screening assays for endocrine disruption developed by the U.S. EPA (U.S. EPA/OPP/HED 2010a, 2011a, p. 5). The results of these Tier 1 screening studies are available and based on these results the EPA concluded:

> *Based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for bifenthrin since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.*
>
> U.S. EPA/OPP 2015, p. 2

The above conclusion from EPA is essentially in agreement with the mammalian study by Jin et al. (2013a). In term of the open literature studies on fish, the U.S. EPA/OPP (2015, p. 8) notes that effects in female fish occurred only in exposures causing over signs of toxicity – i.e., signs of neurotoxicity including erratic swimming, lethargy, and loss of equilibrium.

In terms of functional effects that have important public health implications, effects on endocrine function could be expressed as diminished reproductive performance or abnormal development. As discussed in the following section (Section 3.1.9), bifenthrin does not appear to be associated with specific adverse effects on either fetal development or reproductive performance.

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 and specific protocols for developmental and reproduction studies are established by EPA (U.S. EPA/OPPTS 2000).

As summarized in Appendix 1, Table A1-5, standard developmental toxicity studies in rats (MRID 00154482/ 00141201) and rabbits (MRID 45352301 and MRID 00145997) as well as a developmental neurotoxicity study (MRID 46750501) were submitted to the U.S. EPA in support of the registration of bifenthrin. These studies are summarized in the most recent EPA risk assessment on bifenthrin (U.S. EPA/OPP/HED 2012a). In addition, an abstract of a standard developmental study is published in the open literature (McCarty et al. 2002), which appears to have been conducted by FMC Corporation, the primary registrant for bifenthrin. Nonetheless, the study, which does not appear to have been submitted to EPA, is not summarized in the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2012a).

The developmental studies report signs of neurotoxicity consistent with other studies on bifenthrin, but no signs of developmental toxicity. Based on these studies, the EPA concluded that bifenthrin is not a developmental toxicant (U.S. EPA/OPP/HED 2012a). While the current Forest Service risk assessment concurs with the EPA assessment on developmental effects, several of the developmental studies report neurological effects at doses somewhat below those seen in other types of studies. These data are discussed further in the dose-response assessment (Section 3.3).

3.1.9.2. Reproduction Studies

Reproduction studies involve exposing one or more generations of the test animal to a chemical compound. Generally, the experimental method involves dosing the parental (P or F_0) generation (i.e., the male and female animals used at the start of the study) to the test substance prior to mating, during mating, after mating, and through weaning of the offspring (F_1). In a 2-generation reproduction study, this procedure is repeated with male and female offspring from the F_1 generation to produce another set of offspring (F_2). During these types of studies, standard observations for gross signs of toxicity are made. Additional observations often include the length of the estrous cycle, assays on sperm and other reproductive tissue, and number, viability, and growth of offspring. Typically, the EPA requires one acceptable multi-generation reproduction study for pesticide registration (U.S. EPA/OCSPP 2013).

As summarized in U.S. EPA/OPP/HED (2012a, p. 65), one multigenerational reproduction study in rats is available for bifenthrin (MRID 00157225), and a cleared review of this study is available (DeProspo et al. 1986). No effects on reproduction were noted at dietary concentrations of up to 100 ppm, equivalent to a dose of 5 mg/kg bw/day. The only adverse effects observed were tremors and decreased body weight in females during and shortly after lactation. No effects were noted in male or female rats at a dietary concentration of 60 ppm, equivalent to a dose of 3 mg/kg bw/day.

3.1.10. Carcinogenicity and Mutagenicity

As summarized in Appendix 1, Table A1-4, standard chronic carcinogenicity studies are available in rats (MRID 00157226) and mice (MRID 00157227). No carcinogenic responses were observed in the rat bioassay; however, in mice, there was a significant dose-related trend in the incidence of bladder tumors and a significantly greater incidence of bladder tumors in males

but not females at the high dose, relative to controls. The incidences of other tumor types appeared to be incidental—i.e., there were no dose-related trends or significant increases in other tumor types. In addition, bifenthrin was marginally active in an *in vitro* bioassay for forward mutations in mouse lymphoma cells, but there was no indication of mutagenic activity in five other mutagenicity assays. Based on these data, the EPA classifies bifenthrin as a "*possible human carcinogen*" (U.S. EPA/OPP/HED 2012a, p. 8) but elected to base the dose-response assessment on systemic toxicity, specifically the well-documented neurotoxicity of bifenthrin as discussed further in Section 3.3. This classification reflects and is consistent with the U.S. EPA/OPP/HED detailed review of the mutagenicity and carcinogenicity bioassays on bifenthrin (U.S. EPA/OPP/HED 1992b).

There are no experimental studies or epidemiology studies in the open literature that address the potential carcinogenicity of bifenthrin. The position taken by the EPA (i.e., not to derive quantitative estimates of cancer risk) is consistent with assessments of the carcinogenicity of bifenthrin made by the European Food Safety Authority (EFSA 2011, p. 48), the Food and Agriculture Organization of the United Nations (FAO 2009, p. 18), and the World Health Organization (WHO 2012, p. 21), all of which declined to derive a cancer potency factor for bifenthrin. In the absence of a compelling reason to do otherwise, the current Forest Service risk assessment defers to the U.S. EPA, and carcinogenicity is not assessed quantitatively.

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

As with acute oral toxicity, the U.S. EPA/OPP requires acute assays for skin irritation, skin sensitization, and eye irritation and uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response) for skin and eye irritation. Skin sensitization is classified simply as occurring or not occurring. For each type of assay, the EPA has developed standard protocols (U.S. EPA/OCSPP 2013).

3.1.11.1. Skin Irritation

U.S. EPA/OPP/HED (2012a, p. 63) does not include a detailed discussion about the potential for bifenthrin to cause skin irritation; yet, with reference to MRID 00132521, indicates that bifenthrin is not a skin irritant (Category IV). As summarized in Appendix 1, Table A1-6, MRID 00132521 is associated with the Freeman et al. (1983c) study for which a DER is available. According to the DER, the test compound was technical grade bifenthrin (88.35% purity). As also summarized in Appendix 1, Table A1-6, Freeman et al. (1983c) also assayed a 26.5% w/w a.i. (2 lb a.i./gal) EC formulation of bifenthrin, identified in the DER only as FMC 54800, that also resulted in no signs of skin irritation. As noted in Tomlin (2004), FMC 54800 is a development code for bifenthrin. Thus, the designation in the DER indicates that a formulation of bifenthrin was used but does not help to identify the specific formulation. As summarized in Table 4, the composition of 2 lb a.i./gallon is consistent with two of the formulations explicitly covered in the current risk assessment.

3.1.11.2. Skin Sensitization

As with skin irritation, U.S. EPA/OPP/HED (2012a, p. 63) does not provide a detailed discussion of the skin sensitization studies on bifenthrin but indicates that bifenthrin is not a skin sensitizer referencing MRID 00132523. As summarized in Appendix 1, Table A1-6, MRID 00132523 is associated with Freeman et al. (1983e), a standard skin sensitization study in guinea pigs

conducted with technical grade bifenthrin and in which skin sensitization was not observed following a challenge dose given 14 days after the sensitization doses.

As with skin irritation, a skin sensitization study (Freeman et al. 1983j) is also available on a FMC 54800 (i.e., bifenthrin) formulation containing 26.5% w/w a.i. As noted above, this composition is consistent with 2 lb a.i./gallon formulations covered in the current risk assessment (Table 4). Unlike the case with skin irritation, the formulation did elicit a marked response upon challenge—i.e., severe erythema which had progressed to necrosis. By comparison, the study conducted with the bifenthrin formulation (Freeman et al. 1983j), rather than technical grade bifenthrin (Freeman et al. 1983e), suggests that other ingredients (i.e., *inerts*) in the formulation rather than bifenthrin itself may be associated with skin sensitization.

In contrast to the evaluation in U.S. EPA/OPP/HED (2012a), the European Food Safety review of bifenthrin indicates that bifenthrin is a skin sensitizer; however the review does not provide details on the data supporting this assessment (EFSA 2011, p. 12 and p. 38). As discussed further in Section 3.1.15, FAO (2012) suggests that skin sensitization by bifenthrin may be due to an impurity.

3.1.11.3. Ocular Effects

As with skin irritation (Section 3.1.11.1), U.S. EPA/OPP/HED (2012a, p. 63) does not provide a detailed discussion of the studies addressing the potential for bifenthrin to cause eye irritation; nevertheless, the EPA assessment does indicate that bifenthrin is not an eye irritant (Category IV). This classification is referenced to MRID 00132522. As summarized in Appendix 1, Table A1-7, this MRID is a standard eye irritation study in New Zealand white rabbits with technical grade bifenthrin (Freeman et al. 1983d). While all treated eyes evidenced severe discharges at 1 hour after treatment, all treated eyes were normal by 24 hours and remained so over the 72-hour observation period.

A parallel eye irritation study is available on the FMC 54800 (Freeman et al. 1983i), that is not summarized in U.S. EPA/OPP/HED (2012a). Freeman et al. (1983i) observed discharge and swelling in all treated eyes up to 48 hours after dosing. By 48 hours, however, all eyes were normal. Based on this somewhat more severe response, relative to technical grade bifenthrin, the formulation was classified as Category III for eye irritation.

3.1.12. Systemic Toxic Effects from Dermal Exposure

The acute dermal toxicity studies on bifenthrin and bifenthrin formulations are summarized in Appendix 1, Table A1-8. As with acute irritant effects to the skin and eyes (Section 3.1.11), the U.S. EPA/OPP requires acute dermal toxicity studies for both active ingredients and formulations and classifies the potential for acute dermal toxicity using a Category I (most hazardous) to Category IV (least hazardous) classification system (SERA 2014a, Table 4; U.S. EPA/OPP 2010a).

U.S. EPA/OPP/HED (2012a, p. 63) classifies bifenthrin as Category III for acute dermal toxicity. This classification is based on MRID 00132520. As summarized in Appendix 1, Table A1-8, this MRID number designates the acute dermal limit assay (i.e., single dose) in rabbits conducted by Freeman et al. (1983b) in which no mortality occurred at a dermal dose of 2000 mg/kg bw/day. In the registration process, the U.S. EPA will accept *limit tests* in which the compound

is tested at only a single high dose, typically 2000 or 5000 mg/kg bw. If the compound does not cause mortality rates of 50% or more, the requirement for a full study to determine the LD_{50} value may be waived, which appears to be the case with bifenthrin. Note that the classification of bifenthrin as Category III rather than Category IV may be an artifact of the experimental design. As summarized in the U.S. EPA/OPP (2010, p. 7-2) Label Review Manual, Category III for acute dermal toxicity encompasses acute dermal LD_{50} values of >2000-5000 mg/kg bw. Thus, if the Freeman et al. (1983b) study had been conducted at a dose of 5,000 mg/kg bw bifenthrin could have been classified as Category IV if less than 50% mortality had been observed. As also summarized in Appendix 1, Table A1-8, more recent acute dermal limit tests have been submitted to the U.S. EPA/OPP on technical grade bifenthrin using rats (Tiwari 2002b) and the FMC 54800 formulation using rabbits (Freeman et al. 1983g). Like Freeman et al. (1983b), both of these studies resulted in no mortality at the limit dose of 2000 mg/kg bw.

Although mortality was not observed in the acute dermal studies, signs of neurotoxicity were observed in rabbits (Freeman et al. 1983b) and rats (Tiwari 2002b) in the two acute dermal studies conducted with technical grade bifenthrin. But signs of neurotoxicity were not observed in rabbits in the study conducted with the FMC 54800 formulation (Freeman et al. 1983g). Note that the formulation dose of 2000 mg/kg bw corresponds to a dose of 530 mg a.i./kg bw [2000 mg formulation/kg bw x 0.265 a.i./formulation]. Perhaps this difference is due to the neurotoxicity of bifenthrin and a lack of neurotoxicity in the other ingredients in the formulation.

A single 21-day dermal toxicity study in rabbits is available in which signs of neurotoxicity were observed at 93 mg/kg bw with a NOAEL of 47 mg/kg bw. This study is summarized in all recent human health risk assessments from EPA (U.S. EPA/OPP/HED 2007b, 2010a, 2011a, 2012a), however, an explicit designation of the study is not provided. As summarized in Appendix 1, Table A1-8, this study appears to be the study by Seaman et al. (1984). The DER for this study is dated 1985 and is not consistent with the more recent summaries in the EPA risk assessment, suggesting that the study was reevaluated by EPA. All dose and response data from this study given in Appendix 1 are based on the more recent EPA risk assessments rather than the older DER. As discussed further in Section 3.3, U.S. EPA/OPP/HED (2012a) uses this study to characterize the risk associated with dermal exposures of workers to bifenthrin.

3.1.13. Inhalation Exposure

The standard acute and longer-term toxicity studies required by U.S. EPA/OPP in support of the registration of bifenthrin are summarized in Appendix 1, Table A1-9. Following standard EPA protocols, all of these studies were conducted with rats and an exposure duration of 4 hours.

The most recent EPA human health risk assessment cites a 2003 study involving nose-only exposure to technical grade bifenthrin, and there appears to be no cleared review/DER available for this study. As indicated in Appendix 1, Table A1-9, details of this study are taken from EPA and WHO reviews. Based on the LC_{50} of 1.01 mg/L, U.S. EPA/OPP/HED (2012a) classifies technical grade bifenthrin as Category III (i.e., the second least hazardous classification).

As also summarized in Appendix 1, Table A1-9, two cleared reviews (Maedgen 1983, 1984) are available on acute inhalation studies of bifenthrin formulations. The reported LC_{50} values from the formulation studies are somewhat higher than the LC_{50} for technical grade bifenthrin. The DERs for these studies were prepared in the late 1980s and do not provide detailed summaries of

the test material; moreover, it is not clear whether the LC_{50} values are expressed in units of formulation or active ingredient. These studies are noted for the sake of completeness but are not otherwise used in the current risk assessment.

U.S. EPA/OPP/HED (2012a, p. 7) indicates that an acute neurotoxicity inhalation study is being required for bifenthrin, but further information about its availability is unavailable.

3.1.14. Other Ingredients and Adjuvants

3.1.14.1. Other Ingredients

The EPA is responsible for regulating inerts and adjuvants in pesticide formulations. As implemented, these regulations affect only pesticide labeling and testing requirements. The term *inert* is used to designate compounds that do not have a direct toxic effect on the target species. Although the term *inert* is codified in FIFRA, some inerts may be toxic; therefore, the EPA now uses the term *Other Ingredients* instead of the term *inerts*. For brevity, the following discussion uses the term *inert*, recognizing that *inerts* may be biologically active and potentially hazardous components. The U.S. EPA has classified inerts into one of four lists based on the available toxicity information: toxic (List 1), potentially toxic (List 2), unclassifiable (List 3), and non-toxic (List 4). List 4 is subdivided into two categories, 4A and 4B. List 4A constitutes inerts for which there is adequate information to indicate a minimal concern. List 4B constitutes inerts for which the use patterns and toxicity data indicate that use of the compound as an inert is not likely to pose a risk. These lists as well as other updated information regarding pesticide inerts are maintained by the U.S. EPA at the following web site: http://www.epa.gov/opprd001/inerts/. And the EPA maintains a database, InertFinder, on inerts allowed in pesticides (U.S. EPA/OPP 2014).

The identity of inerts in pesticide formulations is considered proprietary and is not disclosed to the general public. Nonetheless, all inerts are disclosed to and approved by the U.S. EPA/OPP as part of the registration of pesticide formulations. In addition, potentially hazardous inerts are disclosed in Material Safety Datasheets for pesticide formulations. As summarized in Table 4, the disclosed inerts in the representative formulations considered in the current risk assessment include petroleum distillates, ethylene glycol, and propylene glycol. Petroleum distillates, including aromatic hydrocarbons, are complex mixtures. Thus, it is possible that specific inert ingredients vary, at least somewhat, among liquid formulations of bifenthrin. As reviewed by ATSDR (1995), petroleum distillates can induce a wide range of toxic effects, particularly effects on the nervous system. Due to the complexity and variability of petroleum distillates and the limited information available on the identity of the petroleum components in bifenthrin formulations, it is difficult to assess the extent to which the other ingredients in bifenthrin formulations contribute to the toxicity of these formulations. Both propylene glycol and ethylene glycol are approved pesticide inerts that are exempt from tolerance requirements (U.S. EPA/OPP 2014). In plain language, this indicates that the use patterns of these inerts in pesticide formulations are deemed not to pose an unreasonable hazard to human health. In addition, propylene glycol is an approved food additive and is listed by the U.S. Food and Drug Administration as a GRAS (generally recognized as safe) compound (http://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm091048.htm#ftnP).

Another major limitation in assessing the hazards associated with pesticide inerts is that the amounts of the inerts in the formulations are not always specified, as is the case with formulations of bifenthrin. So even if detailed toxicity values were readily available on inerts such as propylene glycol, a quantitative analysis of the potential contribution of the inerts relative to the active ingredient could not be made.

The only remaining approach to assessing the contribution of inerts to the toxicity of the formulation is to compare toxicity values for the formulation, expressed in units of active ingredient, to corresponding toxicity values for the unformulated active ingredient. As discussed in Section 3.1.11.2, comparable studies on skin sensitization of technical grade bifenthrin (Freeman et al. 1983e) and a 26.5% a.i. liquid formulation suggest that components in the formulation other than bifenthrin may be skin sensitizers. Conversely and as discussed in Section 3.1.12, comparable acute dermal toxicity studies on technical grade bifenthrin (Freeman et al. 1983b; Tiwari 2002b) and a 26.5% a.i. liquid formulation (Freeman et al. 1983g) suggest that the inerts in the formulation do not contribute to or augment the neurotoxicity of the bifenthrin.

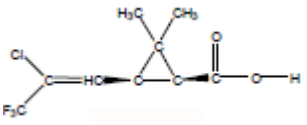
3.1.14.2. Adjuvants

As with most Forest Service risk assessments as well as pesticide risk assessments conducted by the EPA, the current risk assessment does not specifically attempt to assess the risks of using adjuvants, without specific information to suggest that the risks may be substantial. For example, some adjuvants used in glyphosate formulations may be as toxic as, and possibly more toxic than, glyphosate itself; accordingly, these risks are addressed in the Forest Service risk assessment on glyphosate (SERA 2010). Comparable information is not available on adjuvants that might be used with bifenthrin.

3.1.15. Impurities and Metabolites

The U.S. EPA requires the characterization of metabolites for all pesticides, and, as appropriate, may designate metabolites of concern and require toxicity studies on those metabolites. This is not the case with bifenthrin. Neither the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2012a) nor the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a) designates or discusses metabolites of concern. Furthermore, toxic metabolites are not noted in other reviews on the toxicity of bifenthrin (Table 1). Although specific information on the toxicity of bifenthrin metabolites was not identified in the available literature, observations on other pyrethroids, discussed further in Section 3.1.16, suggest that the metabolites of bifenthrin are less toxic than bifenthrin itself.

Information is available on one impurity in technical grade bifenthrin, 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethyl-cyclopropane carboxylic acid, typically abbreviated as TFP-acid.



TFP-acid is both a soil metabolite of bifenthrin (Fecko 1999) and an impurity in the synthesis of technical grade bifenthrin (FAO 2012; U.S. EPA/OPP/HED 1989). This and perhaps other impurities are disclosed to U.S. EPA but are not typically made public. Because specific

information concerning impurities may provide insight into the manufacturing process used to synthesize bifenthrin, information on impurities is considered proprietary, is protected under FIFRA (Section 10), and was not available for the preparation of the current Forest Service risk assessment. The discussion of this impurity in U.S. EPA/OPP/HED (1989) does not address the toxicity of this impurity in detail but does indicate that the impurity is not mutagenic and is viewed by the EPA as *Acceptable*. Conversely, FAO (2012, p. 11) suggests that TFP-acid may be a factor in the skin sensitization reported in a least one European study. The discussion of impurities in FAO (2012) also indicates that bifenthrin may contain technical solvents (e.g., toluene) but that …*the amounts detected are so low that they can be considered as non-relevant* (FAO 2012, p.).

As with most pesticides, concern for impurities in technical grade bifenthrin is reduced because most of the existing toxicity studies were conducted with the technical grade product or formulated products. Thus, the effects of potentially toxic impurities in the technical grade product are likely to be encompassed by the available toxicity studies on technical grade bifenthrin.

3.1.16. Toxicological Interactions

Relatively little specific information is available on the interaction of bifenthrin with other compounds. In an *in vivo* acute toxicity study in rats, Wolansky et al. (2009) noted no deviation from dose-addition in a mixture of 11 pyrethroids including bifenthrin. This observation is consistent with the U.S. EPA's determination to treat pyrethroids as a class of compounds with a common mechanism of action (e.g., U.S. EPA/OPP/HED 2012a, p. 49). Holton et al. (1997) noted that bifenthrin increases the severity of brainstem lesions in rats exposed to 1,3-dinitrotoluene; however, it is not clear if this joint action is additive or greater than additive.

As discussed in ATSDR (2003) and noted in Section 3.1.2.1, bifenthrin as well as other pyrethroids and pyrethrins are metabolized by cytochrome P450 enzyme systems. While there is no specific information available on the toxicity of bifenthrin metabolites (Section 3.1.15), data on other pyrethroids suggest that compounds which stimulate P450 are likely to reduce the toxicity of pyrethroids, and compounds that interfere with the action of cytochrome P450 will increase the toxicity of pyrethroids. These observations provide at least indirect support for the supposition that the metabolism of bifenthrin by cytochrome P450 is a detoxification process. This supposition is consistent with the fact that no toxic metabolites of concern for bifenthrin have been identified by EPA or other organizations. (Section 3.1.15).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

As discussed in Section 2.4.5, the exposure assessments for this risk assessment are detailed in two EXCEL workbooks: Attachment 1 for foliar applications and Attachment 2 for bark applications. These workbooks contain a set of worksheets that detail each exposure scenario discussed in this risk assessment as well as summary worksheets for both workers (Worksheet E01) and members of the general public (Worksheet E02). Documentation for these worksheets is presented in SERA (2011a).

Worker exposure assessments for backpack spray, broadcast ground spray, and aerial spray are given in Attachment 1. In non-accidental scenarios involving the normal application of bifenthrin, central estimates of exposure for workers are approximately 0.0875 mg/kg bw/day for backpack applications, 0.00448 mg/kg bw/day for ground broadcast applications, and 0.00392 mg/kg bw/day for aerial spray. Upper prediction intervals of exposures are approximately 0.064 mg/kg bw/day for backpack applications, 0.336 mg/kg bw/day for ground broadcast applications, and 0.32 mg/kg bw/day for aerial applications. Substantially lower exposures are estimated for bark applications—i.e., a central estimate of 0.00035 with an upper bound of 0.0128 mg/kg bw/day. Much greater exposures are estimated for accidental exposure scenarios. The greatest exposures occur in the accidental scenario for wearing contaminated gloves for a period of 1 hour which is project to result in exposures of greater than1 mg/kg bw per event.

For the general public (Worksheet E03), acute non-accidental exposure levels associated with foliar applications range from very low (e.g., $\approx 1 \times 10^{-7}$ mg/kg bw/day) to about 0.27 mg/kg bw. The upper bound of an exposure of 0.27 mg/kg bw is associated with the consumption of contaminated vegetation. The other acute exposure scenarios lead to lower and often much lower dose estimates. The lowest acute exposure levels are associated with swimming in or drinking contaminated water. Exposure levels associated with bark applications are a factor of about 10 below those for foliar applications based on the assumption that 90% of bifenthrin applied in bark applications remains on the bark.

3.2.2. Workers

3.2.2.1. General Exposures

All general exposures for workers are calculated as the amount a.i. handled by a worker in a single day multiplied by a worker exposure rate (in units of mg/kg bw per lb a.i. handled). Relatively well-documented worker exposure rates are available (SERA 2014b) for bark applications as well as foliar broadcast applications.

3.2.2.1.1. Foliar Application

Worker exposure rates for directed foliar applications are derived in SERA (2014b). In Table 14 of SERA (2014b), three reference chemicals with corresponding worker exposure rates are given for backpack applications—i.e., glyphosate (k_a = 0.00041 hour^{-1}), 2,4-D (k_a = 0.00066 hour^{-1}), and triclopyr BEE (k_a = 0.0031 hour^{-1}). As discussed in Section 3.1.3.2.2 of the current risk assessment, the central estimate of the first-order dermal absorption rate coefficient for bifenthrin is 0.0013 hour^{-1}. This rate coefficient for bifenthrin is about a factor of 2.4 less than the corresponding coefficient for triclopyr BEE [0.0031 hour^{-1} ÷ 0.0013 hour^{-1} ≈ 2.3846] and a

factor of 2 higher than the corresponding coefficient for 2,4-D [0.0013 $hour^{-1}$ ÷ 0.00066 $hour^{-1}$ ≈ 1.9697]. Consequently, the use of the worker exposure rates for either triclopyr BEE or 2,4-D would not involve excessive extrapolation. To minimize extrapolation, 2,4-D is used as the reference chemical for bifenthrin.

The application of the methodology from SERA (2014b) is detailed in Table 5 (backpack applications), Table 6 (ground broadcast applications), and Table 7 (aerial applications). The resulting worker exposure rates are used in Attachment 1 (foliar applications) to derive worker exposures of backpack applications (Worksheet C01a), ground broadcast applications (Worksheet C01b), and aerial applications (Worksheet C01c).

Although applications for termite control are not considered quantitatively in the current risk assessment due to the numerous site-specific considerations that might be involved (Section 2.3.3), it is worth noting that the Worker Health and Safety Branch of the California Environmental Protection Agency derived exposure rates for workers involved in termite control applications (Dong 1995) based on a study involving deposition, which was submitted to the U.S. EPA (U.S. EPA/OPP/HED 1992). The highest reported worker exposure rate is 1.59 µg/kg bw per lb a.i. handled (Dong 1995, Table 3, p. 13) or about 0.002 mg/kg bw per lb a.i. handled. This worker exposure rate is about a factor of 5 below the central estimate of the worker exposure rates for backpack applications detailed in Table 5 [0.0098 ÷ 0.002 ≈ 4.9]. The summary of the worker exposure study given in U.S. EPA/OPP/HED (1992a) notes an average exposure for applicators of 0.0096 mg/kg bw and a maximum exposure of about 0.030 mg/kg bw (U.S. EPA/OPP/HED 1992a, p. 3, lower table). As summarized in Worksheet E01 of Attachment 1 (foliar applications), similar exposures are estimated for backpack applications — i.e., a central estimate of 0.00875 mg/kg bw with an upper bound of 0.064 mg/kg bw. Thus, the use of the worker exposure rates for backpack applications would be a reasonable approach for estimating worker exposures in applications for termite control.

In addition to the application rate and absorbed dose rate, the other factor affecting worker exposure is the number of acres per day that a worker will treat, in that acres treated per day are used in estimating the amount of pesticide that a worker will handle. Estimates of the number of acres per day that a worker might treat are taken from SERA (2014b, Table 2 and Section 1.1). These estimates are as important as worker exposure rates, and estimates of the number of acres treated per day should be adjusted as appropriate for any site-specific application.

3.2.2.1.2. Bark Application

Worker exposure rates for bark applications are derived in SERA (2014b). These rates are based on a study by Middendorf (1992) of workers applying the butoxyethyl ester of triclopyr in a basal bark application. As summarized in Table 14 (p. 82) of SERA (2014b), the worker exposure rate from this study is 0.001 mg/kg bw/day per lb handled with a 95% prediction interval of 0.0001 - 0.02 mg/kg bw/day per lb handled. As 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 rate coefficient for triclopyr (the reference chemical) and the chemical of concern (in this case bifenthrin). This adjustment is detailed in Table 8 of the current risk assessment. In Worksheet C01 of Attachment 2 (the WorksheetMaker workbook for bark applications), the exposure rates from Table 8 are rounded to one significant place (i.e.,

0.0004 [0.00004-0.008] mg/kg bw/day per lb handled) and used to estimate worker exposures to bifenthrin during bark applications.

Standard values for the number of acres treated per day in bark applications are not available, and treatment rates associated with foliar backpack applications are used in Attachment 2. Estimates of acres treated per day may not be viewed as intuitive units for bark applications. In any site-specific use of Attachment 2, Worksheet C01 may be modified to provide more appropriate estimates of the amount of pesticide that a worker will handle per day.

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, and the estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Both sets of exposure scenarios are summarized in Worksheet E01 of the EXCEL workbooks that accompany this risk assessment—i.e., Attachments 1 and 2. Additionally, Worksheet E01 references other worksheets in which the calculations of each exposure assessment are detailed.

Exposure scenarios involving direct contact with solutions of bifenthrin 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 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 rate are essentially constant. For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. For these types of exposures, the rate of absorption is estimated based on a zero-order dermal absorption rate (K_p). Details regarding the derivation of the K_p value for bifenthrin 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).

The details of the accidental spill scenarios for workers consist of spilling a chemical solution on to the lower legs as well as spilling a chemical solution on to the hands, at least some of which adheres to the skin. The absorbed dose is then calculated as the product of the amount of chemical on the skin surface (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the chemical concentration in the liquid), the first-order absorption rate 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 on to the hand) and C03b (spill onto the lower legs).

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 bifenthrin in Forest Service programs appears to be highly variable, depending on which of the various application methods is used. Bifenthrin 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 bifenthrin following either foliar or bark applications. Conversely, members of the general public are less likely to be exposed to bifenthrin in foliar or bark applications made in remote areas.

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., protective 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 bifenthrin, a standard set of exposure assessments used in all Forest Service risk assessments for broadcast applications are considered. These exposure scenarios, with modifications as necessary, are also used for bark applications. As summarized in Worksheet E03 of Attachments 1 and 2, the kinds of exposure scenarios developed for the general public include acute accidental, acute non-accidental, and longer-term or chronic exposures. The accidental exposure scenarios assume that an individual is exposed to the compound of concern either during or shortly after its application. 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 bifenthrin at 0.2 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*). The impact on the risk characterization of lower application rates or single applications of bifenthrin is discussed in Section 3.4.

The nature of the accidental exposure scenarios is intentionally extreme. The non-accidental, acute 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 bifenthrin. 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.

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).

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 allometric 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). As with the accidental exposure scenarios for workers (Section 3.2.2.2), different application methods involve different concentrations of bifenthrin in field solutions, and details of the calculations for these concentrations are given in Worksheet A01of the attachments to this risk assessment. Thus, these exposure scenarios differ slightly for foliar applications (Attachment 1) and bark applications (Attachment 2), due to the different dilution volumes used for foliar applications (Section 2.4.1) and bark applications (Section 2.4.2).

3.2.3.3. Dermal Exposure from Contaminated Vegetation

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

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

The exposure scenario assumes a contact period of 1 hour and further assumes that the chemical is not effectively removed by washing for 24 hours. Other approximations used in this exposure scenario include estimates of body weight, skin surface area, and first-order dermal absorption rates, as discussed in 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 a field solution into a small pond. The calculation of the concentration of bifenthrin in water following the spill is given in Worksheet B04b, and the estimate of the dose to a small child is given in Worksheet D05. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation is considered. Since this exposure scenario is based on assumptions that are somewhat arbitrary and highly variable, the scenario may overestimate exposure. The actual chemical concentrations in the water will vary according to the amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs relative to the time of the spill, 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.

A spill volume of 100 gallons with a range of 20 to 200 gallons is used to reflect plausible spill events. These spill volumes are used in all Forest Service risk assessments involving terrestrial applications. The bifenthrin 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 bifenthrin in a small pond ranges from about 0.036 to about 0.18 mg/L for foliar applications (Attachment 1) and 0.004 to 0.2271 mg/L for bark applications (Attachment 2). As with direct spray scenarios (Section 3.2.3.2.), the estimated nominal concentrations differ slightly for foliar applications (Attachment 1) and bark applications (Attachment 2) due to the different dilution volumes used for foliar applications (Section 2.4.1) and bark applications (Section 2.4.2).

One very unusual aspect of this scenario, as well as other exposure assessments associated with the contamination of surface water, involves the very low water solubility of bifenthrin—i.e., 0.014 µg/L or 0.000014 mg/L. In both the most recent human health risk assessment (U.S. EPA/OPP/HED 2012a, pp. 38-29) and ecological risk assessment (U.S. EPA/OPP/EFED 2012a, p. 147), the EPA caps the concentration of bifenthrin in surface water at the water solubility.

U.S. EPA/OPP/EFED (2012a, p. 224) provides a relatively detailed discussion of the registrant study (MRID 00132518) on which the estimate of the water solubility of bifenthrin is based. The EPA notes that monitoring studies, discussed further in Section 3.2.3.4.5, report concentrations of bifenthrin in surface water that substantially exceed 0.014 µg/L – i.e., the nominal water solubility of bifenthrin. These reported concentrations could be associated with bifenthrin adsorbed to suspended sediment in ambient water and that the bifenthrin sorbed to sediments in ambient water would not be bioavailable. In addition, and for clarity, it is worth noting that many of the reported LC_{50} and EC_{50} values for aquatic organisms discussed in Section 4.1.3 also substantially exceed the water solubility of bifenthrin. In these bioassays as well as bioassays of other compounds with low water solubility, solvents (e.g., acetone or dimethyl formamide) are typically used with appropriate solvent controls. Unlike the case with dissolved sediments, solvents will increase the solubility of bifenthrin in water, and the increased concentrations of bifenthrin may enhance the bioavailability of bifenthrin. As discussed frequently in U.S. EPA/OPP/EFED (2012a, pp. 131, 136, 138), most of the toxicity studies on bifenthrin do not involve centrifugation of the test water and this augments uncertainties in the bioavailability of bifenthrin to the test organisms.

The current Forest Service risk assessment defers to EPA on the approach to handling the low water solubility of bifenthrin. Consequently, the B04b Worksheets in both Attachment 1 and Attachment 2 are modified to cap the concentration of bifenthrin in water following an accidental spill at 0.000014 mg/L. This approach, as discussed below, is also used in estimated concentrations of bifenthrin in surface water that are associated with non-accidental contamination of surface water.

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

This scenario involves 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. For each water body, two sets of drift scenarios are given, one based on fine droplets and the other on coarse droplets. All of the product labels for bifenthrin clearly indicate that applications should be made using coarse droplets to minimize drift. The use of fine droplets would essentially involve a misapplication of bifenthrin. The distinction between fine and coarse droplet sizes applies only to aerial and ground broadcast applications. Drift from backpack and bark applications are always modeled using coarse droplet sizes.

The direct spray and drift scenarios are detailed in Worksheet B04c (small pond) and Worksheet B04d (small stream). As with the estimates of water concentrations following an accidental spill, many of the nominal estimated concentrations associated with direct spray and drift exceed the water solubility of bifenthrin (i.e., 0.000014 mg/L). Worksheets B04c and B04d, however, are not used directly in any exposure scenarios. Consequently, these worksheets present the nominal concentrations and are not modified to cap the concentration of bifenthrin in water at 0.000014 mg/L.

3.2.3.4.3. GLEAMS Modeling

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

As summarized in Table 9, 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 10. 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 0.2 lb a.i./acre.

Table 11 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 bifenthrin (U.S. EPA/OPP/EFED 2012a). The EPA modeling efforts are discussed below (Section 3.2.3.4.4). 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 11 indicate the specific sources of the chemical properties used in the GLEAMS modeling effort.

Table 12 summarizes the modeled concentrations of bifenthrin in surface water by GLEAMS-Driver and details of the GLEAMS-Driver are detailed in Appendix 6. The results of EPA modeling of bifenthrin are discussed in Section 3.2.3.4.4 and the concentrations of bifenthrin in surface water used in the exposure assessments for the current risk assessment are discussed in Section 3.2.3.4.6.

Note that GLEAMS-Driver simulations are conducted only for foliar applications. As discussed in Section 2.4.2, bark applications are treated similarly to foliar applications but with a functional off-target application rate of 10% of the nominal rate for foliar applications—i.e., 0.2 lb a.i./acre x 0.1 = 0.02 lb a.i./acre. Consequently, separate GLEAMS-Driver runs for bark applications are unnecessary.

3.2.3.4.4. Other Modeling Efforts

Other efforts to model bifenthrin concentrations in surface water are summarized in Table 10, which also summarizes the surface water modeling conducted for the current risk assessment (Section 3.2.3.4.3). To estimate concentrations of a pesticide in ambient water as part of a screening level risk assessment, the U.S. EPA typically uses Tier 1 screening models (e.g., GENEEC, FIRST, and SCIGROW). For more refined and extensive risk assessment, the U.S. EPA/OPP typically use PRZM/EXAMS, a more elaborate Tier 2 modeling system. The U.S. EPA/OPP typically models pesticide concentrations in water at the maximum labeled rate.

The discussion of the EPA modeling is complicated by low water solubility of bifenthrin—i.e., 0.014 µg/L. As discussed in Section 3.2.3.4.1, the EPA capped the modeled concentrations of bifenthrin at the water solubility of bifenthrin. Thus, the reported concentrations of bifenthrin from the FIRST modeling and the concentrations used by EPA from PRZM/EXAMS modeling are all reported as 0.014 µg/L and are not directly comparable to the outputs from GLEAMS-Driver.

In an appendix to the most recent EPA ecological risk assessment, the unadjusted modelled concentrations from PRZM/EXAMS are reported (U.S. EPA/OPP/EFED 2012a, Appendix D, pp. 4-5). As summarized in Table 12 (last row) of the current risk assessment, the central estimate of the peak concentration from PRZM/EXAMS based on a normalized application rate

of 1 lb a.i./acre is 0.8 µg/L, somewhat higher than the peak pond concentrations from GLEAMS-Driver (i.e., 0.1 µg/L) but about the same as the upper bound concentration (i.e., 0.7 µg/L). The central estimate of the longer-term concentrations from PRZM/EXAMS (i.e., 0.048 µg/L) is similar to the longer-term concentration modeled by GLEAMS-Driver for the pond (i.e., 0.038 µg/L) and the stream (0.065 µg/L).

The differences between the PRZM/EXAMS and GLEAMS-Driver simulations reflect the nature of the inputs. As summarized in Table 11 (inputs for GLEAMS-Driver modeling), all of the key input parameters for GLEAMS-Driver are given as either ranges or central estimates with lower and upper bounds. The estimates from PRZM/EXAMS modeling are based on upper bound input values. As discussed further in Section 3.2.3.4.6, these differences have little practical impact on the risk assessment because all of the upper bound estimates of the concentration of bifenthrin in water exceed the water solubility of bifenthrin.

3.2.3.4.5. Monitoring Data

No monitoring data are included in compendia published by the U.S. Geological Survey's National Water-Quality Assessment Program (USGS/NAWQA) covering periods from 1992-2001 (Gilliom et al. 2007) or the more recent update covering periods from 1992-2008 (Ryberg et al. 2011). As summarized in the most recent EPA ecological risk assessment, detectable concentrations of bifenthrin are not included in an online USGS/NAWQA database on surface water or groundwater. The EPA also reviewed data from a California Department of Pesticide database in which the maximum reported concentration of bifenthrin in surface water was 5.209 µg/L (U.S. EPA/OPP/EFED 2012a, p. 116). In the conduct of the current Forest Service risk assessment, the California database (http://www.cdpr.ca.gov/docs/emon/surfwtr/surfcont.htm) was searched (June 8, 2015) and 5.209 µg/L is still the highest concentration of bifenthrin reported in the California database. This concentration substantially exceeds the water solubility of bifenthrin—i.e., 0.014 µg/L. A more recent publication by Weston et al. (2014) reports concentrations of bifenthrin in stream water ranging from 0.0016 to 0.024 µg/L. Again the upper bound concentration is higher, albeit modestly, than the water solubility of bifenthrin. As discussed in Section 3.2.3.4.1, monitoring studies reporting water concentrations of bifenthrin that exceed its water solubility probably reflect bifenthrin concentrations in suspended sediment.

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 bifenthrin.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

The calculations of bifenthrin concentrations in surface water used in this risk assessment are summarized in Table 13. These concentrations are based on the GLEAMS-Driver modeling, adopting the approach from EPA surface water modeling of capping the maximum concentration of bifenthrin at the water solubility of 0.014 µg/L. As discussed in Section 3.2.3.4.4, the modeled WCRs from GLEAMS-Driver are reasonably consistent with the modeling from the U.S. EPA, except that the upper bounds from EPA are somewhat higher than the upper bounds from GLEAMS-Driver. In a typical risk assessment, this consideration might lead to adopting

upper bound values from the PRZM/EXAMS modeling. In the case of bifenthrin, doing so would make no difference because all of the upper bound modeled estimates from both GLEAMS-Driver and PRZM/EXAMS exceed the water solubility of bifenthrin (Table 12). Similarly and as discussed in Section 3.2.3.4.5, no monitoring data are available that permit an assessment of the plausibility of the surface water modeling by either GLEAMS-Driver or PRZM/EXAMS.

The estimated concentrations of bifenthrin in surface water following foliar applications are summarized in Table 13. In this table, the water contamination rates (WCRs in units of µg/L per lb a.i./acre) derived from GLEAMS-Driver are given in upper portion of the table and are not capped for water solubility. The estimated concentrations in surface water associated with an application rate of 0.2 lb a.i./acre are given in the center section of the table. These concentrations are simply the WCR multiplied by the application rate and are not capped for water solubility. In the bottom section of Table 13, the concentrations from the center section of the table are capped with the 0.014 µg/L water solubility of bifenthrin. For clarity, bold font is used for the concentrations in the lower section of the table that are capped for water solubility. These capped concentrations include the central and upper bound concentrations for peak exposures and the upper bound concentration for longer-term exposures.

As discussed in Section 3.2.3.4.3, the estimated concentrations of bifenthrin in surface water given in Table 13 apply only to foliar applications (Attachment 1). For bark applications (Attachment 2), these estimated concentrations are reduced by a factor of 10 under the assumption that only 10% of the amount of bifenthrin intended for application to tree bark is lost due to an application efficiency of 90%. The calculations for the concentrations of bifenthrin in surface water are summarized in Table 14, which is constructed similarly to Table 13 except that the functional application is set to 0.02 lb a.i./acre.

The calculations in Table 13 and Table 14 are reproduced in Worksheets B04a in Attachment 1 (foliar applications) and Attachment 2 (bark applications). Following the convention in WorksheetMaker (SERA 2011a), the concentrations in the attachments are in units of mg a.i./L rather than µg a.i./L.

3.2.3.5. Oral Exposure from Contaminated Fish

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

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 bifenthrin 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 bifenthrin in water used for the accidental spill scenario (Section 3.2.3.4.1.) and the surface water exposure estimates (Section 3.2.3.4.6).

Generally, bioconcentration factors for the edible portion of fish (i.e., muscle) are used in the human health risk assessment under the assumption that humans will not generally consume offal. As summarized in Table 3, several bioconcentration factors for bifenthrin are available in fish, mollusks, and other invertebrates but only one study (MRID 163094 and MRID 163095) provides separate bioconcentration factors for edible fish tissue and whole fish. These BCFs are also BCFs reported for fish. The BCF of 2140 L/kg for edible tissue is used in the exposure assessment for humans. As noted in Section 4.2.2.5, the BCF of 6090 L/kg for whole fish is used in the exposure assessments for mammalian and avian wildlife.

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

Some geographical sites maintained by the Forest Service or Forest Service cooperators include surface water in which members of the general public might swim. The extent to which this might apply to areas treated with bifenthrin is unclear.

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 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 bifenthrin, however, the HQs for this scenario are far below the level of concern.

The scenarios for exposures associated with swimming in contaminated water are based on the peak water concentrations of bifenthrin used to estimate acute exposure to drinking water (Section 3.2.3.4.6).

3.2.3.7. Oral Exposure from Contaminated Vegetation

Although none of the Forest Service applications of bifenthrin will involve crop treatment, they may be conducted on some Forest Service lands by individuals or organizations with permission from the Forest Service to use the lands for crop cultivation. All such agricultural applications are subject to U.S. EPA/OPP regulatory constraints (e.g., tolerance limits), and exposures associated with agricultural applications are not explicitly considered in Forest Service risk assessments.

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 vegetation. Two sets of exposure scenarios are provided: one for the consumption of contaminated fruit and the other for the consumption of contaminated vegetation. These scenarios, detailed in Worksheets D03a (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 15. 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 EPA human health risk assessments do not consider exposure scenarios involving direct spray, the residue rates recommended by Fletcher et al. (1994) are used by U.S. EPA/OPP/EFED in their T-REX exposure model for terrestrial organisms (http://www.epa.gov/oppefed1/models/terrestrial/trex/t_rex_user_guide.htm).

The only exception to the use of rates in Table 15 involves bark application. As discussed in Section 2.4.3, the current risk assessment assumes an application efficiency of 90% in bark applications with 10% of the applied amount splashed onto the ground or vegetation adjacent to the treated tree. Consequently, the residue rates from Table 15 are reduced by a factor of 10 in Worksheet A01 of Attachment 3, the WorksheetMaker workbook for bark applications.

The half-lives on vegetation used in chronic exposure scenarios are based on the same rates used in GLEAMS-Driver modeling (Table 11)—i.e., from 2.4 to 23 days. In the attachments to this risk assessment, a central estimate is taken as 12.7 days (the average of the range). As summarized in Table 3, this range of half-lives encompasses reported half-lives for bifenthrin on vegetation from Knisel and Davis (2000), Papadopoulou-Mourkidou et al. (1989), and You et al. (2013). Based on half-lives on peaches of 9-12 days (Papadopoulou-Mourkidou et al. 1989) and half-lives of 2.05 days on tomatoes (Chauhan et al. 2012), the half-times on fruit are taken as 2 - 12 days with a central estimate of 7 days—i.e., the average of the range of half-lives on fruit.

Based on these half-lives on vegetation and fruit, 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 summarized in Worksheet E03 of Attachment 1 (foliar applications), the estimated acute exposures are 0.00234 (0.00108 – 0.0273) mg/kg bw for the consumption of contaminated fruit and 0.0323 (0.00225-0.27) mg/kg bw/day for the consumption of contaminated vegetation. The estimated longer-term exposures are 0.000264 (0.0000345-0.00714) mg/kg bw/day for contaminated fruit and 0.00655 (0.0000866-0.0929) mg/kg bw/day for contaminated vegetation. The exposures estimated for bark applications are summarized in Worksheet E03 of Attachment 2. The exposure estimates for backpack application are a factor of 10 below the estimates for foliar application because of the assumption that 90% of the applied pesticide remains on the bark and only 10% is lost to non-target plants (Section 2.4.2).

As noted above, the U.S. EPA/OPP approach to dietary exposure is very different from the approach used in Forest Service risk assessments. In short, 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 2012a, Table 5.4.6, pp. 41-42), the upper bound (99.9^{th} percentile) acute exposures for bifenthrin range from 0.0011 to 0.003 mg/kg bw/day. The upper bound of this range from EPA is a factor of 90 [0.27 mg/kg bw/day ÷ 0.003 mg/kg bw/day] below the upper bound of the acute exposures estimated in Attachment 1 (foliar applications). The average exposures estimated by EPA (U.S. EPA/OPP/HED 2012a, Table 5.4.6, pp. 41-42) range from 0.00055 to 0.0018 mg/kg bw/day. The upper bound of the range from EPA is a factor of about 50 [0.0929 ÷ 0.0018 mg/kg bw/day ≈ 51.61] below the upper bound of the longer-term exposures estimated in Attachment 1 (foliar applications).

In addition to the EPA dietary assessment (U.S. EPA/OPP/HED 2012a), a more recent dietary exposure assessment for bifenthrin from EPA personnel is published in the open literature (Melnyk et al. 2014). In this paper, which involves monitoring the diets of nine individuals from Apopka, Florida, the maximum intake is reported as 16,000 ng or 16 µg (Individual 2 in Table 1 from Melnyk et al. 2014) and is associated with the consumption of a crab salad. As noted by the authors, this maximum intake value may reflect the high bioconcentration potential of bifenthrin. Melnyk et al. (2014) do not provide information on the body weights of the individuals but note that the participants were females of child-bearing age. Taking 64 kg as an approximate body weight for a young woman (U.S. EPA/ORD 1985), the dose of 16 µg or 0.016 mg would correspond to a dose of about 0.0003 mg/kg bw [0.016 mg ÷ 60 kg bw ≈ 0.00026667 mg/kg bw], which is below the dietary estimates from either U.S. EPA/OPP/HED (2012a) or the current risk assessment.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

Table 16 provides an overview of the dose-response assessment used in this risk assessment. Following standard practices in Forest Service risk assessments, RfDs are adopted from the values proposed by U.S. EPA. The most recent EPA human health risk assessment differs from previous EPA risk assessments as well as similar assessments from international organizations in that the EPA elected to use an acute RfD for risk characterizations associated with both acute and longer-term exposure scenarios, because the dose-duration relationships for bifenthrin indicate that doses which protect against acute endpoints, specifically neurotoxicity, are also protective of longer-term exposures. This position is supported by both toxicity and pharmacokinetic data on bifenthrin. Consequently, the acute RfD of 0.03 mg/kg bw proposed in U.S. EPA/OPP/HED (2012a) for the general population is adopted in the current Forest Service risk assessment and is applied to both acute and longer-term exposures. This RfD is based on a benchmark dose of 0.33 mg/kg bw and an uncertainty factor of 100 (i.e., a factor of 10 for species-to-species extrapolation and a factor of 10 for potentially sensitive individuals).

The EPA dose-response assessment for bifenthrin is somewhat atypical in that the EPA recommends an additional uncertainty factor of 3 for children under 6-years-old, and the RfD for this group is taken as 0.01 mg/kg bw. This additional uncertainty factor is based on data for pyrethroids as a chemical class rather than data specific to bifenthrin. The lower RfD for children is adopted in the current Forest Service risk assessment but does not have a substantial impact on the risk characterization because none of the exposure scenarios for children exceeds the level of concern.

Dose-severity relationships for bifenthrin are limited by the lack of quantitative data on toxicity in humans and by the limited number of mammalian species on which data are available. Within these constraints, exposures associated with hazard quotients of about 4 would raise concern for mild signs of neurotoxicity and hazard quotients of about 17 could raise concerns for serious and possibly lethal effects.

3.3.2. RfD, General Population

As discussed in Section 3.1.10, U.S. EPA/OPP/HED (2012a, p. 8) classifies bifenthrin as a "*possible human carcinogen*" but the EPA elected to base the dose-response assessment for bifenthrin on systemic toxicity. This position is consistent with European assessments which also recommend that exposure limits for bifenthrin be based on systemic toxicity (EFSA 2011, p. 48; WHO 2012, p. 21).

For systemic toxic effects, the U.S. EPA/OPP will typically derive an acute RfD based on studies involving only a single day of exposure and a chronic RfD based on lifetime exposures. In the EPA's agency-wide database (IRIS), the chronic RfD for bifenthrin is given as 0.015 mg/kg bw/day based on a 1-year feeding study in dogs (Accession No. 264637) which yielded a NOAEL of 1.5 mg/kg bw/day with a corresponding LOAEL of 3 mg/kg bw/day based on tremors (U.S. EPA 1988a,b). The chronic RfD of 0.015 mg/kg bw/day is identical to the chronic ADI (acceptable daily intake) derived by the European Food Safety Authority (EFSA 2011, p. 14).

The U.S. EPA/OPP/HED derived a similar RfD of 0.013 mg/kg bw/day also based on a 1-year dog study and an uncertainty factor of 100 (U.S. EPA/OPP/HED 2010a, 2011a). As summarized in Appendix 1, Table A1-4, both the dog study cited in U.S. EPA (1988) and the dog study cited in U.S. EPA/OPP/HED (2010a) are attributed to a 1985 registrant-submitted bioassay, but neither EPA document gives a full citation to the study. It is likely that both EPA documents refer to the same 1-year bioassay in dogs and that U.S. EPA (1988) refers to nominal doses and U.S. EPA/OPP/HED (2010a, 2011a) refers to the average of measured doses. These types of minor inconsistencies are common among EPA documents prepared at different times or by different groups within EPA. The uncertainty factor of 100 used in the derivation of both RfDs is based on a factor of 10 for species-to-species extrapolation and a factor of 10 for potentially sensitive individuals.

U.S. EPA/OPP/HED (2010a, 2011a) also derives an acute RfD of 0.33 mg/kg bw based on the acute neurotoxicity study in rats, which is summarized in Appendix 1, Table A1-2 (MRID 44862102). The acute RfD is based on a NOAEL of 32.8 mg/kg bw with a corresponding LOAEL of 70.3 mg/kg bw for neurotoxicity. As with the chronic RfD and for the same reasons, U.S. EPA/OPP/HED (2010a, 2011a) uses an uncertainty factor of 100.

The EPA has taken a much different approach to the derivations of the RfD in its most recent human health risk assessment (U.S. EPA/OPP/HED 2012a). The EPA conducted and published studies on the acute neurotoxicity studies in rats (Wolansky et al. 2006, 2007), as summarized in Appendix A1-2. Based on these data, the U.S. EPA/OPP/HED identified a benchmark dose of 3.1 mg/kg bw and derived an acute RfD of 0.03 mg/kg bw for members of the general population using the standard uncertainty factor of 100 (U.S. EPA/OPP/HED 2012a, p. 32). In addition, the EPA elected not to define a chronic RfD:

> *Chronic endpoints have not been chosen for bifenthrin since the toxicology database indicates that the acute endpoints are protective of longer-term exposures.*
>
> U.S. EPA/OPP/HED (2012a, p. 73)

This assessment is supported by a detailed discussion of the acute, subchronic, and chronic studies on bifenthrin (U.S. EPA/OPP/HED 2012a, pp. 71-73). The EPA acute RfD of 0.03 mg/kg bw is supported by and is identical to an acute RfD recommended by the European Food Safety Authority (EFSA 2011, p. 3). The EPA discussion concerning the lack of a dose-duration relationship for bifenthrin is also supported by the fact that the EFSA (2011) acute RfD is based on a 90-day neurotoxicity study in rats rather than the single-dose study used by EPA. Finally, pharmacokinetic considerations specific to bifenthrin indicate that it is not likely to accumulate in the body over prolonged periods of exposure (Section 3.1.3.3) mostly likely due to rapid metabolism by cytochrome P450 enzyme and carboxylesterases (Section 3.1.3.1). Thus, the approach used by EFSA (2011) is consistent with the approach taken by U.S. EPA/OPP/HED in applying an acute RfD to the risk characterization for longer periods of exposure (U.S. EPA/OPP/HED 2012a).

Using an RfD derived by the EPA is standard practice in most Forest Service risk assessments. The U.S. EPA RfDs are used because they generally provide a level of analysis, review, and

resources that far exceed those that are or can be conducted in the support of most Forest Service risk assessments. In addition, it is desirable for different agencies and organizations within the federal government to use concordant risk assessment values. When multiple RfDs are available from EPA, Forest Service risk assessments generally adopt the most recent oral RfDs derived by the U.S. EPA, unless there is a compelling basis for doing otherwise. Compelling reasons for differing from EPA generally involve the availability of data not considered by EPA. In the case of bifenthrin, the most recent EPA risk assessment takes into consideration all the available data, and the current Forest Service risk assessment uses the RfD of 0.03 mg/kg bw/day for the risk characterization of both acute and longer-term exposures.

3.3.3. RfD, Children

The most recent EPA human health risk assessment implements an additional Food Quality Protection Act (FQPA) uncertainty factor of 3 for children under the age of 6 (U.S. EPA/OPP/HED 2012a, pp. 26-27). Earlier EPA risk assessments mention that this uncertainty factor was under consideration but had not been implemented (U.S. EPA/OPP/HED 2010a, 2011a). The uncertainty factor for children is somewhat atypical in that it is not based on data specific to bifenthrin. Instead, the uncertainty factor is based on a consideration of acute toxicity data on pyrethroids indicating that younger animals are generally more sensitive than adult animals to pyrethroids. The EPA derives an RfD for children of 0.01 mg/kg bw based on the benchmark dose of 3.1 mg/kg used for adults and children over 6-years-old (Section 3.3.2) but uses an uncertainty factor of 300 rather than 100.

The current Forest Service risk assessment defers to EPA and applies the RfD of 0.01 mg/kg bw to the risk characterization for all exposure scenarios involving children. As detailed in Section 3.4, this lower RfD has no practical impact on the risk characterization because none of the exposure scenarios for children results in hazard quotients that exceed the level of concern (HQ=1).

3.3.4. Dose-Severity Relationships

While none of the exposure scenarios for children exceed the level of concern, some exposure scenarios for workers and adult members of the general public do exceed the level of concern. Consequently, a consideration of dose-severity relationships is necessary.

Dose-severity relationships can be crudely characterized in terms of the ratio of the LOAEL to the NOAEL on which the RfD is based. As summarized in Table 16 and discussed in Section 3.3.2, the RfD for adults is based on a benchmark dose of 3.1 mg/kg bw which is used by U.S. EPA/OPP/HED (2012a) as a functional NOAEL. The corresponding LOAEL is 12 mg/kg bw based on decreases in motor activity. Based on the relationship of the NOAEL to the LOAEL, an HQ of about 4 would raise clear concern for mild adverse effects [12 mg/kg bw ÷ 3.1 mg/kg bw ≈ 3.871]. The interpretation of HQs above 1 (the standard for no anticipated effects) and HQs below 4 are indeterminate – i.e., potential effects cannot be clearly characterized.

Data on incidents of human poisoning can sometimes be used to refine the dose-severity assessment for lethal or near lethal doses in humans. This is not the case for bifenthrin. Bifenthrin is not included in compendia by Hayes (1982) on pesticides studied in humans, and no incidents of fatal human poisonings, intentional or suicidal, were identified in the available

literature. U.S. EPA/OPP/HED reviewed incident reports in humans and noted that most signs of toxicity were relatively mild (U.S. EPA/OPP/HED 2010b). A total of four fatalities are reported (U.S. EPA/OPP/HED 2010b, p. 4); however, the doses associated with fatal and nonfatal exposures are not provided in the analysis.

The lowest reported LD_{50} for bifenthrin is 53.8 mg/kg bw in females (MRID 00132519). As discussed further in the ecological risk assessment (Section 4.1.2.1), no systematic differences in sensitivity to bifenthrin are apparent among species. In the absence of additional data, an HQ of 17 [53.8 mg/kg bw ÷ 3.1 mg/kg bw ≈ 17.355] could be viewed with substantial concern for severe effects, including death.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

The risk characterizations for workers (Worksheet E02) and members of the general public (Worksheet E04) are summarized in the attachments to this risk assessment—i.e., Attachment 1 for foliar applications and Attachment 2 for bark applications.

None of the central estimates for general exposures of workers results in HQs that exceed the level of concern (HQ=1); however, upper bound exposures for foliar applications are in the range of 4 to 11. In addition, the accidental exposure scenarios for wearing contaminated gloves for 1 hour result in HQs of 4 for foliar applications and 3 for bark applications. A reasonable interpretation of the HQs is that most workers who exercise reasonable care in the application of bifenthrin should be able to do so without adverse effects; however, workers who do not follow prudent handling practices could be at risk of effects that might lead to overt signs of neurotoxicity. A major source of excessive exposure to bifenthrin could involve wearing contaminated gloves.

Except for upper bound HQs associated with the consumption of contaminated vegetation following foliar applications, members of the general public do not appear to be at risk. The scenario for the consumption of contaminated vegetation does lead to upper bound HQs of 9 for acute exposures and 3 for long-term exposures. These are extreme exposure scenarios that should not be viewed as typical or expected in most cases. Based on EPA exposure assessments, typical uses of bifenthrin in agricultural applications lead to exposures that are far below the level of concern.

Bifenthrin does share a common mechanism of action with other pyrethroids and with pyrethrins. If other pyrethroids or pyrethrins are used in Forest Service programs or projects along with bifenthrin, the risks posed by the other pyrethroids or pyrethrins should be considered quantitatively under the assumption of dose addition—i.e., the HQs should be added. The WorksheetMaker program used in the development of Forest Service risk assessments has a utility for conducting such assessments.

3.4.2. Workers

For general exposures, none of the central estimates of the HQs exceeds the level of concern, which is consistent with the risk characterizations for workers given in EPA risk assessments (i.e., U.S. EPA/OPP/HED 2007b, 2011a, 2012a). Only the most recent EPA risk assessment uses the most recent RfD discussed in Section 3.3. For workers involved in backpack spray applications at an application rate of 0.2 lb a.i./acre, EPA estimates an Aggregate Risk Index (ARI) of 2.1 (U.S. EPA/OPP/HED 2012a, Table 6.3.1, p. 45). As implemented by EPA, the ARI is essentially the reciprocal of the hazard quotient (HQ). Thus, an ARI of 2.1 corresponds to an HQ of about 0.5. As summarized in Worksheet A02 of Attachment 1, the central estimate of the HQ for backpack workers at an application rate of 0.2 lb a.i./acre is 0.3. Given the substantially different methods used in EPA and Forest Service risk assessments (i.e., SERA 2009c, Section 4.1), the similarity between the EPA and Forest Service risk characterization for backpack workers is striking.

The upper bound HQ for bark applications is 0.4, below the level of concern (HQ=1). The upper bound HQs for foliar applications, however, are all above the level of concern—i.e., 2 for backpack applications, 11 for ground broadcast applications, and 10 for aerial applications. The relatively modest exceedance for backpack foliar applications (HQ=2) is of concern, but it is not clear that adverse effects would be noted at this HQ. As discussed in Section 3.3.4 (Dose-Severity Relationships), an HQ of about 4 would raise concern for mild adverse effects. The HQs for both ground broadcast applications (HQ=11) and aerial applications (HQ=10) are substantial and are clear concerns because these HQs approach the level at which serious adverse effects could occur (HQ=17).

As detailed in SERA (2013b), the upper bound for workers that is currently used in Forest Service risk assessments is based on prediction intervals, which are more conservative (i.e., higher) than rates based on confidence intervals. The upper bound prediction intervals may be viewed as unlikely to occur in most workers but as reasonable worst-case approximations for some workers. This qualitative risk characterization is reasonably consistent with the discussion of human incident reports from EPA:

> *…bifenthrin exposures may have caused adverse health effects such as dermal and respiratory tract irritation and neurological symptoms such as dizziness and altered sensations. … Many incidents appeared to occur due to improper use, such as overuse of a product, failure to ventilate or a leak/spill resulting in direct contact.*
>
> U.S. EPA/OPP/HED (2010b, pp. 2-3)

The only accidental exposure scenario that leads to HQs of concern involves wearing contaminated gloves for 1 hour. The upper bound HQs are 3 for bark applications and 4 for foliar applications. The difference between bark and foliar applications reflects the difference in field solutions, as discussed in Section 2.4 (Mixing and Application Rates) and detailed in Worksheet A01 in the EXCEL workbooks for foliar application (Attachment 1) and bark application (Attachment 2). Wearing contaminated gloves is the most severe accidental exposure scenario given in Forest Service risk assessments, and taking precautions to avoid wearing contaminated gloves is justified in the application of any pesticide.

3.4.3. General Public

The risk characterization for members of the general public is dependent on the application method, and concerns with the HQs are limited to exposure scenarios associated with the consumption of contaminated vegetation.

For bark applications, none of the HQs exceeds the level of concern (HQ=1), although the scenario for the upper bound HQ associated with the acute consumption of contaminated vegetation (HQ=0.9) approaches the level of concern. For foliar applications, the central estimate of the HQ for the consumption of contaminated vegetation (HQ=1) reaches the level of concern. In the interest of transparency, it is noted that the underlying value of the HQ somewhat exceeds the level of concern (HQ≈1.0452); however, this is inconsequential, and it is reasonable to round HQs to one significant place.

The upper bound HQs for the consumption of contaminated vegetation are a greater concern—i.e., an upper bound HQ of 9 for acute exposures and 3 for longer-term exposures. The upper bound HQ of 9 for the consumption of contaminated vegetation is above the level for potentially overt effects—i.e., an HQ of 4, as discussed in Section 3.3.4. While the exposure scenario for the consumption of contaminated vegetation is a concern, this concern must be appreciated in the context of the underlying 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, much more so than the approach taken in EPA risk assessments. As noted in Section 3.2.3.7, the estimated doses for bifenthrin associated with the consumption of contaminated vegetation are a factor of about 90 above the acute doses estimated by EPA in their total dietary exposure assessment (U.S. EPA/OPP/HED 2012a, Table 5.4.6, pp. 41-42). 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 exposure scenarios should be viewed as extreme exposures which might, in some cases, reflect exposure levels following forestry uses of bifenthrin; however, these exposures should not be viewed as typical or expected, in most cases. As noted in the EPA review of human incident reports, most of the documented incidents associated with human exposure to bifenthrin …*result in low severity outcomes* (U.S. EPA/OPP/HED 2012b, p. 3).

3.4.4. Sensitive Subgroups

For exposures to almost any chemical, there is particular concern for children, women who are pregnant or may become pregnant, the elderly, or individuals with any number of different diseases. As discussed in Section 3.3.3, the EPA has determined that children may be at increased risk, compared with other members of the general population, and this this determination which applied to other pyrethroids was extended by the EPA to include bifenthrin (U.S. EPA/OPP/HED 2012a, pp. 26-27). The potentially greater sensitivity of young children, specifically those under the age of 6, is encompassed quantitatively in the current risk assessment by the use of a lower RfD for young children (Table 16).

As discussed in Section 3.1.3, bifenthrin is detoxified in the liver and metabolites are excreted primarily by the kidney. It is possible that individuals with liver or kidney diseases could be more sensitive than other individuals to bifenthrin. This concern applies to pyrethroids in general (ATSDR 2003).

As noted in EPA's review of human incident data on bifenthrin,

> *People with underlying medical conditions (such as heart and lung diseases) reported that their condition worsened after using bifenthrin.*
>
> U.S. EPA/OPP/HED (2010b, p. 3)

The specific incident reports summarized in the EPA review (U.S. EPA/OPP/HED 2010b, pp. 6-108) clearly support the above statement but do not clearly implicate bifenthrin as a causative agent.

3.4.5. Connected Actions

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions (40 CFR 1508.25) as actions which occur in close association

with the action of concern; in this case, the use of a pesticide. 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 bifenthrin, "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 bifenthrin.

As discussed in detail in Sections 3.1.14, bifenthrin formulations contain inert components; however, the inert ingredients in bifenthrin formulations are not well characterized. This limitation is common in pesticide risk assessments. The inerts that are disclosed to the general public, such as petroleum hydrocarbons, may cause a wide spectrum of toxic effects. The limited data on the toxicity of the formulations do not yield a consistent pattern in terms of the potential impact of the inert ingredients on the toxicity of the formulations. As discussed in Section 3.1.14.1, the limited available information suggests that inerts in bifenthrin formulations do not contribute to or augment the neurotoxicity of the bifenthrin, but inerts in some formulations may contribute to skin sensitization.

3.4.6. Cumulative Effects

The U.S. EPA/OPP has made the assessment that bifenthrin shares a common mechanism of action with other pyrethroids and pyrethrins (U.S. EPA/OPP 2011b). The EPA determination is supported by the ATSDR (2003) review of pyrethroids and pyrethrins, although there are varying opinions on how to approach the cumulative risk assessment for pyrethroids and pyrethrins (e.g., Soderlund et al. 2002). The EPA makes the following assessment: … *given the current state of the science with respect to pyrethroid mixtures, the assumption of dose additivity is both reasonable and appropriate* (U.S. EPA/OPP 2011b, p. 37).

For the current Forest Service risk assessment, the practical implication of the EPA determination is that Forest Service projects or programs involving applications of bifenthrin should explicitly consider applications of other pyrethroids or pyrethrins that are made in geographical and temporal proximity to the application of bifenthrin. The WorksheetMaker program used to develop the attachments to the current risk assessment has utilities for adding new pesticides and for combining the HQs across multiple workbooks—i.e., SERA 2011a, Section 3.4.1 (adding new pesticides) and Section 3.4.3 (combining HQs from different workbooks). The utility for combining workbooks includes the option of adding HQs under the assumption of dose addition. Given the above EPA assessment, the assumption of dose addition should be used in project- or program-specific assessments of applications of more than one pyrethroid pesticide.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Bifenthrin is an effective insecticide used to control numerous insects. The LD_{50} values are about 0.1 to 0.2 mg/kg bw for sensitive species of insects. Other species of insects are much more tolerant with LD_{50} values of up to 500 mg/kg bw. For comparison, the LD_{50} values for mammals range from about 70 to 250 mg/kg bw, and the LD_{50} values for birds are greater than 1000 mg/kg bw. The honeybee appears to be the most sensitive insect species, along with some species of dipterans, lepidopterans, and coleopterans. Nonetheless, there are no clear patterns of sensitivity among insects at the level of the taxonomic order, with some species of coleopterans and dipterans being among the most tolerant insect species. Mammals appear to be somewhat more sensitive than birds. As with insects, neurotoxicity is the most sensitive endpoint for mammals. While relatively few toxicity studies are available in birds, compared with mammals, none of the studies reports signs of neurotoxicity. On the other hand, most of the available avian toxicity studies were submitted to the EPA in support of the registration of bifenthrin. Full copies of these studies were not available for the conduct of the current Forest Service risk assessment. Nonetheless, detailed reviews from the EPA specifically note that signs of sublethal effects were not reported in avian acute toxicity studies.

An overview of the acute toxicity studies in fish and aquatic invertebrates is given in Figure 3. As with terrestrial organisms, sensitive species of aquatic arthropods are more vulnerable than sensitive species of aquatic vertebrates to bifenthrin exposure. The differences in sensitivity among tolerant species of aquatic arthropods and tolerant species of fish are minor. The differences in sensitivity are more pronounced, however, among sensitive species of fish and sensitive species of aquatic invertebrates.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

The toxicity studies used to assess the potential hazards of bifenthrin to humans (Section 3.1 and Appendix 1) are applicable to the risk assessment for mammalian wildlife. As summarized in Section 3.1, bifenthrin's mechanism of action involves interference of the voltage-gated membrane sodium channels of nerve cells, which leads to signs of neurotoxicity. The most sensitive overt sign of toxicity is a decrease in motor activity.

The ecological risk assessment attempts to identify subgroups of mammals that may display greater or lesser sensitivity to a particular pesticide. These differences may be based on allometric scaling (e.g., Sample and Arenal 1999) or differences in physiology. Based on acute oral LD_{50} values for technical grade bifenthrin of 70.1 mg/kg bw in male rats and 53.8 mg/kg bw in female rats (MRID 00132519) (Section 3.1.4), U.S. EPA/OPP/HED (2012a) classifies bifenthrin as moderately toxic to mammals (Category II as discussed in Section 3.1.4). As summarized in Appendix 1 (Tables A1-1 and A1-2), all of the available acute toxicity data on mammals involves rats; thus, these data are insufficient to assess potential differences in toxicity among mammalian species. As discussed in Section 3.1.5, subchronic and chronic studies are available in mice, rats, and dogs. These studies give no indication of remarkable differences in

sensitivity between rats and dogs with LOAELs for neurotoxicity falling in the relatively narrow range of about 4 to 7 mg/kg bw/day. Mice appear to be somewhat more tolerant than rats and dogs with LOAELs for neurotoxicity in the range of about 25 to 30 mg/kg bw/day. In the absence of a systematic relationship between body weight and toxicity across a range of mammalian species, separate toxicity values are not derived for small and large mammals.

4.1.2.2. Birds

Typically, the EPA requires three types of avian toxicity studies for pesticide registration: single gavage dose LD_{50} studies, 5-day dietary toxicity studies, and chronic (≈30-week) dietary reproduction studies. The required studies are usually conducted with mallard ducks and bobwhite quail. As summarized in Appendix 2, this standard set of avian toxicity studies was submitted to the EPA—i.e., acute gavage (Table A2-1), acute dietary (Table A2-2), reproduction (Table A2-3) studies. The open literature includes one additional study conducted with domestic chickens (Shakoori et al. 1993), which is summarized in Table A2-2.

Based on the standard acute gavage and acute dietary studies in birds, the EPA classifies bifenthrin as slightly toxic to birds (U.S. EPA/OPP/EFED 2012a, p. 143). No remarkable differences in toxicity are apparent between quail and mallards. Based on acute gavage studies, quail are somewhat more sensitive than mallards—i.e., LD_{50} values of 1800 mg/kg bw for quail and 2150 mg/kg bw for mallards. Based on acute dietary studies, the opposite pattern is seen, with mallards being somewhat more sensitive than quail—i.e., LC_{50} values of 1280 ppm for mallards and 4450 ppm for quail.

The dietary studies are summarized in both U.S. EPA/OPP/EFED (2012a, Appendix F, p. 5) as well as the recent review by FAO (2012). Neither of these documents reports the doses (in units of mg/kg bw/day) associated with the dietary LC_{50} values. As indicated in Appendix 2, Table A2-2, the dietary LC_{50} values are estimated to correspond to about 1355 mg/kg bw/day for quail and 512 mg/kg bw/day for mallards based on approximate food consumption rates from similar studies on other pesticides for which food consumption rates are available. While these estimates may be viewed as tenuous, they suggest no remarkable differences in the toxicity of bifenthrin to birds exposed by gavage versus dietary routes. This is somewhat unusual in that gavage LD_{50} values are typically lower than estimated dietary LD_{50} values.

The study in chickens by Shakoori et al. (1993) is from the Pakistani literature and involves a Talstar 10 EC formulation. As summarized in Appendix 2, Table A2-2, this study involved gavage dosing to domestic chickens (*Gallus gallus*) using two dose regimes—i.e., 50 mg/kg bw/day x 30 days and 100 mg/kg bw/day x 7 days. The 100 mg/kg bw/day dose for 7 day is similar to the acute dietary studies discussed above. As indicated in Appendix 2, Table A2-2, this dose resulted in 20% mortality by Day 7, and this response seems reasonably consistent with the estimated 8-day LD_{50} of 512 mg/kg bw/day in mallards.

As summarized in Appendix 2, Table A2-3, the EPA summaries of the reproduction studies in both mallards and quail failed to note any adverse effects at the highest dietary concentration assayed, 75 ppm. The estimated NOAEC of 5.25 mg/kg bw/day for both of these studies is similar to the dose of 5 mg/kg bw/day from the reproduction study in rats (MRID 00157225 as summarized in Appendix 1, Table A1-5). The dose of 5 mg/kg bw/day in the rat study, however, caused signs of neurotoxicity in female rats. As noted in U.S. EPA/OPP/EFED (2012a, p. 143),

the acute toxicity and reproduction studies in birds failed to note signs of neurotoxicity. Based on these differences, it appears that birds may be at least somewhat less sensitive than mammals to bifenthrin.

As discussed in U.S. EPA/OPP/EFED (2012a, p. 143), data are not available on passerine species. Concern for this data gap is increased by the Addy-Orduna et al. (2011) study which indicates that a species of canary (*Serinus* sp.) is 13 times more sensitive than cowbirds and doves (two non-passerine species of birds) to a formulation of beta-cyfluthrin (another pyrethroid). This data gap is discussed further in the risk characterization (Section 4.4.2.2).

4.1.2.3. Reptiles and Amphibians (Terrestrial Phase)

There are no data regarding the toxicity of bifenthrin to reptiles or terrestrial phase amphibians in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a) or in the review by Pauli et al. (2000). No other information on the toxicity of bifenthrin to reptiles or terrestrial phase amphibians was identified in the open literature. As noted in the EPA risk assessment, the EPA recommends the use of birds as surrogates for reptiles and terrestrial-phase amphibians.

A concern with the use of birds as a surrogate for amphibians involves the permeability of amphibian skin to pesticides and other chemicals. Quaranta et al. (2009) indicate that the skin of the frog *Rana esculenta* is much more permeable than pig skin to several pesticides and that these differences in permeability are consistent with differences in the structure and function of amphibian skin, relative to mammalian skin. In the absence of data, however, the current risk assessment defers to the EPA, and birds are used as surrogates for reptiles and terrestrial-phase amphibians.

4.1.2.4. Terrestrial Invertebrates

Studies on the toxicity of bifenthrin to terrestrial invertebrates are summarized in Appendix 3. These studies encompass effects on honeybees (Table A3-1), other terrestrial insects (Table A3-2), other terrestrial invertebrates (Table A3-3), and selected field studies (Table A3-4).

The open literature on bifenthrin is abundant. For example, the EPA ECOTOX database lists a total of 1604 records on the toxicity of bifenthrin to terrestrial invertebrates (ECOTOX 2015), and the most recent EPA ecological risk assessment lists these studies as an appendix (i.e., U.S. EPA/OPP/EFED 2012, Appendix H). Consistent with the approach taken in U.S. EPA/OPP (2012a), the current risk assessment for terrestrial invertebrates focuses primarily on the toxicity of bifenthrin to the honeybee, which is the most sensitive arthropod, as well as studies useful for assessing the range of sensitivities among other terrestrial arthropods (Section 4.1.2.4.1). Exposures of soil invertebrates to bifenthrin are fundamentally different from those of above ground organisms. Consequently, soil organisms are also considered separately in Section 4.1.2.4.2.

4.1.2.4.1. Insects and Other Arthropods

The honeybee is the standard test species used by the U.S. EPA to assess toxicity to nontarget terrestrial invertebrates. As summarized in U.S. EPA/OPP (2012a, Table 4-5, p. 19), technical grade bifenthrin is classified as *very highly toxic* to the honeybee with a contact/topical LD_{50} of 0.015 µg a.i./bee using a 0.8% EC (emulsifiable concentrate) formulation. This study is cited in

the EPA risk assessment to "*Atkins (1981)"* for which a full citation was not located in either the EPA document or ECOTOX bibliography. As summarized in Appendix 3, Table A3-1, the study cited by EPA is consistent with Atkins and Kellum (1981), and a cleared review for this study is available.

In a discussion of the honeybee contact assay discussed above as well as other studies summarized in ECOTOX, U.S. EPA/OPP (2012a, p. 144) indicates that the honeybee appears to be the most sensitive species of terrestrial arthropods, based on comparisons in doses of µg a.i./g organism; however, details of the analysis are not given. The cleared review of the study by Atkins and Kellum (1981) does not specify the body weight of the 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, the LD_{50} of 0.015 µg/bee corresponds to a dose of about 0.13 µg/g bw [0.015 µg ÷ 0.116 g ≈ 0.1293 µg/g bw (mg/kg bw)].

While toxicity data are available on many insect species, comparisons among studies are complicated by the diversity of the open literature studies in terms of the types of exposures used and different endpoints assayed. For the comparison to the honeybee assay by Atkins and Kellum (1981), the comparisons are limited to contact bioassays involving topical exposures as well as studies for which LD_{50} values can be expressed in units of µg a.i./g bw (i.e., equivalent to mg a.i./kg bw).

Within the subgroup of studies expressing dose in the units of µg a.i./g bw, comparisons of species sensitivity are complicated by the ability of insect populations to develop resistance, or at least tolerance, to insecticides. As summarized in Appendix 3, Table A3-2, resistance or tolerance to bifenthrin is well documented with apparent resistance factors (i.e., the LD_{50} value in a tolerant population ÷ the LD_{50} in a sensitive population) ranging from about 2.5 (African malaria mosquito in the study by Hougard et al. 2002) to about 136 (bluegrass weevil in the study by Ramoutar et al. 2009). In addressing the issue of resistance, the EPA requires that honeybee studies in support of registration must be from insect populations … *kept in conditions conforming to proper cultural practices* (U.S. EPA/OCSPP 2012a, p. 3), which would preclude substantial prior exposures to pesticides. Consequently, for species on which a range of LD_{50} values are available, the lowest LD_{50} value is used for comparisons to the toxicity value for the honeybee.

Within the above constraints, LD_{50} values in units of µg a.i./g organism are summarized in Table 17 and illustrated in Figure 4. Most of the studies report LD_{50} values in units of µg a.i./g organism. The study by Li et al. (2006) specifies doses in units of µg a.i./organism but provides data on the body weights of *C. suppressalis*; thus, the dose conversion to units of µg a.i./g organism is accompanied by little uncertainty.

The y-axis of Figure 4 represents the cumulative frequencies of the toxicity data for the various species of terrestrial invertebrates, based on ordered sensitivity to bifenthrin. The individual values for the cumulative frequency are based on the following equation:

Equation 1

$$Freq_i = \frac{i - 0.5}{N}$$

where $Freq_i$ is the cumulative frequency for the i^{th} value and N is the number of values in the data set. For example, 10 LD_{50} values in terrestrial invertebrates are available on bifenthrin. The lowest value is the LD_{50} of 0.13 µg a.i./g bw. Thus, the frequency for the first point (i=1) is calculated as (1-0.5) ÷ 10 which is equal to 0.05. Similarly, the second lowest LD_{50} value (i=2) is 0.15 µg a.i./g bw, which is assigned a frequency of (2-0.5) ÷ 10 or 0.15. The x-axis in Figure 4 represents the LD_{50} values, which are given on a logarithmic scale, under the standard assumption that LD_{50} values for species have a lognormal distribution.

The cumulative frequency distributions of toxicity values are related to figures often referred to as *species sensitivity distributions* (e.g., Awkerman et al. 2008; Posthuma et al. 2002). As discussed by Posthuma et al. (2002), species sensitivity distributions can be used quantitatively as tools in probabilistic risk assessment. Probabilistic methods are not routinely used in Forest Service risk assessments. Nonetheless, cumulative distribution plots, like those in Figure 4, are useful for illustrating differences in and among different groups of organisms.

Consistent with the EPA assessment discussed above, the honeybee is apparently the most sensitive species on which data are available. Two species of mosquito (i.e., *Anopheles gambiae* and *Culex quinque-fasciatus*) are almost as sensitive as the honeybee. Overall, there seems to be no clear relationship among the different orders of insects with sensitivity to bifenthrin. Among the dipterans, the common housefly appears to be less sensitive than mosquitos by a factor of 280 [42 ÷ 0.15 = 280]. The sensitivity among lepidopterans is modest, spanning a factor of about 7 [1.321 ÷ 0.19 ≈ 6.953]. The differences among coleopterans, however, are much greater, spanning a factor of about 2000 [542 ÷ 0.27 ≈ 2007.4]. As also illustrated in Figure 4, the distribution of LD_{50} values does not appear to conform to a lognormal distribution—i.e., the points do not form a sigmoidal curve. Given the small number of species on which comparisons may be made, relative to the numerous species of insects, the apparent differences in the magnitudes of the variations in sensitivity as well as the shape of the cumulative distribution may be an artifact of the limited data set.

As discussed in Section 3.1, comparative data on the [S] and [R] enantiomers of bifenthrin clearly and consistently indicate that the [S] enantiomer of the cis-isomer is more potent than the [R] enantiomer in mammals. Based on the study by Liu et al. (2008b) on a species of butterfly, the reverse pattern is apparent with the [R] enantiomer being much more potent than the [S] enantiomer. The studies by Wiltz et al. (2009) on Argentine ants do not indicate an effect of temperature on the toxicity of bifenthrin, while the study by Li et al. (2006) on the rice stem borer notes an increase in the toxicity of bifenthrin as temperature increased. This temperature dependence is a common pattern. As discussed further in Section 4.1.3 (hazard identification for aquatic organisms), the reverse pattern is apparent in fish with increasing toxicity as temperature decreases.

4.1.2.4.2. Soil Invertebrates

The earthworm is the standard test species used by the EPA in the assessment of potential hazards to soil invertebrates (U.S. EPA/OCSPP 2012b). The U.S. EPA risk assessments on

bifenthrin (Table 1) do not cite any information on the toxicity of bifenthrin to earthworms; furthermore, bifenthrin toxicity data are not included in the compendia of earthworm toxicity studies (i.e., Edwards and Bohlen 1992; Potter et al. 1990; Wang et al. 2012).

The open literature on bifenthrin includes two earthworm studies (Potter et al. 1994; Schofield 2007). As summarized in Appendix 3, Table A3-3, Potter et al. (1994) observed no effect on earthworms following applications of a bifenthrin formulation at a rate of 0.11 lb a.i./acre. Similarly, Schofield (2007) noted no effect on earthworms following applications of a bifenthrin formulation equivalent to about 20 lbs a.i./acre.

European regulators have somewhat different testing requirements than those of EPA. As also summarized in Appendix 3, Table A3-3, the recent risk assessment from the European Food Safety Authority (EFSA 2011) summarizes a bioassay in earthworms that yielded an NOAEC of 2.13 mg a.i./kg soil for bifenthrin as well as higher NOAECs (17.8-178 mg a.i./kg soil) for two bifenthrin metabolites. The lower toxicity of the bifenthrin metabolites (i.e., higher NOAECs) is consistent with the mites study by Yang et al. (2001) indicating that bifenthrin appears to be detoxified by esterases, glutathione S-transferases, and cytochrome P450 monooxygenases—i.e., the metabolites of bifenthrin appear to be less toxic than bifenthrin itself.

4.1.2.5. Terrestrial Plants (Macrophytes)

Little information is available on the toxicity of bifenthrin to terrestrial plants. For herbicides, the EPA generally requires relatively sophisticated Tier II bioassays on plants. For insecticides applied to plants, much simpler Tier 1 (i.e., single limit dose) studies are sometimes required. While the most recent EPA ecological risk assessment does not explicitly note that standard Tier 1 toxicity tests on terrestrial plants were waived, that appears to be the case in that the EPA did not identify toxicity data on terrestrial plants, and this lack of information is not identified as a data need (U.S. EPA/OPP/EFED 2012a, p. 145). In the somewhat earlier problem formulation for the registration review of bifenthrin, the EPA notes the following:

> *…it was concluded at the time, that risk to terrestrial plants is unknown due to a lack of data, but that it would also be considered minimal (based on bifenthrin's mode of action).*
>
> U.S. EPA/OPP/EFED (2010b, p. 7)

This assessment is essentially identical to the conclusion in the the European Food Safety Authority risk assessment of bifenthrin (EFSA 2011, p. 30).

Notwithstanding the above assessment, the most recent EPA ecological risk assessment notes that some formulations of bifenthrin registered for the control of turf insects are associated with damage to grass (U.S. EPA/OPP/EFED 2012a, p. 197). It is unclear from the EPA summary whether the damage was due to bifenthrin or other components in the formulation. The only other suggestion of phytotoxicity in the open literature is the study by Corkidi et al. (2009, Table 2, p. 811) that notes dose-related decreases in shoot dry weight, root dry weight, and total dry weight of corn plants. Adverse effects were noted at bifenthrin soil concentrations of 12 ppm and above with an NOAEC of 10 ppm (i.e., mg/kg soil). No effects were noted in corn plants treated with a mycorrhizal inoculum prior to exposure – i.e., corn plants treated with a commercial formulation of beneficial fungi used to promote plant growth.

Bifenthrin is applied extensively to trees (e.g., Elias et al. 2013; Liesch and Williamson 2010; Lowe et al. 1994; McCullough and Smitley 1995; McCullough et al. 1998; Negron and Clarke 1995). For example, bifenthrin applications to urban forests (Miller 1997) and loblolly pine (Burke et al. 2012) did not damage trees. In applications of bifenthrin formulated as SPECKoZ and another formulation (IC2) that does not contain bifenthrin, Elias et al. (2013) specifically noted phytotoxic effects from the IC2 formulation but not the formulation containing bifenthrin. In a study of technical grade bifenthrin for the control of whiteflies, He et al. (2013) suggest that bifenthrin might alter the chemical composition of treated plants; however, there are no reported data to support this supposition.

4.1.2.6. Terrestrial Microorganisms

Effects on terrestrial microorganisms are not addressed in the EPA, EFSA or other risk assessments and reviews on bifenthrin (Table 1). Only one study regarding the potential effects of bifenthrin on microorganisms is available. As noted in the previous section, Corkidi et al. (2009) examined the effects of bifenthrin on corn plants with and without a commercial fungal mycorrhizal inoculum. No effects on mycorrhizal colonization of corn root systems were noted at bifenthrin soil concentrations of 10 to 25 ppm (mg a.i./kg soil).

ECOTOX (2015) indicates that the study by Asi et al. (2010) provides information on the toxicity of bifenthrin to entomopathogenic fungi. A review of the paper by Asi et al. (2010), a group of investigators from Pakistan, conducted as part of the current risk assessment failed to note any data on bifenthrin. While somewhat speculative, this discrepancy may involve the nomenclature of the formulation, which is cited in Asi et al. (2010, Table 1) as “Capture 20 SC”. While some U.S. formulations designated as “Capture” do contain bifenthrin (e.g., Capture 2 EC in CalEPA/DPR 1997), the Capture formulation in Asi et al. (2010) is specified in the publication as containing triflumuron (CAS No. 64628-44-0) rather than bifenthrin (CAS No. 82657-04-3).

4.1.3. Aquatic Organisms

As summarized in Table 3 and discussed in Section 3.2.3.4, the solubility of bifenthrin in water is only 0.014 µg/L. Some of the modeled estimates as well as monitoring data for bifenthrin, however, indicate water concentrations in excess of the water solubility of bifenthrin. Similarly, as detailed in Appendix 3 (fish) and Appendix 4 (aquatic invertebrates), some of the reported LC_{50} values for bifenthrin exceed the water solubility of bifenthrin. This is not surprising in that solvents (as well as appropriate solvent controls) are typically used in aquatic bioassays for compounds with a low solubility in water. The current Forest Service risk assessment adopts the approach taken in U.S. EPA/OPP/EFED (2012a) and discusses the toxicity values for aquatic organisms in terms of the reported nominal concentrations.

4.1.3.1. Fish

4.1.3.1.1. Acute Toxicity

Studies on the acute lethal potency of bifenthrin in fish are summarized in Appendix 3, Table A3-1. The U.S. EPA typically uses 96-hour LC_{50} values in fish to assess the potential for acute risks to fish. An overview of the LC_{50} values in fish is given in Table 18 and illustrated in Figure 5. Acute LC_{50} values, available in seven species of fish, range from 0.15 µg/L (rainbow trout) to 19.8 µg/L (sheepshead minnow). Sheepshead minnow is the only species for which more than one LC_{50} is available—i.e., 17.5 µg/L from MRID 163101 and 19.806 µg/L from the open literature study by Harper et al. (2008). These values are averaged in Figure 5 and are plotted as a single point (18.653 µg/L). The LC_{50} value for gizzard shad involves an 8-day rather than a 96-hour LC_{50}. As illustrated in Figure 6, the available concentration-duration data in trout, bluegill, and zebra fish suggest that substantial additional mortality will not occur after 96 hours, and the longer LC_{50} in gizzard shad is probably comparable to the 96-hour LC_{50} values in Figure 5. Based on the 96-hour LC_{50} of 0.15 µg/L in trout, U.S. EPA/OPP/EFED (2012a, p. 134) classifies bifenthrin as *very highly toxic* to fish on an acute basis.

As also summarized in Appendix 3, Table A3-1, DeMicco et al. (2010) report a 6-day LC_{50} of 190 µg/L for zebra fish embryos, which is substantially higher than the 96-hour LC_{50} of 2.1 µg/L for zebra fish fry reported by Zhang et al. (2010). The difference in LC_{50} values probably reflects the lower uptake of bifenthrin by zebrafish embryos, as noted by Tu et al. (2014)—i.e., BCF values of about 300 to 700 for embryos relative to BCF values in whole fish of about 6,000 (MRID 163094 and MRID 163095).

The LC_{50} values from Drenner et al. (1993) in gizzard shad and Velisek et al. (2009) in common carp involve emulsifiable concentrate (EC) formulations of bifenthrin. In the absence of matched studies in the same species with technical grade bifenthrin, the formulation studies cannot be used to assess the potential contribution of other ingredients in the formulations to the toxicity of the formulations. As summarized in Appendix 4, Table A4-2, Beggel et al. (2010) assayed the effects of both technical grade bifenthrin and a Talstar formulation (7.9% a.i.) on swimming performance in the fathead minnow. Based on the estimated LOAELs of 0.14 µg/L for technical grade bifenthrin and 0.03 µg a.i./L for the Talstar formulation, it appears that the other ingredients in the Talstar formulation contribute to the toxicity of the formulation or the bioavailability of bifenthrin to the organism.

As discussed in Section 3.1.2, the most common sign of toxicity in mammals involves decreased motor activity. Based on the sublethal studies with zebra fish larvae and embryos by Jin et al. (2009), the opposite effect (an increase in spontaneous movements) is seen in fish. The most sensitive endpoint appears to involve endocrine effects. As summarized in Appendix 3, Table A3-2, several studies note changes in hormone regulation (vitellogenin or choriogenin) in several species of fish at sublethal concentrations—i.e., 0.001 to 1.5 µg/L (Beggel et al. 2010; Brander et al. 2012; Crago et al. 2015; DeGroot and Brander 2014; Wang et al. 2007; Forsgren et al. 2013). The lowest adverse effect level is 0.001 µg/L, which was associated with a significant but not a dose-dependent increase in choriogenin over concentrations ranging from 0.001 to 0.1 µg/L (Brander et al. 2012). Based on assays for mRNA expression of vitellogenin, the NOAEC for endocrine-related effects appears to be 0.005 µg/L (Crago et al. 2015), although effects on mRNA were noted with co-exposure to surfactants. As with mammals (Section 3.1.2), the [S]

enantiomer appears to be more potent than the [R] enantiomer (Jin et al. 2013b ; Wang et al. 2007). The only exception to this pattern is the report by Jin et al. (2010) indicating that [R] enantiomer was more effective than the [S] enantiomer in causing curvature of body axis and pericardial edema in zebrafish larvae.

In terms of practical significance to the current risk assessment, endocrine disruption in fish should be reflected in full life-cycle reproduction studies. One full life-cycle study is available on bifenthrin (McAllister et al. 1988a,b). While the authors of this study indicate that 0.04 µg/L should be viewed as a NOAEC, this study is classified as "*Invalid*" by EPA due to poor control survival and poor study documentation. The EPA data evaluation record for this study is detailed and well documented. Consequently, the current Forest Service risk assessment defers to the EPA evaluation, and the McAllister et al. (1988a,b) study is not used quantitatively in the current risk assessment.

4.1.3.1.2. Longer-term Toxicity

The EPA risk assessments (Table 1) do not discuss any valid or acceptable longer-term studies on the effects of bifenthrin in fish, and no such studies were identified in the open literature. The review by the Food and Agriculture Organization of the United Nations (FAO 2012, p. 33) provides a brief description of an early life-cycle assay (48 days) in rainbow trout reporting an NOEC of 0.012 µg/L. As summarized in Appendix 4, Table A4-3, this reported NOEC is somewhat unusual in that the concentration designated as the NOAEC is not one of the experimental concentrations—i.e., 0.0044, 0.0088, 0.018, 0.035, or 0.070 µg/L. The geometric mean of the second and third doses is about 0.012 µg/L [$(0.0088 \times 0.018)^{0.5} \approx 0.01259$], and the NOEC indicated in FAO (2012, p. 33) may be intended as the MACT (Maximum Acceptable Tolerance Concentration), which is generally calculated as the geometric mean of the NOAEC and LOAEC. This trout study is not discussed in any EPA risk assessments. Rainbow trout is a standard test species approved by the U.S. EPA, and it is unusual for such a study not to be submitted to and discussed by the EPA.

Given the lack of an acceptable chronic study in fish, the most recent EPA ecological risk assessment on bifenthrin proposes a surrogate chronic NOAEC of 0.004 µg/L for fish (U.S. EPA/OPP/ EFED 2012a, pp. 136-137 and Appendix J). This NOAEC is essentially the lowest NOAEC for any pyrethroid. In an open literature study, Fojut et al. (2012) also note the lack of a suitable chronic toxicity value for fish and derive a surrogate chronic value of 0.0006 µg/L. This recommended chronic value is based on a probabilistic analysis of bifenthrin data yielding an estimated acute value of 0.00803 µg/L to which a default acute-to-chronic ratio of 12.3 is applied [$0.00803 \div 12.3 \approx 0.000637$ µg/L]. Note that the acute value of 0.00803 µg/L is not an estimate of an acute NOAEC but the 5th percentile of the LC_{50} values based on a log-logistic distribution (Fojut et al. 2012, p. 69).

As summarized in Appendix 4, Table A4-4, there are three field studies that address the effects of bifenthrin on fish (Sherman 1989; Pennington et al. 2014; Weston et al. 2015). The study by Weston et al. (2015) is particularly notable in that the study assayed for but did not note changes in vitellogenin or sex steroid levels in both Chinook salmon and steelhead trout following exposure to concentrations of up to 0.0146 µg/L.

4.1.3.2. Amphibians (Aquatic Phase)

As with terrestrial phase amphibians, there are no data on the toxicity of bifenthrin to aquatic phase amphibians. The EPA risk assessments (Table 1) on bifenthrin do not cite any registrant-submitted studies on aquatic phase amphibians. The general lack of toxicity data on aquatic phase amphibians extends to the open literature and the compendia of amphibian toxicity studies by Pauli et al. (2000). As noted in the EPA's most recent risk assessment on bifenthrin (U.S. EPA/OPP/EFED 2012a, p. 85), the EPA uses fish as a surrogate for aquatic phase amphibians.

4.1.3.3. Aquatic Invertebrates

A large and diverse body of literature is available on the toxicity of bifenthrin to aquatic invertebrates, which is summarized in Appendix 5. Bifenthrin is extensively bound to sediment, and several bifenthrin toxicity studies express exposures and toxicity values as concentrations in sediment, either as µg/kg sediment or µg/g organic carbon in sediment (e.g., Picard 2010a; Maul et al. 2008a; Harwood et al. 2014; Weston et al. 2009). Because of the partitioning of bifenthrin to sediment, potential risks to benthic organisms are an obvious concern. Nonetheless, consistent with the approach used in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a), the focus of the current risk assessment is on studies that report toxicity values for bifenthrin in units of the concentration of bifenthrin in the water column. This approach parallels the exposure assessment (Section 3.2.3.4), and concerns for benthic organisms are addressed by considering the bifenthrin concentration in sediment pore water – i.e., the water between the soil particles in the sediment (e.g., U.S. EPA/OPP/EFED 2012a, Table 3-2).

4.1.3.3.1. Acute Toxicity

As summarized in Appendix 5, Table A5-1, acute toxicity values expressed in units of water concentration consist primarily of LC_{50} values (concentrations estimated to cause 50% mortality) and EC_{50} values (concentrations estimated to cause a non-lethal response in 50% of the organisms assayed) for aquatic invertebrates. As discussed further in Section 4.3.3, the dose-response assessment is concerned primarily with estimated no effect levels; however, LC_{50} and EC_{50} values are generally preferable in estimating differences in sensitivity among species (e.g., Awkerman et al. 2008). For aquatic invertebrates, the distinction between LC_{50} and EC_{50} values is often unclear in publications, and the two terms may be used loosely and sometimes interchangeably. As summarized in Table 19, Weston and coworkers (Weston and Jackson 2009; Weston et al. 2015), explicitly report both LC_{50} and EC_{50} values in five species of aquatic invertebrates with four replicate assays in one of the species (*Hyalella azteca*). Based on these data, the LC_{50} values for bifenthrin are factors of about 1.2 to 2.7 higher than the corresponding EC_{50} values, with an average difference of about a factor of 2. While these differences are not substantial, the endpoints are addressed separately below.

By definition, EC_{50} values are more sensitive endpoints than LC_{50} values, and the EC_{50} is the endpoint used in most EPA risk assessments. U.S. EPA/OPP/EFED (2012a, p. 137) classifies bifenthrin as *very highly toxic* on an acute basis to aquatic invertebrates. This classification is based on an EC_{50} of 1.9 ng/L in the scud, *Hyalella azteca*, from the open literature study by Weston and Jackson (2009). As detailed in Appendix 5, Table A5-1 and noted above, Weston and Jackson (2009) report four replicate EC_{50} values ranging from 1.9 to 3.5 ng/L, based on swimming impairment in the scud. The EPA assessment selects and focuses on the lowest EC_{50} value for risk characterization.

An overview of all of the available EC_{50} values for aquatic invertebrates is given in Table 20, and the data for aquatic arthropods are illustrated in Figure 7. Figure 7 is constructed in a manner similar to Figure 4 (terrestrial invertebrates), as discussed in Section 4.1.2.4.1. For species on which more than one EC_{50} value is available—i.e., *Hyalella azteca* and *Daphnia magna*—the EC_{50} values in Figure 7 are plotted as the geometric mean of the available values for each species. Note that the EC_{50} of 285,000 ng/L for the bivalve *Crassostrea virginica* (Eastern oyster) is not included in Figure 7. Based on the single available bioassay from the registrant-submitted study by Ward and Dose (1987), Eastern oyster is more tolerant than the most tolerant arthropod by a factor of about 125 [285000 ÷ 2277 ≈ 125.17] and more tolerant than the most sensitive arthropod by a factor of nearly 100,000 [285,000 ÷ 2.91 ≈ 97,787.2].

There is some uncertainty in the number of species on which data are available because both Weston et al. (2015) and FAO (2012) report EC_{50} values for species from the genus *Hexagenia* but do not identify the organism to the level of species. This uncertainty is noteworthy because the 96-hour EC_{50} from Weston et al. (2015) is lower than the 48-hour EC_{50} reported by FAO (2012) by a factor of about 25 [390 ÷ 15.3 ≈ 25.49]. Of the 15 or 16 species of arthropods on which data are available, 11 of the species are reported in studies by Weston and coworkers (Weston and Jackson 2009; Weston et al. 2015). For these species, concerns for differences in the experimental methods are minimal. Even with these studies, however, there are differences in the durations of the bioassays which range from 48 to 96 hours. Also, as summarized in Weston et al. (2015, Table 1), these studies were conducted at different times and at different temperatures appropriate for the species used in the bioassays. These types of experimental differences are common and virtually inevitable in comparisons of bioassays on different species.

Within the above limitations and consistent with the assessment from U.S. EPA/OPP/EFED (2012a, p. 137), *Hyalella azteca* is clearly the most sensitive species. Based on the data from Ye et al. (2004) and a registrant-submitted study (MRID 41156501), *Daphnia magna*, a very common test species in aquatic toxicology, is among the least sensitive species.

The sensitivities of aquatic insect larvae are highly variable even within the same order. For example, data from Weston et al. (2015) indicate a difference in sensitivity among Trichoptera of a factor of about 20—i.e., the 96-hour EC_{50} of 251 ng/L in a *Helicopsyche* species and the 96-hour EC_{50} of 12.8 ng/L in a *Hydropsyche* species [251 ÷ 12.8 ≈ 19.61]. These two bioassays were conducted at different times—i.e., November for *Helicopsyche* species and February for *Hydropsyche* species—and used somewhat different endpoints to assess response—i.e., the ability to cling for the *Helicopsyche* species and thrashing when prodded for *Hydropsyche* species. Nonetheless, the organisms were collected from the same creek and the bioassays were conducted at about the same temperatures (i.e., 12°C and 13°C). Another noteworthy difference in sensitivities among aquatic invertebrates involves amphipods. As noted above, *Hyalella azteca* is the most sensitive amphipod with an average EC_{50} of about 2.91 ng/L (Weston et al. 2015) but another amphipod, *Gammarus pulex* (EC_{50}=110 ng/L), is less sensitive by a factor of nearly 40 [110 ÷ 2.91 ≈ 37.74].

An overview of all of the available LC_{50} values for aquatic invertebrates is given in Table 21 and the LC_{50} values for aquatic arthropods are illustrated in Figure 8. As with the sensitivities in

EC_{50} values, the most sensitive species is *Hyalella azteca*. Taking the geometric mean of the multiple LC_{50} values for *Hyalella azteca* (i.e., 4.55 ng/L), the mysid shrimp, *Americamysis bahia*, is the most sensitive species. In any event, the LC_{50} values consistently indicate that members of the Class Malacostraca (i.e., mysids, amphipods, and decapods) are among the more sensitive species with LC_{50} values ranging from 1.5 to 24 ng/L. As noted in the above discussion of EC_{50} values, however, the scud (*Gammarus pulex*, Amphipoda: Malacostraca) is an exception with an EC_{50} of about 110 ng/L, based on mobility. The Branchiopoda (i.e., Cladocera and Anostraca) are among the more tolerant species with the cladoceran *Daphnia magna* being substantially less sensitive than the cladoceran *Ceriodaphnia dubia*. The observations on the cladocerans are consistent with the EC_{50} data; however, EC_{50} values are not available on the order Anostraca. Also, consistent with the EC_{50} data, dipterans appear to be relatively tolerant. Patterns of sensitivity in other orders and classes of aquatic invertebrates (e.g., Trichoptera and Ephemeroptera) are highly variable.

Unlike the case in fish (Section 4.1.3.1) and mammals (Section 3.1.2), the studies by Liu et al. (2005a,c) in cladocerans indicate that the [R] enantiomer of cis-bifenthrin is more toxic than the [S] enantiomer. Based on LC_{50} values in *Ceriodaphnia dubia*, the difference in potency (i.e., [S] ÷ [R]) is a factor of about 18 [1.342 µg/L ÷ 0.076 µg/L ≈ 17.658]. Based on LC_{50} values in *Daphnia magna*, the difference in potency is about a factor of 22 [1.803 µg/L ÷ 0.081 µg/L ≈ 22.259].

As summarized in Appendix 5, Table A5-1, Siegfried (1993) conducted more or less standard bioassays on several species of aquatic insects, which are summarized in Table 21. Also, as summarized in Appendix 5, Table A5-1, Siegfried (1993) conducted topical bioassays on several species of aquatic invertebrates. The LD_{50} values in the study range from 0.1 to 4 ng/mg bw. Topical bioassays on aquatic insects are extremely unusual. While these results are not used quantitatively in the current risk assessment, they do suggest that the sensitivities of aquatic insects are similar to the sensitivities of terrestrial insects when assayed topically and when doses are expressed in units of ng/mg bw.

4.1.3.3.2. Longer-term Toxicity

Information on the chronic toxicity of bifenthrin to aquatic invertebrates is summarized in Appendix 5, Table A5-2, and an overview of the available studies is given in Table 22. Consistent with the acute toxicity data, *Hyalella azteca* (Malacostraca: Amphipoda) is the most sensitive species with a NOAEC for reproduction of 0.17 ng/L. Also consistent with the acute LC_{50} values, mysids are also among the most sensitive species with an NOAEC of 1.2 ng/L in *Mysidopsis bahia* (Malacostraca: Mysida), based on reproduction. The data on *Daphnia magna* (Branchiopoda: Cladocera) are generally consistent with the acute toxicity data indicating that daphnids are generally more tolerant than the Malacostraca. The one exception is the reported NOAEC of 1.3 ng/L in *Daphnia magna* from a registrant-submitted study (MRID 41156501), which is similar to the NOAEC of 1.2 ng/L in *Mysidopsis bahia*.

One clear difference between the acute and chronic studies involves the magnitude of the differences in sensitivity. Based on the geometric means of acute EC_{50} values (Table 20), *Hyalella azteca* is more sensitive than *Daphnia magna* by a factor of about 780 [2,277 ng/L ÷ 2.91 ng/L ≈ 782.47]. Based on the geometric means of acute LC_{50} values (Table 19), *Hyalella azteca* is more sensitive than *Daphnia magna* by a factor of about 124 [546.34 ng/L ÷ 4.55 ng/L

≈ 124.03]. Based on the range of chronic NOAECs for reproductive effects in *Daphnia magna* (Table 22), the difference in chronic sensitivity between *Hyalella azteca* and *Daphnia magna* ranges from a factor of about 8 [1.3 ÷ 0.17 ≈ 7.65] to 120 [20 ÷ 0.17 ≈ 117.65]. All of the higher reproductive NOAECs for *Daphnia magna* are from the open literature (Brausch et al. 2010; Wang et al. 2009b; Zhao et al. 2009) and are reasonably consistent with each other—i.e., NOAECs ranging from 10 to 20 ng/L. The experimental details of the open literature studies are well documented in the publications. A DER for the registrant study (MRID 41156501) is not available but the study is well-described in EPA risk assessments as well as FAO (2012). In addition, U.S. EPA/OPP/EFED (2012a, Table 4-1, p. 133) classifies this study as *Acceptable*. In the absence of additional information, there is no basis for questioning either the registrant study or the open literature studies, and the differences between the studies may reflect normal biological variability in different populations of daphnids or other unidentified factors in the experiments.

4.1.3.4. Aquatic Plants

The most recent EPA ecological risk assessment does not include information on the toxicity of bifenthrin to aquatic plants (U.S. EPA/OPP/EFED 2012a, p. 140). As explicitly noted in the EPA's problem formulation for the registration review of bifenthrin,

> *No toxicity data are currently available to assess the risk of bifenthrin to aquatic nonvascular plants. Since bifenthrin has residential outdoor uses, Tier I/II aquatic nonvascular plant studies are required.*
>
> U.S. EPA/OPP/EFED (2010b, p. 71)

New studies on the toxicity of bifenthrin to aquatic plants were not, however, identified in the EPA literature.

One algal bioassay summarized in the European regulatory literature reports an indefinite EC_{50} value of > 8 mg a.i./L for a formulation of Talstar 8SC assayed in *Desmodesmus subspicatus*, a species of freshwater green algae (EFSA 2011, p. 84). EFSA (2011) also reports a definitive EC_{50} of 0.822 mg/L, based on a reduction in dry weight for *Pseudokirchneriella subcapitata*, another species of freshwater algae.

In mesocosm studies conducted over 7- to 14-day periods of exposure, bifenthrin had mixed effects on algal populations and chlorophyll levels at concentrations ranging from about 0.1 to 3 µg/L (Drenner et al. 1993; Hoagland et al. 1993). Increases in algal populations may have been associated with decreases in invertebrate grazing. Decreases in algal populations and chlorophyll levels may have been associated with changes in nutrients.

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 bifenthrin. Attachment 1 details the exposure assessments for foliar applications at the maximum single application rate for forestry of 0.2 lb a.i./acre. Attachment 2 covers bark applications, again at the maximum anticipated application rate of 0.2 lb a.i./acre. As discussed in Section 2 (Program Description), bark applications are treated similarly to foliar applications with the assumption that bark applications will be conducted at an application efficiency of 90% (i.e., 10% of the applied bifenthrin is lost to nontarget vegetation). As with the exposure assessment for human heath (Section 3.2), all exposure assessments involving applications of bifenthrin are expressed in units of active ingredient (a.i.).

As in the human health risk assessment, three general types of exposure scenarios are considered: accidental, acute non-accidental, and longer-term. 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 applications of any pesticide to vegetation. The highest exposures are associated with the consumption of contaminated short grass by a small mammal or bird.

Exposures of aquatic animals and plants are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water (Section 3.2.3.4.6).

4.2.2. Mammals and Birds

All of the exposure scenarios that are more or less standard in Forest Service risk assessments for broadcast applications are not relevant to the foliar and bark application methods considered in the current risk assessment of bifenthrin.

Table 23 provides an overview of the mammalian and avian receptors considered in the current risk assessment. These data are discussed in the following subsections. Because of the relationship of body weight to surface area as well as to the consumption of food and water, the dose for smaller animals is generally higher, in terms of mg/kg body weight, than the dose for larger animals. Consequently, 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).

4.2.2.1. Direct Spray

Direct spray scenarios are relevant to the foliar applications of virtually any pesticide. In a scenario involving exposure to direct spray, the amount of pesticide absorbed depends on the application rate, the surface area of the organism, and the rate of absorption. For this risk assessment, two direct spray or broadcast exposure assessments are conducted. 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. This exposure assessment assumes first-order dermal absorption using the first-order dermal absorption rate coefficient (k_a) discussed in 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.

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

4.2.2.2. Dermal Contact with Contaminated Vegetation

As discussed in the human health risk assessment (Section 3.2.3.3), the 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. The lack of data regarding the kinetics of this process precludes a quantitative assessment for this exposure scenario.

For bifenthrin, the failure to quantify exposures associated with dermal contact adds relatively little uncertainty to the risk assessment, since the consumption of contaminated vegetation is the greatest source of exposure, as discussed below (Section 4.2.2.3).

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

The exposure scenarios for the consumption of contaminated vegetation are similar to the exposure scenarios considered in the human health risk assessment (Section 3.2.3.7), except that the ecological risk assessment considers a wider variety of vegetation—i.e., long and short grass, in addition to fruit and broadleaf vegetation, which are considered in the human health risk assessment. As with the human health risk assessment, residues on nontarget vegetation following bark application are assumed to be one-tenth of the residues following broadcast application.

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 to birds or larger mammals which 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).

As summarized in Table 23, 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 by the U.S. EPA/ORD (1993) of estimates from Nagy (1987). 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 24. Most of the specific values in Table 24 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).

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating bifenthrin concentrations in water are identical to those used in the human health risk assessment. As summarized in Table 13 and discussed in Section 3.2.3.4.6.1, the current Forest Service risk assessment adopts the approach used in all recent EPA risk assessments, and the estimated concentrations of bifenthrin in surface water are capped at the water solubility of bifenthrin (i.e., 0.014 µg/L).

Body weight and water consumption rates are the major differences in the exposure estimates for birds and mammals, relative to humans. 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 23.

Like food consumption, water consumption in birds and mammals varies substantially with diet, season, and many other factors. Quantitative estimates regarding the variability of water consumption by birds and mammals are not well documented in the available literature and are not considered in the exposure assessments. As discussed further in Section 4.4.2.1 (risk characterization for mammals) and Section 4.4.2.2 (risk characterization for birds), exposures associated with the consumption of contaminated surface water are far below the level of concern (HQ=1). Consequently, extreme variations in the estimated consumption of contaminated water by mammals and birds would have no impact on the risk characterization for mammals and birds.

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 bifenthrin. 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*), which is an endangered species that actively feeds on fish (Reid 2006). As summarized in Table 22, the 5 kg mammal is representative of a fox, and the 2.4 kg bird is representative of a heron.

Bifenthrin exposure levels associated with the consumption of contaminated fish depend on the bifenthrin concentration in water and the bioconcentration factor for bifenthrin in fish. The concentrations of bifenthrin in water are identical to those discussed in Section 4.2.2.4. The bioconcentration factor for whole fish is taken as 8720 L/kg from the registrant-submitted study of bioconcentration in bluegill sunfish (MRID 163094 and MRID 163095). As summarized in Table 3, this is the highest bioconcentration factor reported for bifenthrin.

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

Estimated levels of exposure associated with broadcast terrestrial applications of bifenthrin are detailed in Worksheet G09 of Attachments 1 and 2 (the EXCEL workbooks for bifenthrin). In Attachment 1 (foliar applications), Worksheet G09 is a custom worksheet which includes aerial, ground broadcast (high boom and low boom), and backpack applications. In Attachment 2, the worksheet is limited to bark applications.

Honeybees are used as a surrogate for other terrestrial insects, and honeybee exposure levels associated with broadcast applications are modeled as a simple physical process based on the application rate and planar surface area of the bee. The planar 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 Section 4.1.2.4.1 and detailed further in Section 4.3.2.3 (dose-response assessment for terrestrial invertebrates), toxicity data on other

terrestrial invertebrates suggest that honeybees are the most sensitive species of terrestrial invertebrates for which data are available.

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

Like terrestrial mammals and birds, terrestrial invertebrates may be exposed to bifenthrin through the consumption of contaminated vegetation or contaminated prey. As with consumption scenarios for humans (Section 3.2.3.7) and mammalian wildlife (Section 4.2.3.2), estimates of residues on contaminated vegetation or prey are based on estimated residue rates (i.e., mg/kg residues per lb applied) from Fletcher et al. (1994), as summarized in Table 15. In Attachment 1 (foliar applications), these rates are used directly. Also as with humans and mammalian wildlife, the rates for bark applications (Attachment 2) are reduced by a factor of 10, under the assumption that 10% of the bifenthrin nominally applied to the bark is lost to nontarget vegetation.

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

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

A summary of the estimated exposures in terrestrial herbivorous insects is given in Worksheet G08a, and details of the calculations for these scenarios are provided in Worksheets G07a, G07b, G07c, and G07d of the EXCEL workbooks that accompany this risk assessment (Attachments 1 and 2). These levels pertain to the four food items included in the standard residue rates provided by Fletcher et al. (1994), as summarized in Table 15.

4.2.3.3. Concentrations in Soil

As discussed in Section 4.1.2.4.2, toxicity data on earthworms are available for bifenthrin and bifenthrin metabolites. The bifenthrin toxicity data from studies in the open literature (Potter et al. 1994; Schofield 2007) are expressed in units of application rate, and no explicit exposure assessment is necessary.

The toxicity data from the European Food Safety Authority (EFSA 2011) are expressed in units of mg a.i./kg soil. The GLEAMS modeling discussed in Section 3.2.3.4 provides estimates of soil concentration as well as estimates of off-site movement (runoff, sediment, and percolation). Based on the GLEAMS modeling, bifenthrin concentrations in clay, loam, and sand soil textures over a broad range of rainfall rates are summarized in Appendix 6 for foliar applications.

Table A6-2 gives the estimated concentration of bifenthrin in the top 12 inches of the soil column at a normalized application rate of 1 lb/acre. The peak concentration in the top 12 inches of soil is 0.34 mg a.i./kg soil per lb a.i./acre. At an application rate of 0.2 lb a.i./acre, the peak concentration corresponds to 0.068 mg a.i./kg soil [0.34 mg a.i./kg soil per lb a.i./acre x 0.2 lb a.i./acre]. As discussed further in Section 4.4.2.4.2, this concentration is substantially below the NOAEC for earthworms.

4.2.4. Terrestrial Plants

Terrestrial plants, particularly trees treated with bifenthrin, will certainly be exposed to bifenthrin in any application that is effective in the control of insect pests on trees. Several different exposure assessments typically made for herbicides could be made for terrestrial plants including, direct spray, spray drift, runoff, wind erosion, and the use of contaminated irrigation water. For bifenthrin, however, the development of such exposure assessments would serve no purpose. As discussed in Section 4.1.2.4 (Hazard Identification for Terrestrial Plants), there is no basis for asserting that bifenthrin will cause adverse effects in terrestrial plants. While some damage to grasses has been noted following applications of bifenthrin formulations, the damage may be related to adjuvants rather than bifenthrin. Given the widespread use of bifenthrin on plants with no clear reports indicating that it is toxic to plants, no formal exposure assessment is conducted for terrestrial plants.

4.2.5. Aquatic Organisms

An assessment of the effects of bifenthrin on aquatic organisms is based on estimated water concentrations identical to those used in the human health risk assessment. These values are summarized in Table 13 and discussed in Section 3.2.3.4.6.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

Table 25 provides an overview of the dose-response assessments used in the ecological risk assessment. The derivation of each of these values is discussed in the following subsections. Available toxicity data support separate dose-response assessments in six groups of organisms: terrestrial mammals, birds, terrestrial invertebrates, fish, aquatic invertebrates, and aquatic algae. No explicit dose-response assessments are justified for terrestrial plants, terrestrial or aquatic phase amphibians, and terrestrial or aquatic macrophytes. Different units of exposure may be used for different groups of organisms, depending on the nature of exposure and the way in which the toxicity data are expressed.

As with many insecticides, the most sensitive groups of organisms are terrestrial and aquatic invertebrates. Based on estimates of acute NOAELs, the honeybee is more sensitive than mammals by a factor of over 2000 [3.1 mg/kg bw ÷ 0.013 mg/kg bw ≈ 2384] and more sensitive than birds by a factor of about 4000 [51 mg/kg bw ÷ 0.013 mg/kg bw ≈ 3923]. Chronic toxicity values for terrestrial invertebrates cannot be developed. While the longer-term toxicity values for mammals (3.1 mg/kg bw) and birds (5.25 mg/kg bw) are similar, this similarity is an artifact of the data used for the two groups. As with the human health risk assessment, the dose-response assessment for longer-term exposures of mammalian wildlife is based on the same toxicity value used for acute exposures. For birds, the toxicity value is based on a free-standing NOAEC.

As with terrestrial invertebrates, aquatic invertebrates are much more sensitive than aquatic vertebrates (i.e., fish) to bifenthrin, but the differences are less striking. Based on NOAECs for sensitive species, aquatic invertebrates are more sensitive than fish by a factor of over 500 [0.094 µg a.i./L ÷ 0.00017 µg a.i./L ≈ 552.9]. Based on NOAECs for tolerant species, aquatic invertebrates are more sensitive than fish by a factor of only about 8 [0.005 mg a.i./L ÷ 0.0006 mg a.i./L ≈ 8.333…]. Little information is available on aquatic algae. Based on a NOAEC of 0.04 mg a.i./L estimated from a definitive EC_{50} for growth, algae appear to be much less sensitive than aquatic animals to bifenthrin.

4.3.2. Terrestrial Organisms

4.3.2.1. Mammals

In characterizing risk 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). A more elaborate approach is used if sufficient data are available to characterize variable sensitivities among subgroups of mammals, which is not the case for bifenthrin (Section 4.1.2.1).

As discussed in Section 3.3, an unusual aspect of the dose-response assessment for mammals is that U.S. EPA/OPP/HED (2012a) uses a $BMDL_{1SD}$ rather than a NOAEL to derive the RfD. Specifically, the $BMDL_{1SD}$ is the 95% lower limit of the dose associated with a 20% decrease in locomotor activity, relative to the controls (U.S. EPA/OPP/HED 2012a, pp. 18-19). Another unusual aspect of the dose-response assessment for bifenthrin is that the EPA elected to derive only an acute RfD under the assumption that preventing acute neurological effects will prevent

longer-term effects. As also discussed in Section 3.3, this approach appears to be reasonable, based on a detailed consideration of dose-duration relationships as well as the pharmacokinetics of bifenthrin.

As summarized in Table 16, the $BMDL_{1SD}$ is estimated as 3.1 mg/kg bw based on a decrease in locomotor activity from the Wolansky et al. (2006, 2007) studies. This dose is used in the current risk assessment as a surrogate NOAEL for the characterization of risks associated with both acute and longer-term exposures to bifenthrin.

It should be noted that the dose-response assessment for mammals in the current risk assessment differs from the dose-response assessment used for mammals in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED (2012a, p. 144). For acute exposures, the EPA uses the oral LD_{50} of 53.8 mg a.i./kg bw (MIRD 00132519). As discussed in SERA (2009c), the use of an LD_{50} in the risk characterization for acute effects in mammals is a standard practice by U.S. EPA/OPP/EFED; however, the Forest Service prefers to use an acute NOAEL.

4.3.2.2. Birds

In general, Forest Service risk assessments defer to the U.S. EPA/OPP on study selection, unless there is a compelling reason to do otherwise. For characterizing risks to birds, the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a) uses a 5-day dietary LC_{50} of 1280 mg/kg diet (MRID 132535, summarized in Appendix 2, Table A2-2) to characterize risks associated with acute exposures. U.S. EPA/OPP/EFED (2012a) also uses an acute single-dose gavage LD_{50} of 1800 mg/kg bw (MRID 132532). For risk characterization of longer-term exposures, the EPA uses the reproductive NOAEC of 75 mg/kg diet (MRID 163097, summarized in Appendix 2, Table A2-3 of the current risk assessment). All of these studies were conducted on bobwhite quail. The EPA's use of these studies for risk characterization is noted in a tabular summary of risk quotients in U.S. EPA/OPP/EFED (2012a, pp. 178-179).

As summarized in Appendix 2, Table A2-2, the acute dietary LC_{50} of 1280 ppm (MRID 132535) corresponds to a dose of about 512 mg/kg bw. The estimated dose associated with the acute dietary LC_{50} is lower than the gavage LD_{50} of 1800 mg/kg bw by about a factor of about 3.5 [1800 mg/kg bw ÷ 512 mg/kg bw ≈ 3.516]. To characterize risks of acute exposure for birds, the current Forest Service risk assessment uses only the dietary study. The available EPA summaries of the acute dietary study in quail (MRID 132535) do not specify a NOAEC. Following standard practice in Forest Service risk assessments (SERA 2014a, Section 4.3.2, pp. 98-99), the estimated dose of 512 mg/kg bw associated with the acute dietary LC_{50} is divided by 10 to approximate an NOAEC of 51 mg/kg bw. This estimated NOAEC is used to characterize the risk acute exposures to bifenthrin in birds.

As summarized in Appendix 2, Table A2-3, the reproductive NOAEC in quail of 75 ppm (MRID 163097) corresponds to a dose (NOAEL) of about 5.25 mg/kg bw/day. In this study as well as in the study in mallards (MRID 163099) the dietary NOAEL of 75 ppm is the highest concentration used. Thus, the NOAEL of 5.25 mg/kg bw/day is free standing—i.e., an adverse effect level has not been defined. Consequently, the NOAEL of 5.25 mg/kg bw/day may be conservative (i.e., underestimated). As discussed further in the risk characterization for birds (Section 4.4.2.2), the potential underestimation of the NOAEL is important in that several of the longer-term HQs for birds exceed the level of concern (HQ=1).

4.3.2.3. Reptiles and Amphibians (Terrestrial Phase)

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

4.3.2.4. Terrestrial Invertebrates

4.3.2.4.2. Contact Toxicity Value

The effects of direct spray or spray drift to terrestrial insects are typically assessed using the results of contact toxicity studies—i.e., studies in which the pesticide is applied by pipette to the insect. As discussed in Section 4.1.2.4.1 and illustrated in Figure 4, contact toxicity assays are available on several species of terrestrial invertebrates. Consistent with the most recent ecological EPA risk assessment (U.S. EPA/OPP 2012a, p. 144), the honeybee appears to be the most sensitive species.

The current Forest Service risk assessment uses the contact bioassay in honeybees by Atkins and Kellum (1981) as the basis for the dose-response assessment. As discussed in Section 4.1.2.4.1, this appears to be the same study used in EPA (U.S. EPA/OPP 2012a, Table 4-5, p. 19) to classify bifenthrin as *very highly toxic* to the honeybee. While a DER is available for the study by Atkins and Kellum (1981), it is not detailed, does not indicate responses at different doses, and does not report a NOAEL. In the absence of a reported NOAEL, the LD_{50} of 0.13 µg/g bw (equivalent to mg/kg bw) is divided by a factor of 10 to approximate a NOAEL of 0.013 mg/kg bw. The rationale for this approach is identical to that used for birds (Section 4.3.2.2) and is discussed further in SERA (2014a, Section 4.3.2, pp. 98-99).

4.3.2.4.2. Oral Toxicity Value

Oral toxicity values are used in Forest Service risk assessments to characterize risks to phytophagous insects. No oral toxicity studies on terrestrial invertebrates were identified in which doses are expressed as µg/g bw or other comparable units. As summarized in Table 17 and discussed above, the honeybee, with a topical LD_{50} of 0.13 mg/kg bw appears to be the most sensitive insect for which data are available; however, some phytophagous insects are almost as sensitive—e.g., the rice stem borer (*Chilo suppressalis*) with a topical LD_{50} of 0.19 mg/kg bw.

As discussed in Section 4.2.3.2, terrestrial insects will be exposed to bifenthrin via contaminated vegetation, and it does not seem appropriate to forego a risk characterization for these insects. In the absence of oral toxicity data, the estimated topical NOAEL 0.013 mg/kg bw in the honeybee is applied to potentially sensitive species of phytophagous insects.

4.3.2.4.3. Earthworms

While HQs are not developed for soil invertebrates, concentrations of bifenthrin in soil can be estimated (Section 4.2.3.2) and toxicity data in earthworms are available, specifically the NOAEC of 2.13 mg a.i./kg soil from EFSA (2011), as discussed in Section 4.1.2.4.2). This NOAEC is used to characterize risks to earthworms as discussed in Section 4.4.2.4.3.

4.3.2.5. Terrestrial Plants (Macrophytes)

No dose-response assessment is proposed for terrestrial plants. As discussed in Section 4.1.2.5, there is no basis for asserting that bifenthrin is likely to damage terrestrial plants. This approach is identical to the position articulated in the U.S. EPA/OPP/EFED problem formulation for the registration review of bifenthrin (U.S. EPA/OPP/EFED 2010b, p. 7).

4.3.2.6. Terrestrial Microorganisms

As with terrestrial plants, little information is available on the toxicity of bifenthrin to terrestrial microorganisms (Section 4.1.2.6). Moreover, the limited information does not support an assertion that bifenthrin is likely to damage soil microorganisms. Consequently, no dose-response assessment is developed for this group of organisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish

4.3.3.1.1. Acute Toxicity Values

As summarized in Table 18 and illustrated in Figure 5, acute LC_{50} values in fish indicate a wide range of sensitivities, with rainbow trout being the most sensitive species (LC_{50} = 0.15 µg/L) and sheepshead minnow being the least sensitive species (average $LC_{50} \approx 18$ µg/L). This range of sensitivities spans a factor of 120 [18 µg/L ÷ 0.15 µg/L]. The Forest Service elects to use NOAEC values rather than LC_{50} values as the basis for the dose-response assessment, and NOAECs are available for both the most sensitive and tolerant species.

For sensitive species, the NOAEC of 0.094 µg/L in rainbow trout (MRID 163156) is used. This is the same study used in the most recent EPA ecological risk assessment to characterize risks to fish based on the LC_{50} of 0.15 µg/L (U.S. EPA/OPP/EFED 2012a, p. 151). It should be noted that the LC_{50} is only a factor of about 1.6 greater than the NOAEC [0.15 µg/L ÷ 0.094 µg/L ≈ 1.5957], and this steep dose-response relationship is discussed further in the risk characterization (Section 4.4.3.1).

For tolerant species of fish, the NOAEC of 5 µg/L (0.005 mg/L) in sheepshead minnow is taken from the open literature study by Harper et al. (2008). In this case, the LC_{50} of 19.806 µg/L reported in Harper et al. (2008) is a factor of about 4 greater than the NOAEC [19.806 µg/L ÷ 5 µg/L = 3.9612]. This relationship has no impact on the risk characterization, because plausible exposures to fish are far below the NOAEC in the sheepshead minnow.

4.3.3.1.2. Longer-term Toxicity Values

As discussed in Section 4.1.3.1.2 and detailed further in Appendix 4, Table A4-3, open literature on bifenthrin does not include longer-term toxicity studies in fish. The recent EPA risk assessments and related documentation indicate that valid longer-term toxicity studies of bifenthrin in fish were not submitted by registrants. This situation is unusual, given that bifenthrin has been registered for many years (Section 2.2).

In the most recent EPA risk assessment, the chronic NOAEC for bifenthrin is taken as 0.004 µg a.i./L (U.S. EPA/OPP/ EFED 2012a, pp. 136-137 as well as Appendix J). This NOAEC, however, is not based explicitly on bifenthrin data, but is simply the lowest NOAEC in fish for any pyrethroid. Specifically, the NOAEC for bifenthrin is based on the experimental NOAEC of 0.00397 µg a.i./L for tefluthrin in fathead minnows (MRID 41705101) rounded to one significant place. In an open literature publication, Fojut et al. (2012) also note the lack of an acceptable chronic study on bifenthrin and derive a lower estimate of a chronic NOAEC, 0.0006 µg/L, based on a probabilistic analysis of acute toxicity data on bifenthrin and chronic toxicity data on other pyrethroids.

FAO (2012, p. 33) reports an experimental NOAEC in an early life-stage study in rainbow trout; however, the study is not described in detail, and the NOAEC is not clearly reported. The only other experimental longer-term toxicity value for bifenthrin is a NOAEC of 0.0405 µg/L from a registrant-submitted full life-cycle study in fathead minnows (McAllister et al. 1988b, MRID 40791301). While a relatively detailed DER for this study is available, the study is classified by the EPA as … *invalid for quantitative use* (U.S. EPA/ OPP/EFED 2010b, p. 2). This study is cited in the most recent EPA ecological risk assessment (U.S. EPA/ OPP/EFED 2012a, p. 260) but is not used or discussed in the risk assessment.

In the absence of additional information, the current Forest Service risk assessment defers to EPA and uses the concentration of 0.004 µg a.i./L as a longer-term toxicity value for fish. As discussed above, this value is not based on a study using bifenthrin but is the lowest NOAEC in fish for any pyrethroid (U.S. EPA/OPP/ EFED 2012a, pp. 136-137 as well as Appendix J). Given the approach used by EPA—i.e., the lowest longer-term NOAEC for an pyrethroid— the NOAEC of 0.004 µg a.i./L is applied to presumably sensitive species of fish.

Given the well-documented, substantial variability of acute toxicity values in fish, as discussed in Section 4.3.3.1.1 and illustrated in Figure 5, consideration is given to the use of the acute-to-chronic ratio approach (e.g., NAS 2013) to estimate a chronic toxicity value in presumably tolerant species of fish. As noted in Section 4.3.3.1.1, the ratio of the LC_{50} in the most tolerant species of fish (sheepshead minnow) to the LC_{50} in the most sensitive species of fish (rainbow trout) is about 120. Using this ratio, a longer-term NOAEC for tolerant species of fish could be estimated at 0.48 µg a.i./L [0.004 µg a.i./L x 120]. This estimated NOAEC is supported by the NOAEC of 0.2 µg a.i./L for sheepshead minnow from the 28-day mesocosm study reported in the open literature (Pennington et al. 2014). As summarized in Appendix 4, Table A4-4, the only significant effects noted at the concentration of 0.2 µg a.i./L were significant increases in growth which were likely secondary to increased food availability.

The above approach for estimating a longer-term toxicity value for tolerant species of fish is viewed as marginal. Nonetheless, the differences in the sensitivity of fish to bifenthrin in acute exposures are clear. As a modestly conservative approach, the experimental NOAEC of 0.2 µg a.i./L (0.0002 mg a.i./L) from Pennington et al. (2014) is used rather than the somewhat higher estimated NOAEC of 0.48 µg a.i./L. The NOAEC of 0.2 µg a.i./L is applied to potentially tolerant species of fish.

4.3.3.2. Amphibians (Aquatic Phase)

No data are available on the toxicity of bifenthrin to aquatic phase amphibians (Section 4.1.3.2). Consequently, no dose-response assessment is developed for this group of organisms.

4.3.3.3. Aquatic Invertebrates

4.3.3.3.1. Sensitive Species

As discussed in Section 4.1.3.3, *Hyalella azteca* (Malacostraca: Amphipoda) is the species of aquatic invertebrate most sensitive to bifenthrin. The most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a See Table 4-1 and Table 5-2, p. 155) uses toxicity values for this species in the risk characterization of both acute and chronic exposures of aquatic

invertebrates. Specifically, the EPA uses the acute EC_{50} of 1.9 ng/L from the open literature study by Weston and Jackson (2009) and the chronic NOAEC of 0.17 ng a.i./L from the open literature study by Amweg et al. (2005).

As with other groups of organisms, Forest Service risk assessments do not use EC_{50} values directly for risk characterization. Weston and Jackson (2009) do not report an NOAEC associated with the EC_{50} of 1.9 ng/L. Typically, a Forest Service risk assessment would divide the EC_{50} by a factor of 20 to approximate an acute NOAEL of 0.095 ng/L [1.9 ng/L ÷ 20] (SERA 2014a, Section 4.3.2, pp. 98-99). This approximated NOAEC, however, would be below the chronic NOAEC of 0.17 ng/L from Amweg et al. (2005), and it makes no sense to use an acute NOAEC that is lower than the chronic NOAEC. In this instance, the chronic data simply indicate that the standard approach for approximating an acute NOAEC from an acute EC_{50} is overly conservative for bifenthrin. Consequently, the chronic NOAEC of 0.17 ng a.i./L (0.00000017 mg a.i./L) from Amweg et al. (2005) is used for the risk characterization of sensitive species of aquatic invertebrates for both acute and chronic exposures. While the acute EC_{50} of 1.9 ng a.i./L for *Hyalella azteca* is not used directly for risk characterization, this EC_{50} would be associated with an acute HQ of about 11 [1.9 ng a.i./L ÷ 0.17 ng a.i./L ≈ 11.175]. This relationship is discussed further in the risk characterization for aquatic invertebrates (Section 4.4.3.4).

4.3.3.3.2. Tolerant Species

As illustrated in Figure 7 (acute EC_{50} values in aquatic invertebrates) and summarized in Table 22 (chronic NOAECs for aquatic invertebrates), *Daphnia magna* (Branchiopoda: Cladocera) is the most tolerant species of aquatic arthropods. As summarized in Table 20, the lowest EC_{50} reported for *Daphnia magna* is 1.6 µg a.i./L (MRID 41156501). As summarized in Appendix 5, Table A5-1, this study is classified as *Acceptable* by the U.S. EPA and reports a NOAEC of 0.6 µg a.i./L. The NOAEC of 0.6 µg a.i./L (0.0006 mg a.i./L) is used in the risk characterization of tolerant species of aquatic invertebrates following acute exposures. While the NOAEC of 0.6 µg a.i./L is close to the EC_{50} of 1.6 µg a.i./L, this proximity does not have an impact on the risk characterization, because anticipated exposures for aquatic invertebrates are below the NOAEC (Section 4.4.3.4).

As summarized in Table 22, several chronic NOAECs, ranging from 1.3 ng/L (MRID 41156501) to 20 ng/L (Brausch et al. 2010) are available in *Daphnia magna*. The current risk assessment uses the lowest NOAEC of 1.3 ng/L (0.0000013 mg a.i./L), because this study has been reviewed and classified as *Acceptable* by the U.S. EPA, and the study is cited in FAO (2012).

As discussed further in Section 4.4.3.4 (risk characterization for aquatic invertebrates), the use of the lowest NOAEC for *Daphnia magna* may be viewed as conservative and does impact the risk characterization. If the highest NOAEC in *Daphnia magna*—i.e., 20 ng a.i./L from the study by Brausch et al. 2010—were used, then the longer-term HQs would be reduced by a factor of about 15 [20 ng a.i./L ÷ 1.3 ng a.i./L ≈ 15.385].

4.3.3.4. Aquatic Plants

The dose-response assessment for aquatic plants is limited by the substantial lack of data on this group of organisms (Section 4.1.3.4). No toxicity data are available on aquatic macrophytes. The only definitive toxicity value is reported in a brief summary by EFSA (2011)—i.e., an EC_{50} of 0.822 mg/L based on a decrease in dry weight in *Pseudokirchneriella subcapitata*, a species of freshwater algae. Following the standard procedure (SERA 2014a, Section 4.3.2, pp. 98-99), the NOAEC is approximated as 0.04 mg a.i./L by dividing the EC_{50} by a factor of 20 [0.822 mg/L ÷ 20 = 0.0411 mg a.i./L].

4.4. RISK CHARACTERIZATION

4.4.1. Overview

In the ecological risk assessment, as in the human health risk assessment, the quantitative expression of the risk characterization is the hazard quotient (HQ), the ratio of the anticipated dose or exposure to a no-observed-effect level or concentration (NOEL/NOEC) using 1 as the level of concern—i.e., an HQ of ≤ 1 is below the level of concern. The specific HQs discussed in this risk characterization are based on a single application of 0.2 lb a.i./acre. The toxicity data on and exposure estimates for bifenthrin support quantitative risk characterizations in mammals, birds, terrestrial insects as well as other invertebrates, fish, aquatic invertebrates, and to a limited extent, aquatic plants. Risk characterizations for reptiles and amphibians as well as terrestrial plants are not possible because of the lack of toxicity data.

The organisms at greatest risk are the invertebrates, both terrestrial and aquatic. Adverse effects are virtually certain in sensitive species of phytophagous insects. Bifenthrin will be applied to and will contaminate terrestrial vegetation, and sensitive species of phytophagous insects that consume the contaminated vegetation will likely be killed. This risk characterization pertains to virtually any effective insecticide applied to vegetation. Based on toxicity data in the honeybee, sensitive species of flying insects could be harmed by direct spray or drift. Similarly, sensitive species of aquatic invertebrates will be adversely impacted by foliar or bark applications of bifenthrin to areas near surface water, if effective measures are not taken to limit the contamination of surface water from drift, runoff, percolation, and sediment losses. This severe risk characterization is limited to sensitive species of invertebrates. There is little basis for asserting that tolerant species or populations of both terrestrial and aquatic invertebrates will be adversely affected by applications of bifenthrin. Based on the available data, however, generalizations concerning sensitivity or tolerance to bifenthrin cannot be made at the level of taxonomic orders.

Vertebrates are generally less sensitive than invertebrates to bifenthrin. Nonetheless, foliar applications of bifenthrin could result in exposure levels for some terrestrial mammals and birds that substantially exceed the level of concern. In all cases, risks to mammals and birds are associated with the consumption of contaminated vegetation, and risks are greatest for smaller animals consuming contaminated grasses or food items with bifenthrin concentrations comparable to those associated with contaminated grasses. Risks to sensitive species of fish are limited to longer-term rather than acute exposures.

Risks to vertebrates following bark applications are less than those associated with foliar applications. Specifically, risks to mammals (highest HQ=4), birds (highest HQ=2) and sensitive species of fish (highest HQ=3) are a concern.

The risk characterization for bifenthrin focuses on the potential for direct toxic effects. Nonetheless, there is a potential for secondary effects in virtually all groups of nontarget organisms. Terrestrial applications of any effective insecticide, including bifenthrin, are likely to alter insect and other invertebrate populations within the treatment area. This alteration could have secondary effects on terrestrial or aquatic animals and plants, including changes in food availability, predation, and habitat quality. These secondary effects may be beneficial to some

species and detrimental to others; moreover, the magnitude of secondary effects is likely to vary over time.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

The HQs for mammals are given in Worksheet G02a of the attachments to this risk assessment—i.e., Attachment 1 for foliar applications and Attachment 2 for bark applications. As with the human health risk assessment (Section 3.3), both acute and chronic risks are characterized with a single toxicity value. As discussed in Section 4.3.2.1, the toxicity value for mammalian wildlife is taken as 3.1 mg/kg bw, the 95% lower limit of the dose associated with a 20% decrease in locomotor activity, relative to the controls (U.S. EPA/OPP/HED 2012a, pp. 18-19).

None of the exposure scenarios associated with contaminated water is a concern. The highest HQ is $7x10^{-7}$, below the level of concern (HQ=1) by a factor of about 1.5 million [$1 \div 7x10^{-7} \approx$ 1,428,571]. As discussed in Section 3.2.3.4.6, the concentrations of bifenthrin in ambient water are capped at the water solubility of bifenthrin (0.014 µg/L). Nonetheless, the very low HQs associated with the concentration of bifenthrin in surface water suggest that this route of exposure will not pose a risk to mammalian wildlife.

As is common for pesticides applied to foliage, the risks to mammals associated with the consumption of contaminated vegetation are much higher than those associated with contaminated water. For bifenthrin, several of the central estimates of the HQs and most of the upper bound estimates of the HQs exceed the level of concern following foliar applications. For bark applications, the levels of bifenthrin are taken as a factor of 10 lower than those associated with foliar applications, and only some of the upper bound HQs for bark application exceed the level of concern.

For foliar applications, the risk characterization for mammals is similar to that developed in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, Table 5-12, pp. 184-185). Several of the acute exposures developed by EPA exceed the level of concern with risk quotients (RQs) ranging from 0.12 to 1.84 with a level of concern of 0.1. These RQs correspond to acute HQs of 1.2 to 18.4. In the current Forest Service risk assessment (Attachment 1, Worksheet G02a), acute HQs exceeding the level of concern (HQ=1) range from 1.2 to 9 based on central estimates and 3 to 25 based on upper bound estimates. For chronic exposures, the EPA chronic RQs (which are equivalent to HQs used in Forest Service risk assessments) that exceed the level of concern range from 1.34 to 34.7. The corresponding HQs in the current Forest Service risk assessment (Attachment 1, Worksheet G02a) range from 4 to15. The EPA does not evaluate bark applications, so the risk characterization for bark applications in the current Forest Service risk assessment cannot be compared with an EPA risk characterization.

A major concern with the relatively harsh risk characterization for mammals involves exposure assumptions. As noted in Section 4.2.2.3, the exposure assessments for the consumption of contaminated vegetation or prey involving mammals and birds assume that 100% of the diet is contaminated. While this might, in some cases, be a reasonable assumption for a small mammal with a limited range, this assumption is less likely for larger mammals which may spend only a limited period of time in the treated areas. In addition, the diets of most mammals are diverse.

As indicated in Table 15, the highest residue rates are associated with short grass. As indicated in Attachment 1, Worksheet G02a, the exposure scenario for the consumption of short-grass leads to the highest HQs—i.e., 9 (1 to 45). As summarized in Worksheet G01a, the upper bound HQ is associated with a dose of 138 mg/kg bw for a small (20 g) mammal and 18 mg/kg bw for a large mammal, such as a deer. As discussed in Section 3.1.4 and summarized in Appendix 1, Table A1-1, the acute LD_{50} values for small mammals range from 53.8 to 265 mg/kg bw. Based on the estimated upper bound exposures and the LD_{50} values, lethality might be expected in some field populations of small mammals that consume short grass. As discussed in Section 4.1.2.1, mice appear to be somewhat more tolerant than rats and dogs to bifenthrin. While the toxicity data do not support separate toxicity values for small versus large mammals, risks to very small mammals may be less than suggested by the HQs. Although bifenthrin has been in use for a prolonged period of time (Section 2), field reports of death in small mammals were not encountered in the open literature and are not reported in the EPA incident database (i.e., U.S. EPA/OPP/EFED 2012a, Appendix K). Nonetheless, field surveys that look for carcasses of small mammals are exceedingly difficult and the lack of field reports of effects on small mammals should not viewed strong support for the suggestion that small mammals may be less sensitive than larger mammals to bifenthrin.

While the above discussion is not intended to lessen concern for the high HQs for mammals, this discussion underlies the need to consider species-specific and site-specific factors (e.g., nature of the vegetation) in any site-specific application of bifenthrin.

4.4.2.2. Birds

The risk characterization for birds is less severe than that for mammals, which reflects the substantially higher estimated acute NOAEC for birds (51 mg/kg bw), relative to mammals (3.1 mg/kg bw/day), and the somewhat higher longer-term NOAEC for birds (5.25 mg/kg bw/day), relative to mammals (3.1 mg/kg bw/day as with acute effects).

For bark applications (which are based on the assumption that only 10% of applied bifenthrin will reach nontarget vegetation), none of the acute HQs exceed the level of concern (HQ=1) (Attachment 2, Worksheet G02b). The only longer-term HQ to exceed the level of concern is the upper bound HQ associated with the consumption of contaminated short grass (HQ=2) by a small bird. While small birds may not typically consume large amounts of grasses in the vegetative stage, many birds will consume significant amounts of grass seeds (USDA/NRCS 1999). Thus, concern for the scenario involving the consumption of contaminated grasses by small birds may be most relevant to contaminated grasses with seeds.

For broadcast applications (Attachment 1, Worksheet G02b), the central estimates of the HQs that exceed the level of concern involve the acute consumption by a small bird of short grass (HQ=1.4) and the longer-term consumption by a small bird of short grass (HQ=3), tall grass (HQ=1.2), and broadleaf vegetation (HQ=1.5). These same food items result in HQs that exceed the level of concern for a small bird (HQs from 10 to 22) and a large bird (HQs from 1.2 to 3).

As discussed in Section 4.3.2.2, the chronic NOAEC of 5.25 mg/kg bw is free-standing—i.e., doses associated with adverse effects have not been defined. Consequently, the consequences

associated with longer-term HQs that exceed the level of concern (i.e., HQs of 3-22) cannot be defined.

The acute risk characterization for birds given in the current risk assessment is similar to, albeit somewhat harsher than, that given in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, Table5-7, pp. 177-178). As discussed above, the acute HQs that exceed the level of concern in the current risk assessment range from 1.4 to 7. In the EPA assessment, the acute risk quotients (RQs) that exceed the level of concern (RQ=0.1) are 0.11 to 0.2, equivalent to HQs of 1.1 to 2. The longer-term HQs that exceed the level of concern in the current risk assessment range from 1.2 to 22. In the EPA assessment, the chronic dietary risk quotients (RQs) that exceed the level of concern (RQ=1) are 1.05 to 3.04. As discussed in Section 4.3.2.2, the chronic dose response assessments in the EPA and current Forest Service risk assessment are based on the same study. The higher HQs in the current risk assessment, relative to the EPA assessment, involve the use of metabolic rates and caloric values for different food items used in the current risk assessment (Sections 4.2.2 and 4.2.3.2), relative to the EPA's direct use of experimental concentrations of bifenthrin in toxicity studies and the residues rates from Fletcher et al. (1997).

As with mammals, all of the exposure scenarios for birds are based on the assumption that 100% of the diet is contaminated. This is a standard assumption used in all Forest Service risk assessments but may overestimate and in some cases grossly overestimate exposures in some site-specific applications, particularly those in which bifenthrin is not broadcast over a wide area. These factors cannot be further considered in a generic assessment but could and should be considered quantitatively in site-specific assessments.

As discussed in Section 4.1.2.2, no data are available on the toxicity of bifenthrin to passerines (i.e., perching birds of the order Passeriformes). By analogy to other pyrethroids, U.S. EPA/OPP/EFED (2012a, p. 143) raises the concern that passerines may be more sensitive than other taxonomic orders of birds to bifenthrin. While this reservation is noted, the lack of data on passerines precludes further or quantitative consideration of risks to passerines.

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). Within the reservations discussed in Section 4.1.2.3, the current Forest Service risk assessment is consistent with the most recent EPA ecological risk assessment on bifenthrin (U.S. EPA/OPP/EFED 2012a) and recommends the use of birds as a surrogate for reptiles and terrestrial-phase amphibians (Section 4.4.2.2).

4.4.2.4. Terrestrial Invertebrates

4.4.2.4.1. Honeybees

The risk characterization for honeybees following direct spray and spray drift is summarized in Worksheet G09 of the EXCEL workbooks that accompany this risk assessment. Bifenthrin is an effective insecticide, and the direct spray of a bee at an application rate of 0.2 lb a.i./acre leads to an HQ of 1056, and this HQ is associated with a dose of about 13.7 mg/kg bw (Attachment 1, Worksheet G09). This dose is above the topical LD_{50} of 0.13 mg/kg bw (Atkins and Kellum

1981) by a factor of over 100 [13.7 mg/kg bw ÷ 0.13 mg/kg bw ≈ 105.38]. The risk characterization for direct spray requires little elaboration. If a honeybee is directly sprayed with bifenthrin at an application rate that is effective in insect control, the exposure will be lethal. This risk characterization pertains to most effective insecticides.

The risk characterization for spray drift is more nuanced. For bark applications (Attachment 2, Worksheet G09), the incidental direct spray of a bee would probably be lethal; nonetheless, the HQs for drift at 25 feet or greater from the application site are below the level of concern. For foliar applications (Attachment 1, Worksheet G09), HQs above the level of concern vary from lows of about 3 to 9 for backpack applications at distances of 25 to 100 feet downwind to highs of 13 to 253 at distances of 900 to 25 feet downwind. As specified in this worksheet, HQs may be reduced by foliar interception.

A reasonable verbal interpretation of the risk characterization for honeybees is that risks appear to be minimal for bark application and could be modest for backpack applications. These are the application methods that would be most commonly used in Forest Service programs and projects. Foliar broadcast applications could lead to bee mortality if bee populations are near the application sites. While reports of bee mortality following bifenthrin applications were not identified in the open literature, credible incidents involving bee mortality associated with bifenthrin applications have been reported to the EPA (e.g., U.S. EPA/OPP/EFED 2012a, Appendix K, pp. K-3 to K-4).

4.4.2.4.2. Phytophagous Insects

If bifenthrin is applied to vegetation at an effective rate, adverse effects on sensitive species of phytophagous insects are unavoidable. Given the use of bifenthrin to control damage to vegetation from phytophagous insects, this risk characterization is essentially a tautology. In addition, this severe risk characterization is to be expected given the higher sensitivity of insects to bifenthrin relative to mammals (Section 4.3.1) and the relatively severe risk characterization for mammals consuming contaminated vegetation (Section 4.4.2.1).

The specific HQs for phytophagous insects are summarized in Worksheet G08b of the EXCEL workbooks that accompany this risk assessment. For foliar applications (Attachment 1), the lower bound HQs range from 30 to 277. The upper bound HQs range from over 500 to over 8000. The HQs for bark applications (Attachment 2) are lower by a factor of 10, but this has little impact on the risk characterization.

The only nuances in this risk characterization involve differences in sensitivity among different species or populations of insects. As summarized in Table 17 and discussed in Section 4.1.2.4.1, differences in acute topical LD_{50} values for bifenthrin span a factor of 4000 [542 mg/kg bw ÷ 0.13 mg/kg bw ≈ 4169.23]. Systematic differences in terms of taxonomic groups, however, cannot be identified. Nonetheless, it seems likely that some species of tolerant phytophagous insects might not be severely impacted following applications of bifenthrin. As also discussed in Section 4.1.2.4.1, some populations of terrestrial insects may develop resistance to bifenthrin, and resistance factors of up to 136 have been documented (i.e., bluegrass weevil in the study by Ramoutar et al. 2009). Given the high upper bound HQs for bifenthrin, adverse effects in tolerant or resistant insect populations to bifenthrin cannot be ruled out. Nonetheless, in some

cases involving lower exposures, some tolerant or resistant populations of insects might be unaffected or only minimally affected by bifenthrin applications.

4.4.2.4.3. Earthworms

Neither EPA nor Forest Service risk assessments typically derive formal HQs for earthworms. While earthworms are not included in the attachments to this risk assessment, the review by the European Food Safety Authority (EFSA 2011) notes an NOAEC of 2.13 mg/kg soil for earthworms (Section 4.3.2.4.3) and the concentrations of bifenthrin in the top 12 inches of soil are estimated at about 0.34 mg a.i./kg soil (Section 4.2.3.3). Based on these values, a soil based HQ could be estimated at about 0.2 [0.34 mg a.i./kg soil ÷ 2.13 mg/kg soil ≈ 0.1596]. While the available data on earthworms are not extensive, no risks to earthworms are apparent.

4.4.2.5. Terrestrial Plants

As discussed in Section 4.3.2.5, the available data on terrestrial plants does not support a formal dose-response relationship for terrestrial plants. The most recent EPA ecological risk assessment notes the following reservation:

> *Although effects on terrestrial plants are not expected based on the mode of action of bifenthrin, the large number of minor incidents suggests there is a potential of bifenthrin to cause adverse effects on terrestrial plants at least when applied to turf grass using the aforementioned formulations.*
>
> U.S. EPA/OPP/EFED (2012a, p. 197)

As discussed in Section 4.1.2.5, the incident data reported in the EPA risk assessment (U.S. EPA/OPP/EFED 2012a, Appendix K) support the above statement; however, the incident reports suggest that damage to the terrestrial plants may have been associated with other ingredients in the formulation. As also discussed in Section 4.1.2.5, bifenthrin formulations have been applied to trees for many years with no reports of substantial damage. The assessments by U.S. EPA/OPP/EFED (2010b) and EFSA (2011) suggest that substantial adverse effects to terrestrial plants are unlikely based on the widespread use of bifenthrin on trees and other plants with no clear reports indicating that bifenthrin is toxic to plants. This assessment seems reasonable.

4.4.2.6. Terrestrial Microorganisms

Little information is available on the effects of bifenthrin on terrestrial microorganisms, and the data do not support a hazard identification (Section 4.1.2.6) or a dose-response assessment (Section 4.3.2.6). Consequently, no risk characterization for terrestrial microorganisms is developed.

4.4.3. Aquatic Organisms

4.4.3.1. Fish

As summarized in Worksheet G03 of the attachments to this risk assessment, none of the acute HQs for sensitive species of fish approaches the level of concern. As discussed in Section 4.3.3.1, the acute toxicity data in fish are extensive and the acute toxicity values for fish are based on well-documented NOAELs.

A reservation with the benign acute risk characterization for fish involves the exposure assessment. As discussed in Section 3.2.3.4.6, the current risk assessment adopts the approach

used by EPA in both human health and ecological risk assessments by capping the estimated concentrations of bifenthrin in surface water at the water solubility of bifenthrin (0.014 µg/L). As summarized in Table 13, the nominal modelled peak concentrations of bifenthrin in surface water at a foliar application of 0.2 lb a.i./acre are 0.07 (0.01-0.8) µg/L. If these concentrations were used in the exposure assessment for foliar applications (Attachment 1), the upper bound of the acute HQ for sensitive species of fish would be 9, substantially above the level of concern (HQ=1). The HQs for tolerant species of fish would remain below the level of concern with an upper bound HQ of 0.2 for tolerant species of fish. As discussed in Section 3.2.3.4.6, the nominal water contamination rates for bark applications (Attachment 2) are a factor of 10 below those for foliar application. Using the nominal rather than capped concentrations of bifenthrin in surface water, the upper bound HQ for sensitive species of fish would be 0.9, modestly below the level of concern.

For foliar applications, the upper bound HQs for longer-term exposures in sensitive species of fish are 3 (0.2 to 4). For bark applications, the corresponding HQs are 0.3 (0.02 to 3). While HQs are typically related linearly to functional application rates, this is not the case for bifenthrin, because the estimated concentrations in surface water are capped. As with the acute risk characterization for fish, the capping of the concentrations of bifenthrin in surface water is a reservation in the risk characterization. A greater reservation, however, involves the nature of the chronic toxicity data in fish. As discussed in Section 4.3.3.1.2, no acceptable studies are available on the chronic toxicity of bifenthrin to fish. This is an unusual situation for a pesticide that has been in use for many years. The toxicity value estimated by EPA for sensitive species of fish—i.e., the selection of the lowest NOAEC for any pyrethroid—as well as the use of the acute-to-chronic ratio approach developed in the current risk assessment should be viewed as marginal at best. Consequently, confidence is low for the risk characterization associated with chronic exposures of fish to bifenthrin.

4.4.3.2. Amphibians (Aquatic phase)

Because data on aquatic phase amphibians are not available, no explicit risk characterization is developed for this group of organisms. The most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, p. 132) uses fish as a surrogate for aquatic phase amphibians, which is a standard practice in EPA ecological risk assessments. As discussed above, there are serious concerns with the available data on the chronic effects of bifenthrin on fish, and the extension of the chronic risk characterization of fish to amphibians is tenuous at best. In addition, concerns with capping the concentration of bifenthrin at the water solubility of this compound adds to the uncertainty in the risk characterization for aquatic phase amphibians.

4.4.3.4. Aquatic Invertebrates

The HQs for aquatic invertebrates are summarized in the EXCEL workbooks which accompany this risk assessment—i.e., Attachment 1 for foliar applications and Attachment 2 for bark applications. Based on the most sensitive species (i.e., *Hyalella azteca*), the acute and chronic HQs are substantially above the level of concern based on central estimates as well as lower and upper bounds. The only exception is the lower bound HQ of 0.5 for chronic exposures following bark applications. The upper bound HQ for longer-term exposures to sensitive species of aquatic invertebrates is 71, only modestly below the corresponding HQs of 82 for foliar applications. As summarized in Table 25 and discussed in Section 4.3.3.3.1, both the acute and chronic HQs for sensitive species are based on the chronic NOAEC of 0.00000017 mg/L (0.17 ng a.i./L). This

approach should not be viewed as overly conservative in that an alternate acute NOAEC based on acute toxicity data would be below the chronic NOAEC. Given the high HQs for sensitive species of aquatic invertebrates, the capping of estimated concentrations of bifenthrin in surface water at the water solubility of bifenthrin (0.014 µg/L) has no substantial impact on the qualitative risk characterization. If bifenthrin is applied near surface waters, adverse effects on aquatic invertebrates would be likely, unless extraordinary measures are taken to limit the contamination of surface water. This severe risk characterization for sensitive species of aquatic invertebrates is consistent with the risk characterization given in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, Table 5-2, pp. 151-155).

As discussed in Section 4.3.3.3.2, the risk characterization for tolerant species of aquatic invertebrates is based on acute and chronic bioassays in *Daphnia magna*, the least sensitive aquatic arthropod on which data are available with an acute NOAEC of 0.6 µg/L and a chronic NOAEC of 1.3 ng a.i./L. There is little uncertainty with the NOAECs in that the tolerance of *Daphnia magna* to bifenthrin is documented in several acute studies (Tables 20 and 21) as well as chronic studies (Table 22). In selecting toxicity values, preference is given to values used by the EPA, which are also the lowest toxicity values for *Daphnia magna*. For acute exposures, this conservative approach does not have an impact on the risk characterization, because all HQs are below the level of concern (HQ=1). For chronic exposures, the chronic HQs for tolerant species of aquatic invertebrates are 10 (0.6 to 11). As summarized in Table 22 and discussed in Section 4.1.3.3.2, some open literature studies report chronic NOAECs for *Daphnia magna* up to 20 ng/L, a factor of about 15 [20 ng/L ÷ 1.3 ng a.i./L ≈ 15.385] higher than the chronic toxicity value used in the current risk assessment. If the highest NOAEC were used, all of the chronic HQs for tolerant species would be below the level of concern. Based on these considerations, it appears that tolerant species of aquatic invertebrates would not be adversely affected based on peak exposures to bifenthrin. For longer-term exposures, adverse effects could occur in some but perhaps not all populations of tolerant aquatic invertebrates.

Given the substantial differences in the risk characterization for sensitive and tolerant species of aquatic invertebrates, there may be uncertainty and perhaps substantial uncertainty in site-specific assessments of bifenthrin applications. Depending on the sensitivities of the species and populations of aquatic invertebrates, bifenthrin applications could be associated with little impact or substantial adverse impacts on aquatic invertebrates. As illustrated in Figures 5 and 6, generalizations based on taxonomic order do not appear to be justified. In addition, as discussed above, bioassays on the most commonly tested species, *Daphnia magna*, suggest that different populations of aquatic invertebrates may differ substantially in sensitivities to bifenthrin.

4.4.3.4. Aquatic Plants

Based on the available information, there is no basis for asserting that bifenthrin is likely to have an adverse impact on aquatic plants. This risk characterization, however, is based on limited toxicity data. While the substantial lack of data diminishes confidence in the risk characterization for aquatic plants, the risk characterization developed by EPA seems reasonable:

> *…given the low toxicity of other pyrethroids to aquatic plants … and the mode of action of bifenthrin, risks to aquatic plants at its limit of solubility (0.014 µg ai/L) are considered very low.*
>
> U.S. EPA/OPP/EFED (2012, p. 201).

A qualitatively similar risk characterization for algae is given in the analysis of bifenthrin by the European Food Safety Authority (EFSA 2011, p. 25).

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.

CDPR01	**Copies of full studies courtesy of the California Department of Pesticide Registration via David Bakke (USDA/Forest Service)**
Carbaryl	**Papers from the Forest Service risk assessment on carbaryl (SERA 2009a).**
ClRev	**Cleared reviews from http://iaspub.epa.gov/apex/pesticides.**
CRLF01	**Papers from U.S. EPA/OPP/EFED 2012a not otherwise identified in initial searches.**
E-Docket01	**E-Docket EPA-HQ-OPP-2010-0384 associated with registration review (17 support documents)at www.regulations.gov.**
FS	**Comments from the USDA/Forest Service.**
Sec	**Summary of citation from a secondary source.**
SET00	**Papers from preliminary scoping.**
Set01	**Initial TOXLINE search.**
Set02	**Update search in April 2015.**
Set03	**Additional scoping.**
Set04	**Screen of Set 02.**
Set05	**Screen of Set 03.**
Std	**Standard references used in most Forest Service risk assessments.**

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Table 1: Relevant Reviews and Related Documents on Bifenthrin

Reference [# pages][1]	Comment
ATSDR 2003 [328 pp]	Toxicological Profile for Pyrethrins and Pyrethroids
CalDFG 2000 [5 pp.]	Brief summary of ecological data on aquatic species.
CalEPA/DPR 1997 [31 pp.]	HHRA focused on greenhouse applications.
Fecko 1999	Environmental fate. Mostly EPA studies.
ECOTOX 2014	EPA database on ecotoxicity values for both terrestrial and aquatic species. For bifenthrin, EXCOTOX contains about 350 records on aquatic species and over 1800 records on terrestrial species.
EFSA 2011 [101 pp.]	Review of studies relevant to environmental fate, human health, and ecological effects. Mostly unpublished studies. Contains studies not included in U.S. EPA reviews (i.e., studies only required in Europe).
EFSA 2011 [61 pp.]	Review of allowable residues in Europe with discussion of dose-response.
FOA0 2009 [7 pp.]	Brief summary of data relevant to WHO's ADI.
FAO 2012 [45 pp.]	Summary of human health and ecological effects data (unpublished) with cursory references to the specific studies. Appears to be similar to WHO 2012. Probably contains studies not included in U.S. EPA reviews (i.e., studies only required in Europe).
HSDB 2011 [64 pp.]	Summary reliant on other secondary sources. Little primary literature.
NPIC 2011 [12 pp.]	Short review but with full references.
U.S. EPA/OPP 2011a [22 pp.]	Bifenthrin Final Work Plan for Registration Review.
Palumbo et al. 2010 [51 pp.]	Primary literature relevant to human health and ecological effects.
Schleier and Peterson 2011	General review of pyrethrins and pyrethroids.
U.S. EPA/OPP/EFED 2010a [98 pp.]	EFED Registration Review Problem Formulation for Bifenthrin
U.S. EPA/OPP/EFED 2010b [106 pp.]	Revised EFED Registration Review Problem Formulation for Bifenthrin
U.S. EPA/OPP/EFED 2012a [265 pp.]	EFED risk assessment for threatened and endangered species. Includes many appendices and attachments.
U.S. EPA/OPP/HED 2007a [57 pp.]	Acute and Chronic Dietary (including drinking water) exposure assessment.
U.S. EPA/OPP/HED 2007b [54 pp.]	HHRA in support of new uses on several crops.
U.S. EPA/OPP/HED 2010a [31 pp.]	U.S. EPA/OPP Health Effects Division scoping level risk assessment in support of registration review.
U.S. EPA/OPP/HED 2010b [109 pp.]	Review of human incidents.
U.S. EPA/OPP/HED 2012a [83 pp.]	U.S. EPA/OPP Health Effects Division Human Health Risk Assessment for New Uses
Von Stacklberg 2012 [36 pp.]	Review focused on mammalian toxicity and potential risks to humans. Includes open literature and some unpublished registrant studies.
WHO 2012	Summary of human health and ecological effects data (unpublished) with cursory references to the specific studies. Appears to be similar to FAO 2012.
Wolansky and Harrill 2008	General review on neurotoxicity of pyrethroids.

[1] Key reviews are indicated by light green shading. Some U.S. EPA/OPP tolerances and other narrowly focused documents – e.g., exposure assessments, registration status, use applications, etc. – are not summarized above but are discussed in the text as appropriate and are listed in Section 5 (References).

See Section 1.1. for discussion.

Table 2: Summary of Open Literature Most Relevant to Risk Assessment

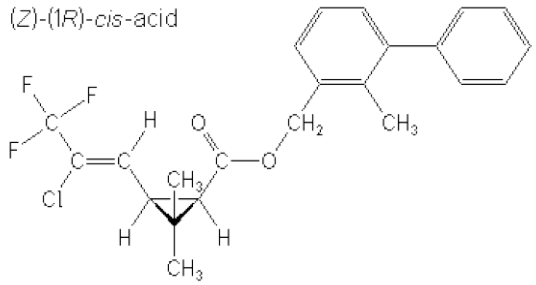
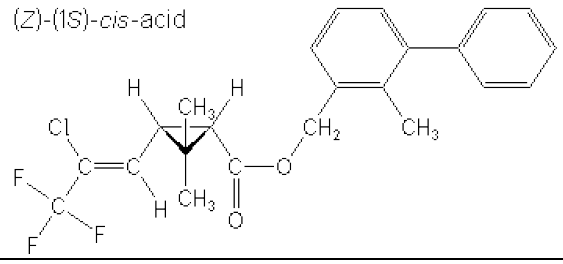
Topic	Citations[1]
Human Health	
Dermal Absorption	Hughes and Edwards 2010
Estrogenic Effects	Brander et al. 2012; Schlenk et al. 2012; Wang et al. 2007; Wang et al. 2009b; Yang et al. 2009a; Zhao et al. 2010
Immune function	Hoffman et al. 2006; Zhao et al. 2010
Mechanism/ Neurotoxicity As[2]	Cao et al. 2011a,b; Choi and Soderlund 2006; Clark and Matsumura 1987; Clark and Symington 2008; Nandi et al. 2006; Scollon et al. 2011; Tran et al. 2006; Wolansky et al. 2007; [many more]
Pharmacokinetics	Scollon et al. 2005;
Reproductive Effects	Liu et al. 2011a,b; McCarty et al. 2002
Worker Exposure/Effects	Dong 1995; Lebailly et al. 1998; Srivastava et al. 2005; U.S. EPA/OPP/HED 1992a;
Terrestrial Species	
Birds	Shakoori et al. 1993;
Bees	Dai et al. 2010; Estesen et al. 1992; Mao et al. 2011; Qualls et al. 2010; Zhang et al. 2008;
Other nontarget inverts	Elias et al. 2013; Hamby et al. 2013; Hoang et al. 2011; James et al. 1995; Yang et al. 2001;
Insect Resistance	Bynum and Archer 2002; Parkman and Pienkowski 1989; Shakoori et al. 1994; Van Leeuwen and Tirry 2007;
Sublethal Effects Inverts	Tufail et al. 1994
Aquatic Species	
Fish	Harper et al. 2008; Jin et al. 2009, 2010, 2013; Riar et al. 2013; Schlenk et al. 2012; Velisek et al. 2009; Zhang et al. 2010
Invertebrates	Brausch et al. 2010; Harper et al. 2008; Harwood et al. 2013; Holzer 2011; Hook et al. 2014; Maul et al. 2008a,b; Putt 2005; Trimble et al. 2010; Wang et al. 2009a,b; Wheelock et al. 2006; Ye et al. 2004; Zhao et al. 2009
Field/Mesocosm	Drenner et al. 1993; Pennington et al. 2014; Weston et al. 2006
Environmental Fate	
Fate on vegetation	Chauhan et al. 2012; Mukherjee et al. 2010; Papadopoulou-Mourkidou et al. 1989; You et al. 2013
Other media	Gan et al. 2005; Harris 2004; Laskowski 2002; Peterson 2012a,b; Sharma and Singh 2012; Yang et al. 2006
Other	
Chirality	Liu et al. 2005ab, 2008a,b; 2009; Lu 2013; Wang et al. 2007; Yang et al. 2009; Zhao et al. 2009;
Forestry Uses	Burke et al. 2012; Cranshaw 2014; Fettig et al. 2006, 2013; Hiskes 2014; Liesch and Williamson 2010; Lowe et al. 1994; McCullough and Smitley 1995; McCullough et al. 1998; Miller 1997; Montana DNRC 2014; Monture Creek Land Management, Inc. 2014; Negron and Clarke 1995;

[1] Full bibliographic citations are given in Section 5.

[2] Papers on mechanisms, neurotoxicity, and other related topics.

See Section 1.1. for discussion.

Table 3: Chemical and Physical Properties

Item	Value	Reference[1,2]
	Identifiers	
Common name:	Bifenthrin	
CAS Name	2-Methylbiphenyl-3-ylmethyl-(Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate	ChemIDplus
IUPAC Name	2-methylbiphenyl-3-ylmethyl (Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate	TalstarOne Multi-Insecticide label
CAS No.	82657-04-3 [Primary] Alternate CAS Numbers 107497-60-9 107538-32-9 92880-79-0	ChemIDplus 2014
Chemical Group	Pyrethroid	ChemIDpus 2014
Development Codes	FMC 54800	FMC product labels, Tomlin 2004
Molecular formula	$C_{23}H_{22}CLF_3O_2$	USDA/ARS 2002
EPA PC Code	128825	U.S. EPA/OPP/EFED 2012a
Mode of Action	Neurotoxin/ Sodium channel modulator	IRAC 2013
Smiles Code	`Cc1c(cccc1c2ccccc2)COC(=O)[C@@H]3[C@@H](C3(C)C)/C=C(/C(F)(F)F)\Cl`	ChemIDpus 2014
Structure		U.S. EPA/OPP/EFED 2012a
		U.S. EPA/OPP/EFED 2012a
Isomeric composition	≥97% cis-isomer, ≤3% trans-isomer	Tomlin 2004
	Chemical Properties(1)	
Aqueous photolysis	0.0033 day^{-1}	USDA/ARS 2002
	Stable	MRID 163084
Henry's Law Constant	>101.5 Pa m^3/mol	USDA/ARS 2002
Hydrolysis (abiotic)	Stable	USDA/ARS 2002
	Stable at pH values of 5, 7, and 9.	MRID 132539
K_{ow}	3,000,000 at 20ºC	Laskowski, 2002
	1,000,000 [log Kow = 6]	USDA/ARS 2002
	>1,000,000 [log Kow > 6]	Tomlin 2004; U.S. EPA/OPP/ HED 2012a, p. 13

<table>
<tr><th>Item</th><th>Value</th><th>Reference[1,2]</th></tr>
<tr><td>Molecular weight</td><td>422.9 g/mole</td><td>Laskowski, 2002</td></tr>
<tr><td></td><td>422.88 g/mole</td><td>USDA/ARS 2002</td></tr>
<tr><td>Specific gravity</td><td>1.212 g/mL at 25ºC/4ºC</td><td>HSDB 2011</td></tr>
<tr><td>Vapor pressure</td><td>0.024 mPa</td><td>USDA/ARS 2002</td></tr>
<tr><td></td><td>Non-volatile under field conditions</td><td>U.S. EPA/OPP/EFED 2012a</td></tr>
<tr><td>Water solubility</td><td>0.000014 mg/L (0.014 µg/L) @ 22ºC
This value is used by U.S. EPA/OPP/EFED 2012a.</td><td>MRID 132518; Laskowski, 2002</td></tr>
<tr><td></td><td>0.0001 mg/L</td><td>USDA/ARS 2002</td></tr>
<tr><td></td><td>< 0.0001 mg/L (p. 13, Table 3.2)
0.014 µg/L or 0.000014 mg/L (p. 36)</td><td>U.S. EPA/OPP/ HED 2012a, p. 13</td></tr>
<tr><td></td><td>< 0.001 mg/L</td><td>Tomlin 2004</td></tr>
<tr><td></td><td>0.1 mg/L (appears to be for Talstar formulation)</td><td>Knisel and Davis 2000</td></tr>
<tr><td></td><td>Environmental Properties</td><td></td></tr>
<tr><td>Bioconcentration in various aquatic organisms (BCF, L/kg)</td><td>
<table>
<tr><th>Species</th><th>Lower bound</th><th>Upper bound</th></tr>
<tr><td>Daphnia magna</td><td>270</td><td>440</td></tr>
<tr><td>Asellus [isopod][1]</td><td>71</td><td>82</td></tr>
<tr><td>Asellus [isopod] [2]</td><td>120</td><td>180</td></tr>
<tr><td>Pimephales promelas [fathead minnow]</td><td>45</td><td>63</td></tr>
<tr><td>Corbicula [clam] [1]</td><td>41</td><td>74</td></tr>
<tr><td>Corbicula [clam] [3]</td><td>92</td><td>140</td></tr>
</table>
[1] Water exposure
[2] Water and sediment exposure
[3] Soil phase.
</td><td>MRID 42529902</td></tr>
<tr><td></td><td>Bluegill sunfish
Whole fish: 6,090 L/kg
Edible tissue: 2,140 L/kg
Offal: 8,720 L/kg
Working Note: The values for whole fish and edible tissues used in WorksheetMaker.</td><td>MRID 163094 and MRID 163095 from U.S. EPA/OPP/ EFED 2012a, pp. 129-130</td></tr>
<tr><td></td><td>Daphnia magna
Water Exposure: 2,500 to 4,600
Water and Suspended solids: 800-4,300</td><td>Yang et al. 2006
Also summarized in U.S. EPA/OPP/EFED 2012a.</td></tr>
<tr><td></td><td>Hyalella azteca: 1180 ± 542</td><td>Holzer 2011 (p. 13)
Also summarized in U.S. EPA/OPP/EFED 2012a.</td></tr>
<tr><td></td><td>Zebrafish (Danio rerio) embryos:
708.4 (at 2 µg/L)
278.4 (at 20 µg/L)</td><td>Tu et al. 2014</td></tr>
<tr><td>Field dissipation</td><td>26 (7-62) days</td><td>USDA/ARS 2002</td></tr>
<tr><td>Foliar washoff fraction</td><td>0.4</td><td>Knisel and Davis 2000</td></tr>
<tr><td>Foliar half-life</td><td>7 days (NOS)</td><td>Knisel and Davis 2000</td></tr>
<tr><td></td><td>9-23 days (peach foliage)</td><td>Papadopoulou-Mourkidou et al. 1989</td></tr>
<tr><td></td><td>2.4-10.5 days (wheat seedlings)</td><td>You et al. 2013</td></tr>
<tr><td></td><td>12.7 (2.4-23)
Note: These values are used in WorksheetMaker for half-lives on fruit based on the above to studies.</td><td>Based on above.</td></tr>
<tr><td>Fruit half-life</td><td>9-12 days (peach pulp)</td><td>Papadopoulou-Mourkidou et al. 1989</td></tr>
</table>

<table>
<tr><th>Item</th><th>Value</th><th>Reference[1,2]</th></tr>
<tr><td></td><td>2.05 days (tomatoes, room temperature, NOS)
2.32 days (tomatoes, 4°C)</td><td>Chauhan et al. 2012</td></tr>
<tr><td></td><td>7 (2 to 12)
Note: These values are used in WorksheetMaker for half-lives on fruit based on the above to studies.</td><td>Based on above.</td></tr>
<tr><td>K_{oc}</td><td>240,000</td><td>Knisel and Davis 2000</td></tr>
<tr><td></td><td>236,750 (Average of four values: 131000, 239000, 302000 and 275000.)</td><td>MRID 00141203, U.S. EPA/ OPP/EFED 2012a, Table 3-3</td></tr>
<tr><td></td><td>237,000
Note: Appears to be a rounding of MRID 00141203.</td><td>Amweg et al. 2005</td></tr>
<tr><td></td><td><table><tr><th>Soil</th><th>Kd</th><th>Koc</th></tr><tr><td>Sandy loam</td><td>4160</td><td>239,000</td></tr><tr><td>Silt loam</td><td>5429</td><td>302,000</td></tr><tr><td>Clay loam</td><td>3688</td><td>275,000</td></tr><tr><td>Sand</td><td>992</td><td>131,000</td></tr></table></td><td>USDA/ARS 2002</td></tr>
<tr><td></td><td><table><tr><th>Soil</th><th>Kd</th><th>Koc</th></tr><tr><td>Sandy loam</td><td>4192</td><td>239,000</td></tr><tr><td>Silt loam</td><td>5430</td><td>302,000</td></tr><tr><td>Clay loam</td><td>3690</td><td>275,000</td></tr><tr><td>Sand</td><td>992</td><td>131,000</td></tr></table>Above very similar (slight differences in Kd) to values reported above from USDA/ARS 2002.</td><td>MRID 141203</td></tr>
<tr><td>Kds</td><td>485-21,290 [Table 3 of paper]</td><td>Gan et al. 2005</td></tr>
<tr><td>Sediment half-life</td><td>318-870 days (field sediment, Table 5)
485-870 days (creek sediment, Table 5)</td><td>Lee et al. 2004</td></tr>
<tr><td></td><td>Aerobic:
578±24days ([R-cis])
630±34days ([S-cis])
Anaerobic:
630±45days ([R-cis])
408±36days ([S-cis])</td><td>Qin et al. 2006</td></tr>
<tr><td>Soil half-life (NOS)</td><td>26 days</td><td>Knisel and Davis 2000</td></tr>
<tr><td>Soil half-life, aerobic</td><td><table><tr><th>Soil</th><th>Half-life (days)</th><th>Label</th></tr><tr><td>Sandy loam</td><td>132</td><td>Cyclopropyl</td></tr><tr><td>Sandy loam</td><td>116</td><td>Phenyl</td></tr><tr><td>Silt loam</td><td>250</td><td>Cyclopropyl</td></tr><tr><td>Silt loam</td><td>155</td><td>Phenyl</td></tr><tr><td>Silty clary loam</td><td>128</td><td>Cyclopropyl</td></tr><tr><td>Silty clary loam</td><td>97</td><td>Phenyl</td></tr></table></td><td>Composite of many MRIDs as summarized in Table 2.2 U.S. EPA/OPP/EFED 2012a.</td></tr>
<tr><td>Soil half-life, aerobic</td><td>95 (65-125) days</td><td>USDA/ARS 2002</td></tr>
<tr><td></td><td>8-17 months</td><td>Gan et al. 2005</td></tr>
<tr><td></td><td>147 days (not sterilized)
330 days (sterilized)</td><td>Sharma and Singh 2012</td></tr>
<tr><td></td><td>277±19days ([R-cis])
330±28days ([S-cis])
Difference not significant at p=0.06.</td><td>Qin et al. 2006</td></tr>
<tr><td>Soil half-life anaerobic</td><td>Stable</td><td>MRID 163088</td></tr>
<tr><td>Soil dissipation half-life</td><td>35 to 345 days [several specific values given]</td><td>Composite of many MRIDs as summarized in Table 2.2 U.S. EPA/OPP/EFED 2012a.</td></tr>
</table>

Item	Value	Reference[1,2]
	2.89-4.3 days [Note: field dissipation and not degradation]	Mukherjee et al. 2010
	200 (at 7.5 cm) and 235 days (at 15 cm) in vegetated soil 345 (at 7.5 cm) and 390 days 235 days (at 15 cm) in non-vegetated soil.	Peterson et al. 2012a
Soil photolysis half-life	147 days (cyclopropyl label) 106 days (phenyl label)	MRID 163085
Water Dissipation half-life	No discernable dissipation from ponds over a 12 month period.	Composite of many MRIDs as summarized in Table 2.2 and p. 43 of U.S. EPA/OPP/EFED 2012a.

[1] MRID studies taken from U.S. EPA/OPP/EFED 2012a unless otherwise specified.
[2] 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 4: Representative Formulations

Formulation, Supplier, EPA Registration Number	Composition/ Characteristics	Application Information, Methods and Rates[1]
Onyx Insecticide FMC Corporation EPA Reg. No. 279-3177 U.S. Patent No. 4,238,505 Label date: Dec. 31, 2008 Commercial applicators only. Patent granted on Dec. 9, 1980 to John F. Engel, FMC Corp. [http://www.google.com/patents/US4238505]	Liquid, 23.4% a.i. (w/w) 2 lbs a.i./gallon (equiv. 0.015625 lb/fl.oz.) 97% cis isomers Contains petroleum distillates and ethylene glycol (CAS No. 107-21-1).	General: Addition of spreader stickers not necessary. Surfactants recommended only for turf applications. Maximum Single Application Rate: 0.2 lb a.i./acre. Maximum annual application rate not specified. <u>Ground Broadcast Applications</u> 0.26 to 1.28 fl. oz. formulation/10 gallons water applied at a rate of 10 gallons/4,356 ft^2 (0.1 acre). Equivalent to ≈0.041 to 0.2 lb a.i./acre with an application volume of 100 gallons/acre. Low and high volume applications are allowed but not specified for tree applications. Low and high application volumes are specified as 2 to 10 gallons/1000 ft^2, corresponding to 87.12 to 435.6 gallons/acre [43,560 ft^2/acre], in the discussion of turf applications. <u>Bark Treatments for *Dendroctonus* bark beetles</u> Preventative: Solutions of 0.25 to 0.5 lbs. a.i./100 gallons [≈300 to 600 mg/L] sprayed on main trunk from base to half way to live crown at rates of 1 to 4 gallons/tree. This corresponds to 0.0025 lb a.i./tree to 0.02 lb a.i./tree. Total applications cannot exceed 0.2 lb a.i./acre. Treatment of Infested Trees: 2 pints formulation per 100 gallons of water [0.5 lb a.i./100 gallons or 600 mg a.i./L] applied at about 1 to 4 gallons/tree or 0.005 lb a.i. to 0.02 lb a.i./tree. <u>Bark Treatments for other bark beetles (e.g., Ambrosia beetles, Elm bark beetles and Emerald Ash borer):</u> Preventative: As above but specifies 6 to 12 gallons/tree. This is equivalent to 0.015 to 0.03 lb a.i./tree [0.25 lb a.i./100 gallons x 6 to 12 gallons/tree] May also be applied to grass. Aerial: Not permitted.
Biflex SFR Termiticide/ Insecticide FMC Corporation EPA Reg. No. 279-3177 Commercial applicators only.	Liquid, 23.4% a.i. (w/w) 2 lbs a.i./gallon (equiv. 0.015625 lb/fl.oz.) 97% cis isomers Contains petroleum distillates.	Essentially identical to Onyx Insecticide for applications to trees and shrubs but also labelled for termite control in and around buildings. See Section 2.2 for discussion. Applied as a 0.6% suspension (≈1,400 mg a.i./L) for subterranean applications. May not be used in greenhouses or nurseries.

Formulation, Supplier, EPA Registration Number	Composition/ Characteristics	Application Information, Methods and Rates[1]
Talstar GC Flowable FMC Corporation EPA Reg. No. 279-3156 Restricted use pesticide.	Flowable, 7.9% a.i. (w/w) ⅔ lbs a.i./gallon (equiv. ≈ 0.00521 lb/fl.oz.) 97% cis isomers Contains <6.2% propylene glycol (CAS No. 57-55-6).	Maximum Single Application Rate: 0.1 lb a.i./acre. Maximum Seasonal Application Rate: 0.2 lb a.i./acre/year. <u>Ground Broadcast Applications</u> 0.125 to 1.0 fl. oz. formulation/1,000 ft^2 (equiv. ≈0.00065 to 0.00521 lb/1000 ft^2 or 0.0283 to 0.227 lb a.i./acre. [The rate of 0.227 lb a.i./acre is a rounding issues that does imply that the maximum seasonal rate can be exceeded.] Application volumes of about 33 to 435 gallons/acre. Not specifically labelled for bark application but applications to woody trunks of ornamentals is specified. May also be applied to grass. Aerial Application: Not permitted.
Talstar One Multi-insecticide FMC Corporation EPA Reg. No. 279-3156 U.S. Patent No. 4,238,505 Label date: Dec. 31, 2008 Restricted use requirement noted only for termiticide applications.	Flowable, 7.9% a.i. (w/w) ⅔ lbs a.i./gallon (equiv. ≈ 0.00521 lb/fl.oz.) 97% cis isomers Contains <6.2% propylene glycol (CAS No. 57-55-6).	Maximum labeled rate: 1 fl oz/1000 ft^2 (≈0.2269 lb a.i./acre). <u>Ground Broadcast Applications</u> Application Rates: 0.125 to 1 fl oz. formulation/1000 ft^2. Equiv. to ≈ 0.0283 to 0.2269 lb a.i./acre. Application Volume: 100 to 300 gallons/acre. <u>Bark Treatments</u> Specific directions for bark treatments given only for carpenter ants. Labelled directions for Ground Broadcast Applications indicate that trunks, stems, and twigs in addition to foliage should be sprayed for the control of beetles, borers and weevils. Also labeled for the control of termites.

[1] Unless otherwise noted, application rates and directions are for ornamentals and trees.

Table 5: Backpack Foliar - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.2.1.3.	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	0.005	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.001	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.02	SERA 2014b, Table 14	7
Subject Chemical	Bifenthrin		8
First-order dermal absorption rate coefficient for subject chemical ($hour^{-1}$) [ka_P]	0.0013	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	1.96969697		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.00984848	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.001969697	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.039393939	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 ratio 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 3.2.2.1.1 for discussion.

Table 6: Ground Broadcast - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.2.1.3.	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	0.000002	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.005	SERA 2014b, Table 14	7
Subject Chemical	Bifenthrin		8
First-order dermal absorption rate coefficient for subject chemical ($hour^{-1}$) [ka_P]	0.0013	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	1.96969697		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.00019697	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.000003939	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.009848485	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 ratio 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'.

Table 7: Aerial - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.2.1.3.	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	0.0000005	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.0008	SERA 2014b, Table 14	7
Subject Chemical	Bifenthrin		8
First-order dermal absorption rate coefficient for subject chemical ($hour^{-1}$) [ka_P]	0.0013	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	1.96969697		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.00003939	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.000000985	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.001575758	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.

Working Note: Triclopyr BEE is a factor of 2.38 more. 2,4-D is a factor of 1.96 less. Use 2,4-D.

- 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 ratio 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'.

Table 8: Bark Applications - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	Triclopyr-BEE	Section 3.2.2.1.3.	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	0.001	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.0001	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.02	SERA 2014b, Table 14	7
Subject Chemical	Bifenthrin		8
First-order dermal absorption rate coefficient for subject chemical ($hour^{-1}$) [ka_P]	0.0013	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	0.41935484		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.00041935	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.00004194	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.0083871	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 ratio 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'.

Table 9: Precipitation, Temperature and Classifications for Standard 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.

Table 10: 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

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

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

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

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

Table 11: Chemical parameters used in Gleams-Driver modeling

Parameter	Values	Note/Reference
Half-lives (days)		
Aquatic Sediment	485 to 870	Note 1
Foliar	2.4 to 23	Note 2
Soil	150 (110-180)	Note 3
Water	300 (220-360)	Note 4
Soil $K_{o/c}$, mL/g	236750 (175264-298236)	Note 5
Sediment K_d, mL/g	3576 (2043-5109)	Note 6
Water Solubility, mg/L	0.00002	Note 7
Foliar wash-off fraction	0.4	Knisel and Davis 2000
Fraction applied to foliage	0.5	Standard assumption
Depth of Soil Incorporation	1 cm	Standard assumption
Irrigation after application	none	Section 2
Initial Application Date	June 15	Standard assumption

Notes

Number	Text
1	From the open literature publication by Lee et al. (2004, Table 1, creek sediment). Somewhat more conservative than value from Qin et al. (2006) for [R] and [S] enantiomers. U.S. EPA/OPP/EFED (2012a, p. 102) assumes *stable*.
2	Encompasses the range of values from Knisel and Davis (2000), Papadopoulou-Mourkidou et al. (1989), and You et al. (2013).
3	Based on six soil aerobic half-times used by U.S. EPA/OPP/EFED (2012a, p. 102) including the average as well as 10^{th} and 90^{th} percentiles. EPA used only 90^{th} percentile.
4	Consistent with approach used by used by U.S. EPA/OPP/EFED (2012a, p. 102) in doubling the soil half-lives. This is a common EPA practice in the absence of studies on aqueous metabolism.
5	Based on four Koc values used by U.S. EPA/OPP/EFED (2012a, p. 102) including the average as well as 10^{th} and 90^{th} percentiles. EPA used only the average value.
6	Based on four Kd values associated with the Kd used by U.S. EPA/OPP/EFED (2012a, p. 102) including the average as well as 10^{th} and 90^{th} percentiles. See Table 1, MRID 141203. Very similar to Kd values from USDA/ARS 2002. Gan et al. (2005)
7	This is slightly higher than the value of 0.000014 mg/L used by U.S. EPA/OPP/EFED 2012a and is used to accommodate rounding characteristics in GLEAMS. This is not a sensitive parameter.

Table 12: Summary of Modeled Concentrations in Surface Water

Scenario/Source	Peak Concentrations (ppb or µg/L)	Long-Term Average Concentrations (ppb or µg/L)
Water Contamination Rates (1 lb a.i./acre)		
Directed Foliar Application (Appendix 6) [1]		
Pond, Section 3.2.3.4.3.2	0.10 (0.014 – 0.7) [2]	0.038 (0.004 – 0.24) [2]
Stream, Section 3.2.3.4.3.2	0.35 (0.05 – 4) [2]	0.065 (0.004 – 0.6) [2]
Application Rate of 0.2 lb a.i./acre		
Directed Foliar Application		
Pond, Section 3.2.3.4.3.2	0.020 (0.0028 – 0.14)	0.0076 (0.0008 – 0.048)
Stream, Section 3.2.3.4.3.2	0.07 (0.01 – 0.8)	0.013 (0.008 – 0.12)
EPA Modeling		
FIRST [3]	0.014	0.014
SCI-GROW (ground water) [3]	0.003	N/A
PRZM/EXAMS[4]	0.014	0.014
PRZM/EXAMS[5]	0.40 (0.36 – 0.96)	0.024 (0.0046 – 0.046)
PRZM/EXAMS[6]	0.80 (0.72 – 1.92)	0.048 (0.0092 – 0.092)

[1] Applies only to broadcast. The estimate for bark applications is lower by a factor of 10.

[2] See Appendix 6, Table A6-5 through A6-8. Values are a composite of clay, loam, and sandy soils. The central estimate is taken as the average of the central estimates from clay, loam, and sand textured soils. The lower bound is taken as the minimum of the non-zero 25th percentiles for clay, loam, or sand textured soils. The maximum is the maximum value from clay, loam, or sand textured soils.

[3] U.S. EPA/OPP/HED (2007b, p. 7.; 2012a, p. 37), Modeling based on application rate of 0.5 lb a.i./acre.

[4] U.S. EPA/OPP/EFED (2012a, pp. 104-115.). Modeling based on a range of application rates from about 0.1 to 2.2 lb a.i./acre. Concentrations capped at water solubility.

[5] U.S. EPA/OPP/EFED (2012a, Appendix D, pp. 4-5.). Modeling for California citrus based on application rate of 0.5 lb a.i./acre. Not adjusted for water solubility. Concentrations given as average (minimum-maximum) converted to WCR values. Note that EPA uses only the upper bounds for risk characterization and the upper bound values are capped at 0.014 µg/L.

[6] The results from U.S. EPA/OPP/EFED (2012a, Appendix D, pp. 4-5) normalized for an application rate of 1 lb a.i./acre

See Section 3.2.3.4 for discussion.

Table 13: Estimated concentrations in surface water (foliar applications)

Foliar Broadcast	Peak	Longer-term
Water Contamination Rates (i.e., at an application rate of 1 lb a.i./acre	**Peak WCR**[1] (µg/L per lb a.i./acre)	**Longer-term WCR**[1] (µg/L per lb a.i./acre)
Central	0.35	0.065
Lower	0.005	0.004
Upper	4.0	0.6
Nominal Concentrations at an application rate of 0.2 lb a.i./acre	**Nominal Concentration (µg/L)** [2]	**Nominal Concentration (µg/L)** [2]
Central	0.07	0.013
Lower	0.01	0.0008
Upper	0.8	0.12
Adjusted Concentrations at 0.2 lb a.i./acre	**Adjusted Concentration (µg/L)** [3]	**Adjusted Concentration (µg/L)** [3]
Central	**0.014**	0.013
Lower	0.01	0.0008
Upper	**0.014**	**0.014**

[1] WCR (Water contamination rates) – concentrations in units of µg a.i./L expected at an application rate of 1 lb a.i./acre. In the EXCEL workbooks (Attachments 1 and 2) units of mg a.i./L are used. The WCRs are based on the stream concentrations from the GLEAMS-Driver simulations given in Table 12. The estimated concentrations of bifenthrin in surface water are capped to the water solubility of bifenthrin in water (0.014 µg/L) in Worksheet B04a of Attachment 1 (foliar applications).

[2] Calculated as the WCR multiplied by the application rate.

[3] The lower of the adjusted concentration or the water solubility (0.014 µg/L). Bold font is used to indicate that the concentration is limited by the water solubility.

See Attachment 1, Worksheet B04a for details of calculations.

See Section 3.2.3.4.6 for discussion.

Table 14: Bark Applications: Estimated concentrations in surface water

Foliar Broadcast	**Peak**	**Longer-term**
Water Contamination Rates (i.e., at an application rate of 1 lb a.i./acre	**Peak WCR**[1] (µg/L per lb a.i./acre)	**Longer-term WCR**[1] (µg/L per lb a.i./acre)
Central	0.35	0.065
Lower	0.005	0.004
Upper	4.0	0.6
Nominal Concentrations at an application rate of 0.02 lb a.i./acre	**Nominal Concentration (µg/L)** [2]	**Nominal Concentration (µg/L)** [2]
Central	0.007	0.0013
Lower	0.001	0.00008
Upper	0.08	0.012
Adjusted Concentrations at 0.02 lb a.i./acre	**Adjusted Concentration (µg/L)** [3]	**Adjusted Concentration (µg/L)** [3]
Central	0.007	0.0013
Lower	0.001	0.00008
Upper	**0.014**	0.012

[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. The WCRs are based on the stream concentrations from the GLEAMS-Driver simulations given in Table 12. The estimated concentrations of bifenthrin in surface water are capped to the water solubility of bifenthrin in water (0.014 µg/L) in Worksheet B04a of Attachment 2 (bark application).

[2] Calculated as the WCR multiplied by the application rate.

[3] The lower of the adjusted concentration or the water solubility (0.014 µg/L). Bold font is used to indicate that the concentration is limited by the water solubility.

See Attachment 2, Worksheet B04a for details of calculations.

See Section 3.2.3.4.6 for discussion.

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

Food Item	Central [a]	Lower [b]	Upper [a]
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

All concentrations given in units of ppm (mg agent/kg food) per lb a.i./acre.

[a] The central and upper bound values are taken from the U.S. EPA/EFED (2001, p. 44) as adopted from Fletcher et al. (1997).

[b] The EPA does not provide lower bound estimates. The lower bound estimates used in the current Forest Service risk assessment are calculated as: Central values × (Central Value ÷ Upper Value).

See Section 3.2.3.7 for discussion.

Table 16: Summary of toxicity values used in human health risk assessment

Acute – General Population (adults and children >6 years old), single exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2012a, Table 4.5.4, p. 34
Study	Wolansky et al (2006, 2007)
$BMDL_{1SD}$	3.1 mg/kg bw
LOAEL	12 mg/kg bw [2]
LOAEL Endpoint	Decreased locomotor activity.
Species, sex	Rats, male
Uncertainty Factor/MOE	100
Equivalent RfD	0.031 mg/kg bw

Acute – children (≤ 6 years old), single exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2012a, Table 4.5.4, p. 34
Study	Wolansky et al (2006, 2007)
BMD_{1SD}	3.1 mg/kg bw
LOAEL	12 mg/kg bw/day [1]
LOAEL Endpoint	Decreased locomotor activity.
Species, sex	Rats, male
Uncertainty Factor/MOE	300
Equivalent RfD	0.01 mg/kg bw

[1] As discussed in U.S. EPA/OPP/HED (2012a, pp. 18-19), the $BMDL_{1SD}$ is the lower 95% confidence limit of the Benchmark Dose (BMD) value and the $BMDL_{1SD}$ is used as a surrogate for the NOAEL. For bifenthrin, the EPA selected a BMD_{20} (a 20% decrease in locomotor activity relative to control) as the basis for the estimate.

[2] See discussion of LOAEL in U.S. EPA/OPP/HED 2012a, p. 20 as well as Figure 1A in Wolansky et al. 2006 and Figure 4 in Wolanksy et al. 2007.

See Section 3.3 for discussion.

Table 17: Topical LD_{50}s in Terrestrial Insects

Group	Species	LD_{50} (µg/g)	Reference
Hymenoptera	*Apis mellifera*	0.13	Atkins and Kellum 1981
Diptera	*Anopheles gambiae*	0.15	Hougard et al. 2002
Diptera	*Culex quinque-fasciatus*	0.16	Hougard et al. 2002
Lepidoptera	*Chilo suppressalis*	0.19	Li et al. 2006
Coleoptera	*Diabrotica virgifera*	0.27	Meinke et al. 1998
Lepidoptera	*Ostrinia nubilalis*	1.1	Siegfried 1993
Lepidoptera	*Heliothis virescens*	1.321	Leonard et al. 1988
Coleoptera	*Hippodamia convergens*	6.5	Siegfried 1993
Diptera	*Musca domestica*	42	Siegfried 1993
Coleoptera	*Sphenophorus venatus vestitus*	542	Doskocil et al. 2012

See Section 4.1.2.4.1 for discussion.
See Figure 4 for illustration.

Table 18: Acute LC_{50} Values in Fish

Species	96-h LC_{50} (µg/L)	Reference
Rainbow trout	0.15	MRID 163156
Gizzard shad [Capture 2EC]	0.207	Drenner et al. 1993 [8-days]
Bluegill sunfish	0.35	MRID 132536
Fathead minnow	0.78	Fojut et al. 2012
Zebra fish	2.1	Zhang et al. 2010
Common carp [Talstar EC]	5.75	Velisek et al. 2009
Sheepshead minnow	17.5	MRID 163101
Sheepshead minnow	19.806	Harper et al. 2008
Sheepshead minnow	18.653	Average of above two values

See Figure 5 for illustration.
See Section 4.1.3.1 for discussion.

Table 19: Relationship of LC_{50} and EC_{50} Values in Aquatic Invertebrates

Species	Duration (Hours)	EC_{50} (ng/L)	EC endpoint	LC_{50} (ng/L)	$LC_{50} \div EC_{50}$	Reference
Diphetor hageni	48	18.7	swimming	50.9	2.72	Weston et al. 2015
Fallceon quille	48	183	swimming	443	2.42	Weston et al. 2015
Serratella micheneri	48	79.4	swimming	97.4	1.23	Weston et al. 2015
Isoperla quinquepunctata	96	16.3	clinging	28.5	1.75	Weston et al. 2015
Hyalella azteca	96	1.9	swimming	2.7	1.42	Weston and Jackson 2009
Hyalella azteca	96	3.1	swimming	7.3	2.35	Weston and Jackson 2009
Hyalella azteca	96	3.5	swimming	8	2.29	Weston and Jackson 2009
Hyalella azteca	96	3.5	swimming	8.2	2.34	Weston and Jackson 2009

See Appendix 3, Table A3-1, for details.
See Section 4.1.3.3.1 for discussion.

Table 20: Acute EC_{50} Values in Aquatic Invertebrates

Class	Order	Species	Duration (Hours)	EC_{50} (ng/L)	Endpoint for EC_{50}	Reference
Malacostraca	Amphipoda	*Hyalella azteca*	96	1.9	swimming	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	3.1	swimming	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	3.5	swimming	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	3.5	swimming	Weston and Jackson 2009
		Hyalella azteca		2.91	Geometric mean	
Insecta	Trichoptera	*Hydropsyche sp*	96	12.8	movement	Weston et al. 2015
Insecta	Ephemeroptera	*Hexagenia sp.*	96	15.3	swimming	Weston et al. 2015
Insecta	Plecoptera	*Isoperla quinquepunctata*	96	16.3	clinging	Weston et al. 2015
Insecta	Ephemeroptera	*Diphetor hageni*	48	18.7	swimming	Weston et al. 2015
Insecta	Ephemeroptera	*Baetis tricaudatus*	48	35.5	swimming	Weston et al. 2015
Insecta	Plecoptera	*Taenionema sp.*	96	36.5	swimming	Weston et al. 2015
Insecta	Diptera	*Chironomus tentans*	96	51	growth	Putt 2005b
Insecta	Ephemeroptera	*Serratella micheneri*	48	79.4	swimming	Weston et al. 2015
Malacostraca	Amphipoda	*Gammarus pulex*	48	110	NOS	FAO 2012
Insecta	Ephemeroptera	*Fallceon quille*	48	183	swimming	Weston et al. 2015
Insecta	Trichoptera	*Nectopsyche sp.*	96	186	swimming	Weston et al. 2015
Insecta	Trichoptera	*Helicopsyche sp.*	96	251	movement	Weston et al. 2015
Branchiopoda	Cladocera	*Ceriodaphnia dubia*	24	310	NOS	FAO 2012
Insecta	Ephemeroptera	*Hexagenia sp.*	48	390	NOS	FAO 2012
Branchiopoda	Cladocera	*Daphnia magna*	48	1,600	immobility	MRID 41156501
Branchiopoda	Cladocera	*Daphnia magna*	24	3,240	hyperactivity	Ye et al. 2004
		Daphnia magna		2,277	Geometric mean	
Bivalva	Ostreoida	*Crassostrea virginica*	48	285,000	growth	Ward and Dose 1987

See Appendix 5, Table A5-1 for details of studies
See Section 4.1.3.3 for discussion.
See Figure 7 for illustration of aquatic arthropods.

Table 21: Acute LC_{50} Values in Aquatic Invertebrates

Class	Order	Species	Duration (hours)	LC_{50} (ng/L)	Reference
Malacostraca	Mysida	Americamysis bahia	96	3.97	MRID 00163102
Malacostraca	Amphipoda	*Hyalella azteca*	96	1.5	Graves et al. 2014
Malacostraca	Amphipoda	*Hyalella azteca*	96	2.7	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	7.3	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	8.0	Weston and Jackson 2009
Malacostraca	Amphipoda	*Hyalella azteca*	96	8.2	Weston and Jackson 2009
		Hyalella azteca		**4.55**	**Geometric mean**
Insecta	Plecoptera	*Isoperla quinquepunctata*	96	28.5	Weston et al. 2015
Malacostraca	Decapoda	*Palaemonetes pugio*	96	20.0	Harper et al. 2008
Malacostraca	Decapoda	*Palaemonetes pugio*	24	38.0	Harper et al. 2008
Malacostraca	Decapoda	*Palaemonetes pugio*	24	48.0	Harper et al. 2008
		Palaemonetes pugio		**33.17**	**Geometric mean**
Insecta	Ephemeroptera	*Diphetor hageni*	48	50.9	Weston et al. 2015
Branchiopoda	Cladocera	*Ceriodaphnia dubia*	48	70.0	Mokry and Hoagland 1990
Branchiopoda	Cladocera	*Ceriodaphnia dubia*	96	79.0	Liu et al. 2005b
Branchiopoda	Cladocera	*Ceriodaphnia dubia*	96	144	Liu et al. 2005a
		Ceriodaphnia dubia		**92.69**	**Geometric mean**
Insecta	Ephemeroptera	*Serratella micheneri*	48	97.4	Weston et al. 2015
Insecta	Ephemeroptera	*Fallceon quille*	48	443	Weston et al. 2015
Branchiopoda	Cladocera	*Daphnia magna*	48	175	Liu et al. 2005a
Branchiopoda	Cladocera	*Daphnia magna*	48	370	FAO 2012
Branchiopoda	Cladocera	*Daphnia magna*	48	860	Brausch et al. 2010
Branchiopoda	Cladocera	*Daphnia magna*	48	1600	MRID 41156501
		Daphnia magna		**546.34**	**Geometric mean**
Insecta	Odonata	*Enellagma and Ishnura spp.*	24	1100	Siegfried 1993
Insecta	Diptera	*Simulium vitallium*	24	1300	Siegfried 1993
Insecta	Ephemeroptera	*Heptageniidae sp.*	24	2300	Siegfried 1993
Insecta	Coleoptera	*Hydrophilus sp.*	24	5400	Siegfried 1993
Branchiopoda	Anostraca	*Thamnocephales platyurus*	24	5700	FAO 2012
Insecta	Trichoptera	*Hydropsyche and Cheumatopsyche sp.*	24	7200	Siegfried 1993

Note: For species with more than one value, the geometric mean of the values for the species is given in shaded rows.

See Appendix 5, Table A5-1 for details of studies
See Section 4.1.3.3 for discussion.
See Figure 8 for illustration.

Table 22: Chronic Toxicity in Aquatic Invertebrates

Species (Class: Order)	NOAEC (ng/L)[1]	LOAEC (ng/L) [1]	Reference [Comment]
Hyalella azteca (Malacostraca: Amphipoda)	0.17	0.34	Amweg et al. 2005
Mysidopsis bahia (Malacostraca: Mysida)	1.2	1.3	FAO 2012
Daphnia magna (Branchiopoda: Cladocera)	1.3	2.9	MRID 41156501
Daphnia magna (Branchiopoda: Cladocera)	4	20	Ye et al. 2004 [Lower NOAEC/LOAEC for growth, 1 ng/4 ng/L]
Leptocheirus plumulosus (Malacostraca: Amphipoda)	5	13	Putt 2005a [Based on growth rather than reproduction.]
Daphnia magna (Branchiopoda: Cladocera)	10	20	Wang et al. 2009b
Daphnia magna (Branchiopoda: Cladocera)	10	20	Zhao et al. 2009
Daphnia magna (Branchiopoda: Cladocera)	20	40	Brausch et al. 2010

[1] NOAEC and LOAEC values based on reproduction unless otherwise specified in comments.

See Appendix 5, Table A5-2, for details.
See Section 4.1.3.3.2 for discussion.

Table 23: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

MAMMALS [1]

Animal	Representative Species	BW[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	BW[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	BW[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 24: 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 25: Summary of toxicity values used in ecological risk assessment

Group/Duration Organism		Endpoint	Toxicity Value (a.i.)	Reference
Terrestrial Animals				
Acute				
Mammals (including canids)		NOAEL Neurotoxicity	3.1 mg/kg bw	Section 4.3.2.1.
Birds		Dietary LD_{50} ÷ 10	51. mg/kg bw	Section 4.3.2.2
Herbivorous insects		Use contact LD_{50} value.	0.013 mg/kg bw	Section 4.3.2.4
Honey Bee (contact)		LD_{50} ÷ 10	0.013 mg/kg bw	Section 4.3.2.4
Longer-term				
Mammals		Use acute value	3.1 mg/kg bw	Section 4.3.2.1
Bird		Freestanding Repro. NOAEC.	5.25 mg/kg bw	Section 4.3.2.2.
Aquatic Animals				
Acute				
Fish	Sensitive	NOAEC, trout	0.000094 mg/L	Section 4.3.3.1
	Tolerant	NOAEC, sheepshead minnow	0.005 mg/L	
Invertebrates	Sensitive	*Hyalella azteca* chronic value	0.00000017 mg/L	Section 4.3.3.3
	Tolerant	NOAEC, *Daphnia magna*	0.0006 mg/L	
Longer-term				
Fish	Sensitive	EPA analogy to other pyrethroids	0.000004 mg/L	Section 4.3.3.1
	Tolerant	28-day NOAEC in minnows	0.0002 mg/L	
Invertebrates	Sensitive	*Hyalella azteca* NOAEC	0.00000017 mg/L	Section 4.3.3.3
	Tolerant	*Daphnia magna* NOAEC	0.0000013 mg/L	
Aquatic Plants				
Algae	Sensitive	Not identified	N/A	Section 4.3.3.4
	Tolerant	LC_{50} ÷ 10 [*P. subcapitata*]	0.04 mg/L	Section 4.3.3.4
Macrophytes	Sensitive	No data identified.	N/A	Section 4.3.3.4
	Tolerant	No data identified.	N/A	Section 4.3.3.4

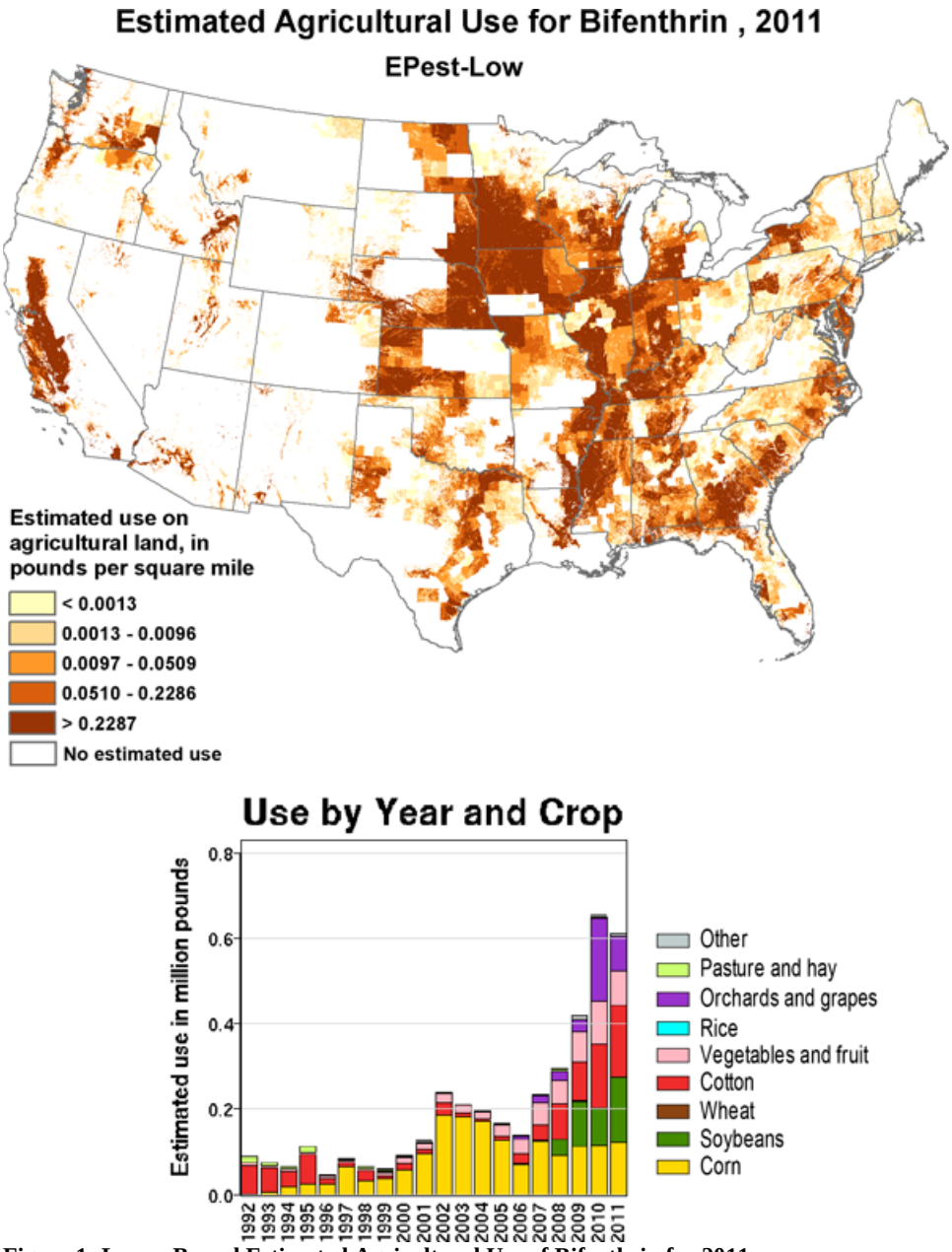


Figure 1: Lower Bound Estimated Agricultural Use of Bifenthrin for 2011

Source: USGS(2013)
See Section 2.5 for discussion.

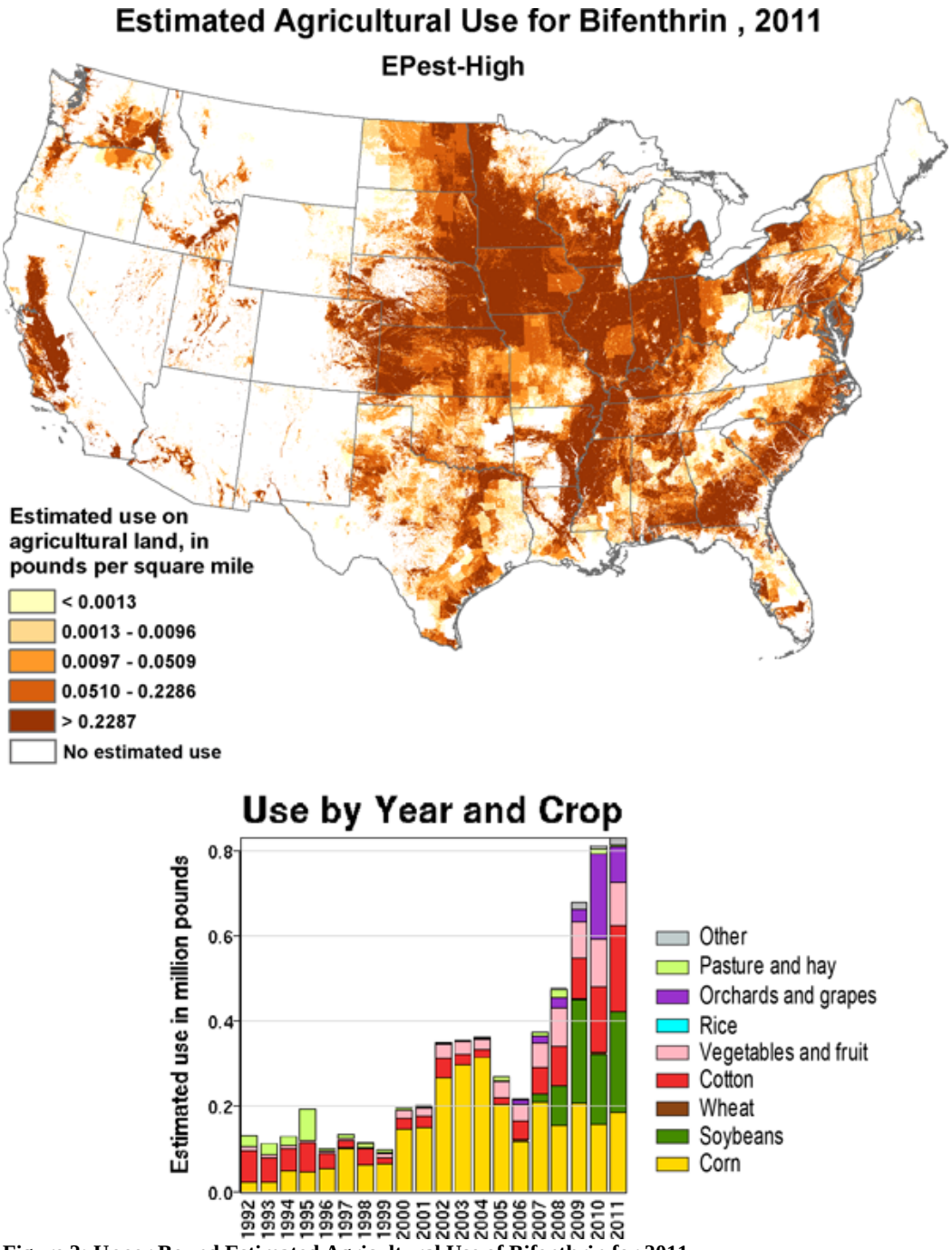


Figure 2: Upper Bound Estimated Agricultural Use of Bifenthrin for 2011

Source: USGS(2013)
See Section 2.5 for discussion.

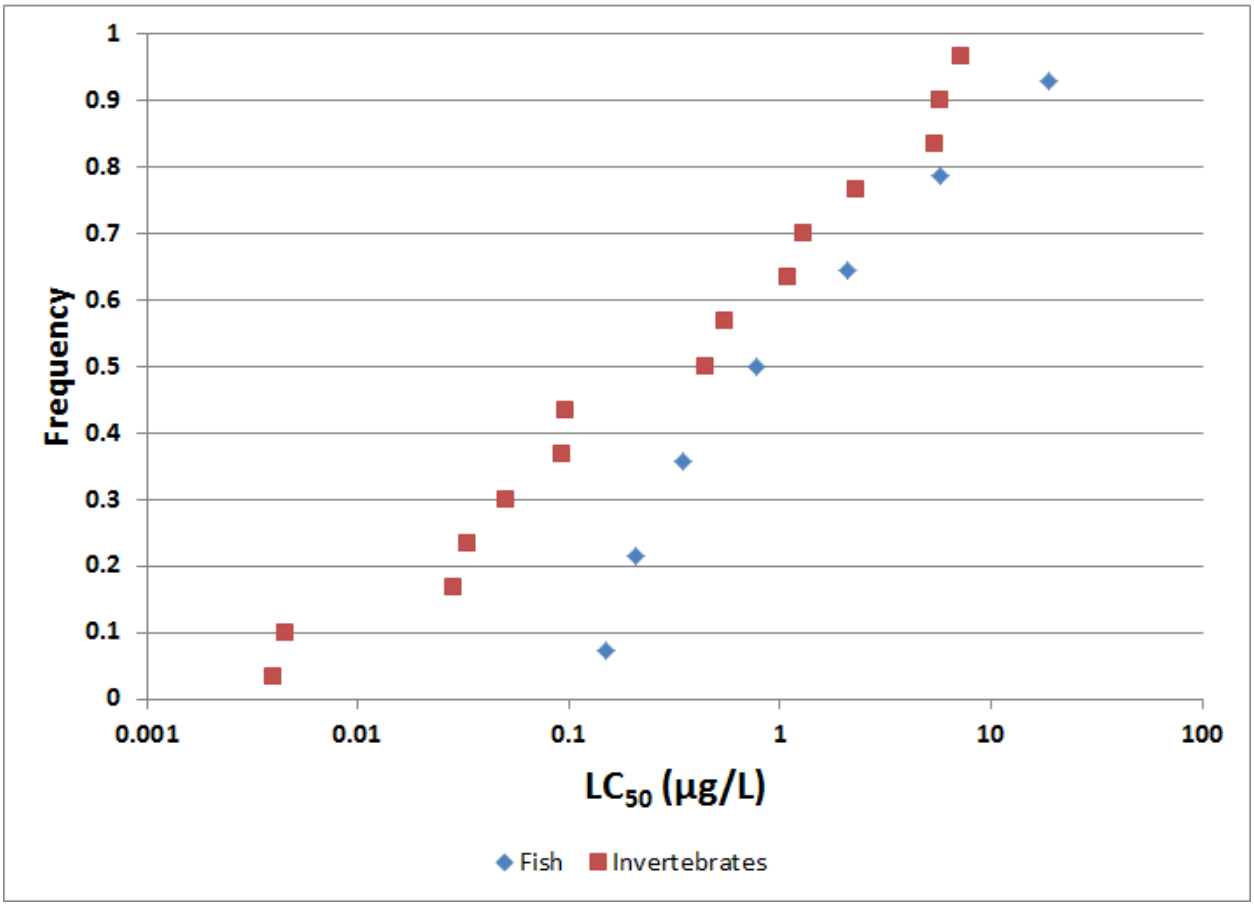


Figure 3: Comparison of LC_{50} Values in Fish and Aquatic Invertebrates

See Figure 5 (fish) and Figure 8 (aquatic invertebrates) for details.
See Section 4.1.1 for discussion.

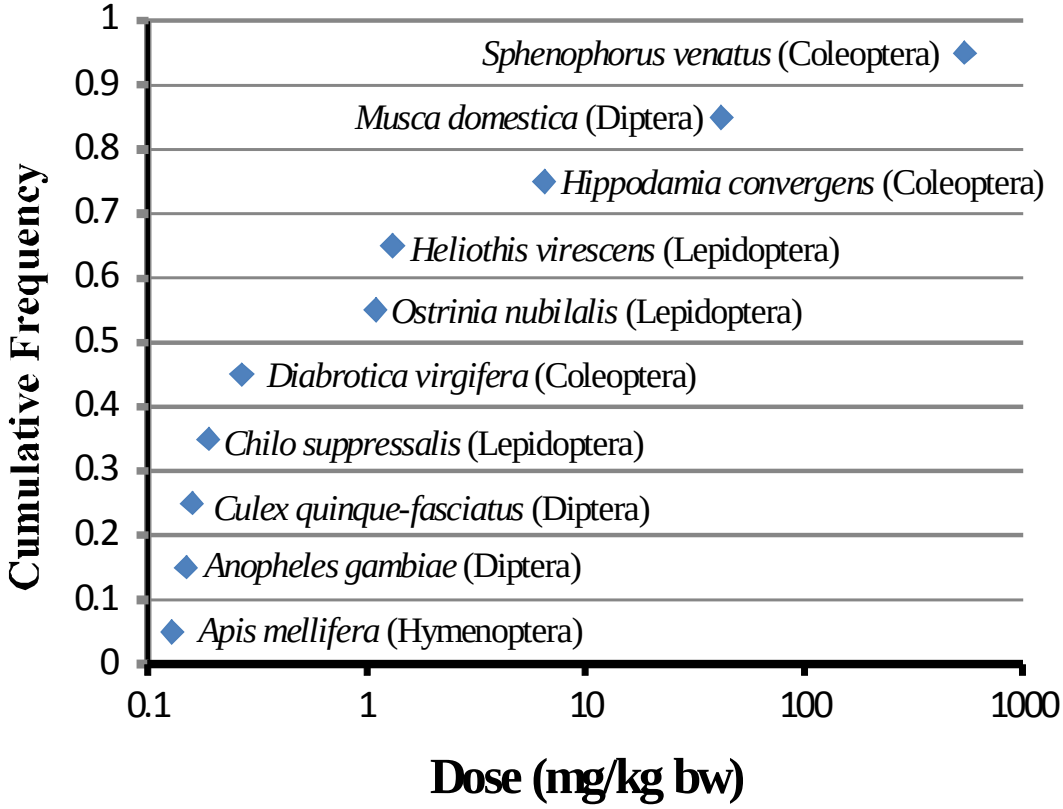


Figure 4: Topical LD_{50} Values in Terrestrial Insects

See Table 17 for data.
See Section 4.1.2.4.1 for discussion.

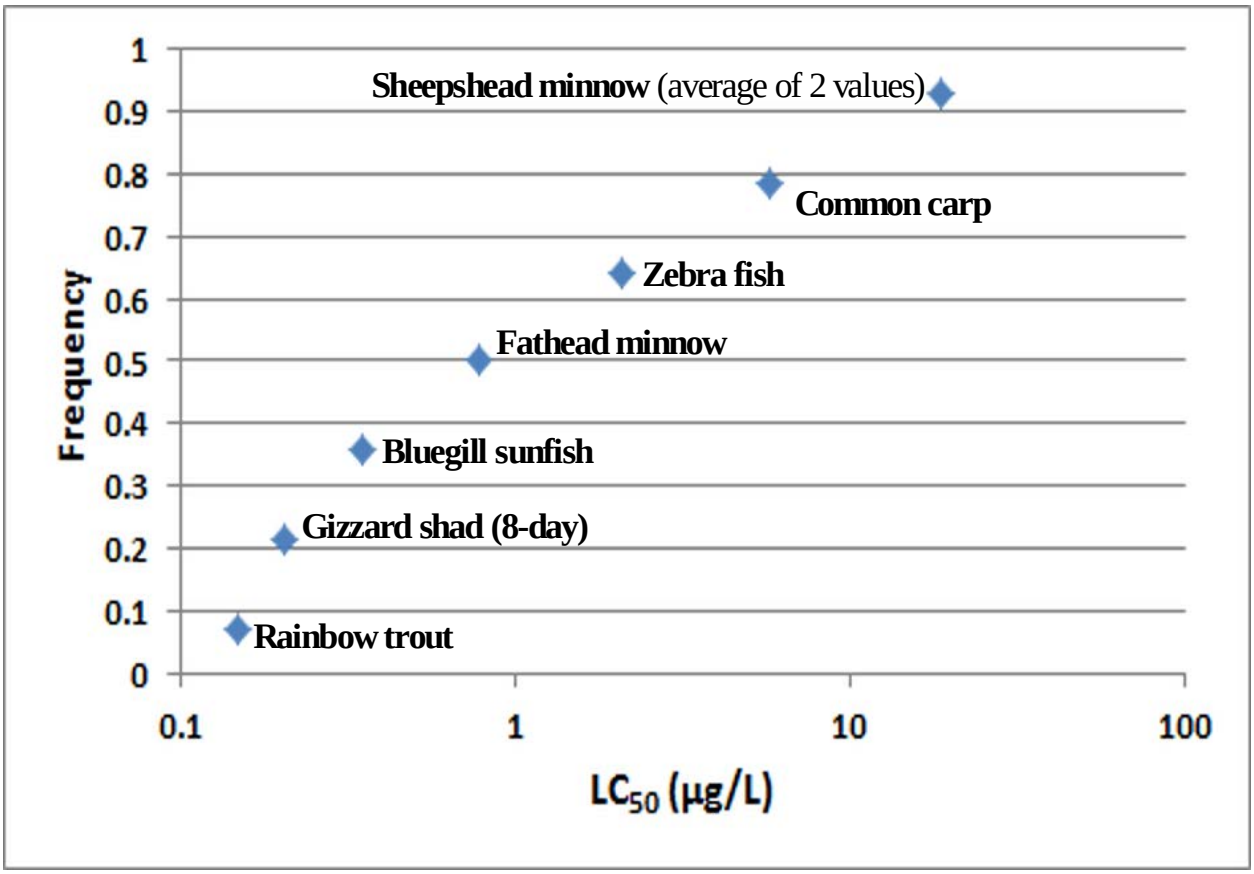


Figure 5: Acute 96-hour LC_{50} Values in Fish

See Table18 for data.
See Section 4.1.3.1 for discussion.

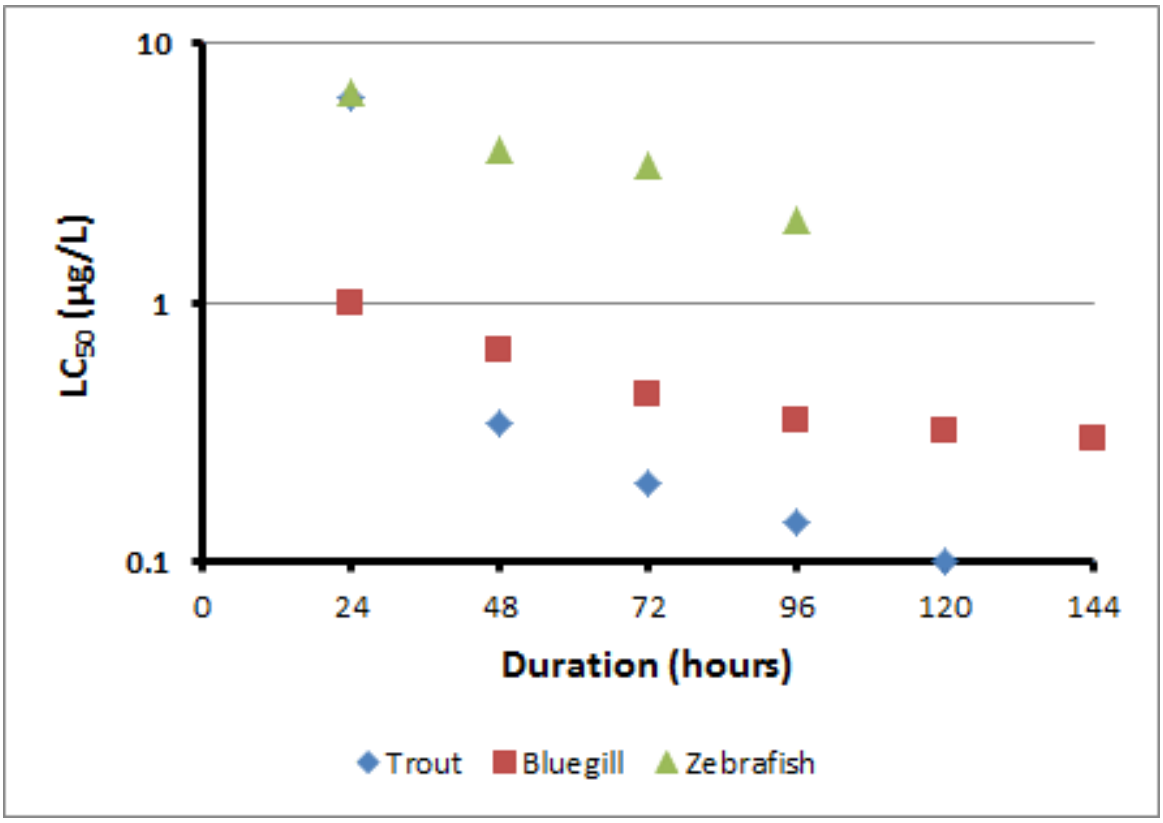


Figure 6: Concentration-Duration Relationships of LC_{50} Values in Fish

See Appendix 3, Table A3-1 for data.
See Section 4.1.3.1 for discussion.

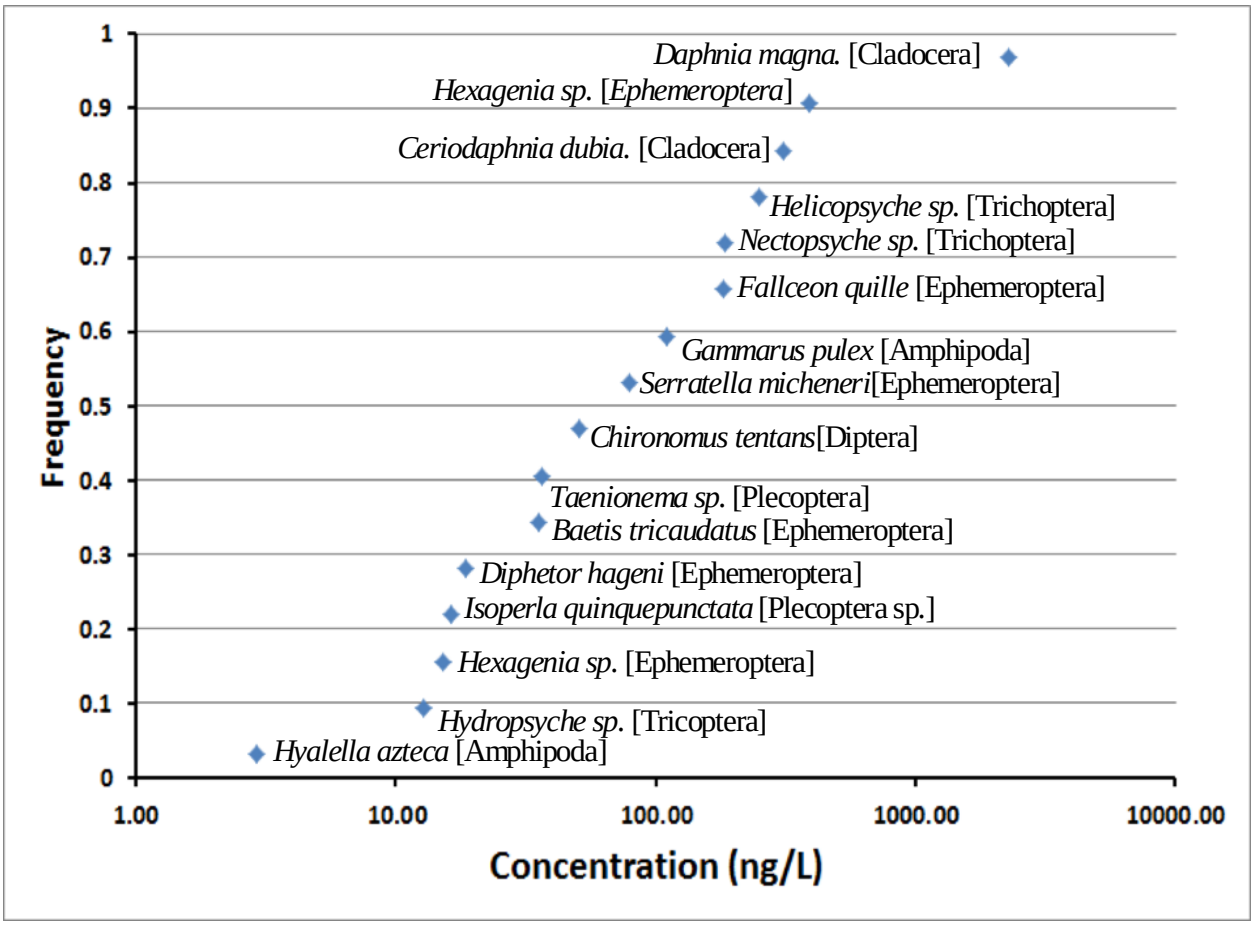


Figure 7: Acute EC_{50} Values for Aquatic Arthropods

See Table 20 for data.
See Section 4.1.3.3.1 for discussion

Note: The multiple EC_{50}s for *Hyalella azteca* (Weston and Jackson 2009) and *Daphnia magna* (MRID 41156501 and Ye et al. 2004) in Table 20 are plotted as geometric means in the above figure.

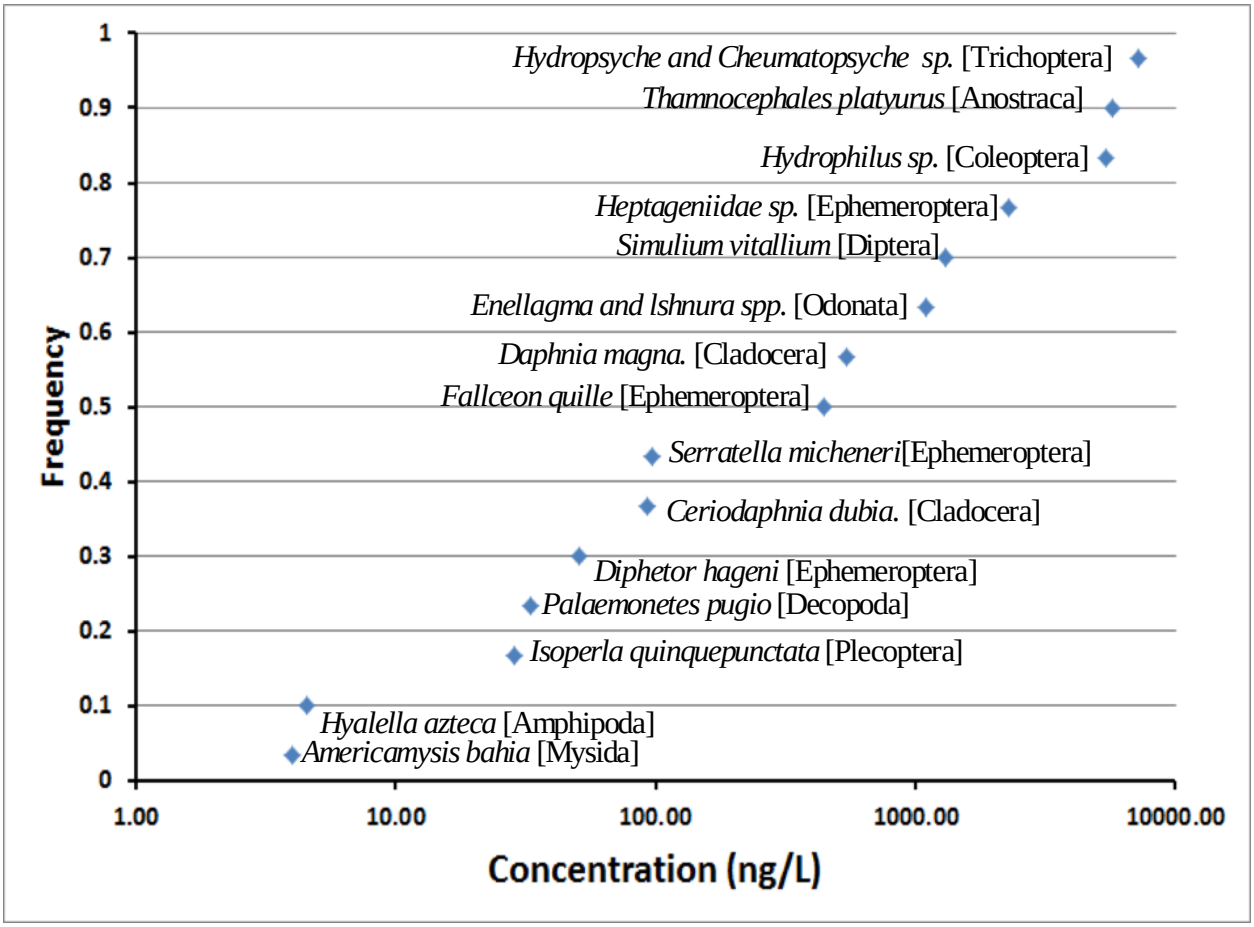


Figure 8: Acute LC_{50} Values for Aquatic Arthropods

See Table 21 for data.
See Section 4.1.3.3.1 for discussion.

Appendix 1: Toxicity to mammals.

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A1 Table 1: Acute Oral LD_{50} Values

Organism	Exposure	Response	Reference
Gavage			
Rats, Wistar, 9 weeks old, 5/dose/sex	TGAI, 99.2% a.i. Single doses: 0, 50, 79, and 125 mg/kg bw. Observation to 14 days.	LD_{50}s: Males: 66.19 (54.48-77.90) mg/kg bw Females: 91.89 (26.67-316.83) mg/kg bw All deaths within 24 hours of dosing.	Tiwari 2002a MRID: 456544-04 Acceptable Not cited in U.S. EPA/OPP/HED 2012a
Rats, Sprague-Dawley, young adults	TGAI, 91.4% a.i. Single doses: 20, 40, 60, 80, 90, or 100 mg/kg	LD_{50} values: Males: 70.1 (± 13.04) mg/kg Females: 53.8 (± 4.92) mg/kg Clinical signs of toxicity included death, clonic convulsions, tremors, ataxia, loss of muscle control, decreased activity, chromorhinorrhea, chromodacryorrhea and oral discharge. Signs were observed from 3 hours to 5 days after dosing. Weight of surviving rats increased over the course of the study.	Freeman et al. 1983a MRID: 00132519 Summarized in U.S. EPA/OPP/HED 2012a and Soderlund et al. 2002 Toxicity Category II
Rats, Sprague-Dawley, young adults	FMC 54800, 2EC, 26.5% w/w a.i. (2 lb/gal a.i.), 100, 150, 200, 250, 300, or 400 mg/kg	LD_{50} values: Males: 265 (± 26.2) mg/kg Females: 262 (± 39.9) mg/kg Clinical signs of toxicity included death, clonic convulsions, tremors, ataxia, decreased activity, chromorhinorrhea, and oral discharge. Signs were observed from 3 hours after dosing and mainly during first 24 hours. Weight of surviving rats increased over the course of the study. Gross necropsy showed blood filled intestines (which appeared to be dose related in both sexes) in eight animals that died during the study.	Freeman et al. 1983f No MRID in DER Not summarized in U.S. EPA/OPP/HED 2012a Toxicity Category II

See Section 3.1.4 for general discussion.

A1 Table 2: Acute Sublethal Toxicity Studies

Organism	Exposure	Response	Reference
Gavage			
Rats, Long-Evans, male, 4- per group	Bifenthrin, 98% Single gavage dose of 0, 0.1, 1, 2, 4, 6, 8, 12, 16 mg/kg) with assays at 4 hours post-dosing Single gavage dose of 0.05, 0.5, 1, 3, 4.5, 6, 9 mg/kg) with assays at 7 hours post-dosing	Dose-dependent decrease in body locomotor activity. See Figure 3 of paper. Concentrations of bifenthrin in brain correlated better with decrease in activity than did concentrations in blood.	Scollon et al. 2011
Rats, Long-Evans, male, 55-57 days old, 8-18 animals/group (NOS)	Bifenthrin, 89% a.i. (100% 1R cis). Gavage, 1 mL/kg corn oil. 9 sublethal doses from 0.03-28 mg/kg bw.	Dose-dependent decrease in motor activity. ED_{30}: 3.21 (2.59-3.83) mg/kg bw NOAEC: 1.28 mg/kg bw LOAEC: 12 mg/kg bw	Wolansky et al. 2006 Also cited in Wolansky et al. 2009 **This is the study used by U.S. EPA/OPP/ HED 2012a to derive the acute RfD which is also applied to longer-term exposures.**
Rats, Long-Evans, male, 55-58 days old	Bifenthrin, 89% a.i. (99% 1R cis). Gavage, 1 or 5 mL/kg corn oil. Doses from 0.1-26 mg/kg bw (see Table 1 of paper for details). Assays conducted at 3 separate laboratories.	Dose-dependent decrease in motor activity. EC_{30} values varied with time after dosing, laboratory and dosing volume ≈ 4-6 mg/kg bw at 1 mL/kg at 4 hours post dosing ≈ 5-8 mg/kg bw at 1 mL/kg at 7 hours post dosing ≈ 11-12 mg/kg bw at 5 mL/kg at 4 hours post dosing ≈ 8-13 mg/kg bw at 5 mL/kg at 7 hours post dosing See Figure 3 of paper for details. Overall average ED_{30} for motor activity: 4.6 mg/kg at 1 mL/kg dose volume Overall average ED_{30} for standard functional observational battery: 5.5 mg/kg at 1 mL/kg dose volume	Wolansky et al. 2007
Rats, Sprague-Dawley, young adult males (10/dose group)	Bifenthrin, Gavage, 0, 40, or 55 mg/kg in corn oil (1 mL/kg)	BMD_{L20} = 0.4 mg/kg BMD_{20} = 14.3 mg/kg based on multiple FOB changes	Weiner/WIL Study 2009 Summarized in U.S. EPA/OPP/HED 2012a

Organism	Exposure	Response	Reference
Rats, Sprague-Dawley, 10/sex/dose group	TGAI, 93.7% a.i., Single gavage doses: 0, 10, 35, or 75 mg/kg or (0, 9.4, 32.8, or 70.3 mg/kg bw)	o treatment-related differences were observed in body-weights, body-weight gains, gross observations or neuropathological examinations in any treated group (the latter only examined in control and high dose groups). No treatment-related findings were observed at 10 or 35 mg/kg. OAEL = 32.8 mg/kg/day OAEL = 70.3 mg/kg/day based on clinical signs of toxicity, FOB findings, altered motor activity, and mortality (females only)	MRID 44862102 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012 **Basis of acute RfD in U.S. EPA/OPP/ EFED 2010a.**
Intraperitoneal			
Rats, Sprague-Dawley, 21-26 days old	Bifenthrin (99.5%). Intraperitoneal doses of 0, 0.5 and 5 mg/kg bw doses in corn oil. After 48 hours, injection of human chorionic gonadotropin hormone to induce ovulation.	At high dose, a significant inhibition of human chorionic gonadotropin inducible gene expression.	Liu et al. 2011b

A1 Table 3: *In Vitro* Studies

System	Exposure	Response	Reference
Human ovarian carcinoma cell line, human estrogen receptor.	Bifenthrin (NOS)	Estrogen antagonism (Figure 3 of paper). In discussion, authors contribute lack of estrogen agonist activity to lack of metabolism in test system. See fish data for *in vivo* agonist activity.	Brander et al. 2012
Mice cerebro-cortical neuron culture	95% a.i.	Only a modest increase in sodium influx but not a significant concentration response relationship. Less potent than most other pyrethroids tested.	Cao et al. 2011a
Mice cerebro-cortical neuron culture	95% a.i.	Concentration dependent increase in calcium influx. EC_{50}: 7.95 µM (3.362 mg/L) Less potent than most other pyrethroids tested.	Cao et al. 2011b
Rat brain synaptosomes	Technical grade	Low potency (NOS) for calcium influx.	Clark and Symington 2008
Human CD4+ H9, and Jurkat cell lines	Technical grade (NOS)	Reduced cell viability at 10^{-4}M (≈0.042 mg/L). Stimulation of T-cell response (inflammation). Authors speculate on link to asthma. `Working Note: A link to asthma and other allergic responses not confirmed by U.S. EPA/OPP 2009.`	Hoffman et al. 2006
Human amnion epithelial cells	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	In various assays for cytotoxicity (levels of reactive oxygen species) and genotoxicity (comet assay), the [S] enantiomer was more toxic than [R] enantiomer at concentrations above threshold (7.5 mg/L).	Liu et al. 2008b China
human hepatocellular liver carcinoma cells (Hep G2)	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	Based on assays for cytotoxicity (including apoptosis), [S] enantiomer more toxic than [R] enantiomer. Activity may be mediated by MAPK signaling pathway.	Liu et al. 2009 China
Rat ovarian granulosa cells	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	Synthesis progesterone and prostaglandin E2 decreased by [S] enantiomer but not by [R] enantiomer. Response apparently mediated via protein kinase C.	Liu et al. 2011a China
Rat ovarian granulosa cells	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	Decrease in levels of mRNA luteinizing hormone-inducible genes.	Liu et al. 2011b China
Rat PC12 cells	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	[S] enantiomer more active than [R] enantiomer in induction of mRNA levels associated with superoxide dismutase, glutathione transferase, and catalase (Figure 2 of paper). All response indactive of greater oxidative stress associated with [S] enantiomer.	Lu 2013 China

System	Exposure	Response	Reference
Rat PC12 cells	cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers	Changes in several parameters indicative of oxidative stress. The [S] enantiomer was more toxic than [R] enantiomer.	Lu et al. 2011 China
Rat PC12 (nerve precursor) cells	Bifenthrin (NOS) 24 hours after application of nerve growth factor	No cytotoxicity at concentrations up to 10^{-4}M (42.29 mg/L). Retraction of neurites at 10^{-5}M (4.229 mg/L) in almost all cells by 48 hours after dosing. Authors speculate on a possible risk of neurodegenerative diseases (Alzheimers and Parkinsons disease). No supporting epidemiology.	Nandi et al. 2006
A549 (human lung adenocarcinoma) cell line	98% a.i.	Reduced responses to various stress proteins at concentrations of 75-400 mg/L. Talstar formulation was somewhat more toxic with LOECs of 1-100 mg/L. A Kiros EV formulation was much more toxic with LOECs of 0.5-3 mg/L.	Skandrani et al. 2006 France
Rat PC12 (nerve precursor) cells	Bifenthrin technical grade. Purity not specified	No cytotoxicity at concentrations up to 10^{-3}M (422.9 mg/L). Inhibition (35%) of normal nerve cell growth at concentrations as low as 10^{-3}M (0.4229 mg/L). A formulation (Ortho Home Defense) was much more toxic.	Tran et al. 2006
Human breast carcinoma cell line MCF-7 (endocrine assay)	cis-bifenthrin (99.5%) with enantiomers separated	1S-cis- bifenthrin more toxic than 1R-cis-bifenthrin based on cell proliferation.	Wang et al. 2007 China
Human cervical carcinoma (Hela) and Chinese Hamster ovary (CHO) cells	cis-bifenthrin, 99.5%	EC50s for cytotoxicity/cell death Hela cells: 4.0×10^{-5} M (≈0.017 mg/L) CHO cells: 3.2×10^{-5} M (≈0.014 mg/L)	Wang et al. 2009b China
Rat cerebro-cortical neuron culture	98% a.i.	Apparent interactions of both closed and open sodium channels – i.e., mixed Type I and Type II activity.	Yang and Li 2015
Human breast carcinoma cell line MCF-7 (endocrine assay)	cis-bifenthrin (99.5%) with enantiomers separated	1S-cis- bifenthrin more toxic than 1R-cis-bifenthrin based on cell proliferation, cell viability, apoptosis. 1S-cis- bifenthrin displayed significantly great estrogenic activity at 10^{-9} M ($4.2\text{x}10^{-6}$ mg/L) to 10^{-5} M (0.0042 mg/L). See Figure 1B of paper.	Zhao et al. 2010
Macrophage cells (RAW264.7) (immune assay)	cis-bifenthrin (99.5%) with enantiomers separated	No significant difference in viability between 1S and 1R enantiomers at concentrations of 10^{-6}M and less. At 10^{-5}M, the S-enantiomer was modestly more toxic (Figure 3B of paper)	Zhao et al. 2010

System	Exposure	Response	Reference
JEG-3 choriocarcinoma cells (estrogen receptor model)	cis-bifenthrin (99.5%) with enantiomers separated	Significant cytotoxicity (inhibition of proliferation at 5×10^{-6} with S-enantiomer somewhat more potent than R-enantiomer over 96 hour period (Figure 1 of paper). S-enantiomer more potent in inducing progesterone (Figure 2 of paper) and significant stimulation of progesterone receptor and human leukocyte antigen G genes.	Zhao et al. 2014

A1 Table 4: Subchronic and Chronic Toxicity Studies

Organism	Exposure	Response	Reference
Gavage			
Rats, Wistar, 150-250g	Biflex formulation (2.5% a.i.) 5.8 mg a.i./kg bw/day for 20 days or 30 days.	Significant change in the blood levels of several indices of oxidative stress – i.e., increases in malondialdehyde and superoxide dismutase as well as decreases in catalase, glutathione S-transferase, glutathione peroxidase, and glutathione S-transferase. See Table 1 of paper.	Dar et al. 2013 India
Rats, 5 per group, one group	Talstar, 10% EC, ICI Agro Chemicals, UK 0.5 mg/day for 21 days.	Significant decrease (≈13%, $p<0.01$) in body weight (Table 1). Significant decrease in T3 and T4 (Figures 1 and 2) and significant increase in thyroid stimulating hormone (Figure 4).	Akhtar et al. 1996 Pakistan
Dietary			
Mice, young (4 weeks old), n=21	Bifenthrin (NOS), mixed in basal diet at 10 or 20 mg/kg diet for 3 weeks.	High Dose: Decrease (N.S.) in body weight. Significant decrease in absolute and relative thymus weight and absolute spleen weight (Table 2 of paper). Significant increases mRNA of some genes (TNF and IL2 in spleen and IL2 in thymus) associated with immune response (Figures 2 and 3 of paper). Significant decreases in total antioxidant capacity and superoxide dismutase activity as well as decrease in glutathione peroxidase. Significant increase in liver glutathione (Table 3 of paper).	Jin et al. 2014 China
Mice, adult (7 weeks old) , n=21	Bifenthrin (NOS), mixed in basal diet at 10 or 20 mg/kg diet for 3 weeks.	No effect on body weight or weights of spleen and thymus at either dose. High dose: Significant increases mRNA of one gene (IL2 in thymus) associated with immune response (Figure 3). Significant increase in liver glutathione (Table 3 of paper).	Jin et al. 2014 China
Rats (NOS)	Bifenthrin (NOS) Doses: 0, 0.88, 3.8, 7.5, or 15 mg/kg/day (M); 0, 1.04, 4.3, 8.5, or 17.2 mg/kg/day (F) for 90 days	NOAEL = 3.8 mg/kg/day (males); 4.3 mg/kg/day (females) LOAEL = 7.5 mg/kg/day (males), 8.5 mg/kg/day (females), based on increased incidence of tremors.	MRID 00141199 Summarized in U.S. EPA/OPP/HED 2012a; von Stackelberg 2012

Organism	Exposure	Response	Reference
Dogs, purebred beagles, 22- to 26-weeks-old, 20 males, 20 females, 4/sex/group	TGAI, 88.35% a.i., repeated daily dose (gelatin capsules) for 90 days Nominal doses of 0, 2.5, 5, 10, or 20 mg/kg Recalculated doses based on a.i. of 2.21, 4.42, 8.84, or 17.7 mg/kg/day a.i.	NOAEL = 2.21 mg/kg/day (males and females) LOAEL = 4.42 mg/kg/day (males and females) based on increased incidence of tremors.	Serota 1984 MRID 00141200 Summarized in U.S. EPA/OPP/HED 2012a
Dogs (NOS)	Bifenthrin (NOS), repeated daily doses of 0, 0.66, 1.3, 2.7. or 4.4 mg/kg/day 52 week	NOAEL = 1.3 mg/kg/day LOAEL = 2.7 mg/kg/day based on increased incidence of tremors Working Note: This study appears to be the same study as Accession No. 264637, summarized below. HED cites a 1985 study. The difference in doses may reflect a reanalysis by HED.	MRID 00163065 Summarized in U.S. EPA/OPP/HED 2012a, U.S. EPA 1988a,b, and von Stackelberg 2012. **Basis for chronic RfD in U.S. EPA/OPP/HED 2010a.**
Dogs, beagles, 4 dogs/sex/dose	Bifenthrin (NOS), repeated daily doses of 0, 0.75, 1.5, 3.0 or 5 mg/kg/day 52 week	NOAEL = 1.5 mg/kg/day LOAEL = 3.0 mg/kg/day based on intermittent tremors from Week 15 o 23. In high dose group, tremors from Week 15 to Week 29. No tremors beyond Week 29.	Accession No. 264637 cited to FMC Corporation. 1985. Summarized in U.S. EPA 1988a,b. **Basis for chronic RfD in U.S. EPA 1988b (IRIS).**
Rats (NOS)	Bifenthrin (NOS), repeated daily doses: 0, 0.6, 2.4, 4.7, or 9.7 mg/kg/day (males) 0, 0.7, 3.0, 6.1, or 12.7 mg/kg/day (females)	NOAEL = 3.0 mg/kg/day (females); 4.7 mg/kg/day (males) LOAEL = 6.1 mg/kg/day (females), based on increased incidence of tremors; 9.7 mg/kg/day (males), based on increased incidence of tremors. Carcinogenicity - No conclusive evidence of carcinogenic potential. **Classification: Acceptable-Guideline**	MRID 00157226 Summarized in U.S. EPA/OPP/HED 2012a; von Stackelberg 2012
Mice (NOS)	Bifenthrin (NOS) repeated daily doses: 0, 6.7, 25.6, 65.4, or 81.3 mg/kg/day (males) 0, 8.8, 32.7, 82.2, or 97.2 mg/kg/day (females)	NOAEL = 6.7 mg/kg/day (males); 8.8 mg/kg/day (females) LOAEL = 25.6 mg/kg/day (males) and 32.7 mg/kg/day (females), based on increased incidence of tremors. Carcinogenicity: carcinogenic potential was evidenced by a dose-related increase in the incidence of hemangiopericytoma in the urinary bladder, a significant dose-related trend for combined hepatocellular adenomas and carcinomas in males, and a significantly higher incidence of combined lung adenomas and carcinomas in females. **Classification: Acceptable-Guideline**	MRID 00157227 Summarized in U.S. EPA/OPP/HED 2012a; von Stackelberg 2012

Organism	Exposure	Response	Reference
Rats, Sprague-Dawley, 10/sex/dose group	TGAI, 93.7% a.i. Dietary doses of 50, 100, or 200 ppm; equivalent to 0, 2.7, 5.6, or 11.1 mg/kg/day (M); 0, 3.5, 6.7, or 13.7 mg/kg/day (F)	No treatment-related differences were observed at any dose level in body-weights, bodyweight gains, food consumption, home cage FOB examination, motor activity measurements, or gross or neuropathological examinations. NOAEL = 2.7 mg/kg/day (males); 3.5 mg/kg/day (females) LOAEL = 5.6 mg/kg/day (males); 6.7 mg/kg/day (females) based on neuromuscular findings (tremors, changes in grip strength, and landing foot-splay) in both sexes.	MRID 44862103 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012
Intraperitoneal			
Mice, Swiss albino, female, 18-24 g, 8 per dose	Bifenthrin (99%). Intraperitoneal doses of 0, 4, and 8 mg/kg bw/day for 28 days.	Impaired response in memory assay (step-through passive avoidance task) on Day 2. Differences not significant on Days 7, 14, 28. Decrease locomotion. Significant but slight decreases in body weight (Figure 7). High Dose: Significant ($p<0.05$) increases in white blood cell counts, ALT, and superoxide dismutase activity. Decrease in glutathione peroxidase activity. Low Dose: Significant increase in white blood cell counts.	Nieradko-Iwanicka et al. 2015

See Section 3.1.5 for discussion.

A1 Table 5: Reproductive and Developmental Studies

Species	Exposure	Response	Reference
Developmental			
Mice, female, ICR	cis-bifenthrin with enantiomer resolution. 15 mg/kg bw either before or during pregnancy	1S-cis-bifenthrin significantly reduced transcription of genes associated with testosterone production in male offspring when females were dosed during but not prior to pregnancy.	Jin et al. 2013a China
Rats, Sprague-Dawley, 25 per dose	Bifenthrin (NOS) Gavage doses: 0, 0.5, 1, and 2 mg/kg bw/day on Days 6-15 of gestation.	Intermittent tremors at 2 mg/kg bw/day. No adverse effects on developmental parameters noted. No effects at doses of 1 mg/kg bw/day or below.	McCarty et al. 2002 [Abstract only]
Rats, Sprague-Dawley, 25 per dose	Bifenthrin (NOS) Dietary doses: 0, 30, 90, and 200 ppm on Days 6-20 of gestation. 200 ppm = 16.3 mg/kg bw/day 90 ppm = 7.4 mg/kg bw/day	200 ppm: Tremors and other signs of neurotoxicity. Decreased maternal body weights and food consumption. No effects on developmental parameters. 90 ppm: No effects `Working Note: The comparison of matched gavage and dietary exposures illustrates standard increased toxicity associated with bolus exposures.`	McCarty et al. 2002 [Abstract only]
Rats, Sprague-Dawley, mated females, 10/sex/dose group	TGAI, 88.35% a.i. in corn oil Gavage doses: 0, 0.5, 1.0, 2.0, or 2.5 mg/kg/day equivalent to 0, 0.44, 0.88, 1.77 or 2.2 mg/kg/day on days 6-15 of gestation (*`range-finding study`*)	Maternal NOAEL = 0.88 mg/kg/day LOAEL = 1.77 mg/kg/day based on sporadic tremors during gestation days 7-18 Developmental NOAEL= 0.88 mg/kg/day LOAEL was not established (fetuses were not examined)	MRID 00154482 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012
Rats, Sprague-Dawley, pregnant females, 25/dose group	TGAI, 88.35% a.i. in corn oil Gavage doses: 0, 0.5, 1.0, 2.0, or 2.5 mg/kg/day equivalent to 0, 0.44, 0.88, 1.77 or 2.2 mg/kg/day on days 6-15 of gestation Positive control: aspirin in 2% Carboxymethyl-cellulose	Maternal toxicity was characterized as tremors in 18/25 dams at 1.77 mg/kg/day during days 10-19. There were no deaths during the study, and no significant differences between groups or dose-related trends with respect to mean maternal bodyweight gains or food consumption were noted Maternal NOAEL = 0.88 mg/kg/day LOAEL = 1.77 mg/kg/day based on the incidence of tremors during gestation. Developmental NOAEL = 0.88 mg/kg/day LOAEL = 1.77 mg/kg/day based on increased fetal and litter incidence of hydroureter without nephrosis.	MRID 00141201 Summarized in U.S. EPA/OPP/HED 2012a and in von Stackelberg 2012

Appendix 1: Toxicity to mammals *(continued)*

Species	Exposure	Response	Reference
Rats, Sprague-Dawley, CD	TGAI, 95.3% a.i. Dietary doses: 0, 30, 60, 90, or 200 ppm, equivalent to 0, 2.4, 4.8, 7.1, or 15.5 mg/kg/day on days 6-20 of gestation	No treatment-related developmental findings were noted at any dose tested. Maternal NOAEL = 7.1 mg/kg/day LOAEL = 15.5 mg/kg/day based on clinical signs and decreased food consumption, body weight gains, and body weight gains adjusted for gravid uterine weight. Developmental NOAEL = 15.5 mg/kg/day LOAEL = not observed.	MRID 45352301 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012
Rats, Sprague-Dawley, females, 25/dose group	TGAI, 94.8% a.i. Doses: 0, 3.6, 7.2, or 9.0 mg/kg/day (gestation); 0, 8.3, 16.2, or 20.7 mg/kg/day (lactation)	No dams died during the study, and maternal body-weight, body-weight gain and food consumption were unaffected by treatment. Maternal NOAEL = 3.6 mg/kg/day during gestation and 8.3 mg/kg/day during lactation LOAEL = 7.2 mg/kg/day during gestation and 16.2 mg/kg/day during lactation based on clinical signs of neurotoxicity (tremors, clonic convulsions, and increased grooming counts) evelopmental NOAEL = 3.6 mg/kg/day during gestation and 8.3 mg/kg/day during lactation. evelopmental LOAEL = 7.2 mg/kg/day during gestation and 16.2 mg/kg/day during lactation based on clinical signs of neurotoxicity (increased grooming counts).	MRID 46750501 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012
New Zealand white rabbits, pregnant females, 20/dose group	TGAI, 88.35% a.i. in corn oil Gavage doses: 0, 2.67, 4.0, or 8.0 mg/kg/day, equivalent to 0, 2.36, 3.5, or 7 mg/kg/day on days 7-19 of gestation	here was no developmental toxicity demonstrated at any dose level. laternal NOAEL= 2.36 mg/kg/day OAEL = 3.5 mg/kg/day based on treatment-related incidence of head and forelimb twitching evelopmental NOAEL = 7 mg/kg/day OAEL not observed	MRID 00145997 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012

Species	Exposure	Response	Reference
Reproduction			
Rats, Sprague-Dawley, 8-weeks-old, 25/sex/dose group	TGAI, 88.35% a.i., Dietary doses: 0, 30, 60, or 100 ppm (equivalent to 0, 1.5, 3, or 5 mg/kg/day) over two consecutive generations.	No mortality was observed; at 100 ppm, tremors were observed in 1st generation lactating dams; reduced body-weight gain observed in 1st generation females on days 7 and 14 of lactation period; decreased food consumption observed in 2nd generation males at 100 ppm during a single week of exposure. No treatment-related effects observed on reproductive performance or litter size, litter weight, or survival of offspring. Parental/Systemic Toxicity: NOAEL = 3.0 mg/kg/day (females) and 5.0 mg/kg/day (males) LOAEL = 5.0 mg/kg/day (females), based on tremors and decreased body weight; not observed in males Reproductive/Offspring Toxicity: NOAEL = 5.0 mg/kg/day LOAEL not observed	DeProspo et al. 1986 MRID 00157225 Summarized in U.S. EPA/OPP/HED 2010a; U.S. EPA/OPP/HED 2007b; von Stackelberg 2012

See Section 3.1.9 for discussion.

A1 Table 6: Skin Irritation and Sensitization Studies

Source: U.S. EPA/OPP/HED 2011a unless otherwise specified.

Species	Exposure	Response	Reference
Skin Irritation			
New Zealand white rabbits, young adults, 3 males, 3 females	TGAI, 88.35% a.i., 0.5 mL applied to right-side abraded skin and left-side intact skin with semi-occlusion; test material removed with acetone 4 hours post application	No signs of skin irritation on any animal at any time after dosing.	Freeman et al. 1983c. MRID: 00132521 Summarized in U.S EPA/OPP/HED 2012a Toxicity Category IV
New Zealand white rabbits, young adults, 3 males, 3 females	FMC 54800, 2EC, 26.5% w/w a.i. (2 lb/gal a.i.), 0.5 mL applied to right-side abraded skin and left-side intact skin with no occlusion; test material removed with gauze pad 4 hours post application	No signs of skin irritation on any animal at any time after dosing.	Freeman et al. 1983c. No MRID in DER Not summarized in U.S EPA/OPP/HED 2012a Toxicity Category IV
Skin Sensitization			
Guinea pigs, Hartly, young adult males, n=20	TGAI, 88.35% a.i., 0.5 mL (10 animals); 0.5 mL 0.15% DNCB (10 animals) with occlusion for 6 hours 3x/week until all animals dosed a total of 10 times. Challenge dose applied 14 days after last dose.	No response to challenge dose observed in test animals. Positive controls showed expected response.	Freeman et al. 1983e. MRID: 00132523 Summarized in U.S EPA/OPP/HED 2012a Toxicity Category IV
Guinea pigs, Hartly, young adult males, n=20	FMC 54800, 2EC, 26.5% w/w a.i. (2 lb/gal a.i.), 0.5 mL (10 animals); 0.5 mL 0.15% DNCB (10 animals) with occlusion for 6 hours 3x/week until all animals dosed a total of 10 times. Challenge dose applied 14 days after last dose.	At challenge, seven animals had moderate to severe erythema which had progressed to necrosis in three. Positive controls exhibited the expected response.	Freeman et al. 1983j. No MRID in DER Not summarized in U.S EPA/OPP/HED 2012a

See Section 3.1.11 for discussion.

A1 Table 7: Eye Irritation Studies

Species	Exposure	Response	Reference
New Zealand white rabbits, young adults, 3 males, 6 females	TGAI, 88.35% a.i., 0.1 mL applied to right eye of each rabbit; eyes of three rabbits washed with 100 mL tap water 20-30 seconds post application; eyes of remaining six rabbits went unwashed.	At 1 hour post dosing, unwashed eyes showed mild conjunctival redness; all nine treated eyes showed severed discharge; all eyes were normal at 24 hours and remained normal at 72 hours.	Freeman et al. 1983d. MRID: 00132522 Summarized in U.S EPA/OPP/HED 2012a Toxicity Category IV
New Zealand white rabbits, young adults, 9 females	FMC 54800, 2EC, 26.5% w/w a.i. (2 lb/gal a.i.), 0.1 mL applied to right eye of each rabbit; eyes of three rabbits washed with 100 mL tap water 20-30 seconds post application; eyes of remaining six rabbits went unwashed.	At 1 hour post dosing, mild conjunctival redness appeared in all unwashed eyes, mild to moderate chemosis in all eyes and a severe discharge in all eyes. The redness persisted through 48 hours, the chemosis through 48 hours, and the discharge through 24 hours. All eyes were normal at 48 hours.	Freeman et al. 1983i. No MRID in DER Not summarized in U.S EPA/OPP/HED 2012a Toxicity Category III

See Section 3.1.11.3 for discussion.

A1 Table 8: Acute and Repeated Dose Dermal Toxicity

Species	Exposure	Response	Reference
Acute			
Rats, Wistar, 9 weeks old, 5/sex	TGAI, 99.2% a.i., 2000 mg/kg bw (limit test) with occlusion	LD_{50}s: >2000 mg/kg bw (both sexes) No mortalities. Tremors in 9/10 on Day 3. Tremors with piloerection in 2/10 on Day 4-5. All rats normal on Days 6-14.	Tiwari 2002b MRID: 456544-05 Acceptable Not cited in U.S. EPA/OPP/HED 2012a
New Zealand white rabbits, young adults, 5 males, 5 females	TGAI, 88.3% a.i., 2000 mg/kg applied under gauze pad and covered with plastic	LD_{50} >2000 mg/kg No mortality No compound related toxicity. Erythema at application site in all rabbits at 24 hours; desquamation in four rabbits on day 24; no compounded related effects seen on necropsy.	Freeman et al. 1983b. MRID: 00132520 Summarized in U.S EPA/OPP/HED 2012a Toxicity Category III
New Zealand white rabbits, young adults, 5 males, 5 females	FMC 54800, 2EC, 26.5% w/w a.i. (2 lb/gal a.i.), 2000 mg/kg applied to shaved skin under gauze pad and covered with plastic sheet for 24 hours, then removed with guaze pad.	LD_{50} >2000 mg/kg No mortality No compound related toxicity. Dermal irritation including erythema, dehydration, fissuring, eschar and exfoliation observed in all treated animals. Eschar and exfoliation present in all rabbits at 14 days.	Freeman et al. 1983g No MRID in DER Not summarized in U.S. EPA/OPP/HED 2012a Toxicity Category III
Repeated Dose			
Rat (NOS)	Bifenthrin (NOS), doses of 0, 23, 47, 93, or 932 mg/kg/day, 6 hours/day, 5 days/week for 21/28 days	NOAEL = 47 mg/kg/day LOAEL = 93 mg/kg/day based on staggered gait and exaggerated hind limb flexion	MRID 45280501 Summarized in U.S. EPA/OPP/HED 2010a; von Stackelberg 2012; FAO 2012
New Zealand white rabbits, adults, 2.0 – 3.0 kg, 6/sex/dose	TGAI, 88.35% a.i., applied to shaved backs at doses of: 0, 25, 50, 100, or 500 mg/kg/day (equivalent to 0, 22, 44, 88, or 442 based on bw) for 6 hours/day for 21 consecutive days. Test material removed first with acetone wetted gauze pad and then with water-wetted pad.	NOAEL = 88 mg/kg/day LOAEL = 442 mg/kg/day based on loss of muscle coordination and increased incidence of tremors.	Seaman et al. 1984 MRID 00141198 Summarized in U.S. EPA/OPP/HED 2010a; von Stackelberg 2012

See Section 3.1.12 for discussion.

A1 Table 9: Acute Inhalation Toxicity

Species	Exposure	Response	Reference
Rat, males and females (NOS)	TGAI, 94.8% a.i., 4-hour nose only exposure to 0.56, 0.99, or 2.3 mg/L	LC_{50}: 1.10 mg/L males 1.01 mg/L combined 0.8 mg/L females Heated to 100° C for testing	MRID 46008101 Summarized in U.S. EPA/OPP/HED 2012a and FAO 2012
Rats, Sprague-Dawley, young adult	FMC 54800 2EC formulation (NOS), 4-hours, mean measured concentrations of 1.82 mg/L to 4.98 mg/L (9 concentrations used).	LC_{50}: 1.943 mg/L males 1.861 mg/L females Signs of neurotoxicity included tremors and loss of hind limb motor control. **Working Note: The composition of the formulation is not specified and it is not clear if the LC_{50} values are expressed in units of formulation or a.i.**	Maedgen 1983
Rats, NOS	FMC 54800 100 g/L formulation (NOS), 4-hours, nominal concentrations of 2.20 mg/L to 5.84 mg/L (5 concentrations used).	LC_{50}: 4.943 mg/L males and females combined. **Working Note: The composition of the formulation is not specified and it is not clear if the LC_{50} value is expressed in units of formulation or a.i.**	Maedgen 1984

See Section 3.1.13 for discussion.

Appendix 2: Toxicity to birds

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A2 Table 1: Acute Oral/Gavage Toxicity to Birds

Species	Exposure	Response	Reference[1]
Bobwhite quail (*Colinus Virginianus*), 5/sex	TGAI, 88.35% a.i. in corn oil Gavage doses: 0, 464, 681, 1000, 1470, or 2150 mg/kg 21 day observation period.	LD_{50} = 1800 mg/kg bw	MRID 132532 U.S. EPA/OPP/ EFED 2012a, Appendix F, p. 4 Summarized in FAO 2012
Mallard *Duck* (*Anas platyrhynchos*), 10/dose group	TGAI, 88.35% a.i. in corn oil Gavage doses: 0, 1470 or 2150 mg/kg 21 day observation period.	LD_{50} = 2150 mg/kg bw	MRID 132534, EFED 2012a, Appendix F, p. 4-5 Summarized in FAO 2012

A2 Table 2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference[1]
Bobwhite quail (*Colinus Virginianus*), 10/dose group	TGAI, 88.35% a.i. in corn oil Dietary doses: 0, 312, 625, 1250, 2500, or 5000 ppm for 5 days; birds maintained on plain feed for 3-day recovery period	8-day LC_{50} = 4450 ppm Equivalent mg/kg bw dose [1]: LD_{50}: ≈1335 mg/kg bw	MRID 132533, EFED 2012a, Appendix F, p. 5. Summarized in FAO 2012
Mallard Duck (*Anas platyrhynchos*), 10/dose group	TGAI, 88.35% a.i. in corn oil Dietary doses: 0, 312, 625, 1250, 2500, or 5000 ppm for 5 days; birds maintained on plain feed for 3-day recovery period	8-day LC_{50} = 1280 ppm Equivalent mg/kg bw dose [1]: LD_{50}: ≈512 mg/kg bw	MRID 132535, EFED 2012a, Appendix F, p. 5. Summarized in FAO 2012
Domestic *chicken* (*Gallus gallus*). 2-weeks-old, 10/dose group	Talstar 10 EC: 100 mg/kg/day for 7 days or 50 mg/kg/day for 30 days by intubation.	<u>100 mg/kg/body weight (7 days)</u>: 13% mortality within 24 hours; 20% mortality by day 7. Decreases in concentrations of AkP (55%), AcP (17%), GOT (43%), GPT (72%), and glycogen (33%) in gastrocnemius muscles Increases in LDH activity (100%) and DNA content (27%) in gastrocnemius muscles <u>50 mg/kg/day (15 days)</u>: Increases in concentrations of AkP (24%), GPT (50%), LDH activity (20%), protein (11%), glycogen (24%), and RNA (44%) in gastrocnemius muscle <u>50 mg/kg/day (30 days)</u>: Mortality: 24% Decreases in muscle protein (25%), glycogen (18%), and RNA (38%).	Shakoori et al. 1993 Pakistan

[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.

A2 Table 3: Reproductive and Subchronic Toxicity to Birds

Species	Exposure	Response	Reference[1]
Reproduction			
Bobwhite quail (*Colinus Virginianus*), 10/sex/dose group	TGAI, 88.35% a.i. Dietary dose levels: 0, 25, 50, or 75 ppm for 24 weeks (12 weeks prior to start of egg production and 12 weeks during egg production)	NOAEC = 75 ppm Equivalent mg/kg bw dose [1]: NOAEC: ≈5.25 mg/kg bw No treatment-related effects were observed for body weight, food consumption, chick mortality, egg production, numbers of cracked or broken eggs, egg shell thickness, or embryo mortality.	MRID 163097, EFED 2012a, Appendix F, p. 5. Summarized in FAO 2012
Mallard *Duck* (*Anas platyrhynchos*) 2 males and 4 females/dose group	TGAI, 88.35% a.i. Dietary dose levels: 0, 25, 50, or 75 ppm for 24 weeks (12 weeks prior to start of egg production and 12 weeks during egg production)	NOAEC = 75 ppm Equivalent mg/kg bw dose [1]: NOAEC: ≈5.25 mg/kg bw No treatment-related effects were observed for egg production, number of cracked or broken eggs, shell thickness or chick survival	MRID 163099, EFED 2012a, Appendix F, p. 5. Summarized in FAO 2012

[1] Dietary concentrations (ppm) 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).

Appendix 3: Toxicity to Terrestrial Invertebrates.

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General Notes on Appendix 3:

Unless otherwise specified, U.S. EPA/OPP/EFED (2012a) is references as EFED 2012a.

Values in parentheses are 95% confidence limits unless otherwise specified.

References to tables or figures typically refer to the tables or figures in the paper being addressed. Cross references to tables within this appendix are always made with reference to this appendix – e.g., "Table A3-2".

Subspecies and varieties are given in the first column of the tables when specified in the papers.

NOTE: Unlike other appendices, the doses/concentrations are identical to those given the cited publications in both the Exposure and Response columns. Take particular care when developing comparisons to the units of exposure or dosing. For dose conversions, note that ng/mg = µg/g = mg/kg.

A3 Table 1: Toxicity to Bees

Species	Exposure	Response	Reference
Lethality			
Apis mellifera	Bifenthrin, 0.8% EC	96-hour-LD_{50}: 0.015 µg/bee Approximate dose [1] = 0.015 µg/bee ÷ 0.116 g ≈ 0.13 µg/g bw (mg/kg bw) Working Note: This value is referenced to Atkins 1981. A full citation for this reference has not been located in the EFED risk assessment and supporting files. Rounding to two significant places, this toxicity value is identical to Atkins and Kellum 1981 as summarized below.	EFED 2012a, p. 19, and p. 142, as well as Appendix J, p. 6 Acceptable "Very highly toxic"
Apis mellifera Contact assay	Bifenthrin, 0.8 EC	LD_{50}: 0.01462 µg/bee Approximate dose [1] = 0.01462 µg/bee ÷ 0.116 g ≈ 0.13 µg/g bw (mg/kg bw) Working Note: DER does not contain many details.	Atkins and Kellum 1981 Cleared review.

Species	Exposure	Response	Reference
Apis mellifera ligustica 3 replicates, 20 bees/replicate per concentration.	FMC 2.5 EC Oral exposure in 1:1 sucrose:water vehicle Concentrations: 4.0, 7.9, 15.5, 30.6, and 60.2 mg a.i./L. Observations at 48 hours.	LC_{50}: 16.7 (12.4-22.6) mg/L LC_{05}: 6.9 (3.0-9.9) mg/L	Dai et al. 2010 China
Apis mellifera Worker bees, 6 replicates per dose, 10 bees per replicate	Topical, acetone solvent Concentrations [n=6] not specified. With or without oral exposure to tablets containing fluvalinate (miticide).	Alone: LD_{50}: 0.034 (0.023-0.058) µg/µL In combination with fluvalinate (miticide): LD_{50}: 0.018 (0.016-0.020) µg/µL Working Note: Table 1 specifies that the units of LD_{50} are µg/µL. These values are referenced as LD_{50}s but should be LC_{50}s. Note that the LC50s are comparable to Dai et al. 2010 – i.e., 34 mg/L vs 16.7 mg/L.	Ellis et al. 1997
Apis mellifera	Bifenthrin (TalstarP, 7.9% a.i.), 10 serial dilutions from 39.5 µg/mL (NOS) Contact assay in bottles coated with different concentrations.	24-minute knockdown EC_{50}: 0.42 µg/mL. 35 µg/mL: 100% mortality at 15 minutes. 0.035 µg/mL: no mortality at 30 minutes. See Table 1 of paper.	Qualls et al. 2012
Sublethal			
Apis mellifera ligustica Five bee colonies (NOS)	FMC 2.5 EC 1:1 sucrose:water vehicle Colony Exposure: 6.9 mg a.i./L (EC_5 for mortality), 400 mL/day x 20 days. Queen Exposure: 6.9 mg a.i./L (EC_5 for mortality), 5 µL every 5 days for 20 days. 3 year observation period (2006-2008). Stored honey removed every 3 days to limit cross exposure.	Decrease in hive fecundity in all 3 years. Slight increases in egg weight and egg development time with decrease in cap rate in first 2 years. Slight decrease in larval weight and hatch rate in 3rd year. Significant decrement in "success rate of development" in all 3 years (i.e., 76-82% of controls). Working Note: The terms "success rate of development" is not a common term in the literature on bee toxicology and is not clearly defined in the paper.	Dai et al. 2010 China
Field Simulation			
Apis mellifera Worker bees in cages.	Capture 2EC, 2 lbs a.i./gallon Applied to seed alfalfa at 0.05, 0.1, and 0.2 lb a.i./acre.	*Capture 2 EC killed 57 to 79% of caged bees at flyover; suppressed foraging 26-28% for 1-2 days; killed 5-19 bees per colony per day for 3 days. Foliar residue (bees confined on treated foliage) mod. to high in toxicity for 1-2 days.* Working Note: DER does not contain many details. Above summary taken from cleared review.	Atkins and Kellum 1986 Cleared review.

Species	Exposure	Response	Reference
Apis mellifera	Bifenthrin (Capture 2 EC, FMC) applied at 0.56 kg a.i./ha (≈0.05 lb a.i./acre) applied to cotton.	Initial residues on cotton leaves of about 0.5 µg/cm^2, dropping rapidly to < 0.1 µg/cm^2 (Figure 1). No statistically significant mortality in bees placed on freshly treated cotton leaves (See Table 2).	Estesen et al. 1992
Apis mellifera	Bifenthrin (TalstarP, 7.9% a.i.), applied to butter daisies (*Melampodium paludosum*) and golden dewdrop (*Duranta erecta*) at 0, 9.7, 19.5, and 29.5 mL/liter of water. Observations at 15 minutes to 24 hours.	No mortality in bees at 24 hours following exposure periods of 15 to 60 minutes. At 9.7 ml/liter, no mortality after 2 weeks in 24-hour exposure group. Working Note: The actual exposures are unclear. The mg/L "*application rates*" may refer to the 39.5 µg/mL stock solutions.	Qualls et al. 2012

[1] Body weight of the bees not reported . Mg/kg bw doses are calculated based on the body weight of 0.116 g or 116 mg from Winston (1987). Note that ng ÷ mg = µg/g = mg/kg.

A3 Table 2: Toxicity to Other Terrestrial Insects

Species	Exposure	Response	Reference
Blattodea			
Reticulitermes flavipes (eastern subterranean termite), workers	Bifenthrin, Talstar, 7.9% a.i. Soil LC_{50} in petri dishes.	3-Day LC_{50} 0.074 (0.056–0.092) mg/kg soil. No substantial increase in mortality by extending the observation period to 7 days.	Peterson 2012a
Reticulitermes flavipes (eastern subterranean termite), workers	Bifenthrin, as Transport formulation (1 : 1.2 acetamiprid : bifenthrin by weight) Note: Acetamiprid is a neonicotinoid.	3-Day LC_{50} in units of bifenthrin: 0.066 (0.051–0.064) mg/kg soil. Working Note: The presence of the neonicotinoid did not substantially impact the LC_{50} for bifenthrin. This is consistent with the observations from Larson et al. (2014) in toxicity of ground beetle.	Peterson 2012b
Coleoptera			
Sphenophorus venatus vestitus (Hunting Billbug), Adult, field collected in low pesticide area. 10 beetles/ replicate, 6 replicates per dose	Bifenthrin (>95%) Topical Observations at 24 hours.	LD_{50}: 542 (457 -942) mg/kg bw Working Note: The above is not a typographical error. See Table 1 of paper. This study is listed in ECOTOX as Reference No. 156768 and the dose unit is correctly listed in ECOTOX as "mg/kg". In U.S. EPA/OPP/EFED (2012a, Appendix H, p. H-60), the dose unit is list as ppm, which is consistent with mg/kg but is ambiguous.	Doskocil et al. 2012
Diabrotica virgifera virgifera (Western corn rootworm) 16 populations. 10 beetles/ replicate, 3 replicates per dose	Bifenthrin (91.3%) Topical Observations at 24 hours.	LD_{50}s for different populations (Table 4 of paper): Low: 0.27 ng/mg bw High: 0.87 ng/mg bw Maximum Resistance Factor: ≈3.2	Meinke et al. 1998
Listronotus maculicollis (Bluegrass weevil) 8 populations,	Bifenthrin (>95%, Sigma-Aldrich) Topical application	LD_{50}s for different populations (Table 1 of paper): Low: 1.8 ng/weevil High: 244.67 ng/weevil Maximum Resistance Factor: ≈136 Working Note: Unable to identify body weight. Working Note: U.S. EPA/OPP/EFED (2012a, p. 144) summarized the lowest LD_{50} from this study as 0.018 µg/organism. As noted above, the correct conversion would be 0.0018 µg/organism.	Ramoutar et al. 2009

Appendix 3: Toxicity to Terrestrial Invertebrates *(continued)*

Species	Exposure	Response	Reference
Tribolium castaneum (red flour beetle)	Bifenthrin formulation from FMC, Pakistan Contact LC_{50} in Petri dishes	LC_{50}s 589 mg/L (PAK malathion resistant strain) 537 mg/L (FSS-II strain malathion tolerant strain). See tables in papers for changes in activity of a large number of enzymes. No consistent pattern in terms of mechanism. Largely descriptive.	Shakoori et al. 1994 Tufail et al. 1994 Pakistan
Hippodamia convergens (Convergent lady beetle) adults	Bifenthrin (94%) Observations at 24 hours. Topical 3 replicates (NOS)	LD_{50}: 6.5 (3.1-16) ng/mg bw	Siegfried 1993
Diptera			
Anopheles gambiae (African malaria mosquito), 50 females/dose	Bifenthrin (91.5% purity, 97% cis-isomer) – i..e. TGAI Topical, 0.1 µL solution	24-hour LD_{50}: 0.15 (0.14-0.16) ng/mg Also gives results for other assays focused on efficacy in applications to treatment of nets with resistant and tolerant strains. Resistance ratios of 2.5 to 3.4 (Table 5).	Hougard et al. 2002
Culex quinque-fasciatus (Southern house mosquito), 50 females/dose	Bifenthrin (91.5% purity, 97% cis-isomer) – i..e. TGAI Topical, 0.1 µL solution	24-hour LD_{50}: 0.16 (0.13-0.19) ng/mg Also gives results for other assays focused on efficacy in applications to treatment of nets with resistant and tolerant strains. Resistance ratios of about 16 to 36 (Table 5).	Hougard et al. 2002
Musca domestica (Housefly) 3rd instar larvae	Bifenthrin (94%) Observations at 24 hours. Topical 3 replicates (NOS)	LD_{50}: 42 (9.1-170) ng/mg bw	Siegfried 1993
Hemiptera			
Bemisia tabaci (whitefly; Aleyrodidae) Adults	Bifenthrin (95% purity) Leaf disc assay Aqueous conc.: 5, 10, 20, 40, 80 and 160 mg a.i./L.	LC_{50}: 52.35 (45.68-62.40) mg a.i./L LC_{10}: 10.02 (7.14-12.89) mg a.i./L	He et al. 2013 China
Bemisia tabaci (whitefly; Aleyrodidae) Adults	Bifenthrin (95% purity) Aqueous conc.: 5, 10 and 40 mg a.i./L.	No significant increase in mortality at 10 mg/L but high and significant mortality at 40 mg/L (Fig. 1). Significant and dose-related decrease in honeydew production (i.e., inhibition of feeding) and egg production at both concentrations (Figs. 2 and 3). Reduction in phloem feeding at 40 mg/L (Fig. 4).	He et al. 2013 China

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Culex quinque-fasciatus</td><td>Bifenthrin (TalstarP, 7.9% a.i.), applied to butter daisies (Melampodium paludosum) and golden dewdrop (Duranta erecta) at 0, 9.7, 19.5, and 29.5 mL/liter of water. Observations at 15 minutes to 24 hours.</td><td>29.5 mg/L: 100% mortality rate up to 4 weeks.
19.5 mg/L: 100% mortality rate up to 2 weeks, partial mortality thereafter.
9.7 mg/L: 100% mortality rate up to 2 weeks, no mortality thereafter.

Working Note: The actual exposures are unclear. The mg/L “application rates” may refer to the 39.5 µg/mL stock solutions.
Note also that the above results are from Table 2 of paper. For the low dose, the discussion in paper (i.e., no mortality after 1 week) does not appear to be consistent with the data in Table 2.</td><td>Qualls et al. 2012</td></tr>
<tr><td>Liriomyza trifolii (American serpentine leafminer), 3 populations
4 replicates, 15 adults/replic-ate/dose</td><td>Bifenthrin (96% from FMC)
Topical application (0.6 µL).</td><td><table><tr><th>Population</th><th>LC_{50} (mg/mL)</th><th>Relative Sensitivity[1]</th></tr><tr><td>California</td><td>0.05 (0.04-0.06)</td><td>1.0</td></tr><tr><td>Florida</td><td>0.06 (0.03-0.12)</td><td>1.2</td></tr><tr><td>Maryland</td><td>0.77 (0.66-0.90)</td><td>15.4</td></tr></table>[1] Expressed relative to California population.
LC_{50} values from Table 1 of paper.
Results in Table 1 of paper are labelled as LD_{50} values but they are clearly LC_{50}s. The LD_{50} values based on 0.6 µL/insect are 0.03 (CA), 0.036 (FL), and 0.462 ng/insect.
Note that Maryland population was taken directly from a greenhouse and subject to recent insecticide applications. Other populations had been reared for several generations without insecticide pressure.</td><td>Parkman and Pienkowski 1989</td></tr>
<tr><td>Hymenoptera (other than bees)</td><td></td><td></td><td></td></tr>
<tr><td>Linepithema humile (Argentine ants)</td><td>Bifenthrin (Talstar F, 7.9% a.i., FMC)
Transfer toxicity of treated ants (n=10) to untreated ants.
Treated ants exposed to 13.7 ppm a.i. in sand.</td><td>LT_{50}s (time to 50% mortality of colonies)
63.7 days at 21-23°C [Table 1]
Number dead at 6 days after exposure (Figure 1):
Control: ≈50
21-23 °C: ≈80
27-29 °C: ≈180
Greater toxicity at higher temperature is in contrast to aquatic species in which greater toxicity is seen at lower temeratures – e.g., Weston et al. 2005, 2011.</td><td>Soeprono and Rust 2004</td></tr>
</table>

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference</th></tr>
<tr><td>Linepithema humile (Argentine ants)</td><td>Bifenthrin (Talstar Flowable, FMC), exposures to 0.06% solution.
Various exposures (see column 3).</td><td>Contact and Topical Application: Almost complete immobility (Figures 1 and 2 of paper).
No effect of temperature (10°C, 20°C, and 30°C) on toxicity (Table 2).

Working Note: This is a comparative study with other insecticides and is not focused on quantitatively describing the toxicity of bifenthrin.
The lack of a temperature effect on toxicity is in contrast to aquatic species – e.g., Weston et al. 2005, 2011.</td><td>Wiltz et al. 2009</td></tr>
<tr><td>Lepidoptera</td><td></td><td></td><td></td></tr>
<tr><td>Heliothis virescens (tobacco budworm) larvae
Two populations, 2-3 replicates per dose, 20 insects per replicate</td><td>Bifenthrin (FMC Corp. NOS), 5-6 doses (NOS)
Topical
Observations at 48 hours.</td><td>LD_{50} values (Table 1 of paper)
Sensitive Strain: 1.321 (0.786-1.429) µg/g larvae
Tolerant Strain: 15.750 (11.571-23.036) µg/g larvae
Resistance Factor: ≈11.9</td><td>Leonard et al. 1988</td></tr>
<tr><td>Chilo suppressalis (rice stem borer), larvae, 9-11 mg/larvae. Minimum of 30 larae per replicate, 3 replicates per dose.</td><td>Bifenthrin (95% a.i.)
Topical
Observations at 48 hours
Temperatures: 17, 27, and 37 °C</td><td><table><tr><th>Temperature °C</th><th>LD_{50} (95% CI) µg/Larvae</th><th>LD_{50} µg/g bw</th></tr><tr><td>17</td><td>0.0032 (0.0024–0.0048)</td><td>0.32</td></tr><tr><td>27</td><td>0.0050 (0.0025–0.0092)</td><td>0.50</td></tr><tr><td>37</td><td>0.0019 (0.0012–0.0023)</td><td>0.19</td></tr></table>Columns 1 and 2 from Table 1 of paper. Column 3 based on average body weight of 10 mg/larvae.
Working Note: U.S. EPA/OPP/EFED (2012a, p. 144) summarized the lowest LD_{50} from this study as 0.018 µg/organism. As noted above, the correct conversion would be 0.0019 µg/organism.</td><td>Li et al. 2006</td></tr>
<tr><td>Pieris rapae (small cabbage white butterfly), 3rd and 5th instar larvae. 10 larvae per replicate, 4 replicates per dose.</td><td>cis-bifenthrin, 99.5% separated to [R] and [S] enantiomers

Note: Concentrations of compounds in solution are not clear. See Section 2.2 of paper</td><td>LC_{50}s (below) expressed as mL/L. Cannot calculate LD_{50}s.<table><tr><th>Duration (h)</th><th>Racemate</th><th>[S]</th><th>[R]</th></tr><tr><td>8</td><td>2.07</td><td>>300</td><td>1.19</td></tr><tr><td>16</td><td>1.74</td><td>>300</td><td>0.74</td></tr><tr><td>24</td><td>1.11</td><td>>300</td><td>0.54</td></tr></table>See Table 1 of paper for confidence intervals.</td><td>Liu et al. 2008b

China</td></tr>
<tr><td>Ostrinia nubilalis (European corn borer) 3rd instar larvae</td><td>Bifenthrin (94%)
Observations at 24 hours.
Topical
3 replicates (NOS)</td><td>LD_{50}: 1.1 (0.74-1.5) ng/mg bw</td><td>Siegfried 1993</td></tr>
</table>

Appendix 3: Toxicity to Terrestrial Invertebrates *(continued)*

Species	Exposure	Response	Reference
Bombyx mori (silk worm) Larvae, 20 per replicate, 3 replicates per dose.	Bifenthrin (90%, NOS) Petri dish exposures to mulberry leaves immersed in solutions and then dried. Observations at 24 and 48 hours. 5 concentrations (NOS).	24-hr LC_{50}: 0.09 (0.06-0.11) mg/L 48-hr LC_{50}: 0.06 (0.05-0.06) mg/L Note: From Table 1 of paper. The upper bound of the 48-hr LC_{50} is as it appears in paper. In binary mixtures, additive with phoxim (OP) and dichlorvos (Table 2 of paper)	Zhang et al. 2008 China

A3 Table 3: Toxicity to Other Terrestrial Invertebrates

Species	Exposure	Response	Reference
Arachnida			
Spiders			
Oxyopes salticus (Striped lynx spider) Females, wild caught 19 spiders tested individually at both time intervals.	Bifenthrin formulation (Ortho Bug-B-Gon MAX Lawn and Garden Killer) 0.00348% a.i. solution, filter paper contact. 30 minute or 48 hour exposure prior to initiating prey contact (fruit flies)	No mortality in spiders. Substantial and significant increase in time to capture at both 30 minute (5 fold increase) and 48 hour (about 10 fold increase). See Figure 1A of paper. Significant decrease in proportion of spiders that successfully captured prey – i.e., at drop of about 40% for 30 minute exposure and 75% for 48 hour exposure. See Figure 1B of paper	Brown et al. 2015
Oxyopes salticus (Striped lynx spider) Females, wild caught 20 spiders tested individually at both time intervals.	Bifenthrin formulation (Ortho Bug-B-Gon MAX Lawn and Garden Killer) 0.00348% a.i. solution Fruit flies (prey) exposed to bifenthrin on filter paper for 30 minutes.	No significant difference in spider's capture of prey or time to discard prey in bifenthrin and water treated controls. Author's interpretation: Spiders unable to detect bifenthrin residues in prey.	Brown et al. 2015
Mites			
Oligonychus pratensis (Banks grass mite) Different populations	Bifenthrin (FMC, NOS) Vial assay, 0.1 mL at concentrations from 0.01 to 10,000 ppm	LC_{50}s from 0.05 (susceptible population) to 1.13 µg/vial. Resistance factor up to 30.9. See Table 1 of paper. `Working Note: Not generally useful for comparison to other species. Simply assays for resistance.` Separate studies with piperonyl butoxide indicated at strong synergistic response (5 to 38 fold as would be expected.	Bynum and Archer 2002
Galendromus occidentalis (predatory mite) 1 female per replicate, 7 replicates per dose.	Bifenthrin formulation, Brigade WSB from FMC. Contact assay: Direct spray at 0.240 g a.i./L onto cotton leaves in petri dish. Observations at 72 hours.	Significant decrease in survival, fecundity, and fertility (Table 1 of paper). Other assays conducted but results not comparable to other species. Indicates that typical field applications may be slightly harmful.	Hamby et al. 2013
Tetranychus urticae (two-spotted spider mite) Two strains, sensitive and resistant	Bifenthrin, Talstar 8g/L EC Leaf disc assay.	Substantial difference in toxicity in sensitive (LC_{50}=5.5 mg/L) and resistant (LC_{50}>10,000 mg/L) strains. Toxicity substantially enhanced by esterase inhibitor. Resistant strain metabolized bifenthrin more rapidly (7.5) than sensitive strain.	Van Leeuwen and Tirry 2007

Appendix 3: Toxicity to Terrestrial Invertebrates *(continued)*

Species	Exposure	Response	Reference
Oligonychus pratensis (Banks grass mite)	Bifenthrin (TGAI, 93.5%) Vial residue assay with and without 3 synergists (i.e., TPP, DEM, and PBO).	LC_{50}s given in Table 1 of paper. These are useful only for estimating synergistic activity. Synergism ratios of 2.2 to 6, all of which were significantly different from toxicity of bifenthrin without synergist. Most effective synergist was PBO.	Yang et al. 2001
Tetranychus urticae (two-spotted spider mite)	Bifenthrin (TGAI, 93.5%) Vial residue assay with and without triphenyl phosphate synergist.	LC_{50}s given in Table 2 of paper. These are useful only for estimating synergistic activity. Synergism ratios of 4.1 to 6.2, all of which were significantly different from toxicity of bifenthrin without synergist. Most effective synergist was TPP.	Yang et al. 2001
Annelida			
Eisenia foetida (earthworm), 10 worms per replicate, 4 replicates per treatment.	Ortho® Season Long Control (0.115% bifenthrin w/w) Bifenthrin applied at rate equivalent to 4 lbs formulation/1000 ft^2. Equivalent to about 20 lbs a.i./acre [4 lbs form. x 0.00115 a.i./form x 43450 ft2/acre /1000 ft2 = 19.987 lb a.i./acre]	Observations at 3, 7, 14, 21, 28 and 60 days post treatment not significantly different from water controls in terms of mortality based on analysis of variance. At the end of 8 weeks (56 days), 32/10 survival in treated containers and 37/40 survival in water control (Table 1 of paper). Working Note: Combining replicates, the response of 32/40 in treated groups is not significantly different (p=0.09633) from control (3/40) mortality using Fisher Exact test. Consistent with ANOVA done by author.	Schofield 2007
Mixed population: Aporrectodea, Allolobophora, Eisenia and Lumbricus species.	Talstar 10 WP formulation. Soil application at 0.11 lb. a.i./acre applied to surface by low volume sprayer. Observations at 1 and 3 weeks after application. Two applications, one in spring and the other in fall.	No significant decrease in earthworm population following applications in spring or fall.	Potter et al. 1994
Earthworms (NOS)	Talstar 8 SC	NOEC: 2.13 mg a.i./kg soil	EFSA 2011, Section 5.5, p. 29
Earthworms (NOS)	Bifenthrin metabolites TFP-acid: 3-(2-chloro-3, 3, 3-trifluoro-1-propenyl)-2, 2-dimethyl-cyclopropane-carboxylic 4-OH: 4'-hydroxy bifenthrin	Chronic NOECs: TFP: 17.8 mg/kg 4-OH: 178 mg/kg	EFSA 2011, Section 5.5, p. 29

A3 Table 4: Field Studies

Nontarget Species	Exposure	Response	Reference
Harpalus pennsylvanicus (ground beetle, Colleoptera)	Bifenthrin, Talstar Select 7.9%, 0.064 g a.i./ha (≈0.057 lb a.i./acre). Applications to turf for general insect control.	Most feeding ground beetles dead by 12 hours after treatment (Table 1 of paper). Other treatments in combination with clothianidin (neonicotinoid) had adverse effects on other terrestrial invertebrates – i.e., bumble bees and two species of wasps (i.e., Hymenoptera). The addition of bifenthrin did not seem to enhance toxicity (paper, p. 257, col. 2). `Working Note: Above observation consistent with study by Peterson 2012b indicating that co-treatment of termites with a neonicotinoid did not have a substantial impact on potency.`	Larson et al. 2014
Nontarget Colleoptera, Hymenoptera, and Collembola	Bifenthrin as SPECKoZ formulation for the control of *Ixodes scapularis* (deer tick). Application rate not specified. Estimated application rate: 0.22 lb/acre [1] Bifenthrin used as positive control in evaluation of another pesticide. Application to oak-pine forest for the control of deer ticks (*Ixodes scapularis*)	Good control of ticks (adults, nymphs, and larvae) for up to 18 months. No apparent effects on bees and other flower-visiting insects (see Figure 8). No detailed tabular summary of data on bifenthrin and nontargets. Based on Figure 5 of paper, bifenthrin appears to have had the most severe effects on Coleoptera and Hymenoptera. No marked differences (from water treatment reference) on Diptera and Collembola. In discussion, authors note reservations with small sample sizes.	Elias et al. 2013

[1] Note on Elias et al. 2013: SPECKoZ is a company name. Based on the bifenthrin product at the company web site (http://www.speckoz.com), the recommended application rate of 1 oz formulation (EPA Reg. No. 279-3206-72113) per 1000 ft^2 is equivalent to 1oz/128 oz/gal * 0.66 lb/gallon = 0.0052 lb/1000 ft^2 = 0.226512 pound/acre.

Appendix 4: Toxicity to fish.

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NOTE: The concentrations are identical to those given the cited publications in both the Exposure and Response columns. Take particular care when making comparisons to the units of concentration. Unless otherwise specified, all concentrations are in units of a.i. rather than formulation.

SPECIAL NOTE ON WATER SOLUBILITY: As summarized in Table 3 of the current risk assessment, the water solubility of bifenthrin is taken as 0.014 µg/L (MRID 132518; Laskowski, 2002). Many of the toxicity values given in this appendix exceed this water solubility. See Section 4.1.3 and Section 4.4.3 for discussion.

A4 Table 1: Standard Acute Toxicity Bioassays

Species	Exposure	Response	Reference
Freshwater			
Fathead minnow (*Pimephales promelas*), 7 day old larvae	Bifenthrin (99%, 97% cis-isomer) 24-hour exposure, 25 °C.	LC_{50}: (24 hrs) – 1.9 µg/L LC_{10}: (24 hrs) – 0.92 µg/L NOAEC: 0.5 µg/L LOAEC: 1 µg/L	Beggel et al. 2010
Fathead minnow (*Pimephales promelas*), 7 day old larvae	**Talstar (7.9% a.i.)** 24-hour exposure, 25 °C.	LC_{50}: (24 hrs) – 4.85 µg/L LC_{10}: (24 hrs) – 2.99 µg/L NOAEC: Not identified LOAEC: 3 µg/L Working Note: Talstar somewhat less toxic than a.i. alone.	Beggel et al. 2010
Fathead minnow (*Pimephales promelas*), 8 day old larvae	Bifenthrin (97.8%), static renewal	LC_{50}: (96 hrs) – 0.78 µg/L	Fojut et al. 2012, summary of unpublished study.

Appendix 4: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Rainbow trout *(Salmo gairdneri*)	Bifenthrin technical (purity 88.35%); composition: 98% cis/2% trans isomers. Test conducted under flow-through conditions for 120 hours. Water temperature: not specified Nominal concentrations: 0.094, 0.19, 0.38, 0.75, or 1.5 µg ai/L	LC_{50}: (24 hrs) - 6.2 µg/L (48 hrs) - 0.34 µg/L (72 hrs) - 0.20 µg/L (96 hrs) - 0.15 µg/L (120 hrs) ~0.1 µg/L NOEC - 0.094 µg/L Working Note: The 96-hour LC50 is used by U.S. EPA/ OPP/EEFED (2012a, p. 151) to characterize acute risks in fish. EPA notes that the reported LC_{50} exceeds the water solubility of 0.014 µg/L.	MRID 163156 U.S. EPA/OPP/ EFED 2012a and other EFED assessments. *Very highly toxic.* Also summarized in FAO 2012
Bluegill sunfish (*Lepomis macrochirus*), 2.5 g, mean weight; n=20/group	Bifenthrin technical (purity 88.35%) under flow-through conditions for 144 hours. Nominal concentrations: 0.18, 0.27, 0.42, 0.65, or 1.0 µg a.i./L Water temperature: not specified	LC_{50} (24 hrs) >1.0 µg/L (48 hrs) - 0.65 µg/L (72 hrs) - 0.44 µg/L (96 hrs) - 0.35 µg/L (120 hrs) - 0.32 µg/L (144 hrs) - 0.30 µg/L NOEC< 0.18 µg/L **ACCEPTABLE**	MRID 132536 U.S. EPA/OPP/EFED 2012a (Red Legged Frog) (U.S. EPA/ECOTOX 2013) FAO 2012
Common Carp (*Cyprinus carpio* L.), male juveniles, 15.3 ± 4.57 g mean body weight, 75 ± 5.34 mm mean body length, 10/dose group	**Talstar EC 10, 100 g/L a.i.** Concentrations: 0, 20, 40, 60, 80, 100, 120, or 140 µg/L for 96 hours under semi static conditions Water temperature: 19.3 - 19.5°C	96-hour LC_{50} = 57.5 µg formulation/L as Talstar EC 10 Corresponding a.i. 96-hour LC_{50} = 5.75 µg a.i./L bifenthrin No mortality in control aquarium	Velisek et al. 2009
Gizzard shad (*Dorosoma cepedianum*)	**Capture 2EC, 24% a.i.** 8 day exposure	8-day LC_{50}: 207 ng/L bases on average concentrations and 521 ng/L based on peak exposures. Complete mortality at 7,750 ng/L. Working Note: This is a mesocosm study.	Drenner et al. 1993
Zebra fish (*Brachydanio rerio*), fry, 3.0 ± 0.5 cm, 0.3 ± 0.1 g, n= 20	TGAI, 90% a.i. dissolved in acetone Concentrations: five (NOS) Water temperature 23±1 ◦C	24-hour LC_{50} = 0.0065 mg/L (95% CL = 0.0051-0.0093) 48-hour LC_{50} = 0.0039 mg/L (95% CL = 0.0026–0.0050) 72-hour LC_{50} = 0.0034 mg/L (95% CL = 0.0020–0.0046) 96-hour LC_{50} = 0.0021 mg/L (95% CL = 0.0021–0.0041)	Zhang et al. 2010

Species	Exposure	Response	Reference
Zebra fish (*Brachydanio rerio*), **embryos** 20 to 25 per replicate, 3 replicates per dose.	Bifenthrin (99%) 6 day exposure Water temperature 28 ◦C.	6-day LC_{50}: 190 (90-350) µg/L Developmental Notes: Curvature of body axis and tremors at concentrations as low as 50 µg/L (Figures 6 and 7). NOAEC not defined. Pericardial edema and spasms at 100 µg/L with NOACE of 50 µg/L.	DeMicco et al. 2010
Saltwater			
Sheepshead minnow (*Cyprinodon variegatus*), 0.28 g	Bifenthrin technical (purity 88.3%) under flow-through conditions for 96 hours. Water temperature: not specified *Investigators used a co-solvent to facilitate dissolution, and although study does not report precipitates, there is uncertainty regarding the amount of bifenthrin that was bioavailable to the test species.*	No sublethal effects reported. 96-hour LC_{50} = 17.5 µg/L **(*exceeds reported solubility of 0.014* µg a.i./L)** **Acute Toxicity Classification: Very Highly Toxic**	MRID 163101 U.S. EPA/OPP/ EFED 2012a ECOTOX 2015
Sheepshead minnow (*Cyprinodon variegatus*), adults, 1–1½ cm	TGAI [97.2% cis and 2.5% trans] under conditions of static renewal at concentrations of 0, 0.4, 0.2, 1, 5, or 25 µg/L for 96 hours Water temperature: not specified	24-hour LC_{50} >25 µg/L 96-hour LC_{50} = 19.806 µg/L (95% CI = 11.886-47.250 µg/L) NOEC = 5 µg/L LOEC = 25 µg/L Sublethal effects included significant *increasing trends with increasing bifenthrin concentration in glutathione ($p = 0.013$) and catalase ($p = 0.041$).*	Harper et al. 2008

A4 Table 2: Sublethal Toxicity Studies

Species	Exposure	Response	Reference
In Vivo			
Common Carp (*Cyprinus carpio* L.), n=20, 1- to 2-years-old, 832.5 ± 167.89 g mean body weight, 366.25 ± 19.88 mm mean body length	**Talstar EC 10, 100 g a.i./L** Concentrations: 0 or 57.5 µg/L for 96 hours under semi static conditions. Water temperature: 19.5 -19.9°C	Significantly ($p<0.01$) increased levels of plasma glucose, ammonia, aspartate aminotransferase, and creatine kinase; increased relative and absolute monocyte counts; and histopathological changes in organ tissues: teleangioectasiae of secondary gill lamellae and degeneration of epatocytes, compared with controls.	Velisek et al. 2009
Fathead minnow (*Pimephales promelas*), 7 day old larvae	Bifenthrin (99%, 97% cis-isomer) Measured Concentrations: 0.07, 0.14, 0.24, and 0.35 µg/L 24-hour exposure 25 °C.	Swimming performance (assayed after 24 hr exposure) NOAEC: 0.07 µg/L LOAEC: 0.14 µg/L Complete recovery after 6 days transfer to clean water. Growth: No effect over 7 day post-exposure observation period at any concentration. Endocrine Effects: Up-regulation of vitellogenin and down-regulation of growth factor transcripts at lowest concentration.	Beggel et al. 2010
Fathead minnow (*Pimephales promelas*), 7 day old larvae	**Talstar (7.9% a.i.)** Measured Dissolved Concentrations: 0.03, 0.05, 0.08, and 0.16 µg/L 24-hour exposure 25 °C.	Swimming performance (assayed after 24 hr exposure) NOAEC: Not identified LOAEC: 0.03 µg/L Complete recovery after 6 days transfer to clean water. Authors Note: Formulation about 5x more toxic than a.i. Growth: No effect over 7 day post-exposure observation period at any concentration.	Beggel et al. 2010
Fathead minnow (*Pimephales promelas*), male, adult	Bifenthrin (NOS) 1 or 5 ng/L 25±2 °C	No change in mRNA expression of vitellogenin. Effects were seen in co-exposure with surfactant.	Crago et al. 2015

Species	Exposure	Response	Reference
Inland silverside (*Menidia beryllina*) 65-70 days old	Bifenthrin (NOS) Nominal Concentrations: Methanol control, 1, 10, and 100 ng/L Measured Concentrations (0-24 hours): 0.898-0.733, 9.514-6.89, and 111-71 ng/L 14 days, static renewal every 24 hours. Note nanograms units	Significant ($p<0.05$) increase in choriogenin (estrogen-dependent egg coat protein) in all groups but not dose-related (Figures 1 and 2 of paper) Separate assays with ethinylestradiol as positive control did display a standard dose-related increase. Working Note: As discussed by U.S. EPA/OPP (2015, p. 9), *"these results are confounded by several uncertainties including the absence of a negative control and limited exposure measurements"*	Brander et al. 2012
Inland silverside (*Menidia beryllina*) 60 days old	Bifenthrin (NOS) Bifenthrin: 10 ng/L 4-OH Bifenthrin , 10 ng/L Bifenthrin (10 ng/L) + PBO 25 µg/L 7 day "semi-static" exposure	4-OH bifenthrin exposures resulted in significant increase choriogenin from controls (Fig. 1). No significant effect from bifenthrin alone or in combination with PBO.	DeGroot and Brander 2014
Japanese medaka (*Oryzias latipes*), 2.5-3.5 cm in length	1-S cis-bifenthrin (99.5%) with enantiomers separated 10 ng/mL (10 µg/L) 10-day duration 25± 1°C.	Based on assays for liver vitellogenin induction, [S] enantiomer more potent than [R] enantiomer by a factor of about 123 based on concentrations of vitellogenin in liver samples. Working Note: Above is the same pattern seen in mammalian studies.	Wang et al. 2007
Rainbow trout (*Salmo gairdneri*), male, juvenile Working note: a.k.a. *Oncorhynchus mykiss*	Bifenthrin (NOS) 1 or 5 ng/L 15 °C	No change in mRNA expression of vitellogenin. Effects were seen in co-exposure with surfactant.	Crago et al. 2015
Steelhead trout (*Oncorhynchus mykiss*),≈9.5 cm length.	Bifenthrin (NOS) Nominal concentrations: 0.1 or 1.5 µg/L. 14-day exposure 13–15 °C Acclimation for 2 weeks to target salinity (4,8,12,and 16 ppt).	Males: Significant decrease in testosterone at 8 ppt salinity. At both concentrations, a decrease in gonadosomatic index (gonad mass as fraction of body weight) in fresh water (not dose-related) but no effect in saltwater. Females: Increase in follicle diameters at 8 ppt (40%) and 16 ppt (62%) salinities. Increase in estradiol in freshwater (high dose only) but significant dose-related decrease in estradiol at 16 ppt.	Forsgren et al. 2013

Appendix 4: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Steelhead trout (n=175) and Rainbow trout (n=175) (*Oncorhynchus mykiss*),≈9.3 cm length. 3 replicates of 5 fish/resplicate `Working Note: Same species but rainbow trout populations are limited to fresh water and steelheads are andromadus.`	Bifenthrin (99.1% cis-isomer) Nominal Concentrations: 0, 0.1, and 1.5 µg/L. Measured (steelheads): 0.025 1.072 µg/L Measured (rainbow): 0.030, and 0.0608 µg/L. 14-day exposure 11–12 °C Fish acclimated to 0 (freshwater), 8 and 17 g/L salinity.	Mortality: Significant only for rainbow trout at higher concentration (Fig. 1). Hormones: Only statistically significant effect was an increase in 17β-estradiol at high concentration in steelheads (Fig. 4). Na^+/ K^+ ATP-ase mRNA expression: Significant only in steelheads at high concentration and 1.7 g salinity for isoforms α1a.	Riar et al. 2013
Zebrafish (*Brachydanio rerio*), embryos, 24, 48, 72, and 96 hours post-fertilization (hpf)	Bifenthrin (99.5%) Concentrations: (50, 100, 150, and 200 µg/L	Lethality only at 200 µg/L. EC_{50}s in 96 hpf embryos (Table 2 and Fig. 4) 256 µg/L pericardial edema 109 µg/L: curved body axis Dose-related increase in spontaneous movements (LOAEC 50 µg/L). Figure 1. Dose-related increase in hatching rate of 50 hpf embryos (Fig. 2). Increased swimming speed at 96 hpf NOAEC: not determined LOAEC: 50 µg/L Increase in expression of vitellogenin gene I at 150 µg/L.	Jin et al. 2009
Zebrafish (*Brachydanio rerio*), larvae	cis-bifenthrin (99.5%) with enantiomer resolution.	Spontaneous movements and hatching rate at 100 µg/L: Increase wit [R] enantiomer and slight decrease with [S] enantiomer (Fig. 2 and 3). Curved body axis and pericardial edema: [R] more toxic than [S] enantiomer [Table 1] `Working Note: The potencies are the opposite as those seen in mammals. Note that this was not seen in adult fish (Jin et al. 2013b) [see below].`	Jin et al. 2010
Zebrafish (*Brachydanio rerio*), adult, both sexes	cis-bifenthrin (>95%) with enantiomer resolution. Concentrations: 0, 0.3, 1, 3 µg/L for racemate and enanteomers	Assays of mRNA expression for oxidative stress and immune function indicated that [S] enantiomer was more toxic than [R] enantiomer. `Working Note: This is the same pattern seen in mammalian studies but different from the pattern in zebrafish from the study by Jin et al. 2010 [see above].`	Jin et al. 2013b
In Vitro			

Appendix 4: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Rainbow trout (*Oncorhynchus mykiss*) hepatocytes	Bifenthrin (NOS) 1 or 5 ng/L	No evidence of estrogenic effect.	Schlenk et al. 2012
Medaka (*Oryzias latipes*) hepatocytes	Bifenthrin (NOS) 1 or 5 ng/L	No evidence of estrogenic effect. No evidence of metabolism.	Schlenk et al. 2012

A4 Table 3: Longer-term toxicity

Species	Exposure	Response	Reference
Fathead minnow (*Pimephales promelas*), <24 hours old at test initiation, 35 eggs/chamber	^{14}C-FMC 54800, 70% pure a.i. in life-cycle toxicity test under flow-through conditions. Concentrations (mean measured): 0.00374, 0.00902, 0.0192, 0.0405, or 0.0905 µg/L Solvent: acetone Water temperature: 23 -25°C Observation period of 368 days. *The study was classified as unacceptable due to a low performance standard with regards to survival, potential solvent effect on test organisms and variability among the test concentrations.* **(EFED 2012a, APPENDIX F: Ecological Effects Data Summaries).**	Hatchability of eggs not significantly affected at any concentration. Fry survival significantly reduced at the highest test concentration. NOAEC: 0.0405 µg/L. Classified as supplemental and …*deemed* ***invalid*** *for quantitative use in the final risk assessment* (U.S. EPA/ OPP/EFED 2010b, p. 2) DER States: *Data on individual spawning pairs was not available so these data cannot be evaluated statistically, though they are highly suggestive of a sol vent and test material related effect. However, any conclusions on reproduction are unwarranted in light of the poor survival of control fish.*	McAllister et al. 1988a MRID 40791301 DER is available (McAllister et al. 1988b). MRID 40791301 U.S. EPA/OPP/ EFED 2010b (Revised Problem Formulation) ECOTOX 2013
Rainbow trout (*Salmo gairdneri*), embryos, 50/group, larvae	^{14}C-bifenthrin (10.36% a.i.) under flow-through conditions for 48 days. Water temperature: not specified, Exposure to Day 48. Nominal concentrations: 0.0044, 0.0088, 0.018, 0.035, 0.070 µg/L	Reported NOEC = 0.012 µg/L Apparent NOEC = 0.0088 µg/L Working Note: The designation of the NOEC as 0.012 is unclear. 0.012 µg/L is the approximate geometric mean of the 2nd and 3rd lowest doses. The NOEC designation may have been intended as an MATC.	FAO 2012, p. 33 Taken from an FMC embryo larval assay dated 1985. No DER available. Not cited in EPA risk assessments.
Different species with different pyrethroids. See U.S. EPA/OPP/ EFED 2012a, Appendix J.	In the absence of an acceptable chronic study on bifenthrin, data on other pyrethroids are used to derive a surrogate NOAEC.	Estimated NOAEC: 0.004 µg a.i./L Based on the NOAEC of 0.00397 µg a.i./L for tefluthrin in fathead minnows (MRID 41705101).	U.S. EPA/OPP/ EFED 2012a, pp. 136-137 as well as Appendix J.
Different species with different pyrethroids.	Based on a default acute-to-chronic ratio of 12.4 and a recommended acute value of 0.0234 µg/L.	Chronic criterion: 0.0006 µg a.i./L	Fojut et al. 2012

A4 Table 4: Field and Mesocosm Studies

Application	Observations	Reference
Bifenthrin was applied as Capture 2.0 EC (0.1 lb a.i./acre) to the crop areas only of a 50-acre cotton field with a 5-meter buffer strip of grasses between the cotton crop and the pond edge of Hagan's Pond (3.3 acres, maximum depth of approx. 2 meters) in Dallas County, south-central Alabama. Standard aerial applications, made on each of 10 consecutive Monday mornings from June 16 to August 18, 1986, were limited to the crop areas of the field and were not to be sprayed directly on the pond. Aerial applications were made only when wind speeds were not greater than 2 mph. Westbrook pond (2.6 acres and approx. 2 meters deep) was untreated and served as a control pond. Deposition cards were placed on the treated pond and field each spray day to determine the amount of pesticide reaching the field or pond service. Pesticide residues were measured in pond water, runoff water, sediment, soil, and biota through August 1987. ***At the time of the first application (June 16, 1986) drift inadvertently introduced bifenthrin directly into the pond.*** According to EEB review: *Hagan's Pond was not the best choice for a field study because the contours of the surrounding fields did not maximize opportunities for surface runoff and spray drift to enter the pond. It is not unreasonable to assume that under optimal conditions for these events to occur, the residues in a pond adjacent to fields treated with bifenthrin would be much higher*	Twenty-eight fish species were recorded in the treated (Hagan's) Pond from 1985 to 1987. Almost the entire population (i.e., more than 1600) gizzard shad died during the winter following the application of bifenthrin and all tested high for concentrations of bifenthrin in their tissue. **Other fish kills**: Shad – 2 Carp – 2 Crappie – 13 Largemouth bass – 3 Catfish – 1 Bluegill sunfish – 16 Spotted gar – 3	Sherman 1989 MRID 40981801 (DER is available) U.S. EPA/OPP/EFED 2012a (Red Legged Frog) **SUPPLEMENTAL** ***Study hampered by lack of controls; however, study provides evidence of acute and chronic effects in 1986. EEB recommends that these results be considered in total with the full field study analyses, not isolated from other field data.***
Bifenthrin, TGAI (97.2% cis-isomer and 2.5% trans-isomer) dissolved into 100% acetone. Doses of 0.002, 0.02, or 0.2 µg/L were added to mesocosms on days 0, 7, 14, and 21 of the 28-day exposure period, intended to match a possible application pattern for Brigade 2EC. Sheepshead minnows (*Cyprinodon Variegatus*), juvenile, 1-2 cm (TL), 25/tank (uncaged) for 28 days	No significant effect on mortality. Growth and weight affected by treatment with a slight increasing trend with increasing concentration: increased growth ($p=0.0419$), increased weight ($p=0.028$), which might not be a direct effect of treatment, but rather attributed to increased food availability due to mortality in prey species. Oxidative stress (lipid peroxidation, glutathione, and catalase) results were largely inconclusive.	Pennington et al. 2014

Appendix 4: Toxicity to fish *(continued)*

Application	Observations	Reference
Chinook salmon (mean standard length 6.8 ± 0.56 cm, mean body wt 3.77 ±_0.92 g), n=6 Steelhead trout (mean standard length 18.7 ± 2.2 cm, mean body wt 69.8_± 19.9 g), n=1 Exposure: flow-through river water containing urban runoff during storm events. Bifenthrin from urban runoff was found in river water following 5 rain events, reaching 14.6 ng/L.	No mortality was observed. No observations of sublethal effects in vitellogenin or sex steroid levels. Possibility of indirect effects via toxicity to salmonid prey	Weston et al. 2015

Appendix 5: Toxicity to aquatic invertebrates

A5 Table 1: Acute Toxicity 195
A5 Table 2: Chronic toxicity 208
A5 Table 3: Field Studies 213

A5 Table 1: Acute Toxicity

Species	Exposure	Response	Reference
Freshwater			
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7- to 14-days-old, n=10, three replicate beakers/concentration	Bifenthrin (NOS) in unamended water (i.e., no bovine serum albumin) for 96 hours 23°C Toxicity values are based on estimated actual concentrations, not nominal concentrations.	Swimming impairment: 96-hr EC_{50} = 1.9 ng/L (95% CI = 1.5-2.3 ng/L) 96-hr EC_{50} = 3.1 ng/L (95% CI = 2.7-3.7 ng/L) 96-hr EC_{50} = 3.5 ng/L (95% CI = 3.1-3.9 ng/L) 96-hr EC_{50} = 3.5 ng/L (95% CI = 2.9-4.1 ng/L) Medan: 3.3 ng/L Survival: 96-hr LC_{50} = 2.7 ng/L (95% CI = 2.1-3.3 ng/L) 96-hr LC_{50} = 7.3 ng/L (95% CI = 6.1-8.6 ng/L) 96-hr LC_{50} = 8.0 ng/L (95% CI = 6.8-9.4 ng/L) 96-hr LC_{50} = 8.2 ng/L (95% CI = 7.0-9.6 ng/L) Median: 7.7 ng/L	Weston and Jackson 2009
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7-14 days, 3 replicates, 10 organisms/replicate	Bifenthrin technical (98.0% a.i.) for 96 hours in static, water-only exposures.	96-hr LC_{50} =0.0027 µg a.i./L 96-hr EC_{50} = 0.0019 µg a.i./L for swimming impairment (severe and included complete immobility except for limited movement of appendages) and mortality **(APPENDIX F: Ecological Effects Data Summaries).** Working Note: The U.S. EPA only considers the lowest LC and EC50 values from Weston and Jackson. **Acute Toxicity Classification: Very Highly Toxic** Supplemental/Quantitative (open literature study)	U.S. EPA/OPP/EFED 2012a summary of Weston and Jackson 2009 **Used for risk characterization in U.S. EPA/OPP/EFED 2012a See Table 4-1 and Table 5-2, p. 155**

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7-days-old, 10/test concentration, eight replicates	Bifenthrin technical (95.7% a.i.) for 10 days under static renewal conditions Nominal concentrations: 0, 0.25, 0.50, 1.0, 2.0, 4.0, or 8.0 µg a.i./kg dry weight Mean measured sediment concentrations: 0, 0.25, 0.45, 0.92, 1.9, 3.6, or 7.7 µg a.i./kg dry weight Water temperature 23±1°C	**Amphipod survival**: LC_{50} = 3.7 µg a.i./kg (95% CI = 3.3 – 4.1 µg a.i./kg) LOEC = 3.6 µg a.i./kg NOEC = 1.9 µg a.i./kg **Amphipod growth**: EC_{50} >7.7 µg a.i./kg LOEC = 0.92 µg a.i./kg NOEC = 0.45 µg a.i./kg	Picard 2010a
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 3 replicates of 10/ replicate/concentration	EPA protocol. 23°C	LC_{50}: 1.5 ng/L	Graves et al. 2014
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 2- to 3-weeks-old, 10/concentration, three replicates	TGAI, 98.0% a.i. in sediment, whole-sugar-maple-leaf material, or an equivalent mixture of the two on an organic carbon (OC) basis of sediment and leaf for 10 days under continuous renewal. Nominal concentrations: 0, 0.07, 0.18, 0.69, 2.15, or 8.33 µg/g OC Water temperature: 18.9-20.8°C	Sediment: LC_{50} = 0.105 µg/g OC (95% CI = 0.078-0.130 µg/g OC) LOEC = 0.065 µg/g OC Leaf material: LC_{50} = 0.065 µg/g OC (95% CI = 0.044-0.082 µg/g OC) LOEC = 0.065 µg/g OC Mixture of sediment and leaf LC_{50} = 0.152 µg/g OC (95% CI = 0.089-0.199 µg/g OC) LOEC = 0.184 µg/g OC	Maul et al. 2008a
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7- to 10-days-old	Bifenthrin (NOS) in acetone added to 0.9 mL/kg control sediment Test concentrations: five ranging from 0.25 to 3.3 µg/kg for 10 days **Concurrent toxicity test**: bifenthrin-spiked sediment with 0, 4, or 25 µg/L piperonyl butoxide (PBO) in overlying water Solvent controls: acetone carrier for bifenthrin and methanol solvent for PBO 23°C	Addition of PBO to overlying water in control sediment spiked with bifenthrin enhances toxicity. **Bifenthrin + Control Sediment** 10-day LC_{50} = 1.3 µg/kg (95% CI = 1.1-1.5 µg/kg) Equivalent to 0.62 µg/g OC (95% CI = 0.52-0.71 µg/g) **Addition of 4 µg/L PBO** 10-day LC_{50} = 0.38 µg/g OC (95% CI = 0.33-0.43 µg/g OC) **Addition of 25 µg/L PBO** 10-day LC_{50} = 0.27 µg/g OC (95% CI = 0.24-0.30 µg/g OC)	Weston et al. 2006

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7- to 10-days-old, 10/concentration	Bifenthrin (NOS) dissolved in acetone with 0.2-0.8 µL acetone/g wet sediment. Five to seven concentrations varying a factor of 1.7 ng/g for 10 days Temperatures: 18 or 23°C	18°C: LC_{50} = 0.45 µg/g organic carbon (95% CI = 0.39-0.51 µg/g OC) 23°C: LC_{50} = 0.99 µg/g organic carbon (95% CI = 0.97-1.02 µg/g OC) LC_{50} ratio (23°C/18°C): 2.2 µg/g OC Working Note: Several other bioassays with field collected sediments indicate an increase in toxicity with decreasing temperature. See Table 2 of paper.	Weston et al. 2009
Amphipod (scud), (*Hyalella azteca*: Amphipoda), adult	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 0.579 µg/g TOC (95% CI 0.544–0.614) 10-day EC_{50} = 0.495 µg/g TOC (immobilization) (95% CI = 0.460–0.530)	Harwood et al. 2014
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 7- to 10-days-old	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 0.768 µg/g TOC (95% CI 0.57–0.961) 10-day EC_{50} = 0.697 µg/g TOC (immobilization) (95% CI = 0.636–0.758)	Harwood et al. 2014
Mayfly (*Hexagenia* sp.: Ephemeroptera), 5 mm	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 1.77 µg/g TOC (95% CI = 1.09–2.46) 10-day EC_{50} = 0.845 µg/g TOC (immobilization) (95% CI = 0.697–0.993)	Harwood et al. 2014
Mayfly (*Hexagenia* sp.: Ephemeroptera), 10 mm	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 3.11 µg/g TOC (95% CI = 2.33–3.89) 10-day EC_{50} = 2.35 µg/g TOC (immobilization) (95% CI = 1.79–2.90)	Harwood et al. 2014
Mayfly (*Hexagenia* sp.: Ephemeroptera), 25 mm	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 4.30 µg/g TOC (95% CI = 4.01–4.58) 10-day EC_{50} = 1.93 µg/g TOC (immobilization) (95% CI = 1.74–2.12)	Harwood et al. 2014
Mayfly (*Hexagenia* sp.: Ephemeroptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 18°C	96-hr EC_{50} = 15.3 ng/L, based on swimming ability (95% CI = 11.8 – 19.9 ng/L) 96-hr LC_{50} >188 ng/L Control survival: 100%	Weston et al. 2015

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Mayfly (*Baetis tricaudatus*: Ephemeroptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 48 hours under static conditions 7°C	48-hr EC_{50} = 35.5 ng/L, based on swimming ability (95% CI = 19.1 – 66.2 ng/L) 48-hr LC_{50} >146 ng/L Control survival: 100%	Weston et al. 2015
Mayfly (*Diphetor hageni*: Ephemeroptera), 5/concentrations, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 48 hours under static conditions 18°C	48-hr EC_{50} = 18.7 ng/L, based on swimming ability (95% CI = 11.7 – 30.0 ng/L) 48-hr LC_{50} = 50.9 ng/L (95% CI = 33.1 – 78.2 ng/L) Control survival: 100%	Weston et al. 2015
Mayfly (*Fallceon quilleri*: Ephemeroptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 48 hours under static conditions 23°C	48-hr EC_{50} = 183 ng/L, based on swimming ability (95% CI = 123 – 274 ng/L) 48-hr LC_{50} = 443 ng/L (95% CI = 293 – 670 ng/L) Control survival: 90%	Weston et al. 2015
Mayfly (*Serratella micheneri*: Ephemeroptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 48 hours under static conditions 23°C	48-hr EC_{50} = 79.4 ng/L, based on swimming ability (95% CI = 59.1 – 106.7 ng/L) 48-hr LC_{50} = 97.4 ng/L (95% CI = 71.0 – 134 ng/L) Control survival: 100%	Weston et al. 2015
Stonefly (*Taenionema* sp.: Plecoptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 8°C	96-hr EC_{50} = 36.5 ng/L, based on ability to cling (95% CI = 28.6 – 46.6 ng/L) 96-hr LC_{50} >92.8 ng/L Control survival: 100%	Weston et al. 2015
Stonefly (*Isoperla quinquepunctata*: Plecoptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 13°C	96-hr EC_{50} = 16.3 ng/L, based on ability to cling (95% CI = 12.6 – 21.2 ng/L) 96-hr LC_{50} = 28.5 ng/L (95% CI = 21.8 – 37.3 ng/L) Control survival: 90%	Weston et al. 2015
Midge (*Chironomus dilutus*: Diptera) 2nd instar	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 4.49 µg/g TOC (95% CI = 2.91–6.08) 10-day EC_{50} = 1.90 µg/g TOC (immobilization) (95% CI = 1.78–2.02)	Harwood et al. 2014
Midge (*Chironomus dilutus*: Diptera), 3rd instar	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 6.33 µg/g TOC (95% CI = 4.85–7.81) 10-day EC_{50} = 2.65 µg/g TOC (immobilization) (95% CI = 1.85–3.44)	Harwood et al. 2014

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Midge (*Chironomus dilutus*: Diptera), 4th instar	Bifenthrin, purity >98% Bifenthrin sediment concentrations: 0, 5, 10, 15, 20, 25, 30, 35, or 40 µg/g TOC 23°C	10-day LC_{50} = 27.6 µg/g TOC (95% CI = 19.8–35.3) 10-day EC_{50} = 11.1 µg/g TOC (immobilization) (95% CI = 7.68–14.52)	Harwood et al. 2014
Midge (*Chironomus tentans*; aka *Chironomus dilutus*: Diptera), mid- to late-3rd instars, 10/test concentration, five replicates, 10 larvae/replicate, 10 replicates/concentration level	Bifenthrin (NOS) in 800 mL jar containing approximately 50 g of sediment (dry weight) Five or six concentrations (NOS), negative control and solvent control for 10 days with renewal Water temperature: 22.3-23.0°C	LC_{50} = 6.2 µg/g OC (95% CI = 8.7 - 5.1 µg/g OC) $EC_{50\ (Immob)}$ = 2.2 µg/g OC (95% CI = 2.4 - 1.9 µg/g OC) $IC_{50\ (AFDM)*}$ = 2.4 µg/g OC (95% CI = 2.8 - 1.6 µg/g OC) $IC_{20\ (AFDM)*}$ = 1.0 µg/g OC (95% CI = 1.3 – 0.7 µg/g OC) $IC_{50\ (IGR)**}$ = 1.5 µg/g OC (95% CI = 1.6 - 1.2 µg/g OC) $IC_{20\ (IGR)**}$ = 0.6 µg/g OC (95% CI = 0.7 – 0.5 µg/g OC) Lethal to sublethal ratios: $LC_{50}/EC_{50\ (Immob)}$ = 2.9 $LC_{50}/IC_{20\ (AFDM)}$ = 6.5 $LC_{50}/IC_{20\ (IGR)}$ = 10.7 ***AFDM – ash-free dry mass** **** IGR – instantaneous growth rate**	Maul et al. 2008b
Midge (*Chironomus dilutus*: Diptera), 9- to 11-days post-hatch (2nd and 3rd instars), 10/test concentration, eight replicates	Bifenthrin technical (95.7% a.i.) for 10 days under static renewal conditions Nominal concentrations: 0, 16, 31, 63, 130, 250, or 500 µg a.i./kg dry weight Mean measured sediment concentrations: 0, 13, 23, 48, 110, 200, or 400 µg a.i./kg dry weight Water temperature 23±1°C	**Midge survival**: LC_{50} = 350 µg a.i./kg (95% CI = 310 – 400 µg a.i./kg) LOEC = 200 µg a.i./kg NOEC = 110 µg a.i./kg **Midge growth**: EC_{50} = 160 µg a.i./kg (95% CI = 140 – 180 µg a.i./kg) LOEC >110 µg a.i./kg NOEC = 110 µg a.i./kg	Picard 2010b

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Midge (*Chironomus tentans*: Diptera), 2nd - 3rd instar, 10-days-old (with at least 50% at 3rd instar), 0.24-0.45 mm, 0.38 mg dry weight/midge,	[Phenyl ring-^{14}C]bifenthrin, 96.4% radiochemical purity for 10 days under intermittent flow-through conditions in sediment-spiked exposures. Nominal spiked test concentrations: 0 (negative and solvent controls), 90, 180, 350, 700, 1400, or 2800 µg a.i./kg dry sediment Mean measured sediment concentrations: <0.72 (negative controls), <0.71 (solvent controls), 83, 170, 330, 610, 1200, or 2500 µg/kg dry sediment Mean measured pore water concentrations: <0.19 (negative and solve controls), 0.17, 0.33, 0.51, 1.68, 2.85, or 5.35 µg a.i./L Water temperature: 23°C ± 1°C	Estimated Pore Water Concentrations **Survival**: LC_{50} : >0.192 µg a.i./L 95% CI: NA LOAEC = 0.092 µg a.i./L NOAEC = 0.192 µg a.i./L **Growth (Ash-Free Dry Weight)** EC_{50} = 0.051 µg a.i./L (95% CI: 0.038-0.068 µg a.i./L) LOAEC = 0.013 µg a.i./L NOAEC = 0.006 µg a.i./L Bulk Sediment concentrations (mean-measured) **Survival**: LC_{50} : >2500 µg a.i./kg dry sediment 95% C.I.: NA LOAEC = 2500 µg a.i./kg dry sediment NOAEC = 1200 µg a.i./kg dry sediment **Growth (Ash-Free Dry Weight)** EC_{50} = 660 µg a.i./kg dry sediment 95% CI: 500-880 µg a.i./kg dry sediment LOAEC = 170 µg a.i./kg dry sediment NOAEC = 83 µg a.i./kg dry sediment Based on OC-normalized Sediment Concentrations (mean-measured) **Survival** LC_{50} : >45,500 µg a.i./kg TOC 95% CI: NA LOAEC = 45,500 µg a.i./kg TOC NOAEC = 21,800 µg a.i./kg TOC **Growth (Ash-Free Dry Weight)** EC_{50} = 12,000 µg a.i./kg TOC 95% CI: 9100-16,000 µg a.i./kg TOC LOAEC = 3090 µg a.i./kg TOC NOAEC = 1510µg a.i./kg TOC	Putt 2005b MRID 46591502 SUPPLEMENTAL (sufficient mortality not achieved in test concen-trations)

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Midge (*Chironomus dilutus*: Diptera), 3rd instar, 10/ concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 23°C	Test 1; 96-hr EC_{50} >253 ng/L 96-hr LC_{50} >253 ng/L Control survival: 90% Test 2; 96-hr EC_{50} >319 ng/L 96-hr LC_{50} >319 ng/L Control survival: 93%	Weston et al. 2015
Water flea (*Daphnia magna*: Cladocera) 1st instar, 80 test organisms/level	Bifenthrin technical (88.3% a.i.) under static conditions for 48 hours. Six treatment levels: 0.5 to 10 µg a.i./L Concentrations exceeded reported solubility (0.014 ppb) and samples were not centrifuged prior to analysis; therefore, bifenthrin concentration bioavailable to test organisms is uncertain. **U.S. EPA/OPP 2012: APPENDIX F: Ecological Effects Data Summaries).**	48-hr EC_{50} = 1.6 µg a.i./L for mortality and immobilization NOEL = 0.6 µg a.i./L **Acute Toxicity Classification: Very Highly Toxic** Working Note: Not used by EPA for RQ derivation because Weston and Jackson 2009 open literature study reports a more sensitive endpoint **(APPENDIX F: Ecological Effects Data Summaries).**	MRID 41156501 U.S. EPA/OPP/EFED 2010b (Revised Problem Formulation) U.S. EPA ECOTOX 2014 Classified as Acceptable.
Water flea (*Daphnia magna*: Cladocera)	^{14}C-labelled bifenthrin (88.35% a.i.) under flow-through conditions for 48 hours. Concentrations: 0.025, 0.064, 0.12, 0.2, or 0.48 µg/L Control solvent: dimethyl formamide.	24-hr LC_{50} >0.48 µg/L 48-hr LC_{50} =0.37 µg/L NOEC <0.025 µg/L	FAO 2012 Not cited in EPA risk assessments cited in Table 1.
Water flea (*Daphnia magna*: Cladocera)	Bifenthrin technical (NOS) under static conditions for 48 hours. Concentrations: 0.018, 0.056, 0.18, 0.56, or 5.6 mg/L	48-hr EC_{50} = 0.37 µg/L NOEC = 0.056 µg/L	FAO 2012 Not cited in EPA risk assessments cited in Table 1.
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, n=5, four replicates/treatment concentration	Bifenthrin nominal concentrations: 0.24, 0.42, 0.73, 1.28 or 2.25 µg/L for 48 hours under static conditions. Water temperature: 24 ± 1°C	Bifenthrin: 48-hr LC_{50} = 0.86 µg/L (95% CI = 0.70 -1.06 µg/L)	Brausch et al. 2010
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, n=20, four replicates	Bifenthrin, purity 98%, for 48 hours 20 ± 1◦C	24-hr EC_{50} = 3.24 µg/L (95% CI = 2.85 -3.68 µg/L) Working Note: This appears to be a duplicate report of Ye et al. 2004.	Wang et al. 2009a

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Water flea (*Daphnia magna*: Cladocera), <24-hours-old juveniles, 5/test concentration	Bifenthrin, 98% a.i. dissolved in acetone, freshwater renewal Test solution = 20 mL Exposure = 96 hours	24-hr EC_{50} = 3.24 µg/L based on behavioral changes, stimulation and rapid movement, (hyperactivity) (95% CI = 2.85 - 3.68 µg/L) 24-LC_{50} not determined 48-hr EC_{50} = 12.40 µg/L (95% CI = 11.87 - 12.95 µg/L) 96-hr EC_{50} = 1.40 µg/L (95% CI = 0.94 – 2.07 µg/L)	Ye et al. 2004
Water flea (*Daphnia magna*: Cladocera), 1st instar (<24-hours-old), 5/test concentration	Capture, TGAI, 25% a.i. w/v Nominal concentrations: 0, 0.50, 1.00, 3.00, or 9.00 µg/L for 48 hours under static conditions	48-hr LC_{50} = 0.32 µg/L (95% fiducial limit = 0.12-0.94)	Mokry and Hoagland 1990
Water flea (*Ceriodaphnia dubia*: Cladocera), 1st instar (<24-hours-old), 5/test concentration	Capture, TGAI, 25% a.i. w/v Nominal concentrations: 0, 0.50, 1.00, 3.00, or 9.00 µg/L for 48 hours under static conditions	48-hr LC_{50} = 0.07 µg/L (95% fiducial limit = 0.02-0.17)	Mokry and Hoagland 1990
Water flea (*Ceriodaphnia dubia*: Cladocera), <20 hours, n=5 active	*cis*-bifenthrin, >96% separated into (+) and (−) enantiomers Test solution (15 mL) containing a given enantiomer or racemate over a known concentration range (NOS) for 96 hours under static conditions Temperature not specified	LC_{50} = 0.144±0.014 µg/L (racemic mixture) LC_{50} = 0.076±0.016 µg/L (+/R enantiomer) LC_{50} = 1.342±0.165 µg/L (−/S enantiomer)	Liu et al. 2005a,c
Water flea (*Daphnia magna*: Cladocera), adults, n=5 active	*cis*-bifenthrin, >96% separated into (+) and (−) enantiomers Test solution (50 mL) containing a given enantiomer or racemate over a known concentration range (NOS) for 96 hours under static conditions Temperature not specified	LC_{50} = 0.175±0.030 µg/L (racemic mixture) LC_{50} = 0.081±0.014 µg/L (+/R enantiomer) LC_{50} = 1.803±0.211 µg/L (−/S enantiomer)	Liu et al. 2005a,c
Water flea (*Ceriodaphania dubia*: Cladocera), neonates, <20 hours, n=5 active, four replicates	*cis*-bifenthrin, 96% pure, racemically mixed Test solutions containing: 1*R-cis*-bifentrhin or *cis*-bifenthrin at 0 to 0.6 mg/L for 4 days Temperature not specified	LC_{50} = 0.079 µg/L (1*R-cis*) LC_{50} = 0.144 µg/L (Mix)	Liu et al. 2005b
Water flea (*Ceriodaphania dubia*: Cladocera)	Bifenthrin technical (NOS) under static conditions for 24 hours. <u>Concentrations</u>: 0.056, 0.18, 0.56, 1.8, or 5.6 mg/L	24-hr EC_{50} = 0.31 µg/L NOEC = 0.043 µg/L	FAO 2012 Not cited in EPA risk assessments cited in Table 1

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Beaver-tail fairy shrimp (*Thamnocephales platyurus*: Anostraca)	Bifenthrin technical (NOS) under static conditions for 48 hours. Concentrations: 0.032,0.056, 0.18, 0.56, 1.8, or 5.6 mg/L	24-hr EC_{50} = 5.7 µg/L NOEC = 0.032 µg/L	FAO 2012 Not cited in EPA risk assessments listed in Table 1
Mayfly (*Hexagenia* sp.: Ephemeroptera), larvae	Bifenthrin technical (NOS) under static conditions for 48 hours. Concentrations: 0.056, 0.18, 0.56, 1.8, or 5.6 mg/L	48-hr EC_{50} = 0.39 µg/L NOEC = 0.039 µg/L	FAO 2012 Not cited in EPA risk assessments cited in Table 1.
Caddis fly (*Agapetus* sp. Trichoptera), larvae	Bifenthrin technical (NOS) under static conditions for 48 hours. Concentrations: 0.056, 0.18, 0.56, 1.8, or 5.6 mg/L	48-hr EC_{50} = 0.12µg/L NOEC = 0.031 µg/L	FAO 2012
Caddis fly (*Hydropsyche* sp. Trichoptera), 4/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 12°C	96-hr EC_{50} = 12.8 ng/L, based on thrashing when prodded (95% CI = 9.3 – 17.9 ng/L) 96-hr LC_{50} = 92.9 ng/L (95% CI = 76.8 - 113 ng/L) Control survival: 94%	Weston et al. 2015
Caddis fly (*Nectopsyche* sp.: Trichoptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 12°C	96-hr EC_{50} = 186 ng/L, based on ability to crawl (95% CI = 111 – 314 ng/L) 96-hr LC_{50} > 2363 ng/L Control survival: 100%	Weston et al. 2015
Caddis fly Helicopsyche sp.: Trichoptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 13°C	96-hr EC_{50} = 251 ng/L, based on ability to cling (95% CI = 146 – 309 ng/L) 96-hr LC_{50} > 632 ng/L Control survival: 100%	Weston et al. 2015
Caddis fly (*Marilia* sp.: Trichoptera), 5/concentration, three replicates	Bifenthrin technical grade dissolved in acetone. Five to 7 concentrations separated by a factor of 2 for 96 hours under static conditions 23°C	96-hr EC_{50} >158 ng/L, based on ability to crawl 96-hr LC_{50} > 158 ng/L Control survival: 100%	Weston et al. 2015
Amphipod (*Gammarus pulex*: Amphipoda)	Bifenthrin technical (NOS) under static conditions for 48 hours. Concentrations: 0.0032, 0.01, 0.032, 0.1, 0.32, or 1.0 mg/L	48-hr EC_{50} = 0.11 µg/L NOEC = 0.032 µg/L	FAO 2012

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Black fly (*Simulium vitallium*: Diptera), larva, 5-7 mm, n=290	TGAI, 94% a.i. diluted in acetone (0.5 µL) applied to ventral abdomen. Insects held in disposable petri dish at 20°C without light for 24 hours	24-hr LD_{50} = 1.1 ng a.i./mg bw (95% CI=0.76-1.5 ng a.i./mg bw), Table 2 of paper	Siegfried 1993
Caddisfly (*Hydropsyche* and *Cheumatopsyche* spp. .: Trichoptera), larva, 8-10 mm, n=520	TGAI, 94% a.i. diluted in acetone (0.5 µL) applied to ventral abdomen. Insects held in disposable petri dish at 20°C without light for 24 hours	24-hr LD_{50} = 3.2 ng a.i./mg bw (95% CI=2.0-5.4 ng a.i./mg bw), Table 2 of paper	Siegfried 1993
Mayfly (*Heptageniidae*.: Ephemeroptera), nymph, 8-12 mm, n=160	TGAI, 94% a.i. diluted in acetone (0.5 µL) applied to ventral abdomen. Insects held in disposable petri dish at 20°C without light for 24 hours	24-hr LD_{50} = 0.22 ng a.i./mg bw (95% CI=0.14-0.32 ng a.i./mg bw) , Table 2 of paper	Siegfried 1993
Damsefly (*Enellagma* and *lshnura* spp.: Odonata), nymph, 10-15 mm, n=160	TGAI, 94% a.i. diluted in acetone (0.5 µL) applied to ventral abdomen. Insects held in disposable petri dish at 20°C without light for 24 hours	24-hr LD_{50} = 0.10 ng a.i./mg bw (95% CI=0.066-0.16 ng a.i./mg bw) , Table 2 of paper	Siegfried 1993
Water scavenger beetle (*Hydrophilus* spp.: Coleoptera), adult, n=200	TGAI, 94% a.i. diluted in acetone (0.5 µL) applied to ventral abdomen. Insects held in disposable petri dish at 20°C without light for 24 hours	24-hr LD_{50} = 4.0 ng a.i./mg bw (95% CI=2.4-7.4 ng a.i./mg bw) , Table 2 of paper	Siegfried 1993
Black fly (*Simulium vitallium*: Diptera), larva, 5-7 mm, n=240	TGAI, 94% a.i. diluted in 15 mL distilled water. Static exposure in glass petri dishes for 24 hours	24-hr LD_{50} = 1.3 µg/L (95% CI=0.16-11 µg/L), Table 3 of paper	Siegfried 1993
Caddisfly (*Hydropsyche* and *Cheumatopsyche* spp. .: Trichoptera), larva, 8-10 mm, n=120	TGAI, 94% a.i. diluted in 15 mL distilled water. Static exposure in glass petri dishes for 24 hours	24-hr LD_{50} = 7.2 µg/L (95% CI=4.5-10 µg/L) , Table 3 of paper	Siegfried 1993
Mayfly (*Heptageniidae* sp.: Ephemeroptera), nymph, 8-12 mm, n=120	TGAI, 94% a.i. diluted in 15 mL distilled water. Static exposure in glass petri dishes for 24 hours	24-hr LD_{50} = 2.3 µg/L (95% CI=1.7-3.0 µg/L) , Table 3 of paper	Siegfried 1993
Damsefly (*Enellagma* and *lshnura* spp. .: Odonata), nymph, 10-15 mm, n=120	TGAI, 94% a.i. diluted in 15 mL distilled water. Static exposure in glass petri dishes for 24 hours	24-hr LD_{50} = 1.1 µg/L (95% CI=0.68-1.7 µg/L) , Table 3 of paper	Siegfried 1993
Water scavenger beetle (*Hydrophilus* spp. .: Coleoptera), adult, n=100	TGAI, 94% a.i. diluted in 15 mL distilled water. Static exposure in glass petri dishes for 24 hours	24-hr LD_{50} = 5.4 µg/L (95% CI=3.9-7.7 µg/L) , Table 3 of paper	Siegfried 1993
Saltwater			

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Eastern oyster (*Crassostrea virginica*: Ostreoida), embryos, 20, 370/replicate, 3 replicates/level	Bifenthrin (FMC 564800) technical (88.35% a.i.) under static conditions for 48 hours. Nominal concentrations: 0.77, 1.3, 2.2, 3.6, 6.0, 10, or 17 mg/L Average measured concentrations: <0.0235, 0.126, 0.448, 2.265, 1.490, 1.895, or 1.995 mg/L Concentrations exceeded reported solubility (0.014 ppb) and samples were not centrifuged prior to analysis; therefore, bifenthrin concentration bioavailable to test organisms is uncertain. **U.S. EPA/OPP 2012: APPENDIX F: Ecological Effects Data Summaries).**	Acute toxicity to embryos and larvae observed at >0.448 mg/L 48-hr EC_{50} = 0.285 mg/L (embryo/larval development) EPA ECOTOX summary: 48-hr EC_{50} = 295 µg/L (immobilization) NOEL = 0.0235 µg/L **Acute Toxicity Classification: Highly Toxic**	Ward and Dose 1987 MRID 40383501 DER available U.S. EPA ECOTOX 2014 **CORE**
Mysid shrimp (*Americamysis bahia*: Mysida), <24 hours old, 20/treatment	Bifenthrin technical (88.3% a.i.) under flow-through conditions for 96 hours. Concentration range: 0.0031 to 0.005 µg/L (mean-measured concentrations averaged 77 to 117% of nominal concentrations during testing) Control solvent: acetone	96-hr LC_{50} = 0.00397 µg/L NOEL = 0.0025 µg/L No sublethal effects reported **Acute Toxicity Classification: Very Highly Toxic**	MRID 00163102 U.S. EPA/OPP/EFED 2010b(Revised Problem Formulation) U.S. EPA/OPP/EFED 2012a (Red Legged Frog) U.S. EPA ECOTOX 2014
Grass shrimp (*Palaemonetes pugio*: Decapoda), **larvae**, 10/test concentration, 5 treatments with 3 replicates each	Bifenthrin (97.2% cis and 2.5% trans) with pesticide grade acetone used as a carrier (normalized at 0.1%) in 600 mL beaker with 68 g sediment, 400 mL seawater for 24 hours under static conditions. Test concentrations: 0, 0.0625, 0.125, 0.25, 0.5, or 1 µg/L Water temperature: 25°C	24-hr sediment LC_{50} = 0.210 µg/L (95% CI =0.096 – 0.393 µg/L) NOEC = 0.0625 µg/L LOEC = 0.125 µg/L TC^{*} = 0.088 µg/L Sediment resulted in significantly higher 24-hr LC_{50} value ($p<0.0001$), relative to the 24-hr aqueous LC_{50} value, according to the LC_{50} ratio test. *Threshold concentration	Harper et al. 2008

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Grass shrimp (*Palaemonetes pugio*: Decapoda), **adults**, 10/test concentration, 5 treatments with 3 replicates each	Bifenthrin (97.2% cis and 2.5% trans) with pesticide grade acetone used as a carrier (normalized at 0.1%) in 4 L beaker with 340 g sediment and 2 L of 20 ppt seawater for 24 hours under static conditions. Test concentrations: 0, 0.0625, 0.125, 0.25, 0.5, or 1 µg/L Water temperature: 25°C	24-hr sediment LC_{50} = 0.339 µg/L (95% CI =0.291 – 0.381 µg/L) NOEC = 0.25 µg/L LOEC = 0.5 µg/L TC* = 0.354 µg/L *Threshold concentration	Harper et al. 2008
Grass shrimp (*Palaemonetes pugio*: Decapoda), **larvae**, 10/test concentration, 5 treatments with 3 replicates each	Bifenthrin (97.2% cis and 2.5% trans) with pesticide grade acetone used as a carrier (normalized at 0.1%) in in 600 mL beaker with 400 ML seawater for 96 hours under static conditions. Test concentrations: 0, 0.003125, 0.00625, 0.0125, 0.025, or 0.05 µg/L Water temperature: 25°C	24-hr aqueous LC_{50} = 0.048 µg/L (95% CI =0.044 - 0.054 µg/L) NOEC = 0.025 µg/L LOEC = 0.05 µg/L TC* = 0.035 µg/L 96-hr aqueous LC_{50} = 0.013 µg/L (95% CI =0.011 - 0.016 µg/L) NOEC = 0.00625 µg/L LOEC = 0.0125 µg/L TC* = 0.009 µg/L Based on the LC_{50} ratio test, larval grass shrimp were significantly more sensitive than adults in the 96-hr aqueous LC_{50} toxicity tests ($p<0.0001$) *Threshold concentration	Harper et al. 2008
Grass shrimp (*Palaemonetes pugio*: Decapoda), **adults**, 10/test concentration, 5 treatments with 3 replicates each	Bifenthrin (97.2% cis and 2.5% trans) with pesticide grade acetone used as a carrier (normalized at 0.1%) in 4 L beaker with 2 L of 20 ppt seawater for 96 hours under static conditions. Test concentrations: 0, 0.00625, 0.0125, 0.025, 0.05, or 0.1 µg/L Water temperature: 25°C	24-hr aqueous LC_{50} = 0.038 µg/L (95% CI =0.032 - 0.044 µg/L) NOEC = 0.025 µg/L LOEC = 0.05 µg/L TC* = 0.035 µg/L 96-hr aqueous LC_{50} = 0.020 µg/L (95% CI =0.015 - 0.025 µg/L) NOEC = 0.0125 µg/L LOEC = 0.025 µg/L TC* = 0.018 µg/L *Threshold concentration	Harper et al. 2008

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Grass shrimp (*Palaemonetes pugio*: Decapoda), adults, 3 replicates/dose group	Bifenthrin (97.2% cis and 2.5% trans) with pesticide grade acetone used as a carrier (normalized at 0.1%) in 4 L glass jar with 2 L of seawater for 96 hours under with renewal of test solution every 24 hours. Test concentrations: 0, 0.001, 0.002, 0.004, 0.008, or 0.016 µg/L Water temperature: 25°C	Oxidative stress assays were largely inconclusive, but showed some increasing trends toward physiological stress with increased concentrations of bifenthrin. Investigators indicate that oxidative stress assays may not be appropriate for identifying sublethal effects of bifenthrin.	Harper et al. 2008

A5 Table 2: Chronic toxicity

Species	Exposure	Response	Reference
Freshwater			
Amphipod (scud), (*Hyalella azteca*: Amphipoda), 6 to 12 days old, 3 replicates/concentration	Bifenthrin technical (% a.i. not available) for 10 days in sediment toxicity test conducted in gently and continuously aerated beakers. **Used for risk characterization in U.S. EPA/OPP/EFED 2012a See Table 4-1 and Table 5-2, p. 155**	**U.S. EPA/OPP/EFED 2010b:** Average sediment 10-day LC_{50} = 0.18 µg/g $_{OC}$ **U.S EPA/OPP 2012 (Red Legged Frog):** Based on pore water concentrations: 10-day NOAEC = 0.17 ng a.i./L 10-day LOAEC = 0.34 ng a.i./L Based on sediment concentrations normalized to organic carbon: 10-day NOAEC = 40 µg a.i./kg-$_{oc}$ 10-day LOAEC = 80 µg a.i./kg-$_{oc}$ Based on significantly reduced amphipod growth.	Amweg et al. 2005 U.S. EPA/OPP/EFED 2010b(Revised Problem Formulation) U.S. EPA/OPP/EFED 2012a (Red Legged Frog)
Water flea (*Daphnia magna*: Cladocera), 40/group (10/replicate beaker)	^{14}C-labelled bifenthrin (purity 96.2%) for 21 days under flow-through conditions. Nominal concentrations: 0.6, 1.2, 2.5, 5.0, or 10 ng/L Mean-measured concentrations (determined by liquid scintillation counting): 0.30, 0.76, 1.3, 2.9, or 7.6 ng/L Working Note: Temperature not specified in EPA summaries. EPA protocol calls for 20±1°C (U.S. EPA/OPPTS 1996)	Daphnid survival in test concentrations not significantly different from pooled controls. Time to first brood significantly affected at mean-measured concentration of 7.6 ng/L; mean young/adult reproduction after 21 days significantly affected at mean-measured concentrations of 2.9 and 7.6 ng/L; growth significantly reduced at mean-measured concentrations of 2.9 and 7.6 ng/L Growth and Reproduction: 21-day NOAEC = 0.0013 µg/L 21-day LOAEC = 0.0029 µg/L **ACCEPTABLE** **Based on significant effects on reproduction and growth.**	MRID 41156501 DER not available. U.S. EPA/ OPP/EFED 2012a, Appendix F Also summarized in U.S. EPA/ OPP/EFED 2010b Classified as Acceptable. FAO 2012

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, n=1, 10 replicates/treatment concentration	Bifenthrin Bifenthrin nominal concentrations: 0.02,0.04,0.09, 0.17, 0.34, 0.69, or 1.38 µg/L pulsed regimen for 70 days Water temperature: 24 ± 1°C	Significantly decreased survival and reproduction observed at 0.69 and 1.38 µg/L bifenthrin treatment levels ($p<0.05$). No significant interactions between fC_{60} and pesticides observed. <u>Bifenthrin</u>: IC_{25} = 0.22 (0.04-0.42) µg/L for days surviving IC_{50} = 0.55 (0.36-0.80) µg/L for days surviving IC_{25} = 0.37 (0.03-0.48) µg/L for reproduction IC_{50} = 0.49 (0.28-0.72) µg/L for reproduction Working Note: Based on Figure 1A of paper, the NOAEC/LOAEC for reproduction appear to be 0.02 µg/L and 0.04 µg/L.	Brausch et al. 2010
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, 10 replicates/concentration	Analytical standard of racemic *cis*-Bifenthrin (99.5%) for 21 days Nominal concentrations: 0, 0.005, 0.01, 0.02, 0.04, or 0.8 µg/L Temperature: (22 ± 1)°C	Treatment resulted in significant effects on reproduction: all mothers died at the highest concentration; number of neonates decreased to 47.2 at 0.02 µg/L and to 16.8 at 0.04 µg/L; survival was significantly affected at 0.02 and 0.04 µg/L, which led to a decrease in brood size; average brood size and number of first brood/female decreased significantly at 0.04 µg/L ($p<0.05$) LOEC = 0.02 µg/L NOEC = 0.01 µg/L Chronic value (geometric mean value of the NOEC and LOEC) = 0.01 µg/L *The intrinsic rate of natural increase was significantly decreased ($p < 0.05$) to 0.02 µg/L.*	Wang et al. 2009b
Water flea (*Daphnia magna*: Cladocera), <24-hours-old, 5/test concretion, 10 replicates	Bifenthrin, 98% a.i. Test concentrations: 0, solvent control (acetone), 0.001, 0.004, 0.02, 0.1, or 0.5 µg/L for 21 days Temperature: (20 ± 1)°C	Reproduction was significantly reduced ($p<0.05$) at concentrations >0.02 µg/L First brood and the number of broods were decreased at a concentration of 0.5 µg/L Length was adversely affected at concentrations of 0.004, 0.1, and 0.5 µg/L. Growth: NOAEC: 0.001 µg/L LOAEC: 0.004 µg/L [Length] Reproduction: NOAEC: 0.004 µg/L LOAEC: 0.02 µg/L [Reproduction]	Ye et al. 2004

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Water flea (*Daphnia magna*: Cladocera), F_0 generation (<24-hours-old)	Bifenthrin, 98% a.i. Test concentrations: 0, solvent control (acetone), 0.5, 0.1, 0.25, 0.5, 0.75, or 1.0 µg/L for 21 days Offspring (animals from the 1st and 3rd brood) were transferred to a pesticide free medium for a 21-day recovery period Temperature: (20 ± 1)°C	F_0 generation: **Survival**: significantly reduced ($p<0.05$) at 1.0 µg/L (daphnids survived for 5 days and did not reproduce), survival not affected by exposure to lower concentrations. **Length (cm)**: significantly reduced ($p<0.05$) at 0.5 and 0.75 µg/L **Time to first brood**: significantly reduced ($p<0.05$) at 0.5 (increased by 5 days, relative to controls)and 0.75 µg/L **Number of young/female**: significantly decreased ($p<0.05$) at ≥0.25 µg/L F_1 generation (1st brood) transferred to toxicant-free (clean) water during recovery period: **Number of young/female**: offspring of mothers in 0.75 µg/L dose group produced only 115 young, relative to 167 produced in control group; however, this number was greater than the number of young produced in the F_0 generation exposed to 0.75 µg/L (n=61) **Length (cm)**: 3.01 cm, relative to 3.27 in control group F_1(3rd brood) transferred to toxicant-free (clean) water during recovery period: no significant effects except for the length of daphnids from mothers exposed to 0.5 or 0.75 µg/L	Ye et al. 2004
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, from 5th brood, 1/concentration , 10 replicates	Bifenthrin, racemic mixture, 99.5% a.i. **1R-*cis*-bifenthrin** nominal concentrations: 0, 0.008% (ethanol), 0.0025, 0.005, 0.01, 0.02, or 0.04 µg/L for 21 days under renewal conditions.	7 Days: **Survival**: Decreased significantly ($p<0.05$) to 60% at 0.04 µg/L. **LOEC = 0.04 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at 0.02 µg/L, no offspring produced at 0.04 µg/L. **LOEC = 0.02 µg/L** 14 Days: **Survival**: Decreased significantly ($p<0.05$) at ≥0.01 µg/L; 0% survival observed at 0.04 µg/L. **LOEC = 0.01 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at ≥0.01 µg/L, no offspring produced at 0.04 µg/L **LOEC = 0.01 µg/L** 21 Days: **Survival**: Decreased significantly ($p<0.05$) at 0.02 µg/L; 0% survival observed at 0.04 µg/L. **LOEC = 0.02 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at 0.02 µg/L; no offspring produced at 0.04 µg/L **LOEC = 0.02 µg/L** No significant effects on length (mm) observed at 21 days.	Zhao et al. 2009

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Water flea (*Daphnia magna*: Cladocera), neonates, <24-hours-old, from 5th brood, 1/concentration, 10 replicates	Bifenthrin, racemic mixture, 99.5% a.i. **1S-*cis*-bifenthrin** nominal concentrations 0, 0.05, 0.1, 0.2, 0.4, or 0.8 µg/L for 21 days under renewal conditions.	7 Days: **Survival**: No significant effects; survival 100% at 0.8 µg/L. **LOEC >0.8 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at 0.8 µg/L. **LOEC = 0.8 µg/L** 14 Days: No significant effects; survival 100% at 0.8 µg/L. **LOEC >0.8 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at 0.8 µg/L. **LOEC = 0.8 µg/L** 21 Days: **Survival**: Decreased significantly ($p<0.05$) only at 0.05 and 0.1 µg/L; all mother daphnids died during last 3 exposure days at 0.05 and 0.1 µg/L concentrations due to unsuccessful molting. **LOEC = <0.05 µg/L** **Fecundity**: Decreased significantly ($p<0.05$) at the two lowest concentrations (0.05 and 0.1 µg/L) and at the highest dose 0.8 µg/L **LOEC = <0.05 µg/L** Length (mm) was significantly affected at 0.05, 0.1, and 0.08 µg/L	Zhao et al. 2009
Saltwater			
Mysid shrimp (*Mysidopsis bahia*: Mysida), 40/group, 5/replicate test chamber	[Phenyl-^{14}C] bifenthrin, 96.5% purity, in 28-day lifecycle toxicity test under flow-through conditions. Nominal concentrations: 0.00, 0.79, 1.4, 2.8, 5.6, or 1.3 ng/L Mean-measured concentrations: 0.98, (control and solvent [acetone] control), 1.2, 1.3, 1.6, 2.5, or 4.7 ng/L	NOEC = 0.0012 µg/L MATC = 0.00125 µg/L LOAEC: 0.0013 ng/L `Working Note: The LOAEC is inferred from the MATC and mean measured concentrations.`	FAO 2012 (p. 29) Not cited in EPA ecological risk assessments.

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Species	Exposure	Response	Reference
Amphipods (*Leptocheirus plumulosus*: Amphipoda), neonate, 100/level divided into 5 replicates of 20 each	[^{14}C] bifenthrin, 96.4% purity for 28 days in static renewal assay Nominal spiked sediment test concentrations: 0 [solvent and negative control (acetone, 9 mL/0.8330 kg sediment (dry weight basis)], 5.6, 17, 50, 150, 450, or 1350 µg a.i/kg sediment. Mean-measured concentrations: <0.73 (controls), 5.4, 20, 50, 130, 440 or 1500 µg total [^{14}C]bifenthrin residues/kg dw sediment Exposure period: 20 days.	Based on mean-measured sediment concentrations (total radioactive residues): **Mortality:** LC_{50} = 168 µg a.i./kg sediment NOAEC = 50 µg a.i/kg sediment LOAEC = 130 µg a.i./kg sediment **Growth:** EC_{50} >130 µg a.i./kg sediment NOAEC = 50 µg a.i/kg sediment LOAEC = 130 µg a.i./kg sediment Based on *estimated* pore water concentrations(total radioactive residues): **Mortality:** LC_{50} = 0.017 µg a.i./L NOAEC = 0.005 µg a.i./L LOAEC = 0.013 µg a.i./L **Growth:** EC_{50} >0.013 µg a.i./L NOAEC = 0.005 µg a.i./L LOAEC = 0.013 µg a.i./L Based on OC-normalized sediment concentrations (mean-measured): **Mortality:** LC_{50} = 4100 µg a.i./kg TOC NOAEC = 2100 µg a.i./kg TOC LOAEC = 3170 µg a.i./kg TOC **Growth:** EC_{50} > 3170 µg a.i./kg TOC NOAEC = 2100 µg a.i./kg TOC LOAEC = 3170 µg a.i./kg TOC	Putt 2005a MRID 46591501 **SUPPLEMENTAL** ***Reproduction (required endpoint) was not assessed.***

A5 Table 3: Field Studies

Application	Observations	Reference
Bifenthrin was applied as Capture 2.0 EC (0.1 lb a.i./acre) to the crop areas only of a 50-acre cotton field with a 5-meter buffer strip of grasses between the cotton crop and the pond edge of Hagan's Pond (3.3 acres, maximum depth of approx. 2 meters) in Dallas County, south-central Alabama. Standard aerial applications, made on each of 10 consecutive Monday mornings from June 16 to August 18, 1986, were limited to the crop areas of the field and were not to be sprayed directly on the pond. Aerial applications were made only when wind speeds were not greater than 2 mph. Westbrook pond (2.6 acres and approx. 2 meters deep) was untreated and served as a control pond. Deposition cards were placed on the treated pond and field each spray day to determine the amount of pesticide reaching the field or pond service. Pesticide residues were measured in pond water, runoff water, sediment, soil, and biota through August 1987. ***At the time of the first application (June 16, 1986) drift inadvertently introduced bifenthrin directly into the pond.*** According to EEB review: *Hagan's Pond was not the best choice for a field study because the contours of the surrounding fields did not maximize opportunities for surface runoff and spray drift to enter the pond. It is not unreasonable to assume that under optimal conditions for these events to occur, the residues in a pond adjacent to fields treated with bifenthin would be much higher.*	**Treated pond *in situ* invertebrate bioassay**: Caged species exposed to ambient levels of bifenthrin in water of both (treated and untreated ponds) during 1986 **Species**: Adult grass shrimp (*Palaemonetes kadiakensis*) Juvenile crayfish (*Orconectes holti*) Juvenile and adult crayfish (*Procambarus lophotus*) Three-ridge mussel (*Amblema plicata*) Mapleleaf mussel (*Ouadrula*) Adult ramshorn snail (*Planorbella trivolvis*) **Effects**: Shrimp and crayfish: Overspray on first bifenthrin application resulted in pesticide concentration of 14 pptr, which killed all the shrimp (LC_{50} = 4 pptr); crayfish were adversely affected by low oxygen levels at bottom of the pond. Mussels: Mortality (if any) was insignificant (<10%) during 1986 to 1988. Authors attributed the lack of adverse effects to the wide-ranging nature of the species and their tolerance to pollution. Ramshorn snails: Significantly greater mortality and fewer egg masses produced for snails in treated pond. **EEB concludes**: ***the presence of significant effects in the snails located in Hagan's (treated) pond for two of the three runs is important. The snails were not only directly exposed to the chemical in the water, but they were also fed algae that had accumulated bifenthrin residues {these latter residues were not measured). It is reasonable to assume that exposure to bifenthrin from these two routes was responsible for the observed effects.*** **Pond water**: average residues ranged from 0.00195 to 0.179 ppb, peaking after treatment six (detection level = <0.5 pptr). **Pond sediment**: average residues ranged from 2.32 to 52.4 ppb (detection level = <200 pptr). **Runoff water**: average bifenthrin concentration ranged from 0.7 ppb to 3.15 ppb **Sediment portion of runoff**: average bifenthrin concentration ranged from 80 ppb to 5250 ppb.	MRID 40981801 Sherman 1989 (DER) U.S. EPA/OPP/EFED 2012a (Red Legged Frog)

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Application	Observations	Reference
Bifenthrin was applied as Capture 2.0 EC (0.1 lb a.i./acre) to the crop areas only of a 50-acre cotton field with a 5-meter buffer strip of grasses between the cotton crop and the pond edge of Hagan's Pond (3.3 acres, maximum depth of approx. 2 meters) in Dallas County, south-central Alabama. Standard aerial applications, made on each of 10 consecutive Monday mornings from June 16 to August 18, 1986, were limited to the crop areas of the field and were not to be sprayed directly on the pond. Aerial applications were made only when wind speeds were not greater than 2 mph. Westbrook pond (2.6 acres and approx. 2 meters deep) was untreated and served as a control pond. Deposition cards were placed on the treated pond and field each spray day to determine the amount of pesticide reaching the field or pond service. Pesticide residues were measured in pond water, runoff water, sediment, soil, and biota through August 1987. ***At the time of the first application (June 16, 1986) drift inadvertently introduced bifenthrin directly into the pond.*** According to EEB review: *Hagan's Pond was not the best choice for a field study because the contours of the surrounding fields did not maximize opportunities for surface runoff and spray drift to enter the pond. It is not unreasonable to assume that under optimal conditions for these events to occur, the residues in a pond adjacent to fields treated with bifenthin would be much higher*	**On-site bioassay with *Daphnia magna***: 21-day study using actual treatment pond water collected before, during, and after application. Results indicate that bifenthrin caused acute and chronic effects, including mortality during the application period and through October 1986 and decreased reproduction during the application period as well as in the March and May 1987 test. **EEB indicates: *Chronic effects to Daphnia would be expected as the MATC .(0.0013 ppb < MATC > 0.0029 ppb) was exceeded in the treatment pond water consistently from the first application through the 1987 conclusion of the study.*** **Pond water**: average residues ranged from 0.00195 to 0.179 ppb, peaking after treatment six (detection level = <0.5 pptr). **Pond sediment**: average residues ranged from 2.32 to 52.4 ppb (detection level = <200 pptr). **Runoff water**: average bifenthrin concentration ranged from 0.7 ppb to 3.15 ppb **Sediment portion of runoff**: average bifenthrin concentration ranged from 80 ppb to 5250 ppb	MRID 40981801 Sherman 1989 (DER) U.S. EPA/OPP/EFED 2012a (Red Legged Frog) **SUPPLEMENTAL** ***Study hampered by lack of controls; however, study provides evidence of acute and chronic effects in 1986. EEB recommends that these results be considered in total with the full field study analyses, not isolated from other field data.***

Application	Observations	Reference
Bifenthrin was applied as Capture 2.0 EC (0.1 lb a.i./acre) to the crop areas only of a 50-acre cotton field with a 5-meter buffer strip of grasses between the cotton crop and the pond edge of Hagan's Pond (3.3 acres, maximum depth of approx. 2 meters) in Dallas County, south-central Alabama. Standard aerial applications, made on each of 10 consecutive Monday mornings from June 16 to August 18, 1986, were limited to the crop areas of the field and were not to be sprayed directly on the pond. Aerial applications were made only when wind speeds were not greater than 2 mph. Westbrook pond (2.6 acres and approx. 2 meters deep) was untreated and served as a control pond. Deposition cards were placed on the treated pond and field each spray day to determine the amount of pesticide reaching the field or pond service. Pesticide residues were measured in pond water, runoff water, sediment, soil, and biota through August 1987. ***At the time of the first application (June 16, 1986) drift inadvertently introduced bifenthrin directly into the pond.*** According to EEB review: *Hagan's Pond was not the best choice for a field study because the contours of the surrounding fields did not maximize opportunities for surface runoff and spray drift to enter the pond. It is not unreasonable to assume that under optimal conditions for these events to occur, the residues in a pond adjacent to fields treated with bifenthin would be much higher*	**Benthic macroinvertebrates**: Generally, the many seasonal patterns of abundance and diversity observed in the untreated pond were not exhibited in the treated pond, which suggests that bifenthrin application had an adverse impact on invertebrate populations. Due to dissimilarities between treated (Hagan's) and untreated (Westbrook) ponds, which made it difficult to assess the potential impact of bifenthrin, EEB focuses the discussion/review of the registrant study only on results observed in the treated pond: In the spring of 1987 (after treatment in the spring of 1986) there was a decrease in the abundance and diversity of the taxa studied, with a suggestion of possible recovery, except in the case of mayflies (*Caenis*) and damselflies (*Enallagma*) and other surface dwelling gerrids and gyrinds, which were most severely affected. The mayflies disappeared after pesticide application and remained in extremely low abundance in the post-treatment year samples, suggesting that the invertebrate communities may take more than 1 year to recover from bifenthrin exposure. Despite the similarities between temporal variation of chironomid emergence and larvae densities in both the treatment and post-treatment years, the magnitude of emergence was severely reduced in the first post-treatment year (1987). The observation of fewer adults during a period of larval abundance suggested a high rate of mortality in mature larvae (near metamorphosis). The authors speculate that this effect *may be due to cumulative toxicity associated with residual bifenthrin in the sediments where these larvae occur*. The sampling station with the highest bifenthrin residue concentrations showed significantly lower diversities and community uniformity among four the 10 most abundant species. EEB concludes: ***The results obtained in this study (particularly the persistence data) are similar to those obtained in more controlled studies with other synthetic pyrethroids***.	MRID 40981801 Sherman 1989 (DER) U.S. EPA/OPP/EFED 2012a (Red Legged Frog)

Appendix 5: Toxicity to Aquatic Invertebrates *(continued)*

Application	Observations	Reference
*Hyalella sp.*abundance in four urban California streams as it relates to metals, bifenthrin, physical habit metrics and conductivity was assessed between 2006 and 2010.	No statistically significant relationship of *Hyalella* abundance to bifenthrin sediment concentrations in the four California streams (r^2 = 0.139; p = 0.015). The negative relationship between *Hyalella* and % silt was statistically significant; however there was no significant relationship between % silt and bifenthrin in the four California streams (r^2 = 0.110, p = 0.007)	Hall and Anderson 2013
Summary analysis of the relationship of bifenthrin sediment concentrations to grain size and total organic carbon (TOC) in six California waterbodies.	Direct significant and meaningful relationship exists between bifenthrin and TOC which was inversely correlated with large grains (sand and gravel) and directly correlated with fine grains (silt and clay). Bifenthrin sediment concentrations are not likely to be significant in sand/gravel areas which are the preferred habitat for many benthic macroinvertebrates.	Hall and Anderson 2014
Grass shrimp (*Palaemonetes pugio*), adults, dosed four times on days 0, 7, 14, and 21 of 28-day exposure period, designed to mimic possible application pattern for bifenthrin formulation Brigade 2EC®. Study included exposure of caged and uncaged shrimp to bifenthrin (97.2% *cis*-isomer and 2.5% trans-isomer) at doses of 0, 0.002, 0.02, or 0.2 µg/L for 96 hours	Caged shrimp mortality: 24-hr LC_{50} = 0.061 µg/L 96-hr LC_{50} = 0.051 µg/L Uncaged shrimp mortality: 28-day LC_{50} = 0.062µg/L No significant effect on growth and oxidative stress assays were largely inconclusive.	Pennington et al. 2014

Appendix 6: Gleams-Driver Modeling, Foliar Application

Table A6- 1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.000139 (0 - 0.00107)	0.000156 (0 - 0.0016)	0 (0 - 0)
Dry and Temperate Location	0.0003 (8.40E-06 - 0.00127)	0.00035 (0.000004 - 0.00173)	0 (0 - 1.62E-05)
Dry and Cold Location	1.25E-05 (4.10E-07 - 0.000106)	0.000011 (1.44E-07 - 0.000131)	0 (0 - 0)
Average Rainfall and Warm Location	0.00283 (0.00129 - 0.0086)	0.0038 (0.00185 - 0.0113)	3.05E-05 (0 - 0.00051)
Average Rainfall and Temperate Location	0.0035 (0.00135 - 0.008)	0.0045 (0.00198 - 0.0117)	0.000014 (0 - 0.00035)
Average Rainfall and Cool Location	0.00279 (0.00144 - 0.0055)	0.0033 (0.00164 - 0.008)	0 (0 - 0.000114)
Wet and Warm Location	0.0085 (0.0045 - 0.0177)	0.0123 (0.0056 - 0.0241)	0.00043 (0.000066 - 0.00148)
Wet and Temperate Location	0.0205 (0.0126 - 0.034)	0.0267 (0.0153 - 0.049)	0.000252 (0.00006 - 0.00139)
Wet and Cool Location	0.0143 (0.009 - 0.0236)	0.019 (0.0112 - 0.032)	0.000125 (2.15E-05 - 0.00077)
Average of Central Values:	0.0059	0.0078	9.50E-05
25th Percentile:	0.0003	0.00035	0
Maximum:	0.034	0.049	0.00148
Summary:	0.0059 (0.0003 - 0.034)	0.0078 (0.00035 - 0.049)	9.50E-05 (0 - 0.00148)

Table A6- 2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.213 (0.195 - 0.224)	0.195 (0.182 - 0.205)	0.193 (0.181 - 0.205)
Dry and Temperate Location	0.257 (0.243 - 0.266)	0.236 (0.22 - 0.246)	0.236 (0.22 - 0.246)
Dry and Cold Location	0.33 (0.32 - 0.34)	0.303 (0.292 - 0.308)	0.305 (0.287 - 0.309)
Average Rainfall and Warm Location	0.207 (0.193 - 0.216)	0.188 (0.175 - 0.196)	0.189 (0.176 - 0.199)
Average Rainfall and Temperate Location	0.256 (0.243 - 0.268)	0.234 (0.22 - 0.244)	0.233 (0.216 - 0.246)
Average Rainfall and Cool Location	0.285 (0.271 - 0.296)	0.26 (0.245 - 0.269)	0.261 (0.244 - 0.27)
Wet and Warm Location	0.203 (0.193 - 0.215)	0.187 (0.176 - 0.196)	0.187 (0.177 - 0.198)
Wet and Temperate Location	0.272 (0.261 - 0.282)	0.246 (0.231 - 0.257)	0.251 (0.236 - 0.261)
Wet and Cool Location	0.311 (0.273 - 0.32)	0.283 (0.241 - 0.291)	0.284 (0.239 - 0.293)
Average of Central Values:	0.259	0.237	0.238
25th Percentile:	0.213	0.195	0.193
Maximum:	0.34	0.308	0.309
Summary:	0.259 (0.213 - 0.34)	0.237 (0.195 - 0.308)	0.238 (0.193 - 0.309)

Table A6- 3: Concentration in Top 36 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.071 (0.065 - 0.075)	0.065 (0.061 - 0.068)	0.064 (0.06 - 0.068)
Dry and Temperate Location	0.086 (0.081 - 0.089)	0.079 (0.073 - 0.082)	0.079 (0.073 - 0.082)
Dry and Cold Location	0.111 (0.106 - 0.113)	0.101 (0.097 - 0.103)	0.102 (0.096 - 0.103)
Average Rainfall and Warm Location	0.069 (0.064 - 0.072)	0.063 (0.058 - 0.065)	0.063 (0.059 - 0.066)
Average Rainfall and Temperate Location	0.085 (0.081 - 0.089)	0.078 (0.073 - 0.081)	0.078 (0.072 - 0.082)
Average Rainfall and Cool Location	0.095 (0.09 - 0.099)	0.087 (0.082 - 0.09)	0.087 (0.081 - 0.09)
Wet and Warm Location	0.068 (0.064 - 0.072)	0.062 (0.059 - 0.065)	0.062 (0.059 - 0.066)
Wet and Temperate Location	0.091 (0.087 - 0.094)	0.082 (0.077 - 0.086)	0.084 (0.079 - 0.087)
Wet and Cool Location	0.104 (0.091 - 0.107)	0.094 (0.08 - 0.097)	0.095 (0.08 - 0.098)
Average of Central Values:	0.087	0.079	0.079
25th Percentile:	0.071	0.065	0.064
Maximum:	0.113	0.103	0.103
Summary:	0.087 (0.071 - 0.113)	0.079 (0.065 - 0.103)	0.079 (0.064 - 0.103)

Table A6- 4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Dry and Temperate Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Dry and Cold Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Average Rainfall and Warm Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Average Rainfall and Temperate Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Average Rainfall and Cool Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Wet and Warm Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Wet and Temperate Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Wet and Cool Location	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)
Average of Central Values:	4	4	4
25th Percentile:	4	4	4
Maximum:	4	4	4
Summary:	4 (4 - 4)	4 (4 - 4)	4 (4 - 4)

Table A6- 5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.024 (0 - 0.24)	0.028 (0 - 0.29)	0 (0 - 0)
Dry and Temperate Location	0.05 (0.002 - 0.22)	0.05 (0.0008 - 0.3)	0 (0 - 0.0028)
Dry and Cold Location	0.002 (0.00006 - 0.022)	0.0015 (0.00003 - 0.028)	0 (0 - 0)
Average Rainfall and Warm Location	0.3 (0.14 - 1.06)	0.4 (0.21 - 1.84)	0.006 (0 - 0.11)
Average Rainfall and Temperate Location	0.4 (0.11 - 1.06)	0.5 (0.15 - 1.59)	0.0024 (0 - 0.06)
Average Rainfall and Cool Location	0.21 (0.1 - 0.7)	0.26 (0.11 - 1.19)	0 (0 - 0.022)
Wet and Warm Location	0.9 (0.4 - 2.36)	1.33 (0.6 - 4)	0.06 (0.01 - 0.25)
Wet and Temperate Location	1.25 (0.7 - 2.88)	1.64 (0.8 - 3.8)	0.028 (0.006 - 0.18)
Wet and Cool Location	0.9 (0.5 - 1.87)	1.18 (0.7 - 3.05)	0.014 (0.0028 - 0.09)
Average of Central Values:	0.45	0.6	0.0123
25th Percentile:	0.05	0.05	0
Maximum:	2.88	4	0.25
Summary:	0.45 (0.05 - 2.88)	0.6 (0.05 - 4)	0.0123 (0 - 0.25)

Table A6- 6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0025 (0 - 0.019)	0.0029 (0 - 0.028)	0 (0 - 0)
Dry and Temperate Location	0.004 (0.00004 - 0.02)	0.005 (0.000025 - 0.026)	0 (0 - 0.00022)
Dry and Cold Location	0.00019 (0.000007 - 0.0017)	0.00017 (2.4E-06 - 0.0021)	0 (0 - 0)
Average Rainfall and Warm Location	0.07 (0.03 - 0.14)	0.08 (0.04 - 0.18)	0.0005 (0 - 0.008)
Average Rainfall and Temperate Location	0.06 (0.024 - 0.15)	0.08 (0.03 - 0.21)	0.00022 (0 - 0.006)
Average Rainfall and Cool Location	0.04 (0.02 - 0.1)	0.05 (0.024 - 0.12)	0 (0 - 0.0017)
Wet and Warm Location	0.19 (0.11 - 0.31)	0.25 (0.15 - 0.5)	0.007 (0.0013 - 0.021)
Wet and Temperate Location	0.24 (0.17 - 0.4)	0.31 (0.21 - 0.6)	0.0029 (0.0008 - 0.014)
Wet and Cool Location	0.15 (0.1 - 0.24)	0.2 (0.13 - 0.4)	0.0015 (0.0003 - 0.008)
Average of Central Values:	0.084	0.109	0.00135
25th Percentile:	0.004	0.005	0
Maximum:	0.4	0.6	0.021
Summary:	0.084 (0.004 - 0.4)	0.109 (0.005 - 0.6)	0.00135 (0 - 0.021)

Table A6- 7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.007 (0 - 0.06)	0.008 (0 - 0.08)	0 (0 - 0)
Dry and Temperate Location	0.014 (0.0003 - 0.06)	0.016 (0.00018 - 0.07)	0 (0 - 0.0008)
Dry and Cold Location	0.0005 (0.00002 - 0.005)	0.0004 (0.000006 - 0.005)	0 (0 - 0)
Average Rainfall and Warm Location	0.22 (0.11 - 0.4)	0.27 (0.14 - 0.5)	0.0016 (0 - 0.02)
Average Rainfall and Temperate Location	0.21 (0.08 - 0.5)	0.26 (0.12 - 0.7)	0.0006 (0 - 0.017)
Average Rainfall and Cool Location	0.14 (0.07 - 0.27)	0.17 (0.08 - 0.4)	0 (0 - 0.005)
Wet and Warm Location	0.23 (0.13 - 0.4)	0.3 (0.17 - 0.5)	0.006 (0.0015 - 0.024)
Wet and Temperate Location	0.19 (0.14 - 0.28)	0.24 (0.15 - 0.4)	0.0017 (0.0006 - 0.007)
Wet and Cool Location	0.19 (0.11 - 0.3)	0.24 (0.14 - 0.4)	0.0017 (0.00024 - 0.008)
Average of Central Values:	0.134	0.167	0.00129
25th Percentile:	0.014	0.016	0
Maximum:	0.5	0.7	0.024
Summary:	0.134 (0.014 - 0.5)	0.167 (0.016 - 0.7)	0.00129 (0 - 0.024)

Table A6- 8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0031 (0 - 0.027)	0.003 (0 - 0.029)	0 (0 - 0)
Dry and Temperate Location	0.004 (0.000008 - 0.029)	0.005 (0.000005 - 0.04)	0 (0 - 0.00031)
Dry and Cold Location	0.0002 (0.000006 - 0.0017)	0.00016 (2.3E-06 - 0.002)	0 (0 - 0)
Average Rainfall and Warm Location	0.09 (0.05 - 0.19)	0.11 (0.06 - 0.24)	0.0006 (0 - 0.007)
Average Rainfall and Temperate Location	0.09 (0.04 - 0.18)	0.11 (0.05 - 0.24)	0.00021 (0 - 0.007)
Average Rainfall and Cool Location	0.05 (0.03 - 0.11)	0.06 (0.04 - 0.14)	0 (0 - 0.0023)
Wet and Warm Location	0.08 (0.05 - 0.12)	0.11 (0.06 - 0.17)	0.0021 (0.0006 - 0.005)
Wet and Temperate Location	0.07 (0.05 - 0.1)	0.09 (0.06 - 0.13)	0.0005 (0.00014 - 0.0022)
Wet and Cool Location	0.06 (0.05 - 0.09)	0.08 (0.06 - 0.12)	0.0005 (0.00006 - 0.0026)
Average of Central Values:	0.05	0.063	0.00043
25th Percentile:	0.004	0.005	0
Maximum:	0.19	0.24	0.007
Summary:	0.05 (0.004 - 0.19)	0.063 (0.005 - 0.24)	0.00043 (0 - 0.007)