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Trifluralin

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
ALS	acetolactate synthase
APHIS	Animal and Plant Health Inspection Service
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
CCME	Canadian Council of Ministers of the Environment
CDPR	California Department of Pesticide Regulations
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
DER	data evaluation record
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
EHE	2-ethylhexyl ester
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
g	gram
GLP	Good Laboratory Practices
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient
IARC	International Agency for Research on Cancer
IRED	Interim Reregistration Eligibility Decision
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter

lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
m	meter
M	male
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MSMA	monosodium methanearsonate
MW	molecular weight
N.D.	not determined
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
NDMA	N-nitrosodimethylamine
NDPA	N-nitrosodi-n-propylamine
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
NTP	National Toxicology Program
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
Pa	Pascal
PBPK	physiologically-based kinetic
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
T.G.I.A.	Technical grade active ingredient
TIPA	Triisopropanolamine
TRED	Tolerance Reassessment Eligibility Decision
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture

U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
WHO	World Health Organization

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

The Forest Service anticipates applying trifluralin by soil incorporation to sunflower fields used as wildlife food plots. This use of trifluralin is very minor, relative to agricultural uses. In this anticipated use of trifluralin applied by soil incorporation, there is no indication that workers or members of the general public are at risk of exposures leading to systemic toxicity. In the event of an accidental spill, the HQs for members of the general public consuming contaminated fish substantially exceed the level of concern. These HQs, however, may be based on overestimates of plausible exposures. In the event of an accidental spill of a large amount of trifluralin into a relatively small pond, it is likely that fish would be killed or at least show signs of poisoning, in which case, it seems unlikely that individuals would consume the fish. The upper bound exposures associated with the consumption of water from a pond following an accidental spill modestly exceed the level of concern (HQ=2); nonetheless, it is not clear that these exposures would result in overt toxic effects. Based on the potential carcinogenicity of trifluralin, members of subsistence populations consuming fish taken from waters contaminated with trifluralin at expected (non-accidental) concentrations in surface water may be exposed to levels of trifluralin that exceed the level of concern—i.e., HQs of up to about 6 at an application rate of 1 lb a.i./acre.

Terrestrial animals and plants do not appear to be at substantial risk. Except for the consumption of contaminated fish, there is little indication that mammals or birds will be adversely affected by trifluralin. In the case of an accidental spill, the consumption of contaminated fish leads to HQs that are substantially above the level of concern. In the event of an accidental spill of trifluralin into a small pond, severe adverse effects could be seen in virtually all groups of aquatic animals and plants including both sensitive and tolerant species.

Based on peak expected concentrations in water associated with non-accidental exposures, tolerant species of aquatic organisms, including both animals and plants would not be impacted by anticipated upper bound peak or longer-term exposures. This risk characterization also applies to sensitive species of aquatic organisms in terms of longer-term exposures – i.e., all of the upper bound HQs for sensitive species of aquatic organisms are below 1 even at the maximum anticipated application rate.

Based on peak expected concentrations of trifluralin in surface water, sensitive species of fish might be adversely effected at application rates of both 1 lb a.i./acre and 2 lbs a.i./acre with exceedance in the HQ of 1 at both the central estimates of exposure as well as the upper bounds of exposures. Risks to aquatic-phase amphibians are likely to be similar to those for fish. Sensitive species of aquatic macrophytes could be impacted at both the central estimate of exposure as well as the upper bound of exposure but only at the maximum anticipated application rate of 2 lbs a.i./acre. Aquatic invertebrates are much less sensitive than fish to trifluralin. Even at the upper bounds of exposures, there is no basis for asserting that aquatic invertebrates will be adversely impacted by trifluralin.

Most of the HQs for trifluralin that exceed a level of concern involve concentrations of trifluralin that may be found in surface water. The concentrations used in the current risk assessment are highly variable with the range of peak concentrations spanning a factor of 195. This substantial variability is associated primarily with the differences in nine different sites and three soil types used in the Gleams-Driver modeling (Section 3.2.3.4.3). The upper bound HQs discussed in this risk assessment will not be applicable to all sites at which trifluralin may be applied, particularly areas with low rainfall rates. For site-specific applications of trifluralin, refinements to the exposure assessments associated with surface water could be warranted.

1. INTRODUCTION

The USDA Forest Service is considering using the herbicide trifluralin in vegetation management programs. The present document provides human health and ecological risk assessments regarding the consequences of using trifluralin in Forest Service programs.

A Forest Service Information Profile is available on trifluralin (Information Ventures 1995); however, the Forest Service has not previously conducted full human health and ecological risk assessments on trifluralin. Several reviews on the toxicology and environmental fate of trifluralin have been conducted by various governmental groups both within and outside of the United States (e.g., CalEPA 2002; CCME 1999; European Commission 2010a,b; Health Canada 2009; U.S. EPA/OPP 1996a,b, 2003a,b, 2004a,b, 2009a; OSPAR Commission 2005; WHO/IARC 1991; WHO 1996). The U.S. E-Docket (www.regulations.gov) contains 858 items at least peripherally related to trifluralin. In addition to the E-Docket, several cleared reviews of trifluralin are available from the U.S. EPA/OPP (http://www.epa.gov/pesticides/foia/reviews.htm). Much of the relevant information from registrant-submitted studies, however, appears to be available from various EPA risk assessments (U.S. EPA/OPP 1996a,b, 2004a,b, 2009a). Consequently, a FOIA of the cleared reviews was not submitted for the preparation of the current risk assessment.

The published literature on trifluralin was initially identified using TOXLINE (http://toxnet.nlm.nih.gov/). Additional information on trifluralin was identified through standard Internet search engines and databases (e.g., HSDB 2010; PAN 2010). As summarized in Section 5 (References), the open literature on trifluralin is robust with a substantial amount of information concerning its toxicity and environmental fate. Published reviews on the toxicology and environmental fate of trifluralin (e.g., Ebert et al. 1992; Fry 1995; Grover et al. 1997) were consulted but these reviews were used primarily to identify primary studies rather than as sources of information. Trifluralin is included in the U.S. EPA IRIS database (U.S. EPA/ORD 1993a), various reviews by the World Health Organization (WHO/IARC 1991; WHO 1996), the EXtension TOXicology NETwork series (EXTOXNET 1993), and the USDA/ARS Pesticide Properties Database (USDA/ARS 1995). USGS (2003a) provides information on the agricultural use of trifluralin as well as monitoring in surface water from the National Water Quality Assessment Program (USGS 2007).

This document has four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species. Each of the two risk assessment chapters has four major sections, including an identification of the hazards associated with trifluralin, 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 risk assessment, which serves primarily as a technical support document for use by the Forest Service, necessarily addresses some specialized scientific information.

Nevertheless an effort has been made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2007a). The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. The information presented in the appendices and the discussions in chapters 2, 3, and 4 of the risk assessment are intended to be detailed enough to support a review of the risk analyses.

As with all Forest Service risk assessments, almost no risk estimates presented in this document are given as single numbers. Usually, risk is expressed as a central estimate and a range, which is sometimes quite large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations, most of which are relatively simple. They are included in the body of the document.

Some of the calculations, however, are cumbersome. For those calculations, EXCEL workbooks are included as attachments to this risk assessment—i.e., Attachment 1 for liquid formulations and Attachment 2 for granular formulations. 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 (2009).

The EXCEL workbooks are an integral part of the risk assessment. The worksheets 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 (i.e., hazard quotients) are derived and contained in the worksheets. The rationale for the calculations as well as the interpretation of the hazard quotients are contained in this risk assessment document.

2. PROGRAMS DESCRIPTION

2.1. Overview

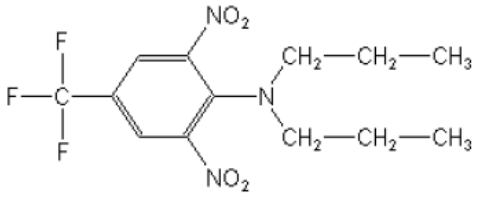
Trifluralin is a herbicide registered for the preemergence control of many broadleaf weeds and grasses. In agricultural applications, trifluralin is used primarily on soybeans, cotton, and alfalfa. The Forest Service anticipates applying trifluralin by soil incorporation to sunflower fields used as wildlife food plots. This use of trifluralin is very minor, relative to agricultural uses.

Trifluralin was introduced in the early 1960s and is now off patent. Consequently, there are numerous formulations of trifluralin available, including both liquid and granular formulations. The current risk assessment explicitly encompasses three liquid formulations (Treflan 4D, Treflan HFP, and Triflurex HFP) and two granular formulations (Treflan 5G and Treflan TR-10). The Forest Service has indicated only that liquid formulations will be used; nonetheless, a discussion of granular formulations is included in the event that the Forest Service considers using them. While the liquid and granular formulations are labeled for aerial application, this application method is not likely to be relevant to Forest Service programs; hence only soil incorporation is considered in this risk assessment.

Both liquid and granular formulations are labeled for a maximum single application rate of 2 lbs a.i./acre. For the liquid formulations, the maximum cumulative annual application rate is 4 lb a.i./acre. One granular formulation, Treflan TR-10, is labeled for a maximum cumulative application rate of 2 lbs a.i./year (i.e., identical to the maximum single application rate). Treflan 5G, another granular formulation, is labeled for higher application rates of up to 12 lbs a.i./year. These extremely high application rates are not likely to be used in Forest Service programs.

2.2. Chemical Description and Commercial Formulations

Trifluralin is the common name for 2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl) benzenamine:



Trifluralin is a pre-emergent herbicide registered for the control of various grasses and broadleaf weeds. As discussed further in Section 4.1.2.5, trifluralin is a mitotic poison similar to colchicine (Bartels and Hilton 1973; Rey et al. 2002). Trifluralin is absorbed by the roots of the developing plant and interferes with the normal development of microtubules during mitosis, blocking cell division and normal plant growth.

The physical and chemical properties of trifluralin are summarized in Table 1. Trifluralin is both highly lipophilic ($K_{ow} \approx 100{,}000$) and volatile (vapor pressure = 1.10×10^{-4} torr). As discussed further in Section 2.3, these two physical properties have an impact on the

effective application of trifluralin. Applying trifluralin to the soil surface may result in significant volatilization, thereby reducing the efficacy of the herbicide. If, however, trifluralin is incorporated into soil, it will bind to soil, thereby reducing volatilization and increasing efficacy.

Trifluralin is stable to hydrolysis, and the biodegradation of trifluralin in soil is relatively slow with aerobic soil half-lives ranging about 100 to 200 days. While no studies were encountered on the soil photolysis of trifluralin, aqueous photolysis is rapid with a half-life of about 0.4 days. As summarized in Table 3, trifluralin may form several metabolites due to biological or photochemical decomposition. While these metabolites are not structurally complex, the general and abbreviated TR-X nomenclature used by U.S. EPA/OPP and summarized in Table 3, is used also in the current risk assessment. The metabolites of trifluralin may be generally classified as reduction of the nitro groups to amines (TR-4, TR-5, TR-6, TR-7), cleavage of the N-propyl groups (TR-2, TR-5, TR-6), or condensation of the N-propyl groups to form heterocyclic benzimidazoles (TR-14, TR-15). The toxicity of metabolites is discussed further in Section 3.1.15 (human health) and Section 4.1.3 (aquatic organisms).

Trifluralin was developed in the early 1960s by Eli Lilly (Tomlin 2004). Trifluralin is no longer under patent protection, and there are numerous commercial formulations of trifluralin available. Based on information in the PAN Pesticide Database (2010), nearly 600 formulations are available in the United States.

Consistent with the approach taken in the most recent EPA risk assessment of trifluralin U.S. EPA/OPP (2009a), no attempt is made in the current document to consider every available formulation of trifluralin. Instead, representative formulations of trifluralin are selected, including three liquid formulations (Treflan 4D, Treflan HFP, and Triflurex HFP) and one granular formulation (Treflan TR-10), as summarized in Table 2. Treflan HFP is identified in U.S. EPA/OPP (2009a) as having forestry applications, and forestry applications of Treflan HFP are briefly noted in a review by DuPlissis (1998). Unspecified Treflan formulations are also discussed by Sandquist (1979) for use in forest nursery seedbeds. Although the application of Triflurex HFP, used in some Forest Service programs, is not mentioned in the available literature, this formulation is included because the Material Safety Data Sheet (MSDS) for this formulation is somewhat more detailed than MSDSs for other formulations.

The three liquid formulations contain about 43% trifluralin (w/w) with the remainder of the formulations consisting primarily of petroleum distillates. Based on information on the product labels and MSDS, Treflan 4D and Treflan HFP appear to be quite similar to each other. The MSDS for Treflan 4D specifies that naphthalene is present at a concentration of 7%; whereas, the MSDS for Treflan HFP does not specify the concentration of naphthalene in the formulation. The MSDS for Triflurex HFP is somewhat more detailed and specifies that the formulation contains 49.2% aromatic hydrocarbons. Naphthalene is a component in the aromatic hydrocarbons (7% w/w formulation).

While the specific constituents in each formulation are disclosed to the U.S. EPA/OPP, this information is considered proprietary and is not disclosed to the general public. The other ingredients in the trifluralin formulations are discussed further in Section 3.1.14.

Another granular formulation of trifluralin, Treflan 5G, is associated with forestry applications in several sources (Ferrell 2009; Netzer 1984; Information Ventures 1995; Williams-Woodward no date). Treflan 5G is a granular formulation that contains 5% (w/w) trifluralin. The only information on the other ingredients in this formulation is that the formulation contains 2.5% kerosene. As discussed further in Section 3.1.4, Treflan 5G has an atypically low oral LD_{50} of 500 mg/kg bw reported on the MSDS. The very low oral LD_{50} for this formulation suggests that the inerts in the formulation contribute substantially to the toxicity of the formulation. The atypically low LD_{50} for Treflan 5G is a concern, and it is not clear that the current risk assessment of trifluralin would encompass risks associated with applications of Treflan 5G.

2.3. Application Methods

Trifluralin formulations are recommended for the development of wildlife food plots (e.g., Harper 2008). The current risk assessment is developed specifically in response to the use of trifluralin on sunflower fields to prevent crabgrass in wildlife food plots. In these applications, liquid formulations of trifluralin are applied to plowed fields using a tractor mounted sprayer followed by disc incorporation (McKinney 2010). Unlike foliar applications, the intent of trifluralin applications is to deposit the herbicide on the soil surface. All product labels for the liquid formulations included in Table 2 recommend soil incorporation within 24 hours of application. Various types of soil incorporation equipment (e.g., tandem disc, rolling cultivator, bed conditioner) are recommended on the product labels with incorporation depths of 2-4 inches. The product labels for liquid formulations of trifluralin do not specify or recommend irrigation or rainfall for soil incorporation.

Liquid formulations of trifluralin may be used in either aerial or ground applications. The Forest Service generally avoids aerial applications of herbicides. The product labels for liquid formulations of trifluralin indicate that aerial applications should be made at a height of no more than 10 feet above the top of the largest plants present at the treated site. These types of low level aerial applications appear to be applicable to agricultural rather than forestry sites.

Granular formulations such as Treflan 5G are applied using drop or rotary spreaders to distribute the granules relatively evenly over the soil surface. Treflan 5G is not labeled for aerial application. Soil incorporation methods are not explicitly discussed on the product label for Treflan 5G. *Watering-in* is mentioned in a general label note on non-agricultural use requirements; however, it is not clear that watering-in is recommended for trifluralin granules. In a very brief note, Williams-Woodward (no date) indicates that Treflan 5G may be effectively activated by rainfall (and presumably irrigation) within 3 days of application. While granular formulations are discussed in this section for the sake of completeness, the Forest Service does not anticipate using granular formulations of trifluralin (McKinney 2010). Consequently, granular formulations are not included in the exposure assessments (Sections 3.2 and 4.2).

2.4. Mixing and Application Rates

The application rates for trifluralin differ substantially between liquid and granular formulations. Liquid formulations of trifluralin are labeled for maximum single application rates of 2 lbs a.i./acre and maximum cumulative annual application rates of 4 lbs a.i./acre.

The recent EPA ecological risk assessment for trifluralin (U.S. EPA/OPP 2009a) models a maximum single forestry application of 2 lbs a.i./acre for Treflan HFP. Liquid formulations are diluted prior to application. As summarized in Table 2, application volumes of 5-40 gallons/acre are used in ground applications. Application volumes affect the concentrations of the pesticide in field solutions, and these concentrations have an impact on the estimates of absorbed dose in some accidental exposure scenarios. For the current risk assessment, the central estimate of the application volume is taken as 10 gallons/acre with a range of from 5 to 40 gallons/acre.

Treflan TR-10, the granular formulation, is applied as a granule—i.e., the formulation is not mixed with water prior to ground application. The maximum single and cumulative annual application rate for this formulation is 2 lbs a.i./acre.

For weed suppression, the granular Treflan 5G formulation is labeled for maximum annual application rates of up to 12 lbs a.i./acre (240 lbs formulation/acre). This formulation also appears to be used for weed control under paved surfaces. In these applications, rates of up to 16 lbs a.i./acre (320 lbs formulation/acre) are specified on the product label. For forestry uses of granular formulations of trifluralin, U.S. EPA/OPP (2009a, Table 2.3, pp. 33-34) models three individual applications of 4 lbs a.i./acre with a minimum application interval of 60 days—i.e., a cumulative application rate of 12 lbs a.i/acre. This application pattern is consistent with the maximum labeled annual application rate for Treflan 5G, and this application pattern is used as the maximum application in the current risk assessment. Forestry applications of Treflan 5G as low as 1 lb a.i./acre are discussed in the literature (Netzer 1984); nevertheless, this application rate does not appear to have been effective, providing only 18% weed control. In a very brief note, Williams-Woodward (no date) indicates that a single application of 80 lbs Treflan 5G/acre (4 lbs a.i./acre) was used for weed control on a Christmas tree plantation.

2.5. Use Statistics

Most Forest Service risk assessments try to characterize herbicide uses in Forest Service programs relative to their use in agricultural applications. Generally, the information about Forest Service uses comes from Forest Service pesticide use reports (http://www.fs.fed.us/foresthealth/ pesticide/reports.shtml), and information about agricultural uses comes from use statistics compiled by the U.S. Geologic Survey (http://ca.water.usgs.gov/ pnsp/pesticide_use_maps/) and/or detailed pesticide use statistics compiled by the state of California (http://www.calepa.ca.gov/).

Trifluralin is not used extensively in Forest Service programs. Between 2000 and 2004, the most recent year for which use statistics are available at the Forest Service web site, only one application of trifluralin is cited, 10 lbs applied to 2.25 acres in Forest Service Region 5, the Pacific Southwest including California and Hawaii.

A summary of the agricultural uses of trifluralin is illustrated in Figure 1 (USGS 2003a). These use statistics are for 2002, the most recent year for which data are available from the USGS. As indicated in this figure, nearly 9,000,000 lbs of trifluralin were applied to crops annually during 2002. The major areas of trifluralin use appear to be in the central United States, particularly in North Dakota, Iowa, and Missouri with additional areas of concentrated use along the southern Mississippi River as well as in parts of Minnesota, Texas and Kansas. A band of heavy use is also apparent in central California.

More recent use statistics are available for California for the year 2007 (CDPR 2008). According to CDPR (2008, pp. 412-414), the total use of trifluralin in California during 2007 was approximately 900,000 lbs. The only applications related to forestry appear to be in rights-of-way management, which accounted for about 1265 lbs or about 0.14% of the total use. Based on these data, it seems reasonable to assert that forestry uses of trifluralin are likely to be far less than agricultural uses.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

Trifluralin disrupts mitosis, the process by which normal cell division occurs in eukaryote organisms, by interfering with the formation of the spindle fiber. In this respect, trifluralin is similar to colchicine, the classic mitotic poison. While trifluralin causes this effect in both plants and animals, trifluralin is selectively toxic to plants, and it is not clear that spindle fiber disruption is a central mechanism of toxicity in mammals. Trifluralin is extensively metabolized in mammals via N-dealkylation, hydroxylation, and reduction of the nitro-groups. The metabolism of trifluralin is mediated at least in part by cytochrome P-450. In terms of acute toxicity, trifluralin is classified as Category IV (the least toxic classification) for acute oral toxicity and acute dermal irritation and Category III (the second least toxic category) for acute inhalation exposures and eye irritation.

The signs of toxicity associated with longer-term exposures to trifluralin are generally nonspecific, consisting of weight loss, decreased food consumption, and changes in organ weights and blood chemistry. Increased liver weights are noted in several longer-term studies. and this effect could be associated with an induction of cytochrome P-450 rather than a direct toxic effect on the liver. Relatively high doses of trifluralin over a 90-day period of exposure are associated with damage to heart cells; however, this effect is not confirmed in other subchronic and chronic toxicity studies. While there is no indication that trifluralin causes birth defects, adverse effects observed in pregnant animals exposed to trifluralin include reduced food consumption, reduced body weight, and increases in the incidence of fetal mortality at doses associated with signs of maternal toxicity. Both acute and subchronic studies are available in mice, rats, rabbits, and dogs. While the chronic RfD for trifluralin is based on a study in dogs, no systematic differences in toxicity associated with body weight are apparent.

The U.S. EPA/OPP classifies trifluralin as a potential human carcinogen—i.e., a "Group C" carcinogen for which there is limited evidence that trifluralin may pose a carcinogenic risk to humans. As discussed further in the dose-response assessment, cancer risks associated with trifluralin applications are considered quantitatively in the current risk assessment. Trifluralin as well as trifluralin formulations may contain dipropylnitrosamine at concentrations of up to 0.5 ppm. Dipropylnitrosamine is a concern because this contaminant is also classified as a potential human carcinogen. While dipropylnitrosamine is a much more potent carcinogen than trifluralin, considerations of the amount of dipropylnitrosamine in trifluralin formulations suggest that this contaminant does not contribute substantially to the overall risks associated with the potential carcinogenicity of trifluralin.

3.1.2. Mechanism of Action

The most fully characterized mechanism of action of trifluralin involves the disruption of cell division. Trifluralin disrupts the formation of microtubules essential for normal cell division in both plants and animals. In this respect, trifluralin is similar to other dinitroaniline herbicides like oryzalin and pendimethalin as well as colchicine, a classic

mitotic poison. The disruption of tubule formation appears to involve binding to tubulin, a protein necessary for the normal development of microtubules. The disruption of microtubule formation prevents the normal development of spindle fibers and movement of chromosomes during mitosis. Consequently, cells are not able to replicate, and normal growth is disrupted (Felix et al. 1988; Fennel et al. 2006; Fernandes et al. 2009; Foureman 1988a,b; Vaughn and Helnen 1991). While the effects of trifluralin on cell division are generally similar to those of colchicine, trifluralin tends to be less toxic than colchicine to animal cells (e.g., Bartels and Hilton 1973; Fennel et al. 2006).

Trifluralin was assayed as a therapeutic agent against several protozoan parasites (e.g., Carvalheiro et al. 2009; Chan et al. 1993; Esteves et al. 2010; Fennel et al. 2006; Jayanarayan and Dey 2005; Naughton et al. 2008; Salas and Romero 1996; Stokkermans et al. 1996; Zaidenberg et al. 1999, 2006). The potential efficacy of trifluralin against protozoan parasites appears to involve both selective disruption of spindle fibers in protozoan cells as well as a selective action of trifluralin on the accumulation of calcium by the mitochondria of protozoa (Salas and Romero 1996).

Most of the available studies on the effects of trifluralin against various protozoan parasites, however, are preliminary *in vitro* efficacy studies. No clinical trials on the use of trifluralin were identified in the literature. Zaidenberg et al. (2007) conducted preliminary studies in mice related to the potential use of trifluralin for the treatment of Chagas disease, which is caused by a protozoan parasite. Weekly doses of 200 mg/kg bw administered for 90 days resulted in focal lymphocytic myocarditis (i.e., damage to heart cells) which was not seen at weekly doses of 50 mg/kg over the same period of time. While Zaidenberg et al. (2007, p 94) suggest that trifluralin has *potential selective action for the myocardium*, a significant increase in the incidence of damage to heart tissue is not noted in standard subchronic and chronic toxicity studies on trifluralin. Nonetheless, and as detailed further in Section 3.1.5, a recent epidemiology study (Dayton et al. 2010) reports a significant increased risk of myocardial infarction in female farm workers involved in applications of trifluralin.

Trifluralin is shown to induce cytochrome P-450 in mice, albeit at relatively high intraperitoneal doses of 250 mg/kg bw/day over a 3-day period (Moody et al. 1991). In addition, there is indirect evidence in studies on fish that trifluralin induces cytochrome P-450—i.e., co-exposure of fish to trifluralin and piperonyl butoxide, a known inhibitor of cytochrome P-450, increases the amount of trifluralin in fish (Reinbold and Metcalf 1976).

3.1.3. Pharmacokinetics and Metabolism

3.1.3.1. General Considerations

Several *in vivo* studies involving oral exposure are available on the pharmacokinetics and metabolism of C^{14}-trifluralin in rats (Emmerson and Anderson 1966; Erkog and Mezer 1985; Heck et al. 1977; Magnussen 1989). The study by Heck et al. (1977) also employed intraperitoneal administration to rats, and the study by Emmerson and Anderson (1966) involved dosing of unlabelled trifluralin to dogs. In additional to these *in vivo* studies, Nelson et al. (1977) examined the metabolism of trifluralin by rat liver

microsomes, while Golab et al. (1969) and Williams and Feil (1971) assayed the metabolism of C^{14}-trifluralin in ruminants.

In all species tested, trifluralin is extensively metabolized by the liver and excreted primarily in the feces. The *in vitro* studies of Nelson et al. (1977) clearly indicate that trifluralin is readily metabolized by liver microsomes (i.e., cytochrome P-450). As discussed in the previous subsection, mechanistic studies indicate that trifluralin will induce cytochrome P-450.

A simplified and partial overview of the metabolism of trifluralin in rats is illustrated in Figure 2. The major metabolic pathways for trifluralin involve N-dealkylation (i.e., complete or partial removal of the propyl groups from the nitrogen attached to the C-1 carbon of the aromatic ring), hydroxylation of the propyl groups, reduction of the nitro-groups (NO_2) to amines (NH_2), as well as various condensation reactions resulting in the formation of benzimidazoles (heterocyclic compounds). In addition, the metabolites of trifluralin may undergo conjugation with glucuronides and other endogenous compounds, such as sulfates. Figure 1 summarizes only some of the major metabolites of trifluralin in mammals. Many metabolites of trifluralin have not been identified. For example, Magnussen (1989) estimates that 30-40 metabolites of trifluralin are excreted in the urine of rats, with most of these being characterized as relatively polar conjugates. Similarly, in studies on goats, Golab et al. (1969) were able to identify only about 6% of the metabolites by mass. As discussed by Emmerson and Anderson (1966), many of the metabolites of trifluralin appear to be unstable, and, therefore, difficult to identify. Based on studies with C^{14}-trifluralin labeled in both the benzene ring as well as the trifluoromethyl group (Emmerson and Anderson 1966; Erkog and Mezer 1985), there is no indication that trifluralin metabolism involves either cleavage of the aromatic ring or dehalogenation of the trimethyl group. As discussed further in Section 3.1.15.1, the same is also true for the environmental metabolites of trifluralin in soil and vegetation.

Based on the high K_{ow} for trifluralin, preferential accumulation of trifluralin in fatty tissues would be expected. In the short-term and relatively low dose (1 and 10 mg/kg bw) metabolic studies by Erkog and Menzer (1985), however, no substantial accumulation in fatty tissue is noted. Similarly, Golab et al. (1969) note no substantial accumulation of trifluralin in the fatty tissue of ruminants. As summarized in Table 4 of the current risk assessment, Schutz and Donaubauer (1986) did note substantial and preferential accumulation of trifluralin in the fatty tissue of rats, particularly in the high dose group for which the average of the ratio of the concentration of trifluralin in fat relative to blood is about 2000.

In the subchronic study in rats, Zaidenberg et al. (2007) report that trifluralin appeared to be preferentially concentrated in heart tissue, relative to skeletal muscle tissue, by a factor of about 2, in terms of residues expressed as nanograms trifluralin per mg tissue protein. Trifluralin concentrations in heart tissue were noted sporadically in rats in the chronic feeding study by Schutz and Donaubauer (1986). For all but the highest dose level (3200 ppm in the diet), trifluralin levels were below the limit of detection in either the heart or muscle tissue. For the high dose group, the ratio of the concentrations of trifluralin in

heart to muscle tissue is illustrated in Figure 4. This figure shows that the ratio of trifluralin in heart to muscle tissue in male rats increases from month 6 to a maximum of about 16 at month 18 but then decreases to a ratio of about 1 by month 24. In female rats, the heart-to-muscle ratio of trifluralin exceeded a factor of 2 only at month 12. Golab et al. (1969) do not note trifluralin concentrations in the heart tissue of ruminants.

In terms of the current risk assessment, the potential hazards associated with the *in vivo* metabolism of trifluralin following human exposure may be encompassed by the existing *in vivo* toxicity studies in mammals, so long as the metabolism in humans is reasonably similar to metabolism in experimental mammals. Although information on the metabolism of trifluralin by humans is not available and the metabolism of trifluralin has been characterized only incompletely in mammals, the available data do not suggest substantial differences in metabolism among species. In rodents, dogs, and ruminants, most (about 70-80%) of the orally administered trifluralin is excreted in the feces with the remaining amount excreted in the urine (Emmerson and Anderson 1966; Heck et al. 1977; Golab et al. 1969). The only remarkable difference in these studies is that Emmerson and Anderson (1966) detected some (≅8%) unmetabolized trifluralin in the feces of rats while the other studies report virtually complete metabolism of trifluralin — i.e., no unmetabolized trifluralin was recovered from the feces or urine. As discussed by Erkog and Menzer (1985), this difference probably reflects the higher oral doses used in the study by Emmerson and Anderson (1966)—i.e., 100 mg/kg bw—and indicates incomplete absorption of trifluralin or saturable metabolism following high dose exposures.

3.1.3.2. Dermal Absorption

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

Two types of dermal exposure scenarios are considered: immersion and accidental spills. In the scenarios involving immersion, the concentration of the chemical in contact with the surface of the skin is assumed to remain constant or at least nearly so. As detailed in SERA (2007), the calculation of absorbed dose for dermal exposure scenarios involving immersion requires an estimate of the dermal permeability coefficient (K_p) expressed in cm/hour, and the rate of absorption is assumed to be essentially constant. In exposure scenarios involving direct sprays or accidental spills where the compound is deposited directly on the skin, the concentration or amount of the chemical on the surface of the skin is assumed to be the limiting factor in dermal absorption. For these scenarios, first-order dermal absorption rate coefficients (k_a), expressed as a proportion of the deposited dose absorbed per unit time (e.g., hour^{-1}), are used in the exposure assessment.

3.1.3.2.1. First-Order Dermal Absorption

In the absence of experimental data, Forest Service risk assessments generally estimate first-order dermal absorption rates based on quantitative structure activity relationships

(QSAR), as documented in SERA (2007). The algorithm on which these estimates are based is developed from the analysis of dermal absorption rates for compounds with K_{ow} values ranging from 0.0015 to 3,000,000 and molecular weights ranging from 60 to 400 g/mole. Using these methods with the molecular weight of 335.28 g/mole and the K_{ow} of 186,000 from U.S. EPA/OPP (2009a) for trifluralin, the estimated first-order dermal absorption rate coefficients are approximately 0.00686 (0.00213 to 0.0220) $hour^{-1}$. The calculation of these rates is detailed in Worksheet B03b of Attachment 1 (liquid formulations of trifluralin).

One of the available experimental studies can be used to estimate a first-order dermal absorption rate for trifluralin. In an *in vitro* study on rat skin preparations, Brand et al. (2004) assayed the dermal absorption of C^{14}-trifluralin, as Treflan MTF, in rats fed diets with or without ethanol at a rate equivalent to 36% of the caloric value of the diet. Over a 24-hour period, trifluralin absorption was about 2.6±0.34% in rats on an ethanol supplemented diet and 3.6±0.11% in rats on a control diet (Brand et al. 2004, Fig 1, p. 157). Using the higher absorption rate from the rats on an ethanol free diet, the first-order dermal absorption rate can be estimated at about 0.0015 $hour^{-1}$ [ln(1-0.036) ÷ 24 hours]. This estimated dermal absorption rate coefficient is below the QSAR estimates by a factor of about 1.4 [0.00213 $hour^{-1}$ ÷ 0.0015 $hour^{-1}$ ≅ 1.42] based on the lower bound and 4.6 [0.00686 $hour^{-1}$ ÷ 0.0015 $hour^{-1}$ ≅ 4.57] based on the central estimate.

The most recent EPA human health risk assessment (U.S. EPA/OPP 2004a) uses a dermal absorption rate of 3%. As detailed in U.S. EPA/OPP (2003a,b), this dermal absorption rate is based on a study in monkeys treated with ethalfluralin, a preemergence herbicide structurally similar to trifluralin. Based on the brief summary of this study in U.S. EPA/OPP (2003a, p. 16), dermal absorption was estimated at 2.84%. While units of day^{-1} are not explicitly stated in the EPA assessments (U.S. EPA/OPP 2003a,b, 2004), the absorption rate of 2.84% is used with daily exposures and may be viewed as a first-order dermal absorption rate coefficient of 0.0284 day^{-1}, which is equivalent to 0.0012 $hour^{-1}$. This first-order dermal absorption rate coefficient is similar to the corresponding value of 0.0015 $hour^{-1}$ from the study by Brand et al. (2004).

Given the consistency of the estimates of the dermal absorption of trifluralin in rats with the estimated dermal absorption of ethalfluralin in monkeys, there is no basis for using the somewhat higher estimates of dermal absorption based on QSAR. The estimated rates from Brand et al. (2004) are quite similar to the estimates from U.S. EPA/OPP (2003a,b). Preference is given to the data from Brand et al. (2004) because this study involved trifluralin rather than a surrogate and also estimates the variability in the dermal absorption rates. The Brand et al. (2004) study was conducted using four rats. Thus, the reported standard deviation of 0.11% corresponds to a standard error of 0.055%. Using a value of 4.303 for $t_{0.025}$, the 95% confidence interval for the first-order dermal absorption rate is 0.0312 to 0.0407 day^{-1} [0.036 ± 4.303x0.0011]. Expressing the rates in units of $hour^{-1}$, the first-order dermal absorption rates for trifluralin are estimated at 0.0015 $hour^{-1}$ (0.0013 to 0.0017) $hour^{-1}$.

3.1.3.2.2. Zero-Order Dermal Absorption

Another set of exposure scenarios used in this risk assessment involves the assumption of zero-order absorption (i.e., the dermal absorption rate is constant over time). This type of assumption is reasonable when the skin is in contact with a constant concentration of the pesticide. As discussed further in Section 3.2, this type of exposure scenario is assumed for workers wearing grossly contaminated gloves as well as members of the general public swimming in water contaminated with trifluralin. This type of exposure scenario requires an estimate of dermal permeability (K_p) in units of cm/hour.

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 algorithm is discussed in further detail in SERA (2007). As with the algorithm for estimating the first-order dermal absorption rate coefficient (Section 3.1.3.2.1), the EPA algorithm (U.S. EPA/ORD 1992, 2007) is based on molecular weight and K_{ow} values. The values for K_{ow} and molecular weight used to implement the algorithm are identical to those used for the estimates for first-order absorption—i.e., a molecular weight of 335.28 g/mole and a K_{ow} of 186,000 (U.S. EPA/OPP 2009a). The algorithm developed by the EPA 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). This range of values for K_{ow} and molecular weight encompass the estimates of the corresponding values for trifluralin. The algorithm developed by the EPA results in an estimated dermal permeability (K_p) of about 0.0862 (0.0345-0.216) cm/hour. Details of the implementation of the algorithms are given in Worksheet B03a in the EXCEL workbooks that accompany this risk assessment.

The dermal permeability of trifluralin is addressed by Brand and Mueller (2002). This study involved skin preparations from mice using C^{14}-labelled trifluralin. The estimates from this study are reported as log K_p values (Brand and Mueller 2002, Table 2, p. 20). The study does not explicitly state whether the values are expressed in common (base 10) or natural logarithms; however, the log K_{ow} values in the publication suggest that the authors use common logarithms. As summarized in Table 3 of the current risk assessment, Brand and Mueller (2002) assayed 1:10 and 1:40 dilutions of both technical grade trifluralin and Treflan MTF (412 g a.i./L). For both trifluralin and the Treflan formulation, the more concentrated 1:10 solutions yielded somewhat higher estimates of the K_p (i.e., factors of about 2-3) compared with the more dilute 1:40 solutions. Even more remarkable is that the estimated K_p values for the formulation are greater than those for trifluralin by factors of about 3.6 for the 1:10 dilution and 2.6 for the 1:40 dilution.

As with the estimates of the first-order dermal absorption rate coefficients (Section 3.1.3.2.1), the QSAR algorithm for the K_p yields higher estimates than even the highest experimental estimate of K_p from Brand and Mueller (2002). In other words, the central estimate of 0.0862 cm/hour from the QSAR algorithm is about 85 times greater than the maximum K_p of 0.001015 cm/hour from Brand and Mueller (2002) [0.0862 cm/hour ÷ 0.001015 cm/hour ≅ 84.93].

Also as with the estimates of the first-order dermal absorption rate coefficients, the current risk assessment uses the experimental K_p rather than the estimates based on the QSAR algorithm. The liquid formulation of trifluralin used by Brand and Mueller (2002) appears to be similar to the liquid formulations of trifluralin (Treflan 4D and Triflurex HFP) identified in Table 2 of this risk assessment. The highest K_p for the Treflan formulation is reported by Brand and Mueller (2002) as a log K_p of -6.55±0.24. The publication does not specify whether the variability is expressed as the standard deviation or the standard error. In addition, the publication notes that the K_p values are based on 3 to 14 individual experiments but does indicate the number of experiments on which each K_p value is based. Consequently, it is not possible to estimate confidence intervals for the K_p values reported in the study.

For the current risk assessment, the K_p for liquid formulations of trifluralin is taken as 0.0010 cm/hour with no estimates of variability (i.e., the lower and upper bounds of the K_p are taken as 0.0010 cm/hour). The failure to define estimates of the variability in the K_p is discussed further in the risk characterization. As discussed in the program description, the Forest Service may use granular formulations of trifluralin which may contain kerosene at concentrations of about 3%. While it seems reasonable to speculate that dermal absorption from granular formulations of trifluralin might be less than that of liquid formulations, no data are available on dermal absorption rates for granular formulations. In the absence of data, the assumption is made that the dermal absorption of granular formulations will be equal to that of liquid formulations. The impact of this assumption on the risk assessment is discussed further in the risk characterization (Section 3.4).

3.1.3.3. Excretion

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

Equation 1

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

As the number of doses ($\boldsymbol{N}$) increases, the numerator in Equation 2 approaches a value of 1. Over an infinite period of time, the plateau or steady-state body burden ($\boldsymbol{X_{Inf}}$) can be calculated as:

Equation 2

$$\frac{X_{Inf}}{X_1} = \frac{1}{1 - e^{-kt^*}} \cdot$$

Heck et al. (1977) report half-lives of 15 hours in liver and 31 hours in fat following intraperitoneal injections of 0.5 mg/kg bw in rats. For estimating body burden using the plateau principal, whole body excretion rates are generally preferable to urinary excretion rates. Erkog and Menzer (1985, Table II, p. 1064) provide data on the cumulative excretion of C^{14} residues in the feces and urine of rats following a single oral dose of 1 mg/kg bw. Given the extensive metabolism of trifluralin (Section 3.1.3.1), the excretion of C^{14} residues is representative of the body burden of both trifluralin and its metabolites. Erkog and Menzer (1985) do not provide a kinetic analysis of these data. In the conduct of the current risk assessment, the data from Erkog and Menzer (1985) were analyzed using both one-compartment and two-compartment elimination models (e.g., O'Flaherty 1981). These analyses are illustrated in Figure 3. The one-compartment model provided an adequate fit to the data (r^2=0.91, p=0.00198) and yielded an estimated whole-body half-life of about 29 hours. Notwithstanding the fit of the one-compartment model, the excretion data illustrated in Figure 3 indicate a biphasic pattern with an initial half-life of about 0.4 days and a terminal half-life of about 1.8 days. The terminal half-life of 1.8 days corresponds to an excretion rate of about 0.38 day^{-1}. When this value is substituted into Equation 2, the estimated plateau in the body burden after daily doses over a prolonged period of time is about 3.1 [$1 \div (1 - e^{-0.38}) \cong 3.129$]. In other words, daily doses of trifluralin could lead to a modest accumulation in humans over prolonged periods of exposure.

3.1.4. Acute Oral Toxicity

One very basic type of acute toxicity information involves time-specific LD_{50} or LC_{50} values (i.e., doses or concentrations of a toxicant that result in or are estimated to result in 50% mortality of the test species during a specified exposure or observation period). These values can be viewed as an index of acute lethal potency. Information on the acute oral toxicity of trifluralin is summarized in Appendix 1. Table A1-1 summarizes information on trifluralin formulations taken from material safety datasheets (MSDS), and Table A1-2 summarizes information on technical grade trifluralin.

As with many other herbicides, both *definitive* and *non-definitive* LD_{50} values are reported for trifluralin. LD_{50} values expressed as a specific value (with or without confidence intervals) are referred to as *definitive* LD_{50} values. LD_{50} values expressed as greater than a particular value are referred to as *non-definitive* LD_{50} values (e.g., >5,000 mg/kg bw). While *non-definitive* LD_{50} values are often associated with limit tests (i.e., single dose studies), standard multi-dose acute toxicity studies sometimes result in mortalities that are substantially below 50%, and the dose-response relationship may be such that the LD_{50} or other comparable value cannot be estimated. In these instances, a non-definitive LD_{50} is reported in which the *greater than* value is the highest dose or concentration tested.

As summarized in Appendix 1 (Table A1-2), the acute LD_{50} values for technical grade trifluralin are available in four species (dogs, mice, rats, and voles) and range from 1930 mg/kg bw (male rats in the study by Hollander 1979) to >10,000 mg/kg bw (an LD_{50} for dogs from Ebert et al. 1992). Definitive LD_{50} values are available for only mice and rats, and these LD_{50} values do not suggest substantial species differences based on body size— i.e., the definitive LD_{50} values for mice range from 3150 to 5000 mg/kg bw (Ebert et al. 1992) and the definitive LD_{50} values for rats range from 1930 to 2270 mg/kg bw (Hollander 1979; Ebert et al. 1992). While the definitive LD_{50} values for rats are modestly lower than those for mice, the very high non-definitive LD_{50} value for dogs (>10,000 mg/kg bw from Ebert et al. 1992) suggests that larger mammals are not more sensitive than smaller mammals to trifluralin.

As detailed in SERA (2007, Table 3-2), the U.S. EPA/OPP classifies pesticides, based on the results of acute oral toxicity studies as well as other acute endpoints, into four toxicity categories designated as Category I (the most toxic) to Category IV (the least toxic). In its most recent human health risk assessments on trifluralin (U.S. EPA/OPP 2003a,b), the EPA selected a registrant submitted study in rats (MRID 00157486) with a non-definitive LD_{50} of >5,000 mg/kg bw to classify technical grade trifluralin as Category IV (i.e., compounds with acute oral LD_{50} values of >5000 mg/kg bw. U.S. EPA/OPP (2003a,b) do not cite or discuss the lower acute LD_{50} values for trifluralin.

Because LD_{50} values are not used directly in Forest Service risk assessments to quantitatively characterize risk, the inability to associate the oral LD_{50} values for the formulations with specific registrant submitted studies is not a severe limitation in the risk assessment. Nonetheless, as discussed further in Section 3.1.14 (Adjuvants and Other Ingredients), acute oral LD_{50} values are often useful in assessing the potential impact of ingredients in the formulations on potential risk.

As summarized in Appendix 1 (Table A1-1), the acute oral LD_{50} values for the trifluralin formulations explicitly considered in the current risk assessment range from 500 mg/kg bw (Treflan 5G) to >5000 mg/kg bw for Treflan HFP. The interpretation of these LD_{50} values is limited because they cannot be associated with registrant submitted studies. Typically, on MSDS, the acute oral LD_{50} values are expressed in units of mg formulation/kg bw. It is not clear whether or not this is the case with the LD_{50} values on the MSDS for trifluralin formulations.

For formulations of trifluralin such as Treflan HFP, the non-definitive LD_{50} of >5000 mg/kg bw does not raise concern. The dose of 5000 mg/kg bw is often used as a limit dose in acute oral toxicity studies (i.e., the dose that defines a compound as essentially nontoxic in terms of acute lethal potency). Thus, if a dose of 5000 mg/kg bw does not cause 50% mortality in rats, the compound is considered essentially nontoxic for acute oral exposures. At the other extreme, however, the reported definitive acute LC_{50} of 500 mg/kg bw for Treflan 5G does raise concern, because the formulation appears to be substantially more toxic than trifluralin itself following acute oral dosing.

As discussed further in Section 3.1.14, the higher toxicity of the formulation relative to the active ingredient suggests that the formulation contains materials that are more toxic than the active ingredients. Because the identity of other ingredients in the formulation are considered to be propriety information (i.e., the information is not disclosed to the general public) the potential risks of using formulations such as Treflan 5G, which are much more toxic than trifluralin itself, may not be encompassed by the current risk assessment. This issue is discussed further in the risk characterization (Section 3.4.5).

3.1.5. Subchronic or Chronic Systemic Toxic Effects

As summarized in Appendix 1 (Table A1-10), subchronic and chronic toxicity studies on trifluralin have been conducted in rats, dogs, and mice. With the exception of the National Toxicology Program bioassays in rats and mice (NTP 1978), all of the subchronic and chronic toxicity studies are registrant submitted studies required by U.S. EPA/OPP for the registration of trifluralin.

As discussed further in Section 3.3 (Dose-Response Assessment), the 1-year toxicity study by Adams et al. (1992) is used by the U.S. EPA/OPP to derive the RfD for trifluralin. In this study, Adams et al. (1992), administered 0, 0.75, 2.4, or 40 mg/kg/day trifluralin in capsules to beagle dogs for 1 year. No effects were noted at the two lower doses; however, adverse effects, including decreased body weight, increased liver weight, and hematological changes were observed in the dogs dosed at 40 mg/kg bw/day. It is possible that the increase in liver weight was associated with the induction of cytochrome P-450. As discussed in Section 3.1.2, trifluralin is a known inducer of cytochrome P-450, and substantial increases in liver cytochrome P-450 are often accompanied by increases in liver weight. The Adams et al. (1992) study in which trifluralin was administered in capsules is supported by a 1-year dietary study in dogs (MRIDs 00151908 and 00159618). As summarized in U.S. EPA/OPP (1996a), in the dietary study, trifluralin was administered at concentrations of 0, 30, 150, and 750 ppm. Although adverse effects were not observed in dogs at the nominal dose of 30 ppm (corresponding to a dose of 0.75 mg/kg bw), increases in liver weight and methemoglobin levels were noted at 150 ppm (corresponding to a dose of 3.75 mg/kg bw/day).

While dogs appear to be somewhat more sensitive than either rats or mice to trifluralin, the differences are not substantial. For example, the NOAEL of 2.4 mg/kg bw/day in dogs from the study by Adams et al. (1992) is not substantially below the chronic NOAEL of 7.5 mg/kg bw/day in mice (Suter et al. 1987) and is virtually identical to the subchronic NOAEL of 2.5 mg/kg bw/day in rats (Usher 1986). Similarly, the LOAEL of 40 mg/kg/day in dogs from the study by Adams et al. (1992) is identical to two subchronic LOAELs in rats (Schutz and Donaubauer 1986; MRID 00151906) and similar to the subchronic LOAEL of 10 mg/kg bw/day in rats (Usher 1986) and a 30 mg/kg bw/day LOAEL in female mice (Suter et al. 1987). Thus, while the selection of the dog by the U.S. EPA/OPP as the most sensitive species appears to be appropriate, there is no basis for proposing an allometric relationship for the subchronic and chronic toxicity of trifluralin to mammals.

As noted in 3.1.2 (Mechanism of Action), Zaidenberg et al. (2007) suggest that trifluralin may have … *selective action for the myocardium.* This comment is based on a

preliminary toxicity study on trifluralin to assess the potential therapeutic use of trifluralin for the treatment of Chagas disease, a tropical disease caused by *Leishmania* parasites. In this study, trifluralin was administered weekly to rats at doses of 50 mg/kg bw/week for 30 days and 200 mg/kg bw/week for 30 and 90 days. The 90-day exposures to 200 mg/kg bw/week were associated with focal lymphocytic myocarditis. In addition, the study found that trifluralin concentrations in heart tissue were 2-fold greater than in muscle tissue (i.e., suggestive of the selective concentration of trifluralin in heart tissue).

Concern for the potential cardiotoxicity of trifluralin is enhanced by the recent epidemiology study of female pesticide workers (Dayton et al. 2010). In this study, significant increases in the odds ratios for nonfatal myocardial infarctions were noted for trifluralin among female pesticide applicators who indicated their involvement in trifluralin applications—i.e., an odds ratio of 1.8 (1.0 to 3.1). When, however, women with self-reported angina or arrhythmia were excluded from the analysis, the increased odds ratio was not statistically significant—i.e., an odds ratio 1.3 (0.6 to 2.6). As also noted by Dayton et al. (2010), significant increases in the odds ratios for myocardial infarctions were noted for women who reportedly used chlorpyrifos, coumaphos, carbofuran, metalaxyl, and pendimethalin. Because the reported use of these chemicals was correlated with the reported use of trifluralin, the increased odds ratios for myocardial infarctions cannot be attributed directly to trifluralin (i.e., the apparent increased risks of myocardial infarctions could be due to co-exposure of any or several of the pesticides for which odds ratios were significantly increased). In addition, there was no apparent association with fatal myocardial infarctions. As noted by Dayton et al. 2010:

> *When we included the 48 women with fatal Mls* [myocardial infarctions] *since enrollment, there were only two more cases who had ever applied pesticides and none who reported using the pesticides associated with nonfatal Mls; hence, the results were essentially unchanged from the analysis including the nonfatal Mls only (data not shown).*
>
> Dayton et al. 2010, p. 696.

Notwithstanding the reservations in the results reported by Dayton et al. (2010), the induction of lymphocytic myocarditis by trifluralin reported by Zaidenberg et al. (2007) enhances concern for the results reported in the epidemiology study by Dayton et al. (2010).

Conversely, none of the chronic studies summarized in Appendix 1 (Table A1-10) reports pathological changes in heart tissue that are clearly associated with trifluralin. It should be noted that the U.S. EPA requires the histological examination of heart tissue for all chronic toxicity as well as carcinogenicity studies (U.S. EPA/PPTS 1998a,b). This requirement also holds for carcinogenicity studies conducted under the National Toxicology Program, and the bioassay of trifluralin (NTP 1978) includes data on pathological changes in cardiac tissue. None of the registrant submitted studies notes any pathological changes in heart tissue. In the chronic study in dogs by Adams et al. (1992),

a significant decrease in ratio of heart-to-brain weight was noted in female dogs in the high dose group (40 mg/kg bw/day); however, no pathological changes to heart tissue are reported. In the rat carcinogenicity bioassay by NTP (1978), no pathological changes in heart tissue were observed in males. In females, inflammation of myocardium was observed in 1/12 (≅8%) of rats in the low dose group, relative to 0/50 in the control group, and degeneration of the myocardium was noted in 1/12 rats in the high dose group, relative to 2/50 in the control group. Using the Fisher Exact test, neither of these responses is statistically significant (i.e., $p \cong 0.194$ for inflammation of the myocardium and $p \cong 0.482$ for degeneration of the myocardium).

Zaidenberg et al. (2007) indicate that follow-up studies were being conducted at the time of the 2007 publication. No follow-up studies by this group, however, were found in the literature. In the absence of additional as well as more detailed and focused studies on the effects of trifluralin on heart tissue, an unequivocal assessment of the potential cardiotoxicity of trifluralin cannot be made. Notwithstanding this limitation, both the concentration of trifluralin in heart tissue and the effects of trifluralin on tissue appear to be evident only at high doses, and cardiotoxicity does not appear to be the most sensitive endpoint.

3.1.6. Effects on Nervous System

In severely poisoned animals, virtually any chemical may cause gross signs of toxicity which might be attributed to neurotoxicity—e.g., incoordination, tremors, or convulsions. A direct neurotoxicant, however, is defined as a chemical that interferes with the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of a direct neurotoxicant distinguishes agents that act directly on the nervous system (direct neurotoxicants) from those agents that might produce neurological effects secondary to other forms of toxicity (indirect neurotoxicants). U.S. EPA has developed a battery of assays to test for neurotoxicity (U.S. EPA/OCSPP 2010), and U.S. EPA/OPP requires neurotoxicity studies for pesticides when standard toxicity studies or other considerations such as chemical structure suggest that concerns for effects on the nervous system are credible. In most standard subchronic and chronic rodent bioassays used and accepted by U.S. EPA for pesticide registration, brain morphology is assessed. The spinal cord and peripheral nerves (e.g., sciatic nerve) are usually evaluated only if there are other indications of neurotoxicity

As discussed in Sections 3.1.4, 3.1.5 and 3.1.9, the toxicology of trifluralin was investigated in acute, subchronic, chronic, developmental, and reproduction studies in mammals. There appears to be no basis for asserting that trifluralin is neurotoxic. This assessment is essentially identical to the Hazard Identification made by the Hazard Identification Assessment Review Committee (HIARC) of the U.S. EPA/OPP (2003a, p. 3): *The HIARC concluded that there is not a concern for neurotoxicity resulting from exposure to trifluralin*.

While not required by the U.S. EPA/OPP, a standard delayed neurotoxicity study was conducted in white leghorn hens. At a gavage dose of 5000 mg/kg bw, the only effects noted were marginal disturbances in muscle coordination from days 9 to 11. No signs of

damage to nerve tissue were noted, based on examinations of the brain, spinal cord, and sciatic nerve. In addition, no signs of ataxia were noted after the hens were re-dosed at 500 mg/kg bw (Ebert 1985; U.S. EPA/OPP 2003b).

3.1.7. Effects on Immune System

Some assessment of the potential immunotoxic effects of trifluralin can be inferred from the standard subchronic and chronic toxicity studies (Section 3.1.5) as well as developmental and reproduction studies (Section 3.1.9). These studies 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 the morphology of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected.

The subchronic and chronic toxicity studies on trifluralin provide no indication of potential immunotoxic effects. As discussed further in Section 3.1.9 and detailed further in Appendix 1 (Tables A1-8 and A1-0), there are numerous developmental and reproductive toxicity studies on trifluralin, and these provide only sporadic indications of potential immunotoxicity. In the multigenerational reproduction study in rats (Becker 1984), a decrease in relative thymus weights was noted in both males and females in the high dose group (2000 ppm). Effects on the thymus are noted only in one developmental study in rabbits (MRID 00152421) in which some abnormally small offspring in one litter evidenced thymic hypoplasia. The only other observation which might suggest an effect on the immune system is an increase in spleen weight noted in a developmental study in rats in the high dose group—i.e., 500 mg/kg bw/day (MRID 00151899, 00159620, and 40392310). Given the sporadic nature of these observations, however, U.S. EPA/OPP (2003a, p. 26) concludes that: *Trifluralin does not appear to be an immunotoxicant*. This assessment seems reasonable and the sporadic observations on the thymus could be associated with a non-specific response to stress.

Three studies in the open literature relate to the potential effects of trifluralin on immune function (Blakely et al. 1998, Igarashi et al. 2006, Ohnishi et al. 2008). In the study by Blakely et al. (1998) a significant decrease in T-lymphocyte response to two antigens (phytohemagglutinin and concanavalin A) was noted in rats after oral doses of 17.5 mg/kg bw/day for 28 days. Several other assays of immune function (i.e., immunoglobulin antibody plaque formation, immunostaining of peripheral whole blood, phagocytic responses of peritoneal macrophages) were not affected by trifluralin. The limited responses of the rats to trifluralin were interpreted by Blakely et al. (1998) as having minimal biological significance. In an *in vitro* study of immune function in macrophages, trifluralin evidenced no signs of immunotoxicity at a concentration of 0.1 mM (equivalent to about 33.5 mg/L) (Igarashi et al. 2006, Ohnishi et al. 2008). The results of these studies are consistent with the assessment made in U.S. EPA/OPP (2003a) that trifluralin does not appear to be an immunotoxic agent.

3.1.8. Effects on Endocrine System

The direct effects of chemicals on endocrine function are most often assessed in mechanistic studies on estrogen, androgen, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). The U.S. EPA/OPP has developed a battery of screening assays for endocrine disruption (i.e., http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series890.htm), and trifluralin has been selected as one of the pesticides for which the screening assays are required (U.S. EPA/OPP 2009b). Results of the screening assays were not located in a search of the EPA web site.

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. As with effects on the nervous system and immune function, however, 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.

In terms of functional effects that have important public health implications, effects on endocrine function would be expressed as diminished reproductive performance or abnormal development. This issue is addressed specifically in the following section (Section 3.1.9), while this section is limited to mechanistic assays that can be used to assess potential direct action on the endocrine system.

Several *in vitro* screening assays for endocrine activity were identified for trifluralin: two using yeast cells (Nishihara et al. 2000; Orton et al. 2009), two using human breast cancer cells (Sonnenschein and Soto 1998; Soto et al. 1995) and one using hamster ovary cells (Kojima et al. 2004). No estrogenic or androgenic activity was noted in these assay systems at concentrations of up to 33.5 mg/L (i.e., ≅ 0.1 mM). In the yeast assay by Orton et al. (2009), antiandrogenic activity was noted at concentrations of 5.2 mg/L or greater; yet, no antiandrogenic activity was noted in the hamster ovary cell assays by Kojima et al. (2004) at culture concentrations of up to 3.36 mg/L (10^{-5} M).

As summarized in Appendix 4, Table A4-4, Couch (1984) conducted a 19-month study in sheepshead minnows at trifluralin concentrations ranging from to 1 to 5 µg/L and noted histopathological changes as well as enlargements of the pituitary glands of the fish. While studies in fish are not typically considered in the human health risk assessment, the observations by Couch (1984) are relevant because this study is interpreted in the review by Colburn et al. (1993) as indicating that trifluralin is an endocrine disrupter. The review by Colburn et al. (1993) is, in turn, cited elsewhere in the literature as an indication that trifluralin is an endocrine disrupter (Garry et al. 1996; Harriot and Feldman 2008). Notably, however, the original publication by Crouch (1984) does not attribute the changes in the pituitary glands of the fish specifically to an endocrine mechanism:

> *Abnormal enlargement or variation in sizes of pituitaries from fish of the same age, along with histopathological findings may be related to the environmental quality of the fish's habitat, and provide indications of stress within individuals resulting from toxicant exposure.*
>
> Couch 1984, p. 157

In the absence of mechanistic studies indicating that trifluralin is likely to bind to or otherwise have an impact on estrogen or androgen receptors, using the study by Couch (1984) to classify trifluralin as an endocrine disrupter appears to be tenuous.

3.1.9. Reproductive and Developmental Effects

3.1.9.1. Developmental Studies

Developmental studies are used to assess whether a compound has the potential to cause birth defects—also referred to as teratogenic effects—as well as other effects during development or immediately after birth. These studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required for the registration of pesticides. Very specific protocols for developmental studies are established by U.S. EPA/OPPTS and are available at http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized.

As summarized in Table 5 and detailed further in Appendix 1 (Table A1-8), six developmental studies involving gavage dosing of mice, rats, and rabbits were submitted to the U.S. EPA in support of the registration of trifluralin. A consistent pattern in all of the available studies is that adverse effects on offspring occur only at doses that also cause signs of maternal toxicity. In addition, there is no indication in the mammalian studies that that trifluralin causes birth defects. At doses that cause maternal toxicity, observed adverse effects on offspring include delayed development and fetal mortality (i.e., abortions). As discussed further in Section 3.3.2, the most recent EPA human health risk assessment (U.S. EPA/OPP 2003b) uses the 100 mg/kg bw/day NOAEL in rats from MRID 00151899 as the basis for the acute RfD. The corresponding LOAEL is 500 mg/kg bw/day, which resulted in severe signs of maternal toxicity, including mortality. Adverse effects in offspring included early resorptions (i.e., fetal or embryo mortality).

Garry et al. (1996) conducted an epidemiology study on 34,772 licensed pesticide applicators in Minnesota which involved 4935 live births. Based on combined births with central nervous system, circulatory/ respiratory, urogenital, and musculoskeletal anomalies, the odds ratio for workers who had handled trifluralin was slightly but significantly elevated (i.e., 1.59 with a 95% confidence interval of 1.39-1.80). A slight but significant increase in odds ratios was also noted for all anomalies combined (i.e., 1.35 with a 95% confidence interval of 1.23-1.49). Garry et al. (1996) do not provide any analysis based on differing levels of exposure to trifluralin and the odds ratios for birth defects.

A more recent study by Barr et al. (2010) of a much small group of individuals (n=150) noted a correlation between trifluralin levels in maternal and umbilical cord blood. No correlation, however, is noted between the concentrations of trifluralin and birth weight or other abnormal reproductive outcomes.

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 the offspring.

Table 5 summarizes three multigenerational rat reproduction studies submitted to the U.S. EPA/OPP. Additional details on these studies are provided in Appendix 1 (Table A1-9). As with the developmental studies, effects on the reproductive parameters were not observed at doses that did not cause signs of toxicity in the treated adults. The lowest exposure level associated with any signs of reproductive toxicity is 650 ppm (corresponding to a dose of about 32.5 mg/kg bw/day) in the study by Becker (1984). At this dose level, signs of reproductive toxicity included decreased pup weights and reduced litter sizes.

3.1.10. Carcinogenicity and Mutagenicity

Three types of data are commonly used to assess potential carcinogenicity of a compound. These data include epidemiology studies, bioassays on mammals, and tests for genetic toxicity, including mutagenicity. The literature on trifluralin does not include epidemiology studies which would permit an assessment of the association between exposure to trifluralin and the development of cancer in humans.

As summarized in Appendix 1 (Table A1-10), there are several chronic toxicity studies conducted in rats and mice which are useful for assessing the carcinogenic potential of trifluralin. These studies are reviewed in detail in U.S. EPA/OPP (1996a, 2003a,b); moreover, the EPA classifies trifluralin as a "Group C" carcinogen—i.e., there is limited evidence that trifluralin may pose a carcinogenic risk to humans. This classification is based primarily on a 2-year feeding study in Fischer 334 rats in which trifluralin was administered at dietary concentrations of 0, 813, 3250, or 6500 ppm, equivalent to daily doses of 0, 41, 163 or 325 mg/kg bw/day. In this study, a dose-related increase in neoplasms in the kidneys of male rats was noted along with a dose-related increase in benign bladder neoplasms in female rats. As discussed further in Section 3.3.4 (Dose-Response Assessment for Carcinogenicity), U.S. EPA/OPP (2003b) derives a cancer potency factor for trifluralin, based on combined tumor rates in male rats for follicular cell adenomas, papillary adenoma, cystadenoma, and carcinoma.

Several other cancer bioassays summarized in Appendix 1 (Table A1-10) did not note significant increases in malignant tumors in rats or mice. An exception is the early cancer bioassay in mice conducted by the National Toxicology Program (NTP 1978), which found a significant increase in liver cancer among treated female mice. The, EPA however, does not consider this bioassay useful for the quantitative assessment of potential carcinogenicity because the trifluralin used in the bioassay was contaminated with 84-88 ppm dipropylnitrosamine (U.S. EPA/OPP 2003b).

As also summarized in U.S. EPA/OPP (2003b, p. 25ff), several standard *in vitro* bioassays regarding the mutagenicity of trifluralin indicate that trifluralin is not mutagenic.

Forest Service risk assessments defer to the U.S. EPA/OPP on assessments of carcinogenicity. While the available data on trifluralin may appear quite limited (i.e., carcinogenic activity is noted in only a single study), the EPA classification of trifluralin as a Group C carcinogen with the derivation of a cancer potency factor is sufficient to identify carcinogenicity as an endpoint of concern.

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

The U.S. EPA requires relatively standard assays for skin and eye irritation as well as dermal sensitization. As summarized in Appendix 1 (Tables A1-5 to A1-7), trifluralin does not appear to cause dermal irritation (Category IV) and causes only slight skin and eye irritation (Category III). While trifluralin did not cause dermal irritation in the acute study, several subacute dermal toxicity studies, summarized in Appendix 1 (Table A1-3), do note relatively severe signs of dermal irritation, including bleeding of the skin.

Trifluralin caused dermal sensitization in a standard assay in guinea pigs (Appendix 1, Table A1-6). The sensitizing effect of trifluralin is reported also in a case report in the open literature (Pentel et al. 1994). This case report involves one individual who showed evidence of allergic contact dermatitis following exposures to trifluralin as well as many other pesticides. Based on the results of standard patch tests, the individual appeared to have allergic reactions to trifluralin as well as to chloroxylenol and benefin.

3.1.12. Systemic Toxic Effects from Dermal Exposure

The acute and subchronic dermal toxicity data on trifluralin are summarized in Appendix 1 (Table A1-3). The one available standard acute toxicity study on trifluralin reports a dermal LD_{50} of >2000 mg/kg bw (Category III). Furthermore, the three available subchronic dermal toxicity studies, two on technical grade trifluralin and one on a trifluralin formulation, indicate no signs of systemic toxicity in rats or rabbits at dermal doses of up to 1000 mg/kg bw/day.

The apparent lack of dermal toxicity is important to the current Forest Service risk assessment, because many of the exposure scenarios for trifluralin involve dermal exposures (Section 3.2). The apparently nontoxic responses to trifluralin following dermal exposures may call into question the relevance of the dermal exposure scenarios. As discussed in Section 3.1.3.2 of the current risk assessment as well as in the EPA human health risk assessments (U.S. EPA/OPP 2003a,b), trifluralin is not well absorbed

following dermal exposure. Consequently, the subchronic dermal NOAELs of 1000 mg/kg bw/day are reasonably consistent with the subchronic oral toxicity studies in rats. For example, a 90-day oral study in rats indicates a NOAEL of about 40 mg/kg bw/day (MRID 00151906). As summarized in Section 3.1.3.2.1, the study by Brand et al. (2004) indicates that rats will absorb less than 4% of trifluralin over a 24-hour period following dermal application. Thus, a dermal NOAEL of 1000 mg/kg bw/day is essentially identical, in terms of absorbed dose, to an oral dose of less than 40 mg/kg bw/day.

3.1.13. Inhalation Exposure

As summarized in Appendix 1 (Table A1-4), inhalation exposure to technical grade trifluralin is addressed in two studies: one acute and one subchronic. The acute inhalation study yields an LC_{50} of >4.66 mg/m^3, and the EPA uses this study to classify trifluralin at Category III for potential risks associated with inhalation exposures (U.S. EPA/OPP 1996a). In the subchronic inhalation study, rats were exposed to trifluralin concentrations of 100, 300, or 1000 mg/m^3, 6 hours/day, 5 days/week for up to 30 days. Based on dose estimates developed in U.S. EPA/OPP (2003b), these exposures correspond to about 27, 81, and 270 mg/kg/day. Although no effects were noted at 81 mg/kg bw/day, signs of liver toxicity were observed at 270 mg/kg bw/day. As with the subchronic dermal studies discussed in the previous subsection, these NOAEL and LOAEL values are reasonably consistent with the subchronic oral toxicity data on trifluralin.

3.1.14. Adjuvants and Other Ingredients

The EPA is responsible for regulating other ingredients and adjuvants in pesticide formulations. As implemented, these regulations affect only pesticide labeling and testing requirements. The term *inert* was formerly 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*. This approach is adopted in the current risk assessment.

As summarized in Table 2 and detailed further in Appendix 1 (Table A1-1), very little specific information is available on the other ingredients used in trifluralin formulations. The material safety data sheets (MSDS) for all of the liquid formulations of trifluralin specifically addressed in the current Forest Service risk assessment indicate that the formulations contain naphthalene. U.S. EPA/OPPTS (2003, p. 5-2) encourages but does not require expanded inert statements on product labels that specifically identify the inert ingredients in the product. It appears that Makhteshim Agan, the manufacturer of Triflurex HFP elected to provide somewhat more detail in the MSDS than the other suppliers of trifluralin formulations. The MSDS for Triflurex HFP specifies that this formulation contains 42.78 % trifluralin, 49.2% aromatic hydrocarbons, and 7% naphthalene. Naphthalene is an aromatic hydrocarbon, and it is not clear if the 7% naphthalene is included in the 49.2% aromatic hydrocarbons specified on the product label. The other liquid formulations of trifluralin explicitly covered in the current risk assessment (i.e., Treflan 4D and Treflan HFP) provide less information on the other ingredients used in the formulations and identify only naphthalene. While somewhat

speculative, it seems likely that these other formulations will also contain solvents compatible with the very low water solubility of trifluralin.

The two granular formulations explicitly considered in the current risk assessment do appear to differ from one another other. Treflan 5G, a 5% granular formulation, indicates that the formulation contains 2.8% kerosene. Treflan TR-10, a 10% granular formulation, indicates that the formulation contains clay but does not indicate that the formulation contains kerosene or any other petroleum solvents.

Petroleum distillates, including aromatic hydrocarbons, are complex mixtures (e.g., ATSDR 1995). It is possible that the specific constituents in the different liquid formulations of trifluralin differ at least somewhat from one another. As reviewed by ATSDR (1999), petroleum distillates can induce a wide range of toxic effects, particularly effects on the nervous system. The U.S. EPA/OPP has not yet completed their RED for aromatic hydrocarbons (http://www.epa.gov/pesticides/reregistration/status.htm).

Given the complexity and variability of petroleum distillates as well as the limited information available on the identity of the petroleum components in formulations of trifluralin, it is difficult to assess the extent to which the other ingredients in trifluralin formulations contribute to the toxicity of these formulations. One approach to assessing this issue is to compare the toxicity of the formulations, expressed in units of active ingredient, to the toxicity of the active ingredient itself.

For formulations of trifluralin, however, this approach has only limited utility. As summarized in Appendix 1 (Table A1-1), most of the reported acute toxicity values for the trifluralin formulations are indefinite—i.e., most of the LD_{50} and LC_{50} values are expressed as *greater than* (>) values. One remarkable exception is the oral LD_{50} of 500 mg/kg in rats reported for Treflan 5G. While the MSDS for Treflan 5G does not explicitly state whether the LD_{50} is expressed in units of mg formulation/kg bw or mg a.i./kg bw, MSDS typically report LD_{50} values in units of mg formulation/kg bw. Assuming that the units are in mg formulation/kg bw, an 500 mg formulation/kg bw for a 5% formulation would correspond to 25 mg a.i./kg bw. As summarized in Appendix 1 (Table A1-2), for rats exposed to trifluralin, the oral LD_{50} values range from 1930 mg/kg bw (Hollander 1979) to >5000 mg/kg bw (MRID 00157486 as summarized in U.S. EPA-OPP 1996a and 2009a). Thus, the oral LD_{50} of 500 mg/kg reported in the MSDS for Treflan 5G indicates that Treflan 5G may contain ingredients other than trifluralin which contribute substantially to the toxicity of this formulation. If this is the case, the current risk assessment, which is based on a quantitative consideration of trifluralin, may not encompass risks associated with the use of Treflan 5G.

As also summarized Appendix 1 (Table A1-1), on the MSDS for Triflurex HFP, a liquid formulation of trifluralin, the oral LD_{50} in rats is reported as 500-5000 mg/kg bw. It is not clear why the LD_{50} is reported as such a broad range.

The U.S. EPA/OPP generally requires acute oral LD_{50} values on formulations, and typically these studies are cited and discussed in the EPA risk assessments. Ideally, the acute oral LD_{50} values for the formulations would be associated with registrant submitted studies; however, this is not case for trifluralin. The available EPA risk assessments (U.S. EPA/OPP 1996a,b, 2003a,b, 2004a,b, 2009a) do not cite or discuss studies on the acute oral toxicity of trifluralin formulations.

The lack of clarity concerning the toxicity of different trifluralin formulations adds uncertainty to this risk assessment, particularly in terms of Treflan 5G and possibly Triflurex HFP. If either of these formulations were substantially more hazardous than other trifluralin formulations, one would expect to find a discussion of the differences in toxicity and the reasons for these differences in the EPA risk assessments, given that the EPA has access to the full studies as well as information on the other ingredients used in the formulations. Such discussions are not found in the EPA risk assessments (U.S. EPA/OPP 1996a,b, 2003a,b, 2004a,b, 2009a).

3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

As discussed in Section 3.1.3, trifluralin is extensively metabolized by mammals. In that all of the toxicity studies used quantitatively in the current risk assessment involve *in vivo* exposures, the formation and toxicity of metabolites formed *in vivo* should be encompassed in the studies used in the dose-response assessment (Section 3.3). This approach to *in vivo* metabolites is essentially implicit in all risk assessments. *In vivo* toxicity studies, however, would not necessarily encompass environmental metabolites (i.e., metabolites that are formed in the environment by either chemical processes or by microbial and/or plant metabolism).

As summarized in U.S. EPA/OPP (2009a) as well as a review prepared for the U.S. EPA by the Dynamac Corporation (1989a), there are several identified trifluralin metabolites. Nevertheless, there is very little toxicity data on trifluralin metabolites and no toxicity data on mammalian exposure to the metabolites. Table 6 summarizes the metabolites discussed specifically in the EPA ecological risk assessment of trifluralin (U.S. EPA/OPP 2009a). The first column of this table indicates the chemical name of the metabolite and briefly summarizes the toxic potency of each metabolite, relative to trifluralin, where information is available. The second column gives the metabolite code used by U.S. EPA (e.g., TR-5), and the third column gives the chemical structure of the metabolite.

As indicated in Table 6, the toxic potencies of the metabolites can be characterized for only TR-6 (5-trifluoromethyl-3-nitro-1,2-benzenediamine) and TR-15 (2-ethyl-7-nitro-5-trifluromethylbenzimidazole). For each of these metabolites, toxicity studies are available in trout, daphnids, and a species of algae (*Selenastrum capricornutum*). In each of these three species and for each of the two metabolites, the toxicity of the metabolite is less than the toxicity of trifluralin by factors of about 6 to 147. In addition, and as discussed further in Section 4.1.2.4, the TR-4 metabolite appears to be at least somewhat less toxic than trifluralin based on NOAECs in earthworms. While these relative potencies cannot be applied directly to the human health risk assessment, these are the

only available data, and these data suggest that the metabolism of trifluralin results in detoxification.

All of the EPA risk assessments on trifluralin (U.S. EPA/OPP 1996a,b, 2003a,b, 2004a,b, 2009a) are based on the toxicity of trifluralin, with no quantitative consideration of the metabolites of trifluralin. In the absence of any information suggesting that some metabolites of trifluralin pose risks that are substantially greater than those posed by trifluralin, the current risk assessment adopts the approach used by U.S. EPA/OPP, and risks associated with the use of trifluralin in Forest Service programs are based on exposures to and the toxicity of trifluralin.

3.1.15.2. Impurities

Formulations of trifluralin may contain N-nitrosodi-n-propylamine. In the literature, this compound is sometimes referred to as NDPA or simply nitrosamine. For brevity, the NDPA abbreviation is used in this discussion.

As reviewed in some detail by ATSDR (1989), NDPA is a concern because it is classified as a potential human carcinogen. In the 1970s, some formulations of trifluralin contained NDPA at concentrations in excess of 150 mg/L (ppm) (Ross et al. 1977, 1978). A publication from the early 1980s indicates that the concentration of NDPA in an unidentified trifluralin formulation ranged from 2 to 6 ppm (Day et al. 1982). By 1982, however, the U.S. EPA/OPP required that technical grade trifluralin should contain no more than 0.5 ppm "N-nitrosamine" (Dockter 1989). As part of the re-registration of trifluralin, the EPA required that concentrations of NDPA in formulations of trifluralin may not exceed 0.5 ppm (U.S. EPA/OPP 1996a). In that the recent tolerance reassessment for trifluralin does not propose a different standard (U.S. EPA/OPP 2004a), 0.5 ppm appears to be the current standard for NDPA in trifluralin formulations.

No discussion of the basis for setting 0.5 ppm as the maximum allowable concentration of NDPA in trifluralin formulations was found in the trifluralin literature. Nonetheless, a consideration of the relative carcinogenic potencies of trifluralin and NDPA suggests that the 0.5 ppm level for NDPA will not add significantly to the carcinogenic potency of trifluralin formulations. As discussed in ATSDR (1989), the carcinogenic potency of NDPA is 7 $(mg/kg/day)^{-1}$. As discussed in Section 3.3.4 of the current risk assessment, the carcinogenic potency of trifluralin is 5.79×10^{-3} $(mg/kg/day)^{-1}$. Thus, NDPA may be viewed as more potent than trifluralin by a factor of about 1200 [7 $(mg/kg/day)^{-1} \div 5.79 \times 10^{-3}$ $(mg/kg/day)^{-1} \cong 1208.98$]. As summarized in Table 2 of the current Forest Service risk assessment, the trifluralin formulations explicitly considered in the current risk assessment contain trifluralin at concentrations of 5-43%. These concentrations correspond to 50,000-430,000 ppm (i.e., 1% = 10,000 ppm). Relative to the maximum allowable concentration of 0.5 ppm NDPA, the concentration of trifluralin is greater than that of NDPA by factors ranging from 100,000 to 860,000 [50,000 to 430,000 ppm ÷ 0.5 ppm]. Thus, adjusting for the difference in potency, the carcinogenic risks associated with trifluralin are greater than those associated with NDPA by factors of ranging from about 80 to more than 700 [100,000 to 860,000 ÷ 1200 ≅ 83.33 to 716.67].

These potency weighted differences in concentrations may overestimate rather than underestimate the potential risks associated with NDPA, relative to trifluralin. Dockter (1989) is an EPA memorandum that summarizes assays of NDPA in both technical grade trifluralin as well as various trifluralin formulations. Based on the data in Dockter (1989), the granular formulations of trifluralin contain concentrations of NDPA no greater than 0.04 ppm. Thus, the standard of 0.5 ppm for DNPA appears to be sufficient to reduce the risks of NDPA in trifluralin formulation to levels that would be regarded as inconsequential.

3.1.16. Toxicological Interactions

No specific information on the interaction of trifluralin with other compounds was found in available literature. As discussed in Section 3.1.2, trifluralin will induce and is metabolized by cytochrome P-450. Cytochrome P-450 is a general term for a class of mixed function oxidases involved in the metabolism of a broad range of naturally occurring chemicals (e.g., steroids) as well as xenobiotics (i.e., man-made chemicals typically not found in nature). In general, any compound that serves as a substrate for or is metabolized by a mixed function oxidase may inhibit or alter the metabolism of other compounds that also serve as substrates for the mixed function oxidase. Furthermore, substrates for mixed function oxidases can often induce the production of mixed function oxidases, thereby enhancing their own metabolism as well as that of other compounds (e.g., Coon 2005; Lewis et al. 1998).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

The exposure assessments for trifluralin are summarized in Worksheet E01 for workers and Worksheet E03 for the general public in the EXCEL workbook that accompanies this risk assessment. All exposure assessments are based on the unit application rate of 1.0 lb a.i./acre.

In Forest Service risk assessments involving broadcast foliar applications, a standard set of worker exposure rates based on biomonitoring studies are used. For trifluralin, the only application method considered is soil incorporation, and the standard rates used for broadcast applications are not applicable. In the absence of any worker exposure studies involving soil incorporation of trifluralin, the current risk assessment adopts the worker exposure assessment for soil incorporation developed by the EPA for the Reregistration Eligibility Decision (RED) document on trifluralin (U.S. EPA/OPP 1996a). The worker exposure rate used by the EPA is 3.1×10^{-7} mg/kg bw per lb handled, which is much lower than the worker exposure rates typically used in Forest Service risk assessments for broadcast applications (Table 7). Based on estimates of the amount of trifluralin that a worker might handle in a single day, the estimated doses for workers are about 0.000035 (0.000020 to 0.000052) mg/kg bw/day.

Because only soil incorporation of trifluralin is considered in the current Forest Service risk assessment, several standard exposure scenarios for members of the general public are not developed for trifluralin, including direct spray and contact with contaminated vegetation. In addition, because only applications to sunflower seed beds are specifically considered, the only exposure scenario for the consumption of contaminated vegetation explicitly considered is the acute consumption of sunflower seeds containing trifluralin that has been translocated from the seed bed. Because wildlife food plots treated with trifluralin are posted and human foraging is not permitted, this exposure scenario is viewed as an unlikely and possibly extreme event. Nonetheless, the doses associated with this scenario are very low (i.e., about 7.2×10^{-6} to 2.9×10^{-5} mg/kg bw). Despite the many uncertainties associated with these estimated doses, they are far below the level of concern, as discussed further in the risk characterization (Section 3.4).

Potential exposures associated with the consumption of contaminated water or fish taken from contaminated water are substantially greater than those associated with eating contaminated sunflower seeds. Estimates of the concentration of trifluralin in water and fish are based on both Gleams-Driver simulations as well as monitoring data. Confidence in these assessments is relatively high, compared with the exposure assessments associated with the consumption of sunflower seeds. Because trifluralin is extensively concentrated from water by fish (with a BCF for muscle tissue of over 2000), the greatest doses are associated with the consumption of fish. Because subsistence populations may consume much more wild-caught fish than would most members of the general public, the highest estimated doses to humans are those for subsistence populations consuming wild-caught fish—i.e., acute doses of about 0.04-0.09 mg/kg bw and longer-term doses of about 0.00001-0.06 mg/kg bw/day. As discussed further in the risk characterization

(Section 3.4), these doses are far below the level of concern for systemic toxicity; however, the upper bound chronic dose is of concern in terms of the carcinogenicity of trifluralin.

3.2.2. Workers

3.2.2.1. General Exposures

In most Forest Service risk assessments, the exposure assessments for workers are based on a standard set of exposure scenarios involving applications of terrestrial herbicides and insecticides. Although these exposure assessments vary according to the available data for each chemical, the organization and assumptions used in the exposure assessments are standard and consistent. As summarized in Table 7 and discussed in SERA (2007a), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. Based on analyses of several different pesticides using various application methods, default exposure rates are typically estimated for three different types of applications: directed foliar (backpack), boom spray (hydraulic ground spray), and aerial.

Soil incorporation application is substantially different from the broadcast application methods considered in most Forest Service risk assessments. No worker exposure studies on trifluralin involving soil incorporation are available. In the Reregistration Eligibility Decision (RED) for trifluralin, U.S. EPA/OPP (1996a, Table 1, p. 28), the EPA developed several worker exposure assessments for trifluralin based on data from the Pesticide Handlers Exposure Database (PHED). Of the scenarios developed in U.S. EPA/OPP (1996a), the scenario most relevant to Forest Service applications is designated as Scenario IV, Groundboom applications, which assumes that the worker applies trifluralin to 80 acres at an application rate of 2 lbs a.i./acre (i.e., the worker handles 160 lbs a.i). The total lifetime average absorbed dose for the worker is estimated at 0.000049 mg/kg bw/day. Normalized for the number of pounds of trifluralin handled by the worker, the exposure rate is about 3.1×10^{-7} mg/kg bw per lb handled [0.000049 mg/kg bw/day ÷ 160 lb a.i. = 0.000000306].

A limitation in the usefulness of the above exposure rate to the current Forest Service risk assessment involves the use of protective clothing. The exposure rate developed by the U.S. EPA assumes that the worker wears long pants, long sleeves, but no gloves. All product labels for trifluralin, however, require the use of gloves during applications. The specifications for the gloves on the product labels vary somewhat in specificity but indicate that the gloves should be chemical resistant—i.e., nitrile, butyl, neoprene, or barrier laminate.

One study (Berardinelli et al. 1995) is available on the efficacy of chemically resistant gloves to an emulsifiable concentrate formulation of trifluralin (Treflan-MTF). In this study, nitrile and butyl gloves did not offer adequate protection to the trifluralin formulation. Thus, the use of the worker exposure rate developed in U.S. EPA/OPP (1996a) may be somewhat conservative if effective gloves are used. Conversely, the use of the EPA exposure rates is based on the assumption that standard clothing will provide a typical level of protection in terms of exposure to trifluralin. In a clothing penetration

study by Stone et al. (1992), however, substantial penetration of jeans and under-briefs was noted for a trifluralin formulation specified only as Treflan. Thus, it is possible that the standard deposition estimates from PHED, which are based on standard clothing penetration estimates for numerous pesticides, might underestimate worker exposures involving applications of at least some trifluralin formulations.

In discussing the data on which the worker exposure estimates are based, U.S. EPA/OPP (1996a, Table 2, p. 29) indicates high confidence in the exposure estimates. Given the above considerations, however, confidence in the worker exposure estimates applied to trifluralin seems limited, at best.

As summarized in Table 7, the worker exposure rates used in most Forest Service risk assessments vary substantially. Taking broadcast foliar as an example, the lower bound of the exposure rate is a factor of 20 below the central estimate [0.0002 ÷ 0.00001 mg/kg bw/day per lb handed] and the upper bound of the exposure rate is a factor of 4.5 above the central estimate [0.0009 ÷ 0.0002 mg/kg bw/day per lb handed]. The exposure estimate developed by U.S. EPA/OPP and used in the current risk assessment is given only as a point estimate with no variability. While the variability in the standard Forest Service exposure rates could be used to estimate variability in the U.S. EPA worker exposure rate, there is no direct connection between the data used by U.S. EPA and the data used in developing the standard Forest Service rates. Consequently, the worker exposure rate of 3.1×10^{-7} mg/kg bw per lb handled from U.S. EPA/OPP (1996a) is used with no modification. Uncertainties associated with this estimate are discussed qualitatively in the risk characterization for workers (Section 3.4.2).

In addition to the worker exposure rate, a key factor in estimating doses for workers is the area to be treated—i.e., the product of the application rate (in lbs/acre) and the number of acres treated is used to calculate the amount of pesticide that the worker handles. In standard ground broadcast applications, Forest Service risk assessments typically assume that 112 (66-168) acres are treated per day. These rates are not substantially different from the estimate of 80 (40-200) acres per day used by the U.S. EPA for tractor drawn broadcast spreaders (Sandvig 2001). In the absence of any additional information from the Forest Service, the rates of 112 (66-168) acres per day are used in the current risk assessment for trifluralin. These estimates of acres treated per day are based on the assumption that workers will treat 16 (11-21) acres per hour and will work 7 (6-8) hours per day.

3.2.2.2. Accidental Exposures

Although typical occupational exposures are likely to involve multiple routes of exposure (i.e., oral, dermal, and inhalation), dermal exposure is generally the predominant route for herbicide applicators (Ecobichon 1998; van Hemmen 1992). Typical multi-route exposures are encompassed by the methods used in Section 3.2.2.1 on general exposures. Accidental exposures, on the other hand, are most likely to involve splashing a solution of herbicide into the eyes and may also involve various dermal exposure scenarios. Quantitative exposure scenarios for ocular exposures are not developed in this or other Forest Service risk assessments. As discussed in Section 3.1.11.3 (Ocular Effects),

trifluralin causes only slight eye irritation. Assuming that workers use protective eyewear, significant ocular exposures do not seem plausible.

Accidental dermal exposure to trifluralin is considered quantitatively in this risk assessment. The two types of modeled dermal exposure 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 in the attachments that accompany this risk assessment. Worksheet E01 references other worksheets which provide detailed calculations.

Exposure scenarios involving direct contact with trifluralin solutions are characterized either by immersion of the hands in a field solution for 1 hour or wearing pesticide contaminated gloves for 1 hour. The assumption that the hands or any other part of a worker's body will be immersed in a chemical solution for a prolonged period of time may seem unreasonable; however, it is quite plausible that the gloves or other articles of clothing worn by a worker may become contaminated with a pesticide. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in the pesticide 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—i.e., because the concentration of the pesticide in contact with the skin is constant, or nearly so, the rate of absorption will be constant. For these types of exposures, the rate of absorption is estimated, based on the dermal permeability coefficient (K_p). Details regarding the derivation of the K_p value for trifluralin are provided in 3.1.3.2.2. The amount of the pesticide absorbed per unit time depends directly on the concentration of the chemical in solution. As discussed in Section 2.4.1, the current risk assessment uses an application volume of 20 gallons/acre with a range of 5-40 gallons/acre.

Exposure scenarios involving chemical spills onto the skin are characterized by a spill on to the lower legs as well as a spill on to the hands, and both scenarios are based on the assumption that a certain amount of the chemical adheres to the skin. The absorbed dose is then calculated as the product of the amount of chemical on the surface of the skin (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the chemical concentration in the liquid), the first-order absorption rate coefficient (k_a), and the duration of exposure. Estimates of the first-order absorption rate coefficients are discussed in the hazard identification (Section 3.1.3.2.1).

Numerous exposure scenarios could be developed for direct contact or accidental spills by varying the amount or concentration of the chemical on, or in contact with, the skin surface, the surface area of the affected skin, and the duration of exposure. The impact of

these variables on the risk assessment is discussed further in the risk characterization (Section 3.4.2).

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 pesticides in Forest Service applications is highly variable. In some Forest Service applications, pesticides may be applied in recreational areas, including campgrounds, picnic areas, and trails. In other instances, pesticides may be applied in relatively remote areas and the probability that members of the general public will be exposed to the pesticides is remote.

As discussed in Section 2.3, the current risk assessment on trifluralin specifically addresses applications of trifluralin to sunflower fields to prevent crabgrass in wildlife food plots. As discussed further in Section 3.2.3.6, individuals could harvest and consume sunflower seeds from treated plots; however, the probability of this occurring appears to be low. As discussed in Section 3.2.3.4, surface water may become contaminated with trifluralin and individuals could be exposed to trifluralin through the consumption of the contaminated surface water. The likelihood of this occurring appears to be highly variable depending on the proximity of the treated area to surface water as well as the proximity of the surface water to human populations.

3.2.3.1.2. Summary of Assessments

The exposure scenarios developed for the general public are summarized in Worksheet E03 of the EXCEL workbook that accompanies this risk assessment. As with the worker exposure scenarios, details about the assumptions and calculations used in these assessments are given in the detailed calculation worksheets in the EXCEL workbook (Worksheets D03a to D11).

As summarized in Worksheet E03, the kinds of exposure scenarios developed for the general public include acute accidental, acute non-accidental, and longer-term or chronic exposures. Most Forest Service risk assessments will consider the consumption of contaminated vegetation—i.e. broadleaf leaves and fruit. Because the only use of trifluralin considered in the current Forest Service risk assessment involves the treatment of sunflower fields, the scenarios for the consumption of broadleaf vegetation and fruit are not considered in the current risk assessment. Instead, a custom exposure assessment is developed for the consumption of sunflower seeds. Forest Service risk assessments will also typically consider exposure scenarios associated with direct spray as well as dermal contact with contaminated vegetation. These exposure scenarios are not considered for trifluralin because the only application method considered for trifluralin is soil incorporation Standard exposure scenarios associated with the consumption of contaminated water, the impact of swimming in contaminated water, and the consumption of fish from contaminated water are, however, relevant and are considered for trifluralin.

The following subsections detail the specific exposure scenarios developed for trifluralin. While some standard exposure scenarios are not considered for trifluralin, section designations for these excluded scenarios are given below as a matter of convenience for individuals who regularly use many different Forest Service risk assessments—i.e., the section designations in all Forest Service risk assessments are consistent.

3.2.3.2. Direct Spray

Direct spray scenarios are used for all broadcast applications and involve the accidental direct spray of a woman and a small child. As discussed in Section 2.2, trifluralin is applied directly to soil using a tractor mounted sprayer. In these types of applications, the direct spray of a member of the general public is not plausible, and these scenarios are not developed for the current risk assessment.

3.2.3.3. Dermal Exposure from Contaminated Vegetation

As with the direct spray scenarios, exposures associated with skin contact with contaminated vegetation are relevant to broadcast foliar applications but not relevant to directed soil applications.

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 estimated concentrations of trifluralin in water following an accidental spill are developed in Worksheet B04b. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation is considered. This scenario also assumes instantaneous mixing.

This exposure scenario is based on assumptions that are somewhat arbitrary and highly variable. The actual chemical concentrations in the water will vary according to the amount of compound spilled, the size of the water body into which the chemical is spilled, the amount of contaminated water that is consumed, and the time at which water consumption occurs relative to the time of the spill. For example, if the child ingests water at the spill cite immediately following the spill, the concentration would be higher than the equilibrium concentration. If, on the other hand, the child ingest waters immediately after the spill but on the opposite side of the pond, the concentration of the pesticide in the water would be much less than the equilibrium concentration.

To reflect the variability inherent in this exposure scenario, a spill volume of 100 gallons (range of 20-200 gallons) is used to reflect plausible spill events. The trifluralin 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 the assumptions discussed above, the estimated concentration of trifluralin in a small pond ranges from about 0.23 to about 18 mg a.i./L, with a central estimate of about 4.5 mg a.i./L (Worksheet B04b). It will be noted that the central estimate and upper

bound concentrations are substantially in excess of the solubility of trifluralin in water – i.e., about 0.3 mg/L (U.S. EPA/OPP 2009a, Table 3.2). For the current risk assessment, the conservative assumption will be made that the other ingredients in liquid formulations of trifluralin would permit these excessive concentrations to be maintained in water for a sufficient period of time for exposures to occur. This assumption is discussed further in the risk characterization.

The dose estimates for a small child consuming water from the pond following an accidental spill are developed in Worksheet D05. Based on estimates of the amount of water consumed per day by a young child with a body weight of about 13 kg (≈30 lbs), the estimated dose to the child is about 0.34 (0.01 to 2) mg/kg bw.

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

Forest Service risk assessments concerned with broadcast applications of pesticides typically include estimates of surface water contamination associated with drift of the pesticide into small ponds and small streams. These types of estimates are not appropriate for directed soil applications of trifluralin and are not included in this current Forest Service risk assessment of trifluralin.

3.2.3.4.3. Gleams-Driver 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 (Groundwater Loading Effects of Agricultural Management Systems) 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. Gleams-Driver offers the option of conducting general exposure assessments using site-specific weather files from Cligen, a climate generator program developed and maintained by the USDA Agricultural Research Service (http://horizon.nserl.purdue .edu/Cligen). Details concerning the use of Gleams-Driver are given in SERA (2007b). Gleams-Driver is used in the current risk assessment to model concentrations of trifluralin in a small stream and small pond.

3.2.3.4.3.1. Inputs to Gleams-Driver

The generic site parameters used in the Gleams-Driver simulations are summarized in Table 8, and additional details are available in the documentation for Gleams-Driver (SERA 2007b). For each site modeled, simulations were conducted using clay (high runoff, low leaching potential), loam (moderate runoff and leaching potential), and sand (low runoff, high leaching potential) soil textures. Some input parameters are based specifically on applications to fields used to grow sunflowers. Specifically, the type of site is taken as an agricultural field rather than a meadow or forest because applications of trifluralin are made to freshly plowed fields prior to planting. The other obvious modification involves crop cover parameters which are adapted to sunflowers rather than standard forest cover (e.g., pines or hardwoods). Most of the other soil and site inputs are standard values used in all Forest Service risk assessments as detailed in SERA (2007b). The only exception involves the slope used for sandy soils. The default values used in Gleams-Driver apply a slope of 0.1 for all types of soils. Based on previous peer review comments on other more recent Forest Service risk assessments, a slope of 0.1 is

considered implausible for sandy soils; accordingly, the slope for simulations with sandy soils is taken as 0.05 (i.e., a 5% slope).

The locations of the generic sites selected for modeling include a total of nine sites, as summarized in Table 9. As discussed in SERA (2007b), these locations are standard sites for the application of Gleams-Driver in Forest Service risk assessments and are intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool). For each site and soil texture, Gleams-Driver was used to simulate 100 applications at a unit application rate of 1 lb/acre, and each of the simulations was followed for a period of about 1½ years after application.

Since trifluralin has relatively long metabolic half-lives in both soil and water, the relatively short runs used in the Gleams-Driver simulations could raise concern that trifluralin might accumulate in both soil and water if applied annually over a period of many years. As detailed in U.S. EPA/OPP (2009a, Figure 3.1, p. 81), trifluralin does not appear to accumulate in soil and is not likely to accumulate in water; however, this assessment does not report water concentrations of trifluralin associated with multiple yearly applications. Consequently, a separate simulation was conducted for annual applications of trifluralin over a 30-year period in a cool and wet climate—i.e., Mt. Washington, New Hampshire, as detailed in Table 9. As discussed further in Section 3.2.3.4.3.2, this simulation is consistent with the PRZM/EXAMS simulations of trifluralin in soil documented in U.S. EPA/OPP (2009a), indicating no consistent pattern of increasing concentrations of trifluralin in surface water.

Table 10 summarizes the chemical-specific values used in Gleams-Driver simulations. For the most part, the chemical properties used in the Gleams-Driver simulations are taken from U.S. EPA/OPP (2009a). The EPA modeling efforts are discussed below (Section 3.2.3.4.4). In the current risk assessment, the model input values are based on several sources including environmental fate studies submitted to the EPA by registrants, standard values for GLEAMS modeling recommended by Knisel and Davis (2000), and studies from the published literature. The notes to Table 10 identify the specific sources for each of the chemical-specific values used in the GLEAMS modeling.

Some of the chemical-specific parameters used in Gleams-Driver modeling are based on triangular distributions rather than single values. This approach differs from the EPA approach used to modeling in U.S. EPA/OPP (2009a). As summarized in Table 1, reported soil K_{oc} values for trifluralin are somewhat variable, which is a common characteristic for many pesticides (i.e., soil binding may depend on other factors in addition to soil organic carbon). While this variability is considered in the Gleams-Driver simulations, the range of reported K_{oc} values is relatively narrow, varying by a factor of about 2.5 [12,557 ÷ 4,958 ≈ 2.533].

As indicated in Table 10, the soil half-lives for trifluralin used in the Gleams-Driver modeling range from 91 to 246 days with a central estimate of 169 days. This range of soil half-times is about 2.7 [246 day ÷ 91 days ≈ 2.703], which is only modestly greater than the range of K_{oc} values discussed above – i.e., a range of 2.5. The soil half-lives

used for trifluralin reflect only biological degradation and not soil volatilization. Numerous studies indicate that trifluralin will volatilize rapidly from soil surfaces with half-lives ranging from a matter of hours to a few days, and even shorter half-lives in moist soils (Bedos et al. 2006; Grass et al. 1994; Glotfelty et al. 1984; Harper et al. 1976; Rice et al. 2002; Ruedel 1997; Sanders et al. 1985; Smith et al. 1997; Yen et al. 2008). The high volatility of trifluralin is a major factor limiting the effectiveness of this herbicide in foliar applications. As detailed by Smith et al. (1997), the soil incorporation of trifluralin to a depth of about 5 cm—i.e., the same incorporation depth used in the Gleams-Driver modeling—substantially limits soil volatilization due to soil binding properties—i.e., the high K_{oc} values. The limited volatilization of trifluralin following soil incorporation is also consistent with the relatively long soil half-lives of 10-11 months reported in the microlysimeter study by Malterre et al. (1997). Thus, the use of half-lives based on soil metabolism rather than volatilization may slightly overestimate trifluralin concentrations in soil and subsequently in water. A benefit of using relatively long soil half-lives involves the potential impact of metabolites. As discussed in Section 3.1.15.1, no information is available on the toxicity of trifluralin metabolites in mammals. The use of the relatively long soil half-lives for trifluralin encompasses the half-lives of about 24 to 194 days for the complete mineralization of trifluralin reported by Farenhorst (2007).

In terms of concentrations of trifluralin in water, the most significant parameter is the degradation half-life in water. As summarized in Table 10, the degradation half-lives used in the Gleams-Driver modeling are taken as 0.6 (0.4 to 3.2) days. The lower bound of the half-life (i.e., the most rapid degradation rate) is taken from the PRZM/EXAMS modeling in U.S. EPA/OPP (2009a) which uses an aqueous photolysis half-life of 8.9 hours (≈0.37 days). The somewhat higher (i.e., more conservative) half-times of 0.6-3.2 days is taken from the microcosm studies by Laabs et al. (2007) in which the relatively rapid dissipation of trifluralin from water was attributed primarily to volatilization.

3.2.3.4.3.2. Results from Gleams-Driver

Table 11 summarizes the results for the Gleams-Driver runs as well as other modeling efforts and monitoring data, discussed further in the following subsections. Details of the results for the Gleams-Driver runs are provided in Appendix 7. It is important to note that the concentrations of trifluralin in water from the Gleams-Driver runs are expressed as the median value with upper and lower bounds. The upper bound is the 95% empirical upper bound. In other words, the two extreme upper values from the 100 simulations at each site are dropped. The lower bound, however, is based on the lower 25% or the lower quartile. This approach is taken because the lower empirical 95% bound for most modeled values is zero. While using the lower quartile may be viewed as somewhat conservative, this has no impact on the risk characterization for either the human health risk assessment (Section 3.4) or the ecological risk assessment (Section 4.4).

The peak concentrations of trifluralin in surface water are higher for streams—i.e., 2.21 (0.02 - 28.4) µg/L—than for ponds—i.e., 0.208 (0.004 - 1.36) µg/L. The higher concentrations in streams relative to ponds may reflect simple dilution. For the pond model, pesticide inputs are diluted by the water initially in the pond, which is assumed to

be free of contamination. For the stream model, most of the water flow in all but very arid regions is attributable to runoff. In the Gleams-Driver modeling, all of the runoff into the stream is associated with the treated plot. This is, of course, a very conservative assumption and perhaps unreasonably so. For the generic exposure assessments conducted in Forest Service risk assessments, this conservative approach to the stream model is used consistently. In any site-specific assessment involving the potential contamination of streams, it would be appropriate to re-run Gleams-Driver to consider both inputs from contaminated water from the treated field as well as inputs of uncontaminated water from untreated areas of the drainage basin of the stream. These types of considerations, of course, also apply to ponds.

The longer-term concentrations of trifluralin in surface water are also higher for streams—i.e., 0.075 (0.0002 - 0.4) µg/L— than for ponds—i.e., 0.0074 (0.000025 - 0.04) µg/L. As discussed above, these differences probably reflect the underlying structure of the pond and stream models as well as the rapid dissipation of trifluralin from water due to photolysis and evaporation, as discussed in Section 3.2.3.4.3.1.

As also discussed in Section 3.2.3.4.3.1, a separate simulation of 40 annual applications of trifluralin was conducted to assess the potential accumulation of trifluralin in soil and water. For this simulation, the site in Mt Washington, New Hampshire was selected. As indicated in Table 9, this site is intended to represent locations with high rainfall and low average temperatures. As detailed in Appendix 7, this site yielded the highest estimated longer-term concentrations of trifluralin in both ponds and streams. The results of the 40-year simulations are illustrated in Figure 5 and indicate no systematic or substantial accumulation of trifluralin in either pond water or in the top 12 inches of soil at the treated site. The lack of accumulation in soil is consistent with the PRZM/EXAMS modeling in U.S. EPA/OPP (2009a, Figure 3.1, p. 81).

As discussed further in Section 3.2.3.4.5, the available monitoring data on trifluralin are not sufficient to assess the quality of the Gleams-Driver modeling because the monitoring data are not associated with specific or defined applications of trifluralin. Several field studies, however, indicate that trifluralin has a very low leaching potential (e.g., Duseja and Holmes 1978; Kim and Feagley 2002a; Malterre et al. 1998; Mordaunt et al. 2005; Golab et al. 1979; Rohde et al. 1998). The deepest soil penetration noted in any of the identified studies is about 16 inches (40 cm) (Yen et al. 2008). The low leaching potential of trifluralin is consistent with the Gleams-Driver modeling (Appendix 7, Table A7-4) in which the maximum soil penetration was 12 inches in clay soils, 18 inches in loam soils, and 24 inches in sandy soils.

3.2.3.4.4. Other Modeling Efforts

The recent EPA ecological risk assessment for the California red-legged frog (*Rana aurora draytonii*) (U.S. EPA/OPP 2009a) details numerous PRZM/EXAMS modeling runs for various application scenarios (U.S. EPA/OPP 2009a, Table 3.3, pp. 71-73). The highest peak concentration modeled in the EPA standard farm pond is 6.55 µg/L. As summarized in Table 11 of the current risk assessment, this concentration is higher than the upper bound concentration of 1.36 µg/L modeled in ponds using Gleams-Driver. The concentration of 6.55 µg/L, however, is based on a nursery scenario involving three

applications of trifluralin at 4.48 kg a.i./ha or about 4 lbs a.i./acre without soil incorporation. Thus, the higher concentration of 6.55 µg/L modeled by the EPA is not directly comparable to the concentrations modeled using Gleams-Driver, which are based on a single application of 1 lb a.i./acre with soil incorporation.

The EPA did, however, conduct two simulations comparable to the Gleams-Driver simulations, one involving a single application to a corn field at 1 lb a.i./acre with soil incorporation and the other involving a single forestry application (cottonwood) at 2 lbs a.i./acre also with soil corporation. As summarized in Table 11 of the current risk assessment, these simulations yield estimates of about 0.6 µg/L for peak concentrations in pond water and 0.07 and 0.095 µg/L for longer-term concentrations. The EPA modeled peak concentrations (U.S. EPA/OPP 2009a) are only modestly higher than the central estimate of about 0.2 µg/L from Gleams-Driver and are below the upper bound concentration of about 1.4 µg/L from the Gleams-Driver simulations. The longer-term concentration of 0.07 µg/L modeled by EPA (U.S. EPA/OPP 2009a) is a factor of about 10 higher than the central estimate from Gleams-Driver – i.e., about 0.0074 µg/L. This probably relates to the averaging period. As summarized in Table 11, U.S. EPA/OPP (2009a) reports 60-day averages while the longer-term concentration from Gleams-Driver are reported as annual averages. In any event, the upper bound annual average of 0.04 µg/L from the Gleams-Driver simulations is only somewhat lower than the 60-day averages reported in U.S. EPA/OPP (2009a). As discussed further in Section 3.2.3.4.6, the upper bound estimates of concentrations of trifluralin in water used in the current risk assessment are based primarily on the stream modeling from Gleams-Driver. As discussed in the previous subsection, the concentrations estimated in streams are substantially above those estimated for ponds.

3.2.3.4.5. Monitoring Data

3.2.3.4.5.1. Monitoring Studies Involving Defined Applications

Occasionally, monitoring data or field studies are available which provide estimated concentrations of a pesticide in surface water associated with well-defined applications (i.e., applications at a specified rate to a field of a known size and site characteristics). These data can be used to evaluate the accuracy of the modeled estimated pesticide concentrations in surface water.

The recent monitoring study by Vogel and Linard (2011) provides a reasonable basis for assessing the Gleams-Driver modeling. In the study by Vogel and Linard (2011), approximately 55 kg (≈121 lb) of trifluralin was applied to a 145 ha (≈360 acres) watershed for an average application rate of about 0.34 lb a.i./acre [121 lb ÷ 360 acres ≈ 0.336111 lb a.i./acre]. Based on subsequent monitoring, the maximum concentration in stream water following a storm event was about 0.11 µg/L. Median longer-term concentrations not associated with storm events were about 0.01 µg/L. In terms of water contamination rates (i.e., µg/L per lb a.i./acre), the peak concentration corresponds to about 0.32 µg/L per lb a.i./acre [0.11 µg/L ÷ 0.34 lb a.i./acre ≈ 0.32353 µg/L per lb a.i./acre] and the median longer-term concentration corresponds to about 0.03 µg/L per lb a.i./acre [0.01 µg/L ÷ 0.34 lb a.i./acre = 0.02941 µg/L per lb a.i./acre].

The study by Vogel and Linard (2011) was conducted in Colfax County in northeast Nebraska. The predominant soil is characterized as Nora-Crofton-Moody, a well-drained and predominantly silty soil. The average annual rainfall at the site is specified as 723 mm (≈28 inches). The average annual temperature for Colfax County, Nebraska is about 50 °F (http://www.weather.com/weather/wxclimatology/monthly/graph/6668:20). Based on these characteristics, this site would most closely correspond to the site with average temperature and average rainfall in Table 9. As indicated in Appendix 7 (Table A7-5), the maximum concentration of trifluralin modeled with Gleams-Driver in streams for a site with loamy soil, average temperature and precipitation is 2.41 (0.6 - 9) µg/L. The lower bound of 0.6 µg/L is only modestly higher than the peak water contamination rate of 0.32 µg/L per lb a.i./acre from the study by Vogel and Linard (2011). In this respect, it may be worth noting that the central estimate and the upper bound of the half-lives for water used in the Gleams-Driver modeling (Table 10) are based on microcosm simulations for aqueous dissipation half-lives from Laabs et al. (2007) in which the rapid dissipation was attributed primarily to volatilization. While somewhat speculative, it seems reasonable to suggest that these microcosm studies, which involved non-flowing water, may be relevant to concentrations in ponds but might underestimate the dissipation of trifluralin from flowing waters. The longer-term concentrations from Gleams-Driver (Appendix 7, Table A7-6) is 0.05 (0.02 - 0.11) µg/L. The central estimate of 0.05 µg/L is only modestly higher than the median longer-term water contamination rate of 0.02941 µg/L per lb a.i./acre.

Given that no attempt was made to model the site from Vogel and Linard (2011), the concordance of the Gleams-Driver modeling with the monitoring data from Vogel and Linard (2011) is remarkable. Based on the central estimates, the Gleams-Driver modeling overestimates the peak concentrations relative to the peak concentrations from Vogel and Linard (2011) by about a factor of about 7.5—i.e., 2.41 µg/L ÷ 0.32 µg/L ≈ 7.531. Nonetheless, the estimated longer-tem water contamination rate of 0.03 µg/L per lb/acre is well within the range of the lower bound (0.02 µg/L) and central estimate (0.05 µg/L) from Gleams-Driver. The correspondence of the longer-term term average of 0.05 µg/L from Gleams-Driver to the monitored longer-term concentration of about 0.03 µg/L per lb/acre from Vogel and Linard (2011) may be coincidental. Nonetheless, a consideration of the Vogel and Linard (2011) study with the Gleams-Driver modeling does suggest that the central estimate of the concentration of trifluralin in streams based on Gleams-Driver is reasonable. Nonetheless, the upper bound peak concentrations in streams estimated from the Gleams-Driver simulations – i.e., 9 µg/L in Appendix 7, Table A7-5, for average rain and temperate location with loam soil – is much high than the peak concentration of 0.32 µg/L from Vogel and Linard (2011). This apparent overestimate is discussed further in Section 3.2.3.4.6.

3.2.3.4.5.1. Other Monitoring Data

As summarized in Table 11, other monitoring data in surface water are available but these data cannot be associated with defined applications of trifluralin. Within these limitations, which are substantial, the available monitoring studies on trifluralin are concordant with the estimates of trifluralin concentrations in surface water from Gleams-Driver. The maximum concentration of trifluralin monitored in surface water is 1.5 µg/L.

This report is from the California Department of Pesticide Regulations, as summarized in U.S. EPA/OPP (2009a). This maximum concentration is very close to the maximum peak concentrations in ponds estimated from Gleams-Driver (1.36 µg/L).

Because the current risk assessment is specifically focused on the use of trifluralin in South Carolina, the data from Maas et al. (1994) on levels of trifluralin in well water in neighboring state of North Carolina are particularly relevant. Regrettably, Mass et al. (1994) do not provide specific concentrations of trifluralin in North Carolina well water but do indicate that trifluralin was detected in 1.8% of the samples tested with a limit of detection of 0.42 µg/L. Concentrations in excess of 0.42 µg/L are consistent with the concentrations of trifluralin estimated in both streams and ponds. In addition and as illustrated in Figure 5, concentrations of trifluralin in excess of 0.42 µg/L would be expected to occur only shortly after trifluralin is applied. This pattern is consistent with the infrequent detection of trifluralin in well water noted by Mass et al. (1994). As discussed above, however, this correspondence could well be coincidental because the monitoring data reported by Mass et al. (1994) cannot be associated with defined applications of trifluralin.

Relatively high concentrations of trifluralin (i.e., up to about 8 µg/L) were detected downstream from a chemical plant used to manufacture trifluralin (Spacie and Hamelink 1979). While this report is included for the sake of completeness, it is not directly relevant to assessing concentrations of trifluralin in streams associated with forestry or agricultural uses. Consequently, this report is not summarized in Table 11 and is not directly relevant to the exposure assessment for humans or wildlife. As discussed further in Section 3.2.3.5.1, the study by Spacie and Hamelink (1979) also reports concentrations of trifluralin in fish, and this study is relevant to the exposure scenarios associated with the consumption of wild-caught fish.

The recent report by USGS on pesticides in streams, does not provide information on monitored concentrations of trifluralin in streams but indicates that trifluralin was detected in about 15% of streams in the United States that are located in agricultural areas (Gilliom et al. 2007, Figure 4-2, p. 44).

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

The water concentrations used in the current risk assessment are based on considerations of the Gleams-Driver and U.S. EPA/OPP modeling as well as the available monitoring data. The specific concentrations used are summarized in Table 12. The concentrations given in Table 12 are specified as water contamination rates (WCRs)—i.e., the concentrations in water expected at a normalized application rate of 1 lb a.i./acre, converted to units of ppm or mg/L per lb a.i./acre. In the previous tables discussing concentrations in water, units of exposure are expressed as ppb or µg/L, as a matter of convenience. In Table 12, however, ppb is converted to ppm because ppm (i.e., mg/L) is the unit of measure used in the EXCEL workbooks for contaminated water exposure scenarios in both the human health and ecological risk assessments. The WCR are entered in Worksheet B04Rt in each of the EXCEL workbook that accompanies this risk assessment. The values in Worksheet B04Rt are linked to the appropriate scenario-specific worksheets in the EXCEL workbooks.

As discussed in Section 3.2.3.4.5.1, the monitoring study by Vogel and Linard (2011) suggests that the Gleams-Driver stream modeling presented in this risk assessment is reasonable based on central estimates but may substantially overestimate upper bound concentrations in streams. The upper bound peak concentration of 28.4µg/L modeled with Gleams-Driver is much higher than the estimated water contamination rate from Vogel and Linard (2011) – i.e., 0.32 µg/L – as well as the maximum monitored concentration of trifluralin – i.e., 1.8 µg/L. As also discussed in Section 3.2.3.4.5.1, the apparent overestimate of upper bound concentrations in streams may be associated with the use of dissipation half-lives from water, which are based on volatilization from static (non-flowing) water.

Based on these considerations, the estimated short-term (peak) water contamination rates for trifluralin in surface water are taken as 0.6 (0.02 to 2.2) µg/L per lb a.i./acre. The central estimate of 0.6 µg/L is based on the U.S. EPA/OPP (2009a) pond modeling using PRZM/EXAMS – i.e., 0.55 and 0.585 µg/ as summarized in Table 11 – rounded to one significant place.

The upper bound of 2.2 µg/L is based on the central estimate for streams based on the Gleams-Driver modeling – i.e., 2.21 µg/L as summarized in Table 11. This concentration encompassed the maximum monitored concentration of 1.8 µg/L from CCME (1999). The lower bound of 0.02 µg/L is taken directly from the Gleams-Driver modeling of streams.

As discussed above, the Gleams-Driver modeling appears to have substantially overestimated the upper bound concentrations of trifluralin in streams. This overestimate appears to be attributable to the use of the upper bound half-life of 3.2 days (Table 10). While this half-life may be appropriate for standing water, it does not appear to be appropriate for flowing water. As discussed in Section 3.2.3.4.3.1, U.S. EPA/OPP (2009a) uses a half-life of about 0.4 days based on photolysis. This half-life is very close to the half-life of 0.5114 days estimated from the EPA's EPI Suite program (U.S. EPA/OPPTS 2011) and only modestly below the central estimate of the half-life in water used in the Gleams-Driver modeling (i.e., 0.6 days). Based on these considerations, the upper bound estimate in streams from Gleams-Driver is not used.

The longer-term water contamination rates for trifluralin are taken as 0.068 (0.00015 - 0.6) µg/L, the longer-term concentrations in streams from Gleams-Driver. As discussed in Section 3.2.3.4.5.1, the longer-term concentrations from Gleams-Driver for the site comparable to that in the Vogel and Linard (2011) study are reasonably consistent with the Vogel and Linard (2011) study. Consequently, the overall longer-term concentrations in streams modeled using Gleams-Driver are not adjusted. As summarized in Table 11, the central estimate of concentration of trifluralin in streams from Gleams-Driver is similar to the concentrations modeled in ponds modeled by U.S. EPA/OPP (2009a).

3.2.3.5. Oral Exposure from Contaminated Fish

Many chemicals may be concentrated or partitioned from water into the tissues of animals or plants in the water. This process is referred to as bioconcentration. The

concentration of the pesticide in fish (C_F) is taken as the product of the concentration of the chemical in water (C_W) and the bioconcentration factor (BCF):

Equation 3

$$C_{Fish_{mg/Kg}} = C_{W\ mg/L} \times BCF_{L/kg}$$

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 BCF is 5 L/kg [5 mg/kg ÷ 1 mg/L].

This risk assessment includes three sets of exposure scenarios for the consumption of contaminated fish, and each set includes separate estimates for the general population and subsistence populations. These exposure scenarios consist of one set for acute exposures following an accidental spill (Worksheets D08a and D08b), another set for acute exposures based on expected peak concentrations (Worksheets D09c and D09d), and the third set for chronic exposures based on estimates of longer-term concentrations in water (Worksheets D09a and D09b). The two worksheets in each of these three sets are intended to account for different rates of wild-caught fish consumption in both general and subsistence populations. Details of exposure scenarios involving the consumption of contaminated fish are provided in Section 3.2.3.5 of SERA (2007a).

For the human health risk assessment, the assumption is made that only the edible portion of the fish (i.e., the fillet) is consumed. The only data on the bioconcentration in the edible portion of fish comes from a registrant-submitted study summarized by U.S. EPA/OPP (1996a, 2009a) in bluegill sunfish indicating a BCF of 2041 L/kg. This bioconcentration factor is used in all exposure scenarios involving the consumption of fish by humans.

Most pesticides covered in Forest Service risk assessments do not substantially bioconcentrate in fish; accordingly, the exposure scenarios associated with the consumption of fish do not raise concern. While this is the case for trifluralin in terms of systemic toxicity, trifluralin is classified as a carcinogen (Section 3.1.10). As discussed further in the Risk Characterization (Section 3.4.3), the combination of the carcinogenicity and bioconcentration of trifluralin, does result in exposures that exceed the level of concern for carcinogenicity. Consequently, the following subsections provide a detailed analysis of the plausibility of the exposures scenarios associated with the consumption of fish, both in terms of the bioconcentration factor and the possible extent of wild-caught fish consumption.

3.2.3.5.1. Bioconcentration

As detailed in Worksheets D09a and D09b, the use of this BCF with the estimated longer-term concentrations of trifluralin in water—i.e., 0.075 µg/L (0.0002 to 0.4) µg/L as summarized in Table 12—leads to estimated concentrations of trifluralin in edible fish tissue of about 150 (0.4 to 816) µg/kg fish. This is an extremely broad range, and the variability is due solely to the wide range of trifluralin concentrations estimated for surface water.

There is relatively little monitoring data on trifluralin concentrations in fish taken from surface waters. An assessment by Health Canada (2009) provides a brief summary of a registrant study in which trifluralin was monitored in fish with frequencies of occurrence ranging from 0.7 to 10%. The reported higher concentration in fish tissues (not otherwise specified) is 36 µg/kg fish, a factor of about 4 below the central estimate used in the current risk assessment [150 µg/kg ÷ 36 µg/kg ≈ 4.29]. Similarly, in a fish monitoring study conducted in California and summarized by U.S. EPA/OPP (2009a, p. 78), the maximum concentration of trifluralin detected in fish was 42.1 µg/kg, a factor of about 3.6 below the central estimate of the concentration in fish used in the current risk assessment [150 µg/kg ÷ 42.1 µg/kg ≈ 3.5629].

Spacie and Hamelink (1979) monitored concentrations of trifluralin in surface water of up to about 8 µg/L. This is somewhat higher than the peak concentration of 2.3 µg/L used as a water contamination rate in the current risk assessment. As noted in Section 3.2.3.4.5.1, the surface water monitoring data from the study by Spacie and Hamelink (1979) are not directly relevant to the assessment of water contamination rates in the current risk assessment because they involved a river in which the peak concentrations were detected 0.5 to 1 km downstream of a plant that produced trifluralin. Spacie and Hamelink (1979), however, also report concentrations of trifluralin in the fat of fish taken from this stream. The mean concentrations in the fat of fish ranged from 300 to 440,000 µg/kg fat (Spacie and Hamelink 1979, Table II, p. 819). Spacie and Hamelink (1979) note that the representative concentration of trifluralin in the water over the period in which the fish were caught was 0.874 µg/L. Taking the geometric mean of the range of trifluralin concentrations in the fat of fish as a central estimate, the average concentration in fat may be estimated at about 11,500 µg/kg fat [$(300 \times 440{,}000)^{0.5} \approx 11{,}489$].

Concentrations of trifluralin in fat are not directly comparable to concentrations of trifluralin in muscle. The bioconcentration study used by the EPA in U.S. EPA/OPP (1996a, 2009a), notes that the BCF for trifluralin in offal (the inedible portion of fish) was 9586 L/kg, a factor of about 5 higher than the BCF in muscle [9586 L/kg ÷ 2041 L/kg ≈ 4.6967]. Using this adjustment factor, the concentration of trifluralin in muscle from the study by Spacie and Hamelink (1979) is estimated at 2300 µg/kg edible tissue [11,500 µg/kg fat ÷ $5_{fat/muscle}$]. As noted above, this concentration in fish is associated with a water concentration of 0.874 µg/L. As also noted above, the central estimate of the concentration of trifluralin in water for longer-term exposures is 0.075 µg/L. Adjusting for these differences in concentration, the expected concentration of trifluralin in the muscle tissue of fish is estimated at about 200 µg/kg edible tissue [2300 µg/kg edible tissue x (0.075 µg/L ÷ 0.874 µg/L) ≈ 197.368 µg/kg edible tissue]. This concentration in fish based on the monitoring data from Spacie and Hamelink (1979) is reasonably close to the central estimate of about 150 µg/kg in edible tissue used in Worksheets D09a and D09b. Thus, this component of the exposure assessment for the consumption of contaminated fish appears to be plausible.

3.2.3.5.2. Consumption of Wild-Caught Fish

The other important factor in the exposure scenario for the consumption of contaminated fish involves the amount of fish that is consumed. Based on the most recent finalized version of the U.S. EPA Exposure Factors Handbook (U.S. EPA/NCEA 1997), the current risk assessment uses consumption rates for caught fish of 0.01 kg/day for the general population and 0.081 kg/day for some native Americans and other subsistence populations—i.e., individuals who may consume large amounts of wild caught fish as a primary (rather than recreational) source of food.

As discussed further in Section 3.4 (Risk Characterization), the consumption of wild caught fish is a concern for subsistence populations in terms of potential carcinogenicity. In terms of interpreting this potential risk, it is important to note that the peer review draft of the updated U.S. EPA Exposure Factors Handbook (U.S. EPA/NCEA 2009) no longer explicitly recommends consumption values for subsistence populations but makes the following statement:

> *Recommended values are also not provided for Native American subsistence fish intake because the available data are limited to certain geographic areas and/or tribes and cannot be readily generalized to Native American tribes as a whole. However, data from several Native American studies are provided in this chapter and are summarized in Table 10-6. Assessors may use these data, if appropriate to the scenarios and populations being assessed. These studies were performed at various study locations among various tribes.*
>
> U.S. EPA/NCEA 2009, p. 10-4

As in Section 2 (Program Description), the current Forest Service risk assessment is intended to be used nationally but is specifically focused on applications of trifluralin in South Carolina. No specific information is available on the amount of fish that might be consumed by Native Americans or other subsistence populations in South Carolina. Consequently, the standard values from U.S. EPA/NCEA (1997) are used in the current risk assessment. If information is available on fish consumption by subsistence populations in the course of site specific analyses, this information should be used in preference to the standard values used in the current risk assessment.

3.2.3.5.3. Accidental Exposure Scenarios

As detailed in Worksheets D08a and D08b of the EXCEL workbook that accompanies this risk assessment, the exposure scenarios involving the consumption of contaminated fish involve water concentrations of about 4.5 (0.23 to 18) mg/L as well as bioconcentration factors of 2041. As discussed in the risk characterization, these exposure factors result in very high HQs, particularly at the upper bounds.

These exposure assessments are included in the current risk assessment because they are used as standard exposure scenarios in all Forest Service risk assessment. For trifluralin, however, these exposure assessments are highly unlikely. As discussed further in Section 4.3.3.1 (the dose-response assessment for fish), the 96-hour LC_{50} values for most species

of fish range from about 0.04 to 4 mg/L. Game species such as trout and largemouth bass are very sensitive to trifluralin with 96-hour LC_{50} values in the region of 0.04 mg/L to 0.075 mg/L. Thus, in the event of an accidental spill, fish which might otherwise be consumed by humans would probably die rapidly or at least evidence signs of toxicity. Consequently, the likelihood that these fish would be taken and eaten by humans seems remote.

Another factor which tempers the consequences of these exposure scenarios involves the relatively high bioconcentration factor for trifluralin—i.e., about 2000 in edible tissue. For chemicals that are not extensively bioconcentrated, the time to equilibrium is typically very rapid. This event is an extension of the plateau principle discussed in Section 3.1.3.3. For chemicals such as trifluralin which are extensively bioconcentrated, a longer period of time is required for the fish to reach equilibrium with the water. Because acute BCFs are not available on trifluralin, the equilibrium BCF of 2041 is used, which is likely to grossly overestimate exposures in the event of an accidental spill.

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. Specifically with respect to trifluralin, it is reasonable to assume that some wildlife feed plots might be planted close to surface water; moreover, several examples of feed plots close to surface water are included in the guide to developing wildlife food plots by Harper (2008).

To assess the potential risks associated with swimming in contaminated water, an exposure assessment is developed for a young woman swimming in surface water for 1 hour (Worksheet D11). Conceptually and computationally, this exposure scenario is virtually identical to the contaminated gloves scenario used for workers (Section 3.2.2.2)—i.e., a portion of the body is immersed in an aqueous solution of the compound at a fixed concentration for a fixed period of time.

As in the corresponding worker exposure scenario, the 1-hour period of exposure is somewhat, but not completely, arbitrary, given that longer periods of exposure are plausible. Nonetheless, the 1-hour period is intended as a unit exposure estimate. In other words, the exposure and consequently the risk will increase linearly with the duration of exposure, as indicated in Worksheet 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).

In Forest Service risk assessments, the ingestion of water during swimming is not considered explicitly. U.S. EPA/OPP (2003) uses a model for swimming exposures based on essentially the same approach to dermal absorption used in Worksheet D10. The EPA model, however, incorporates the assumption that an adult will consume water while swimming at a rate of 50 mL/hour. This assumption is based on data from ingestion rates in swimming pools. Based on more recent studies of water ingestion

while swimming in pools (Dorevitch et al. (2010; Dufour et al. 2006), the EPA assumption of 50 mL/hour is a plausible upper bound.

3.2.3.6. Oral Exposure from Contaminated Vegetation

Forest Service risk assessments involving broadcast foliar applications use a standard set of exposure scenarios in which concentrations of the pesticide are estimated in four types of plant matter, including short grass, tall grass, broadleaf vegetation, and fruits/seeds, based on residue rates in units of mg/kg vegetation per lb/acre developed by the U.S. EPA (Fletcher et al. 1994).

This method for estimating exposures is not relevant to soil applications of trifluralin. Based on the Gleams-Driver modeling detailed in Section 3.2.3.4.3, soil concentrations associated with the soil incorporation of trifluralin can be estimated, as detailed in Appendix 7 (Table A7-2). Based on the Gleams-Driver modeling, concentrations in the top 12 inches of soil are estimated at 0.31 (0.26 to 0.38) mg/kg soil (dry weight). These concentrations are entered into Worksheet B05a. The concentrations in Worksheet B05a are in turn linked to the soil concentrations in Worksheets B05b, B05c, and B05d.

Although trifluralin has been extensively studied in plants (Section 4.1.2.5.), relatively few studies permit quantitative estimates of trifluralin in plant tissue based on the concentrations of trifluralin in soil. Two exceptions are the studies by Cessna et al. (1988) and Tiryaki et al. (1997). The residue rates derived from these studies are summarized in Table 13. These residue rates are essentially bioconcentration factors for plants expressed in units of ppm plant/ppm soil (i.e., mg trifluralin/kg plant per mg trifluralin/kg soil). For the sake of brevity, these units are omitted in the following discussion of the derivation of these plant-to-soil bioconcentration factors.

The study by Cessna et al. (1998) involved residues in wheat following soil incorporation of trifluralin at an application rate of 0.74 kg a.i./ha (≈0.66 lb a.i./acre). Concentrations of trifluralin monitored in wheat ranged from 4.8 to 10.5 µg/kg over a period of 56 days after application (Cessna et al. 1998, Table 1, p. 1156). Over the same period, the concentrations in soil remained relatively constant, ranging from 0.44 to 0.47 mg/kg soil. The resulting plant-to-soil bioconcentration factors for three time periods for which both residues are reported in both wheat and soil are 0.0016, 0.0011, and 0.0023. As summarized in Table 13, these data are used to derive BCFs for grass (both short and tall) of 0.0017 (0.0011 to 0.0023). The central estimate of 0.0017 is the mean of the lowest and highest values and is only modestly more conservative than using the mid-range value of 0.0016.

The study by Tiryaki et al. (1997), which was conducted in Turkey, involved the soil incorporation of trifluralin to agricultural fields (sandy loam soil) followed by the planting of melons (*Yuva* variety) native to Turkey. The study encompassed two growing seasons with plantings on May 14, 1991 and June 5, 1992 with the melons harvested on Oct 23, 1991 and Oct 2, 1992. As summary of the data from Tiryaki et al. (1997, Table 2) is given in Table 14 of the current risk assessment. The summary is based on averages from the two growing seasons. Tiryaki et al. (1997) provide data on total, extractable, and bound residues. For the current risk assessment, only total residues are used to

estimate bioconcentration factors. As indicated in Table 13 of the current risk assessment, the estimates of BCF for trifluralin in broadleaf vegetation are based on the concentrations in melon leaves from Tiryaki et al. (1997), taking BCFs from the upper canopy (lower bound), mid canopy (central estimate), and lower canopy (upper bound). Similarly, the estimates of the BCF values for trifluralin in fruit are based on the concentrations in melon: fruit skin (central estimate), fruit flesh (lower bound), and fruit seed (upper bound).

As discussed in Section 2.3, the current Forest Service risk assessment is concerned specifically with applications of trifluralin to fields used to grow sunflowers as a food source for wildlife. In this application, the probability that humans would consume any vegetation contaminated with trifluralin seems remote. Foraging permits are not issued for areas designated as wildlife site improvement areas (wildlife food plot areas). Moreover, pesticide-treated areas are posted to alert users of that area that pesticide treatments have been made, specifying the pesticide and date of application. Reasonable foragers will understand the intended restriction of foraging in these areas and should avoid them, reducing the potential risk from eating sunflower seeds contaminated with trifluralin. Other than the possible, albeit unlikely and infrequent, consumption of sunflower seeds from treated areas, there is no basis for asserting that humans might consume other types of contaminated vegetation (i.e., humans will not consume the leaves or stalks of sunflowers).

Given the above considerations, the only exposure scenario involving the consumption of contaminated vegetation used in the human health risk assessment involves the short-term/single dose consumption of contaminated sunflower seeds. This exposure scenario is presented in Worksheet D03, which is a custom worksheet modified from the standard worksheet developed by WorksheetMaker. Specifically, the concentration in the contaminated material (sunflower seeds) is based solely on the upper bound bioconcentration factor of 0.021 ppm seeds/ppm soil (Table 13). As indicated in Worksheet D03, the estimated concentration of trifluralin in sunflower seeds is about 0.0065 mg/kg.

In typical exposure scenarios, the amount of plant matter consumed is based on estimates of food consumption from the finalized version of the U.S. EPA Exposure Factors Handbook (U.S. EPA/NCEA 1997). For example, the exposure scenario involving contaminated fruit assumes that a young woman consumes 0.00168 to 0.01244 kg fruit/kg bw. No information on the consumption of sunflower seeds is given in U.S. EPA/NCEA (1997) or in the peer review draft update (U.S. EPA/NCEA 2009). In the absence of any specific information, the assumption is made that an individual might consume about 0.5 (0.25 to 1) cup of shelled sunflower seeds incidentally taken from a treated field. Based on information from the National Nutrient Database for Standard Reference (USDA/ARS 2011), 1 cup of shelled sunflower seeds weighs 140 g. Thus, consuming 0.5 (0.25 to 1) cup of shelled sunflower seeds corresponds to 70 (35 to 140 g). Taking 64 kg as a reference body weight for a young woman (U.S. EPA/ORD 1985), the consumption rate is about 0.0022 (0.0011 to 0.0044) kg seeds/kg bw [0.070 (0.035 to 0.140 kg seeds ÷ 64 kg bw]. Based on this consumption rate and the estimated

concentration of trifluralin in sunflower seeds, the estimated dose to the young woman is about 1.4 (0.72 to 2.9) x 10^{-5} mg/kg bw. These calculations are detailed in Worksheet D03 of Attachment 1.

While longer-term exposures to contaminated sunflower seeds do not seem plausible and are not formally assessed, the potential risks of longer-term exposures are addressed semi-quantitatively in the risk characterization (Section 3.4.3).

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

Table 15 provides an overview of the toxicity values used in the current Forest Service risk assessment for human health effects. When the U.S. EPA adopts toxicity values for human health, which is the case for trifluralin, those values are typically adopted and used directly in Forest Service risk assessments. For trifluralin, the U.S. EPA/OPP derived an acute RfD of 1 mg/kg bw as well as a chronic RfD of 0.024 mg/kg bw/day. Both of these RfDs are derived in the most recent U.S. EPA human health risk assessment on trifluralin (U.S. EPA/OPP 2003a,b, 2004a) and are based on NOAELs from studies in experimental mammals divided by an uncertainty factor of 100. An earlier and lower chronic RfD of 0.0075 mg/kg bw/day was developed by U.S. EPA/ORD (1993) based on very slight increases in methemoglobin as well as increases in liver weight which were not associated with histopathological changes in the liver. The more recent EPA assessments (U.S. EPA/OPP 2003a,b, 2004a) appear to appropriately regard these effects as toxicologically insignificant.

To help interpret the risks associated with exposure levels that exceed the RfD, Forest Service risk assessments try to characterize dose-severity relationships based preferably on human data, or systematic and consistent differences in species sensitivity among mammals, or, at very least, consistent dose-response and/or dose-severity relationships in mammals. Human data on trifluralin are not available for defining dose-severity relationships, and the available animal data, while reasonably complete, are not sufficient for proposing quantitative dose-severity relationships for human exposures to trifluralin.

Unlike most pesticides used by the Forest Service, trifluralin is classified as a carcinogen, and the EPA proposes a cancer potency factor of 0.0058 $(mg/kg\ bw/day)^{-1}$ using a linear nonthreshold model (U.S. EPA/OPP 2004a). Based on this cancer potency factor, the dose of 0.0017 mg/kg bw/day is associated with a risk level of 1 in one million. This dose is used to derive HQs associated with the potential carcinogenicity of trifluralin. A reservation with this approach is that trifluralin does not appear to be mutagenic. Consequently, less conservative nonlinear and/or threshold models could be considered for trifluralin. While noting this reservation, the current Forest Service risk assessment defers to the assessment made in U.S. EPA/OPP (2004a).

3.3.2. Acute RfD

U.S. EPA/OPP sometimes derives an acute RfD for pesticide exposures that occur in a single day. Acute RfDs derived by the U.S. EPA/OPP are usually based on developmental studies in which an adverse effect is associated with a single dose of a pesticide. The most recent EPA human health risk assessment of trifluralin (U.S. EPA/OPP 2004a)—i.e., the pesticide tolerance reassessment for trifluralin—recommends an acute RfD of 1 mg/kg bw/day. As summarized in Appendix 1 (Table A1-8), this acute RfD is based on a NOAEL of 100 mg/kg bw/day from a developmental study in rats (MRID 00151899, 00159620 and 40392310). The corresponding LOAEL from this study is 500 mg/kg bw/day which caused frank signs of toxicity in dams as well as increases in liver and spleen weight. The RfD is derived by dividing the NOAEL of 100

mg/kg bw by an uncertainty factor of 100—a factor of 10 for extrapolating from animals to humans as well as a factor of 10 to account for potentially sensitive individuals in the human population.

As summarized in Table 5 of the current risk assessment, the NOAEL of 100 mg/kg bw/day is supported by identical NOAELs in rabbits (MRID 00152421 and Byrd and Markham 1990; Byrd et al. 1995) as well as somewhat higher NOAELs in rats. Thus, the acute RfD of 1 mg/kg bw is used in the current risk assessment for the characterization of all acute exposure scenarios.

3.3.3. Chronic RfD

The U.S. EPA has derived two chronic RfDs for trifluralin, both of which are based on studies in dogs. The initial RfD for trifluralin was 0.0075 mg/kg bw/day (U.S. EPA/ORD 1993). As summarized in Appendix 1 (Table A1-10), this RfD is based on a 1-year feeding study in dogs in which trifluralin was administered in the diet at concentrations of 0, 30, 150, or 750 ppm (MRIDs 00151908, 00159618). Based on food consumption rates, these dietary concentrations corresponded to doses of (0, 0.75, 3.75, and 18.75 mg/kg/day. The NOAEL from this study was set at 0.75 mg/kg bw/day based on increases in liver weight and methemoglobin in male and female rats at the two higher dose levels; however, histological effects were not observed at any dose. As with the acute RfD, the chronic RfD was calculated as the NOAEL of 0.75 mg/kg bw divided by an uncertainty factor of 100. This RfD is still listed as the chronic RfD for trifluralin on the Agency's Integrated Risk Information System on-line database (http://www.epa.gov/ncea/iris/subst/0268.htm), and this RfD was initially accepted by U.S. EPA/OPP (Ghali 1994).

In both the Reregistration Eligibility Decision (RED) document on trifluralin as well as the more recent tolerance reassessment for trifluralin, U.S. EPA/OPP (1996a, 2004a) proposes a higher chronic RfD of 0.024 mg/kg bw/day. As summarized in Appendix 1 (Table A1-10), this study is based on a 1-year study in dogs involving administration of trifluralin in capsules at doses of 0, 0.75, 2.4, or 40 mg/kg/day (Adams et al. 1992, MIRD 42447001). The NOAEL for this study is identified as 2.4 mg/kg bw/day based on a spectrum of effects at 40 mg/kg bw/day, including, decreased body weight; decreased red cells and hemoglobin levels, increased thrombocyte count, methemoglobin, cholesterol, and triglyceride levels, increased liver weight, and increased heart weight.

The rationale for selecting the higher RfD is not discussed in detail in either the RED (U.S. EPA/OPP 1996a) or the EPA tolerance reassessment (2004a). A support document for the tolerance reassessment (U.S. EPA/OPP 2003a, the toxicology chapter) provides the following discussion concerning the initial chronic RfD:

> *The lower NOAEL of 0.75 mg/kg/day established in the other dog study (MRID 00151908) was not selected since the endpoint (increase in liver weights) was not accompanied by any other corroborative changes such as alterations in clinical chemistry parameters or histopathological changes in the liver.*
>
> U.S. EPA/OPP (2003b, p. 34)

In a more detailed synopsis of this study, U.S. EPA/OPP (2003b, p. 22) notes that the methemoglobin levels in dogs at 0.75 mg/kg bw/day from the dietary study were only modestly increased—i.e., *increased in males at months 6 and 9 (1.2-1.5% treated vs 0.8-1.0% controls) and in females at month 12 (1.8% treated vs 0.7-1.1% controls).*

While not explicitly stated in the recent U.S. EPA/OPP risk assessment documents (U.S. EPA/OPP 2003a,b, 2004), the decision to disregard the increased methemoglobin levels appears to be based implicitly on the determination that the slight increases in methemoglobin levels in the dietary study in dogs are not toxicologically significant.

As discussed in some detail in the Forest Service risk assessments on tebufenozide (SERA 2004a) and diflubenzuron (SERA 2004b), methemoglobin is formed by the oxidation of the heme iron in hemoglobin from the ferrous (Hb++) to the ferric state (MetHb+++). At the level of the cell, methemoglobin formation is clearly an adverse effect because red blood cells with methemoglobin are not able to function normally in the transport and distribution of oxygen. Heme group oxidation, however, occurs spontaneously and accounts for approximately 2% of the hemoglobin in normal individuals. Thus, the modest increases in methemoglobin noted in the dietary study in dogs (MRID 00151908) are clearly an index of exposure to trifluralin; nonetheless, the implicit assessment in U.S. EPA/OPP (2003b) that these changes are not toxicologically significant is justifiable.

The current Forest Service risk assessment adopts the most recent chronic RfD of 0.024 mg/kg bw/day (U.S. EPA/OPP 1996a, 2004a) and uses it to characterize risks associated with longer-term exposures to trifluralin.

3.3.4. Dose-Severity Considerations

Forest Service risk assessments typically consider dose-severity relationships to elaborate concerns for modest excursions above the acute or chronic RfD. Confidence in the assessment of dose-severity relationships is highest when human data are available. There are no data regarding adverse effects in humans after exposure to trifluralin. Even the extensive compilation by Hayes (1982) of the early literature on the effects of pesticides in humans does not include information on the effects of trifluralin.

As discussed further in Section 3.4, some accidental exposure scenarios for members of the general public lead to HQs substantially above the level of concern. No chronic HQs approach a level of concern. Consequently, the consideration of dose-severity relationships is limited to a discussion of the acute RfD. As discussed in Section 3.3.2, the acute RfD is based on a NOAEL of 100 mg/kg bw from a reproductive study in rats with a corresponding LOAEL of 500 mg/kg bw based signs of maternal toxicity. In terms of the study on which the acute RfD is based, an HQ of 5 would be a cause for concern. As summarized in Table 5, other developmental toxicity studies suggest that the ratio of the LOAEL to the NOAEL is greater than a factor of 2.

As summarized in Appendix 1 (Table A1-2), the minimum lethal dose in experimental mammals is 1600 mg/kg bw (Hollander 1979). As discussed in Section 3.1.4, acute LD_{50}

values are available in four mammalian species (dogs, mice, rats, and voles), and these data do not suggest any systematic relationship between body size and toxic potency. Similarly, as discussed in Section 3.1.5, there appear to be no remarkable differences in sensitivity among mice, rats, rabbits and dogs based on the available subchronic and chronic toxicity studies. Notwithstanding these relationships, however, the dose of 1250 mg/kg bw should not be viewed as a minimum lethal dose in humans or any other species, because the available acute toxicity values are based on relatively small numbers of healthy laboratory mammals and probably do not reflect sensitivities in large populations of humans or mammalian wildlife. The dose of 1250 mg/kg bw is simply the lowest reported lethal dose in any mammal tested. In humans, exposure a dose of 1250 mg/kg bw would be a clear cause for alarm. Moreover, it is likely that lower doses would cause severe signs of toxicity and perhaps lethality in humans or other mammals. Given the lack of exposure data, it is impossible to define a specific threshold dose for severe signs of toxicity in humans.

3.3.5. Carcinogenicity

As discussed in Section 3.1.10, the EPA classifies trifluralin as a carcinogen (U.S. EPA/OPP 1996a, 2003a,b, 2004). Cancer risk is quantified by the U.S. EPA and many other organizations using a cancer potency factor (often designated as a Q_1*) in units of reciprocal dose such as $(\text{mg/kg bw/day})^{-1}$. In most cancer risk assessments, the EPA (e.g., U.S. EPA/RAF 2005) assumes that cancer is a nonthreshold response and that the dose is linearly related to risk. Under this assumption, cancer risk over a lifetime (***P***) is calculated as the product of the daily dose (***d***) over a lifetime and the potency parameter ($\mathbf{Q_1^*}$):

$$P = d\, Q_1^*$$

and the lifetime daily dose associated with a given risk level is:

$$d = P \div Q_1^*$$

The U.S. EPA has derived two potency factors for trifluralin, $0.0077\ (\text{mg/kg bw/day})^{-1}$ (U.S. EPA/OPP 1996a) and $0.0058\ (\text{mg/kg bw/day})^{-1}$ (U.S. EPA/OPP 2004a). Both of these potency factors appear to be based on the chronic bioassay in rats (MRID 00044337, summarized in Appendix 1, Table A1-10). As discussed in U.S. EPA/OPP (2003a), the latter and somewhat lower potency factor of $0.0058\ (\text{mg/kg bw/day})^{-1}$ is based on an interspecies scaling factor of 0.75 but is otherwise identical to the earlier and somewhat higher potency factor.

Forest Service risk assessments defer to the U.S. EPA in the derivation of cancer potency factors. In deriving cancer potency factors, the EPA has full access to the studies on which the cancer potency factors are based; furthermore, the derivations of the potency factors undergo extensive EPA review. Consequently, the current risk assessment uses the most recent potency factor of $0.0058\ (\text{mg/kg bw/day})^{-1}$ from U.S. EPA/OPP (2004a).

In Forest Service risk assessments, risk characterization for systemic toxic effects is expressed as a hazard quotient (HQ)—i.e., the ratio of the exposure to the RfD. To

employ the same basic approach for carcinogens, Forest Service risk assessments calculate a dose associated with a 1 in one million (i.e., $1 \div 10^{6} = 10^{-6}$) risk of cancer. The dose associated with a risk of 1 in one million is then used to derive an HQ similar to that used for systemic toxicity. For trifluralin, the dose is calculated as above using the potency factor of 0.0058 $(\text{mg/kg bw/day})^{-1}$ and rounding to two significant digits:

$$d = 10^{-6} \div 0.0058\ (\text{mg/kg bw/day})^{-1} = 0.000172313 \approx 0.0017\ \text{mg/kg bw/day}.$$

It is important to note that the above dose is the lifetime average dose (i.e., the individual is assumed to be exposed to this dose from birth to death). From a practical perspective, daily exposures to any chemical from birth to death are unlikely. As discussed in Section 3.2, the unlikelihood of such an occurrence is clearly the case with trifluralin applied to sunflower seed beds. In the EPA occupational risk assessment (U.S. EPA/OPP 1996a), the daily dose is adjusted by the fraction of the lifespan over which exposures are assumed to occur. This approach is also adopted in the current risk assessment for trifluralin, as discussed further in Section 3.4 (Risk Characterization).

As noted in Section 3.1.10, U.S. EPA/OPP (2003b, p. 25ff) summarizes a number of standard *in vitro* bioassays for mutagenicity indicating that trifluralin is not mutagenic. As discussed in the most recent EPA guidelines for cancer risk assessment (U.S. EPA/RAF 2005), the lack of mutagenic activity suggests that a linear non-threshold model—i.e., the approach used for trifluralin—may not be appropriate and that other less conservative assumptions, such as nonlinear or threshold models could, be considered. As noted specifically in the guidelines:

> *Some modes of action are anticipated to be mutagenic and are assessed with a linear approach. This is the mode of action of radiation and several other agents that are known carcinogens. Other modes of action may be modeled with either linear or nonlinear approaches after a rigorous analysis of available data under the guidance provided in the framework for mode of action analysis.*
>
> U.S. EPA/RAF (2005, p. 1-11)

The U.S. EPA, however, has not conducted an analysis on trifluralin involving the use of either a nonlinear or a threshold model for cancer. Forest Service risk assessments will not adopt a less conservative approach than that used by the U.S. EPA unless there is a compelling basis for doing so. As noted above, Forest Service risk assessments defer to U.S. EPA assessments for carcinogenic effects. In the absence of a *rigorous analysis* by the EPA or some other group of similar standing (e.g., ATSDR or WHO), the potential of a threshold for the carcinogenic effects of trifluralin is not considered quantitatively in the current risk assessment but is discussed further in the risk characterization for the general public (Section 3.4.3).

3.4. RISK CHARACTERIZATION

3.4.1. Overview

In the normal and anticipated use of trifluralin applied by soil incorporation, there is no indication that workers or members of the general public are at risk of exposures leading to systemic toxicity. In the event of an accidental spill, the HQs for members of the general public consuming contaminated fish substantially exceed the level of concern. These HQs, however, probably reflect unrealistic exposure scenarios. In the event of an accidental spill of a large amount of trifluralin into a relatively small pond, it is likely that fish would be killed or at least show signs of poisoning, in which case, it seems unlikely that individuals would consume the fish. The upper bound exposures associated with the consumption of water from a pond following an accidental spill modestly exceed the level of concern (HQ=2); nonetheless, it is not clear that these exposures would result in overt toxic effects.

Based on the potential carcinogenicity of trifluralin, members of subsistence populations consuming fish taken from waters contaminated with trifluralin may be exposed to unacceptable levels of trifluralin—i.e., HQs of up to about 6 at an application rate of 1 lb a.i./acre. If trifluralin is used in areas where the contamination of surface water is likely, refinements to the exposure assessments given in the current risk assessment would be warranted. The refinements could include efforts to better define site-specific concentrations of trifluralin in water and fish as well as efforts to determine the amounts of fish that individuals in the area would consume.

3.4.2. Workers

The risk characterization for workers is summarized in Table 16. This table is based on Worksheets E02 (toxicity) and E05 (carcinogenicity) in the EXCEL workbook that accompanies this risk assessment.

Based on both systemic toxicity and carcinogenicity, there is no indication that workers are at risk during applications of trifluralin. For systemic toxicity, the highest HQ is 0.3, the upper bound HQ for the exposure scenario in which contaminated gloves are worn for 1 hour. For this exposure scenario to reach a level of concern, a worker must wear contaminated gloves for about 3 hours. The only reservation in the interpretation of this exposure scenario concerns the study by Berardinelli et al. (1995) indicating that not all types of gloves may provide adequate protection when handling one emulsifiable concentrate formulation of trifluralin (specified as Treflan-MTF). While Treflan-MTF is not specifically addressed in the current risk assessment, there is a concern that some types of gloves might not offer adequate protection from other emulsifiable concentrate formulations of trifluralin. Specifically, nitrile and butyl gloves did not offer adequate protection to the trifluralin formulation in the study by Berardinelli et al. (1995). While it is beyond the scope of the current risk assessment to offer an opinion on the efficacy of protective equipment, individuals involved in applications of trifluralin should be aware that some types of gloves may not offer adequate protection, and this issue may be important in the selection of gloves used during trifluralin applications.

In terms of general exposures—i.e., non-accidental exposures which may occur during normal applications of trifluralin—the upper bound of HQs for systemic toxicity is 0.03, below the level of concern by a factor of over 30. For carcinogenicity, the HQ is 0.3, below the level of concern by a factor of about 3. As discussed in Section 3.3.5 (Dose-Response Assessment for Carcinogenicity), an HQ of 1 for carcinogenicity would be associated with a risk of 1 in one million. Thus, an HQ of 3 would be associated with a risk of about 3 in ten million. At the maximum likely application rate of 2 lbs a.i./acre, the risk would be about 0.6 in one million.

The only substantial reservation with the risk characterization for workers involved in typical applications of trifluralin involves the exposure assessment. As detailed in Section 3.2.2.1, there are no worker exposure studies involving soil incorporation of trifluralin, and the standard exposure rates used in most Forest Service risk assessments for broadcast applications of pesticides are not applicable to soil incorporation. Consequently, the current risk assessment adopts a worker exposure assessment for trifluralin from the Reregistration Eligibility Decision (RED) for trifluralin (U.S. EPA/OPP 1996a) which is based on data from the Pesticide Handlers Exposure Database (PHED). As summarized in Table 7, the exposure rates used in U.S. EPA/OPP (1996a) are much lower than the exposure rates typically used in Forest Service risk assessments. While it seems reasonable that soil incorporation would involve lower rates of exposure, compared with broadcast applications, the worker exposure rates used in U.S. EPA/OPP (1996a) are remarkably low. Studies that specifically address worker exposure involving soil incorporation of pesticides would reduce uncertainties inherent in the exposure rates used in U.S. EPA/OPP (1996a).

The uncertainty in the worker exposure rates, however, is primarily focused on carcinogenicity. As discussed above, the HQs for systemic toxicity are substantially below the level of concern—i.e., a factor of about 30—but the upper bound HQ for carcinogenicity approaches a level of concern (HQ = 0.3, below the level of concern by a factor of about 3). With respect to carcinogenicity, the EPA exposure assessment (U.S. EPA/OPP 1996a) may be overly conservative when applied to trifluralin. As detailed in U.S. EPA/OPP (1996a, Table 1, p. 28), the EPA assumes that the worker applies trifluralin 5 days/week for 35 years. This is a more or less standard approach in occupational exposure assessments. For the use of trifluralin on sunflower fields, however, it does not seem reasonable to assume that a worker would apply trifluralin throughout the year. It is more likely that a worker would apply trifluralin for a relatively short period of time (perhaps a month) prior to the planting season. Once the planting season is over, no further applications of trifluralin would be made until the following season. Thus, the HQ for cancer, while not above the level of concern, may be overestimated by a factor of about 10 or more [365 days ÷ 30 days ≈ 12.17].

3.4.3. General Public

The risk characterization for members of the general public is summarized in Table 17. This table is based on Worksheets E04 (toxicity) and E05 (carcinogenicity) in the EXCEL workbook that accompanies this risk assessment.

3.4.3.1. Systemic Toxicity

In terms of systemic toxicity associated with non-accidental exposures, the risk characterization for trifluralin is benign. The upper bound HQs range from 0.0000006 (swimming for 1 hour) to 0.04 (the longer-term consumption of contaminated fish by subsistence populations). These upper bound HQs are below the level of concern by factors of about 20 to over one million. While all of the exposure assessments are associated with some level of uncertainty, the very low HQs associated with upper bound and conservative exposure assessments suggest that there is no basis for asserting that systemic toxic effects are likely or even plausible in members of the general public in anticipated exposures to trifluralin.

The HQs for systemic toxicity associated with accidental exposures do, at least numerically, exceed the level of concern (HQ=1). The HQs associated with the consumption of contaminated fish are substantial—i.e., upper bound HQs of 84 for typical adult males and 408 for subsistence populations. As discussed in Section 3.2.3.5.3, however, the accidental spill scenario is highly implausible for trifluralin because, in the event of an accidental spill, most fish would die or at least show obvious signs to toxicity. The probability humans would consume the poisoned such fish is remote. As also discussed in Section 3.2.3.5.3, it seems reasonable to assert that fish would die long before equilibrium between trifluralin in the fish and water would be reached. Consequently, the exposure estimates for exposure to trifluralin from the consumption of fish following an accidental spill probably grossly overestimate exposures.

Accidental exposures from the consumption of contaminated water following an accidental spill lead to much lower HQs—i.e., 0.3 (0.01 to 2). As with the exposure scenario for the consumption of contaminated fish, this is a standard accidental exposure scenario which is included in all Forest Service risk assessments. Although this exposure scenario is obviously and intentionally extreme, the consumption of contaminated water is far more plausible than the consumption of contaminated fish. As discussed in Section 3.3.4 (Dose-Severity Relationships), exposures associated with an HQ of 2 are undesirable; however, it is not clear that these exposures would result in adverse health effects. In addition and as discussed in Section 3.2.3.4.1, the upper bound HQ of 2 is associated with concentrations in water of about 18 mg/L, which is substantially in excess of the water solubility of trifluralin (≈0.3 mg/L). While this risk assessment assumes that the other ingredients in liquid formulations of trifluralin would permit excessive concentrations of trifluralin in water for a least a short period of time, this is a conservative assumption that may overestimate exposures.

3.4.3.2. Carcinogenicity

As summarized in Table 17, carcinogenic risks associated with the exposure scenarios involving the contamination of surface water are below the level of concern for the water consumption (upper bound HQ =0.08), approach but do not exceed the level of concern for the consumption of fish by typical members of the general public (upper bound HQ =0.7), and exceed the level of concern for the consumption of contaminated fish by subsistence populations (upper bound HQ = 6). All of these HQs apply to the unit

application rate of 1 lb a.i./acre and would increase linearly as the application rate increases.

The HQs for subsistence populations consuming contaminated fish—i.e., 0.9 (0.002 to 6)—are obvious concerns. Despite the uncertainties in the exposure assessment, as reflected in the broad range of HQs, the central estimate and upper bound of the HQs should not be viewed as extremely conservative. As discussed in Section 3.2.3.4, the estimated concentrations in surface water are based on a combination of surface water modeling using Gleams-Driver as well as monitoring data. The surface water modeling with Gleams-Driver is reasonably consistent with the PRZM/EXAMS modeling for comparable use scenarios in U.S. EPA/OPP (2009a). Although the detailed monitoring study by Vogel and Linard (2011) suggests that Gleams-Driver may have somewhat over-estimated peak concentrations in streams, it is generally supportive of the estimates of longer-term stream concentrations (Section 3.2.3.4.5.1). Only the longer-term concentrations in surface water are used in the assessment of carcinogenic risk. As discussed in some detail in Section 3.2.3.5, the bioconcentration factor used in the exposure assessment appears to be reasonable. While there are substantial uncertainties in the amount of wild-caught fish that might be consumed by subsistence populations, the consumption values used in the current risk assessment may underestimate exposures in some subsistence populations.

As discussed in Section 3.3.5, the dose-response assessment for carcinogenicity is based on a life-time potency factor, which may be modestly conservative in that the consumption of contaminated fish over a complete lifetime (i.e., birth to death) is not a likely event. Nonetheless, assuming exposures over only half of a lifetime would simply lower the upper bound HQ of 8 to an HQ of 4, based on an application rate of 1 lb a.i./acre. As discussed in Section 2.4, application rates of 2 lbs a.i./acre may be used, which would lead to an HQ of 8 for exposures occurring over half of a lifetime. A more substantial concern with the risk characterization for carcinogenicity involves the linear nonthreshold assumption used in the dose-response assessment (Section 3.3.5). Because trifluralin does not appear to be mutagenic, the linear nonthreshold assumption is questionable, and it is possible that cancer risks could be much lower and possibly nonexistent. Despite this recognition, Forest Service risk assessments defer to the U.S. EPA in the assessment of carcinogenic risks. In the absence of an analysis by U.S. EPA or some organization of comparable standing (e.g., ATSDR or WHO), the current risk assessment accepts the linear nonthreshold assumption.

Qualitatively, the risk characterization for trifluralin indicates that the longer-term use of trifluralin in areas near surface waters that serve as a source of fish for subsistence populations could result in exposure levels of unacceptably high carcinogenic risk. If trifluralin is used in such areas, refinements to the exposure assessment would be warranted. The refinements could include efforts to better define site-specific concentrations of trifluralin in water and fish as well as efforts to determine the amounts of fish consumed by individuals in the area.

As noted in Section 3.2.3.6, the longer-term consumption of contaminated sunflower seeds is not explicitly modeled, because such exposures do not seem likely. As indicated in Table 17, the acute consumption of sunflower seeds leads to an upper bound HQ of 0.00003, which is below the level of concern by a factor of over 30,000. This HQ is associated with an acute dose of about 0.00003 mg/kg bw. Using the cancer potency factor of 0.0058 $(mg/kg\ bw/day)^{-1}$ (Section 3.3.5), the lifetime risk of cancer associated with this acute dose would be about $1.7x10^{-7}$ [0.00003 mg/kg bw x 0.0058 $(mg/kg\ bw/day)^{-1} \approx 1.74 \times 10^{-7}$], which is equivalent to about 1 in six million. In other words, even if an individual were to consume sunflower seeds containing trifluralin at estimated peak concentrations every day over the individual's lifetime, the estimated cancer risk would not exceed a level of concern.

3.4.4. Sensitive Subgroups

With all chemicals, exposure is of particular concern for children, women who are pregnant or may become pregnant, the elderly, or diseased individuals. Although trifluralin may be associated with adverse effects on several organ systems (Section 3.1), the liver seems to be the primary target organ, and liver effects are considered in both the acute and chronic RfDs (Section 3.3). Albeit speculative, individuals with liver diseases might be more sensitive than members of the general population to trifluralin.

Trifluralin can induce methemoglobin formation. Some individuals are born with a form of congenital methemoglobinemia and may be at increased risk of adverse effects to compounds that induce methemoglobinemia. Infants less than 3-months-old have lower levels of methemoglobin (cytochrome b5) reductase and higher levels of methemoglobin, compared with older children or adults (Centa et al. 1985). A similar pattern is seen in many species of mammals (Lo and Agar 1986). Thus, it is possible that infants could be more sensitive than adults to the effects of trifluralin and any other substance that induces methemoglobin formation.

One study suggests that trifluralin may be specifically toxic to heart tissue (Zaidenberg et al. 2007), and one epidemiology study reports a significant increase in the odds ratios for nonfatal myocardial infarctions in female pesticide workers who have applied trifluralin. As discussed in Section 3.1.5, the extensive literature on the subchronic and chronic toxicity of trifluralin does not suggest that cardiotoxicity is a critical effect for trifluralin—i.e., the adverse effect noted at the lowest dose. Consequently, it does not seem reasonable to assert that individuals with heart disease are likely to be particularly sensitive to trifluralin.

Some individuals report a high degree of sensitivity to multiple chemicals, resulting in a broad-spectrum of effects, many of which are similar to allergic reactions. This condition is generally referred to as Multiple Chemical Sensitivity. There is no reported association between trifluralin exposures and adverse effects in individuals who report having Multiple Chemical Sensitivity.

3.4.5. Connected Actions

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

occur in close association with the action of concern; in this case, pesticide use. Actions are considered to be connected if they: (i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously, and (iii) Are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this risk assessment, "connected actions" include actions or the use of other chemicals which are necessary and occur in close association with use of trifluralin.

As discussed in Section 3.1.15.1, trifluralin use results in the formation of numerous metabolites. Nevertheless, there is no specific information on the toxicity of trifluralin metabolites to mammals. This lack of information is a limitation common to many pesticides which are extensively metabolized. To some extent, concern for metabolites is reduced by the fact that trifluralin is metabolized extensively by mammals, and the available mammalian toxicity studies necessarily involve concurrent exposure to trifluralin as well as to its metabolites. There is no information suggesting that unique metabolites, which are highly toxic to mammals, occur in the environment as a result of chemical degradation, microbial degradation, or plant metabolism.

As discussed in Section 3.1.14, the use of trifluralin will also involve the use of various adjuvants and other ingredients (i.e., *inerts*) in trifluralin formulations. While the Forest Service has not indicated that granular formulations of trifluralin will be used, this use cannot be ruled out. Based on the limited available information, one formulation of trifluralin, Treflan 5G, appears to have a greater toxicity than would be expected based on the content of trifluralin in the formulation. If this is the case, the current risk assessment, which is based on a quantitative consideration of trifluralin, may not encompass risks associated with the use of the Treflan 5G formulation.

3.4.6. Cumulative Effects

Similar to the issues involved in assessing the use of adjuvants, it is beyond the scope of the current risk assessment to identify and consider all agents that might interact with, or cause cumulative effects with trifluralin, and to do so quantitatively would require a complete set of risk assessments on each of the other agents to be considered.

Addressing cumulative effects, within the context of the Food Quality Protection Act, requires the assessment of chemicals with a similar mode of action. In the recent human health risk assessment on trifluralin, the U.S. EPA states:

> *The Agency has not yet determined whether the chemical class which includes trifluralin exhibits a common mechanism of toxicity. Therefore, the Agency defers any cumulative risk assessment to a later date. For the purposes of tolerance reassessment of trifluralin, EPA is assuming no common mechanism with other compounds.*
>
> – U.S. EPA/OPP, 2004a, p. 3.

Cumulative effects may also be considered to include the consequences of repeated exposures and repeated exposures are explicitly considered in the current risk assessment on trifluralin both in terms of systemic toxicity and carcinogenicity.

4. Ecological Risk Assessment

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Trifluralin is an effective herbicide, which, when applied at recommended rates, will damage at least some species of terrestrial plants. In general, soil applications of trifluralin appear to be more toxic than foliar applications to plants. Furthermore, trifluralin is more toxic to monocots (e.g., grasses) than to dicots (e.g., broadleaf vegetation). Trifluralin does not appear to pose substantial risks to terrestrial animals. Based on acute toxicity studies, U.S. EPA/OPP (2009a) classifies trifluralin as *practically nontoxic* to mammals, birds, and honeybees. The available literature does not include field studies regarding the effects of trifluralin applications on mammalian wildlife populations; moreover, the only trifluralin toxicity studies conducted on mammalian species are the standard studies in mice, rats, rabbits, and dogs generally required for pesticide registration. Thus, the hazard identification for mammalian wildlife is based on the same data used in the human health risk assessment. The signs of toxicity associated with longer-term exposures to trifluralin are generally nonspecific, consisting of weight loss, decreased food consumption, and changes in organ weights and blood chemistry. In birds, longer-term studies typically report changes in eggshell thickness as the primary sign of toxicity, although decreases in body weight and chick survival were observed at high doses in one reproductive study. Trifluralin has a low degree of toxicity to honeybees, and studies on earthworms and other soil invertebrates suggest that adverse effects in these organisms will occur only at very high concentrations.

The toxicity of trifluralin is well characterized in several species of fish and aquatic invertebrates. Trifluralin is highly toxic to at least some groups of fish, particularly salmonids (e.g., trout) and centrarchids (e.g., bluegills and bass). Several other types of fish, such as cyprinids, appear to be much more tolerant to trifluralin. Studies in two sensitive species of fish (bluegills and trout) indicate that the toxicity of trifluralin increases as water temperature increases. This pattern is common and likely to occur in other groups of fish; however, specific studies demonstrating this effect in fish other than bluegills and trout are not available. Aquatic invertebrates appear to be much less sensitive than fish to trifluralin. Among aquatic invertebrates, small organisms are more sensitive than larger organisms to trifluralin. There is only limited information on the toxicity of trifluralin to other groups of aquatic organisms, including algae, macrophytes, and amphibians. Some algae appear to be as sensitive as the more sensitive species of fish to trifluralin. The available data on macrophytes, limited to species of duckweed (*Lemna*), and the available data on amphibians, limited to a single species of toad, all suggest that these species are as sensitive as fish to trifluralin.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

As discussed in the hazard identification for the human health risk assessment (Section 3.1) and detailed further in Appendix 1, numerous standard toxicity studies were conducted with experimental mammals as part of the registration process for trifluralin.

These studies are directly relevant to the hazard identification for mammalian wildlife species. There are, however, no field studies that assess the impact of trifluralin applications on mammalian wildlife communities. Moreover, the available literature on trifluralin does not include toxicity studies which specifically address effects in mammalian wildlife species.

Available metabolism studies in ruminants include Golab et al. (1969) and Williams and Feil (1971). Trifluralin is extensively and rapidly metabolized in ruminants, as in experimental mammals (Section 3.1.3). In addition, Williams and Feil (1971) report that trifluralin did not cause adverse effects on rumen protozoa and bacteria at concentrations of up to 40 mg a.i./L.

Based on acute LD_{50} studies, the most recent EPA ecological risk assessment on trifluralin (U.S. EPA/OPP 2009a) classifies technical grade trifluralin as *practically nontoxic* to mammals. As summarized in Appendix 1 (Table A1-2), this classification is clearly justified. In addition, there are no systematic differences in the toxicity of trifluralin to mammals, based either on acute toxicity (Section 3.1.4) or chronic toxicity (Section 3.1.5). The most sensitive endpoint for trifluralin (i.e., the effect occurring at the lowest dose) involves changes in liver weight. At higher doses, trifluralin causes changes in red blood cells (methemoglobin formation), decreased body weight, changes in the weights of several other organs, and (at sufficiently high doses) frank signs of toxicity. While trifluralin can have adverse developmental and reproductive effects in mammals, these effects are seen only at maternally toxic doses, and there is no indication that trifluralin causes birth defects.

Data on the toxicity of trifluralin formulations to mammals are limited to acute toxicity studies, and the information from these studies is taken primarily from Material Safety Data Sheets (MSDS). The MSDS give no clear indication that liquid formulations of trifluralin (i.e., the formulations that the Forest Service intends to use) are remarkably more toxic than technical grade trifluralin. The MSDS for one granular formulation of trifluralin, Treflan 5G, reports an oral LD_{50} of 500 mg/kg bw, which is about a factor of 10 below the oral LD_{50} for technical grade trifluralin. While the Forest Service has not indicated that granular formulations are likely to be used in anticipated Forest Service programs, Treflan 5G was used in previous Forest Service programs and related activities (Section 2.2). The reason for the apparently high acute oral toxicity of Treflan 5G is not apparent. Moreover, the atypically low LD_{50} for Treflan 5G is a concern and it is not clear that the current risk assessment encompasses risks associated with applications of Treflan 5G.

4.1.2.2. Birds

Toxicity studies in birds are summarized in Appendix 2. These studies include standard acute gavage administration (Table A2-1), acute dietary studies (Table A2-2), and reproduction studies (Table A-3). With the exception of a brief synopsis of an acute dietary study by the U.S. Fish and Wildlife Service (Hill and Camadese 1986) and an open literature study on toxicity to bird eggs in immersion exposures (Hoffman and Albers 1984), all of the available toxicity studies in birds were submitted to the U.S. EPA/OPP in support of the registration or reregistration of trifluralin.

The available acute oral toxicity study indicate that trifluralin is not hazardous to birds. Based on acute gavage LD_{50} values of >2000 mg/kg bw and acute dietary LC_{50} studies of >5000 ppm (mg trifluralin/kg diet), U.S. EPA/OPP (2009a) classifies trifluralin as *practically nontoxic* to birds. Data on food consumption rates are not reported in the studies summarized in U.S. EPA/OPP (2009a). 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. Based on these estimates, the NOAELs for acute dietary exposures correspond to about 1500 mg/kg bw for quail and about 2000 mg/kg bw for mallards.

In a study by the U.S. Fish and Wildlife Service (Hill and Camadese 1986), the only effect noted in Japanese quail was a transient decrease in food consumption at a dietary concentration of 5000 ppm. In the absence of any signs of toxicity in this study, the decrease in food consumption could reflect nothing more than taste aversion. No decrease in food consumption was noted in this study at a dietary concentration of 2500 ppm (NOAEL ≈750 mg/kg bw).

The reproduction studies in birds are unremarkable (Appendix 2, Table A3). As noted above, the lowest acute dietary NOAEC in birds is 2500 ppm (≈750 mg/kg bw). Longer-term NOAECs for reproductive effects are only modestly lower (i.e., about 500 ppm). As with the acute dietary studies in birds, U.S. EPA/OPP (2009a) does not provide data on food consumption for birds in the dietary reproduction studies. In a previous Forest Service risk assessment for which both body weights and food consumption rates were available for quail and mallards (SERA 2007b), approximate food consumption rates during reproduction studies are about 0.07 kg food/kg bw. Thus, the reproduction NOAELs for birds range from about 32 mg/kg bw (MRID 40334706) to 64 mg/kg bw (MRID 40334704).

Virtually all of the LOAELs for birds are based on egg shell thinning rather than signs of systemic toxicity. The only exception is the LOAEL of 1000 ppm (≈70 mg/kg bw) in mallards which is associated with a decrease in body weight in males as well as a decrease in 14-day survival rates in chicks (MRID 40334704 as summarized in U.S. EPA/OPP 2009a).

The only other information on the potential effects of trifluralin in birds is the egg immersion study by Hoffman and Albers (1984). At a concentration of about 18,000 mg a.i./L, no birth defects were noted in chicks. While the route of exposure is not environmentally relevant and the concentrations used are not environmentally plausible (except in the case of an accidental spill), the study by Hoffman and Albers (1984) is consistent with the reproduction studies in birds indicating that trifluralin is not associated with malformations in offspring.

4.1.2.3. Reptiles and Amphibians (Terrestrial-Phase)

The open literature on trifluralin does not include information on the toxicity of trifluralin to reptiles or terrestrial-phase amphibians; furthermore, information on these groups is not summarized in either the recent EPA ecological risk assessment on trifluralin (U.S. EPA/OPP 2009a) or in the compendium of toxicity data on reptiles and amphibians (Pauli et al. 2000).

The available data on the toxicity of trifluralin to aquatic-phase amphibians are summarized in Section 4.1.3.2.

4.1.2.4. Terrestrial Invertebrates

4.1.2.4.1. Honeybees

The honey bee is the standard test organism used by the U.S. EPA/OPP to assess the potential effects of pesticides on terrestrial invertebrates, and acute contact and oral toxicity studies are typically required by the EPA for pesticide registration. As summarized in U.S. EPA/OPP (1996a, 2009a), trifluralin is classified as *practically nontoxic* to honeybees, based on a contact LC_{50} of >24.17 µg/bee and an oral LC_{50} of >50 µg/bee. In the contact study, the dose of 24.17 µg/bee is associated with a mortality rate of 12.85%; there is no detailed information about the indefinite oral LC_{50} of >50 µg/bee.

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 contact dose of 24.17 µg/bee corresponds to about 210 mg/kg bw [0.02417 mg ÷ 0.000116 kg ≈ 208.36 mg/kg bw] and the oral dose of 50 µg/bee corresponds to about 430 mg/kg bw [0.050 mg ÷ 0.000116 kg ≈ 431.03 mg/kg bw]. The dose of 210 mg/kg bw may be viewed a marginal LOAEL—i.e., a dose associated with about 10% mortality. As summarized in Appendix 1 (Table A1-2), the minimal lethal dose in rats is 1600 mg/kg/bw, and this dose is also associated with 10% mortality (Hollander 1979, MRID 00153164). Based on this admittedly limited comparison, trifluralin appears to be more toxic to honeybees than to mammals.

4.1.2.4.2. Earthworms

Several studies are available on the toxicity of trifluralin to earthworms. Based on a contact toxicity study by Roberts and Dorough (1984), trifluralin is classified as relatively nontoxic to earthworms (*Eisenia foetida*) with an LC_{50} of >1000 µg a.i./cm^2 or about >8.92 lbs a.i./acre. This indefinite contact LC_{50} is about 4 times greater than the maximum anticipated application rate for trifluralin in Forest Service programs (2 lb a.i./acre). Consequently, it does not appear that soil applications of trifluralin are likely to pose an acute hazard to earthworms, based on contact exposures.

Although the U.S. EPA/OPP does not generally require toxicity studies on earthworms, standard acute toxicity studies in earthworms involving soil exposures are required by the European Organization for Economic Co-operation and Development (OECD). These studies involve 14-day exposures of earthworms (*Eisenia fetida*) in artificial soil with observations of both mortality and body weight. Several such studies were submitted to the U.S. EPA/OPP, and cleared reviews of these studies are available. The specific studies involve technical grade trifluralin (Rodgers 1999a) as well as bioassays on two

48% a.i. liquid formulations (Gilham 1999a, Hanisch and Bathelt 1994). The formulation assayed by Hanisch and Bathelt (1994) is identified as Elancolan (which does not appear to be a formulation used in the United States), and the formulation assayed by Gilham (1999a) is identified only as an emulsifiable concentrate.

In all three of the soil bioassays using earthworms, the LC_{50} values are specified as >1000 mg/kg soil (dry weight). For the formulations (48% a.i.), the indefinite LC_{50} corresponds to >480 mg a.i./kg soil. In the study by Rodgers (1999a), technical grade trifluralin was assayed at 95, 171, 309, 556, and 1000 mg a.i./kg soil. Based on sublethal effects (a decrease in body weight), an NOAEC was not identified and the LOAEC was 95 mg a.i./kg soil. The unspecified EC formulation assayed by Gilham (1999a) was somewhat less toxic than technical grade trifluralin with an NOAEC of 82 mg a.i./kg soil. For the Elancolan formulation assayed by Hanisch and Bathelt (1994), only two concentrations were tested (5.90 and 28.98 mg a.i./ kg soil) and no effects were noted at either concentration.

4.1.2.4.3. Other Soil Invertebrates

Staak et al. (1998) examined the toxicity of trifluralin in a species of soil isopod (pill bug), *Porcellio scaber* in a model ecosystem. The concentrations of trifluralin in the model ecosystem soils are specified as ranging from 110 to 320 mg a.i./kg soil (dry weight). Over a 3-week period of exposure, no adverse effects were noted based on mortality, feeding, and body weight.

Park and Lees (2005) conducted bioassays on *Proisotoma minuta*, a Collembolan, in artificial sea salt and report a 7-day LC_{50} of 3.48 mg/L. This study appears to be a methods development effort and involved a number of different herbicides. The rationale for conducting the bioassay on this soil invertebrate in sea salt is that most exposures to this small soil invertebrate will occur through soil pore water. As summarized in Table 10, the K_d values for trifluralin range from about 20 to 150. Thus, it is not likely that the soil concentrations of trifluralin, 0.313 (0.263 to 0.38) mg/kg soil (dry weight) would lead to exposure levels that approach the LC_{50} of 3.48 mg/L for *Proisotoma minuta*.

4.1.2.5. Terrestrial Plants (Macrophytes)

As discussed in 3.1.2 (Mechanism of Action), trifluralin is a mitotic poison in animals as well as protozoa. This mechanism of action also occurs in plants and may be a primary mode of action in the phytotoxicity of trifluralin (Schibler and Huang 1991; Sheval et al. 2008). As would be expected from the high K_{ow} of trifluralin, phytotoxicity from soil exposures decreases as the organic matter in the soil increases (Rahman et al. 1978b). Similar to the available data in mammals (Section 3.1.15.1), the trifluralin metabolites are much less toxic than the parent compound to plants (Vaughn and Koskinen 1987).

The testing requirements for the effects of herbicides on terrestrial plants are relatively rigorous since terrestrial vegetation is the typical target group for herbicides. The testing requirements involve bioassays for seedling germination and emergence (soil exposures) as well as vegetative vigor (foliar exposures) in several species of dicots and monocots. Consistent with these requirements, a complete set of studies on seedling germination,

seedling emergence, and vegetative vigor were submitted to the U.S. EPA/OPP in support of the registration of trifluralin, and these studies are summarized in Appendix 3.

Trifluralin is labeled for the control of both grasses (monocots) and broadleaf weeds (dicots). Nonetheless, trifluralin is generally more toxic to monocots than to dicots and is more toxic in soil exposures than foliar applications. As summarized in Appendix 3, the EC_{25} values range from about 0.8 lb a.i./acre (cucumbers) to 2.6 lb a.i./acre for foliar applications (Table A3-1), 0.33 to 4 lb a.i./acre for seed germination (Table A3-2), and 0.09 lb to 4 lb a.i./acre for seedling emergence (Table A3-3). Because the only uses of trifluralin covered in the current risk assessment involve soil incorporation in sunflower fields, toxicity studies on foliar applications are only marginally relevant to the current risk assessment. Nonetheless, it is worth noting that sunflowers are among the more tolerant species in terms of EC_{25} values for reduced height—i.e., about 2.3 lb a.i./acre.

The plant toxicity study most relevant to the current risk assessment is the Tier II seedling emergence study (MRID 43984401) involving the application of a 43.8% a.i. formulation of trifluralin, comparable to the formulations most likely to be used in Forest Service programs (Table 2). In this assay, sunflowers were the most tolerant species based on both the EC_{25} (4.0 lb a.i./acre) as well as the NOAEC (2.0 lb a.i./acre). While bioassays are available on the toxicity of trifluralin or trifluralin formulations to crabgrass (a monocot and the target species in Forest Service uses of trifluralin), other monocots (i.e., corn, sorghum, onion, and wheat) are more sensitive than sunflowers to trifluralin by factors of about 5 to 44 based on EC_{25} values and factors of 4 to 33 based on NOAELs. This selective toxicity of trifluralin to monocots and tolerance by sunflowers probably accounts for the recommended use of trifluralin to control crabgrass and other monocots in sunflower fields (e.g., Harper 2008).

While considerations of efficacy are not a primary concern in the current risk assessment, it is worth noting that some monocots can develop resistance to trifluralin. This is a common phenomenon with many herbicides as well as other pesticides used on organisms with relatively short lifespans. Mudge et al. (1984) reports trifluralin resistance in goose grass (*Eleusine indica*) in North Carolina. No information on resistance of plants in South Carolina, the state in trifluralin is most likely to be used in Forest Service programs.

Because trifluralin is both highly volatile and highly lipophilic, air levels may result in phototoxic concentrations in plants (Bacci et al. 1990; Cessna et al. 1988; De Schampheleire et al. 2008; Dowdy and McKone 1997). From a practical perspective, the potential risk of substantial volatilization following soil incorporation seems remote. With both low (10 ppm) and higher (10,000 ppm) levels of trifluralin incorporated into soil, Dzaantor and Felsot (1991) noted little indication of volatilization of trifluralin over a 1 year post-treatment period.

4.1.2.6. Terrestrial Microorganisms

Few studies are available regarding the effects of trifluralin on soil microorganisms. Dumontet and Perucci (1992) report a concentration-related decrease in soil respiration in soil samples treated with 0.5 or 5 ppm (mg a.i./kg soil dry weight) analytical grade

trifluralin. At the higher concentration, a substantial but transient decrease (≈25% of control respiration) was noted at week 1 after treatment with recovery to about 60% of control activity from weeks 1 to 5 after treatment (Dumontet and Perucci, 1992, Figure 1, p. 263). At the lower concentration of 0.5 ppm, soil respiration was about 75% of control activity over the 5-week period of observation.

Contrary to the study by Dumontet and Perucci (1992), Hang et al. (2001) report no inhibition of mixed bacteria and *Actinomycetes* species following soil treatments with 5 or 10 mg/kg soil (dry weight). Hang et al. (2001) also note that mixed soil microorganisms were able to use trifluralin as a sole source for both carbon and nitrogen.

The only other study involving direct soil exposures (as opposed to cultures of microorganisms from soil samples) is the algal assay by Cullimore and McCann (1997). In this study, trifluralin concentrations in soil of 1 and 100 ppm (mg a.i./kg soil dry weight) reduced the populations of some sensitive genera of soil algae (i.e., *Chlamydomonas*, *Palmella*, *Stichococcus*, and *Ulothrix*) in soil cores. Other genera of algae, particularly *Chlorella*, appeared relatively tolerant to trifluralin. As discussed further in Section 4.1.3.4.1, aquatic assays also suggest that *Chlorella* may be an algal genus that is tolerant to trifluralin.

In artificial media cultures of *Beauveria bassiana* (a soil fungus), Gardner and Storey (1985) note inhibition of germination and growth at trifluralin concentrations of 60 mg/L and higher. As noted above, these concentrations are much higher than soil concentrations expected to occur from the use of trifluralin in Forest Service programs.

4.1.3. Aquatic Organisms

Like the hazard identification for nontarget terrestrial species, the hazard identification for aquatic organisms is concerned with identifying differences in species sensitivity both within and among the various groups of aquatic organisms, including, fish, amphibians, invertebrates, aquatic macrophytes and algae. In addressing differences among species and groups of organisms, the hazard identification for aquatic organisms uses cumulative frequency distributions of LC_{50} or EC_{50} values.

Figure 6 provides an overview of the cumulative frequency distributions of LC_{50} or EC_{50} values for different groups of aquatic organisms. Details of the data for each of these groups of organisms are discussed in the following subsections. As illustrated in Figure 6, aquatic macrophytes and some algal species appear to be the most sensitive aquatic organisms after exposure to trifluralin, which is to be expected with an effective herbicide. Less expectedly, certain species of fish appear to be as sensitive as aquatic plants to trifluralin. As discussed further in Section 4.1.3.1, the wide variability of sensitivity in fish reflects both apparent differences within various families of fish as well as differences in test conditions, particularly temperature. Very little information is available on the toxicity of trifluralin to amphibians, and the available studies involve only a single species, Fowler's toad. Based on these limited data, Fowler's toad is as sensitive to trifluralin as many species of fish. The reasonably extensive data on several different orders of invertebrates (Section 4.1.3.3) indicate that aquatic invertebrates are markedly less sensitive than fish or amphibians to trifluralin.

In Figure 6, the x-axis is the LC_{50} and EC_{50} values and the y-axis is the cumulative frequency of the LC_{50} values for the different groups of organisms. The individual values for the cumulative frequency are based on the following equation:

Equation 4

$$Freq_i = \frac{1-0.5}{N}$$

where $Freq_i$ is the cumulative frequency for the i^{th} value and N is the number of values in the data set. The x-axis in Figure 6 represents the toxicity values on a logarithmic scale, under the standard assumption that LC_{50} and EC_{50} values for different chemicals or different groups of organisms will be distributed lognormally.

While the dose-response assessment for aquatic species (Section 4.3.3) is focused on NOAECs, the comparisons of toxicity in the hazard identification uses LC_{50} or EC_{50} values, because they estimate population means and are more amenable to comparisons, relative to NOAELs which are simply exposure concentrations used in experiments.

Cumulative distribution plots, like those in Figure 6, are useful for illustrating differences in and among different agents or groups of organisms. The cumulative frequency distributions used in this risk assessment, illustrate the variability in data, including variability in reported toxicity values for the same species.

4.1.3.1. Fish

4.1.3.1.1. Acute Toxicity

A summary of the 96-hour LC_{50} values in fish is given in Table 18 and illustrated in Figure 7. Additional details on these studies are provided in Appendix 4. The studies include several registrant submitted studies summarized in EPA risk assessments (U.S. EPA/OPP 1996a, 2009a) as well as studies published in the open literature.

Table 18 does not include bioassays from Hashimoto and Nishiuchi (1981), although information from this study is summarized in Appendix 4. This study reports only 48-hour LC_{50} values. In addition, the LC_{50} values reported by Hashimoto and Nishiuchi (1981) are atypically high where direct comparisons are available. Furthermore, the EPA rejected this study because of the failure to use control groups (U.S. EPA/OPP 2009a, Appendix H, p. H-26). Hashimoto and Nishiuchi (1981) is published in Japanese, and presumably the EPA translated the study as part of their review and evaluation. In the preparation of the current Forest Service risk assessment, only the original publication, which contains an English abstract, was obtained. Consequently, the current risk assessment defers to the judgment made in U.S. EPA/OPP (2009a), and Hashimoto and Nishiuchi (1981) is not used quantitatively in the current risk assessment.

As illustrated in Figure 7, the 96-hour LC_{50} values in fish are highly variable, ranging from 18.5 to 12,000 µg/L—i.e., the range spans a factor about 650 [12,000 µg/L ÷ 18.5 µg/L ≈ 648.65]. Based on the lowest reported LC_{50} of 18.5 µg/L, U.S. EPA/OPP (2009a, p. 90) classifies trifluralin as *very highly toxic* to fish. While there is substantial scatter in

the distribution of LC_{50} values among the different species, the available data suggest that salmonids (e.g., trout) and centrarchids (e.g., bluegills and bass) are more sensitive than cyprinids (e.g., goldfish and minnows), ictalurids (catfish), and poeciliids (e.g., mosquitofish) to trifluralin.

Temperature is a significant factor in the scatter of species included in Figure 7. As detailed in Appendix 4, Macek et al. (1969) assayed groups of bluegills and trout over temperature ranges of about 10 °C (i.e., 1.6 to 12.7 °C) for trout (a cold water fish) and 12.7 to 23.8 °C for bluegills (a temperate water fish). The results of this study are illustrated in Figure 8. For both species, an increase of about 10 °C in temperature led to a substantial decrease in the LC_{50}, about a factor of 4 for bluegills and a factor of 5 for trout. This increase in toxicity with increasing temperature is a common pattern with many chemicals. Because fish species differ in their sensitivity to temperature, the impact of temperature on toxicity somewhat complicates species sensitivity comparisons. For example, based on the data from Macek et al. (1969), at 12.7 °C, trout are more sensitive than bluegills to trifluralin by a factor of about 4.5 [190 µg/L ÷ 42 µg/L ≈ 4.5238]. This comparison, however, somewhat distorts the sensitivity because 12.7 °C is about the recommended temperature for bioassays in trout but is substantially below the recommended temperature for bioassays in bluegills—e.g., about 20 °C (U.S. EPA/OW 2002). Visually interpolating from Figure 8, the LC_{50} for bluegills would be estimated at about 100 µg/L. Thus, based on recommended assay temperatures for the two species of fish, trout would be more sensitive than bluegills by only a factor of about 2.4 [100 µg/L ÷ 42 µg/L ≈ 2.38].

Factors such as temperature that may impact the results of a bioassay are best determined from studies such as Macek et al. (1969) in which the experiments are conducted using organisms from a single stock or culture using identical experimental methods. Otherwise, differences in the populations tested or populations of animals used may confound comparisons of different studies. For example, Table 18 includes three LC_{50} values in bluegills from studies conducted at about the same temperature: 18.5 µg/L (MRID 40098001 conducted at 23.9 °C), 47 µg/L (Macek et al. 1969 conducted as 23.8°C), and 68 µ/L (Cope 1965 conducted at 24°C). These LC_{50} values vary by a factor of about 4 [68 µ/L ÷ 18.5 µg/L ≈ 3.676], similar to the apparent differences in sensitivity between trout and bluegills discussed above from the study by Macek et al. (1969). The reasons for the differences in the three bluegill LC_{50} values, however, cannot be defined and may be due to simple random variability or differences in the sensitivity of the bluegill populations used in these studies.

Fabacher and Chambers (1974) observed that two populations of mosquitofish varied in their sensitivity to trifluralin by a factor of about 2. This difference, however, is relatively minor. In the absence of repeated studies using the two populations of presumably sensitive and tolerant fish, it is not clear that the two populations of mosquitofish assayed by Fabacher and Chambers (1974) are significantly different in their tolerance to trifluralin.

Relatively little information is available on the sublethal effects of trifluralin following short-term exposures. In 14-day assays in carp, Poleksic and Karan (1999) noted damage to gill, liver, and kidney tissue at concentrations of 10 or 20 µg/L. No histopathological effects, however, were noted at 5 µg/L.

A series of studies suggest that trifluralin causes spinal damage in fish. Following an accidental spill of trifluralin into a stream, Wells and Cowan (1982) observed extensive mortality as well as vertebral dysplasia in brown trout (*Salmo trutta*); however, neither the magnitude of the spill nor the water concentration of trifluralin are reported. In a subsequent experimental exposure, trout were exposed to 500 µg/L trifluralin for 11 hours and then observed for 12 months. Vertebral damage in the fish was evident and developed rapidly after exposure. In a related study, Koyama (1996) assayed several species of marine fish for vertebral deformities following a 96-hour exposure to trifluralin. Because this study used a Japanese formulation of trifluralin as well as marine species native to Japan, the LC_{50} values from this study are not summarized in Table 18. As indicated in Appendix 4 (Table A4-1), however, the definitive 96-hour LC_{50} values ranged from 21 to 110 µg/L, which is comparable to those for salmonids and centrarchids. Vertebral deformities in fish occurred at concentrations ranging from 5 to more than 70 µg/L. As discussed further in Section 4.1.3.1.2, vertebral dysplasia has also been noted in sheepshead minnow (a standard saltwater test species) in chronic exposure studies.

As discussed in Section 3.1.15.1 and summarized in Appendix 4 (Table A4-2), acute toxicity studies in rainbow trout were conducted with two metabolites of trifluralin, TR-6 (MRID 47807001) and TR-15 (Marino et al. 2001a). In both assays, the LC_{50} values for exposure to the metabolites were substantially higher for trout—i.e., 991 µg/L for TR6 and 6040 µg/L for TR-15—than the range of reported LC_{50} values for trifluralin in trout—i.e., 41 to 86 µg/L (Table 18) at about 13 °C.

4.1.3.1.2. Chronic Toxicity

Two types of longer-term toxicity studies are available on trifluralin. The first type of study involves relatively standard full life-cycle studies in fathead minnows (Macek et al. 1976) and sheepshead minnows (Parrish et al. 1978) as well as an early life-stage (egg-to-fry) study in rainbow trout (Adams et al. 1990). The second group of studies focuses on the development of vertebral dysplasia in sheepshead minnows (Couch et al. 1979; Couch 1984).

The life-cycle studies in minnows indicate longer-term NOAECs that are virtually identical: 1.9 µg/L in fathead minnows (Macek et al. 1976) and 1.3 µg/L in sheepshead minnows (Parrish et al. 1978). As discussed in Section 4.1.3.1.1, fathead minnows (Cyprinidae) are among the fish that appear to be more tolerant to trifluralin. Rainbow trout, however, are among the more sensitive species, based on acute toxicity. Nonetheless, the early life-stage study in trout yields a NOEC of 2.18 µg/L (Adams et al. 1990). The study in trout was substantially shorter in duration (48-days) relative to the full life-cycle studies (166 days in sheepshead and 245 day in fathead minnows). Consequently, it is not clear that a full life-cycle study in trout would be comparable to the full life-cycle studies in the minnows. The trout study, however, resulted in the

lowest LOAEC of 4.23 µg/L, based on reduced body weights. At an only modestly higher concentration of 4.8 µg/L, the full life-cycle study in sheepshead minnow did not reduce fecundity, an endpoint which would not be detected in the egg-to-fry study in trout.

The studies in vertebral dysplasia in sheepshead minnows yield a 28-day NOAEC of 2.7 µg/L, with concentration-related effects on bone tissue at 5.5 µg/L and higher (Couch et al. 1979). In the longer-term study by Crouch (1984), the concentration over the 19-month exposure period is characterized only as 1 to 5 µg/L, with this range of concentrations apparently reflecting differences in the exposures to a single group of minnows over the course of the study. This exposure is associated with pathological changes to the pituitary gland as well as skeletal defects. While the standard life-cycle study in sheepshead minnow by Parrish et al. (1978) was conducted over a range of concentrations (1.2 to 34.1 µg/L) that exceeded the concentrations used by Crouch et al. (1979) and Crouch (1984), Parrish et al. (1978) do not note signs of skeletal abnormalities. This failure to note skeletal abnormalities, however, may not be contradictory to the studies by Crouch and coworkers because Parrish et al. (1978) do not appear to have conducted an examination of skeletal tissue.

4.1.3.2. Amphibians (Aquatic- Phase)

Three LC_{50} values are reported for Fowler's Toad (*Bufo fowleri*, which is sometimes designated as *Bufo woodhousei fowleri*). These LC_{50} values are virtually identical—i.e., 100 µg/L from Sanders (1970) to 115.4 and 116.15 µg/L from U.S. EPA/OPP (2009a). In Figure 6, these three LC_{50} values appear as an almost vertical line intersecting the cumulative distribution of LC_{50} values for fish at a frequency of about 0.5. In other words, based on the sparse information that is available, it appears that the sensitivity of Fowler's Toad to trifluralin is about the same as the median sensitivity of fish.

The only other information on amphibians is a reported 48-hour LC_{50} of 14,000 µg/L in *Bufo bufo japonicus* and an unspecified Japanese formulation of trifluralin from the publication by Hashimoto and Nishiuchi (1981). As discussed in Section 4.1.3.1.1, Hashimoto and Nishiuchi (1981) report atypically high toxicity values for fish, and this is clearly the case with amphibians. In addition, the EPA rejects this study (U.S. EPA/OPP 2009a, Appendix H, p. H-26). Accordingly, the rejection of this study by the U.S. EPA, the use of an unspecified Japanese formulation, and the atypically high LC_{50} preclude the use of the Hashimoto and Nishiuchi (1981) study in the hazard identification for amphibians.

The observation of hind limb deformities in free-living amphibians substantially increases concern for the effects of xenobiotics on amphibian populations (e.g., Sparling et al. 2000). No developmental studies in amphibians are available. Quellet et al. (1997) surveyed hindlimb deformities in frogs and toads in agricultural habitats which included exposures to unspecified levels of trifluralin. No significant difference in the incidence of malformations between control and exposed populations were noted. Similarly, Reeder et al. (1998) conducted a population survey of frogs (*Acris crepitans*) in several different sites in Illinois with varying concentrations of different pesticides. No associations were noted for the incidence of intersex gonads with concentrations of

trifluralin. While these types of population studies are not always sensitive, the study by Reeder et al. (1998) was able to identify associations with other herbicides (i.e., atrazine) as well as some halogenated heterocyclic compounds.

4.1.3.3. Aquatic Invertebrates

4.1.3.3.1. Acute Toxicity

The acute LC_{50} and EC_{50} values in freshwater invertebrates are summarized in Table 20 and illustrated in Figure 9. Figure 9 also summarizes the range of reported chronic NOAECs in freshwater invertebrates. These studies are discussed in Section 4.1.3.3.1. Additional details on both the acute and chronic studies are provided in Appendix 5. Toxicity studies on aquatic invertebrates are somewhat more diverse than the standard toxicity studies in fish. For small aquatic invertebrates such as daphnids, test durations of 48 hours are common, and the results of acute toxicity studies are often reported as EC_{50} values for immobilization, primarily because it is difficult to clearly determine that very small aquatic invertebrates are dead. For larger invertebrates like crayfish and scuds, test durations of 96 hours are often used, and the results of the bioassays are typically reported as LC_{50} values. Functionally, there is little practical difference between an EC_{50} and an LC_{50} in terms of the ability of the organism to survive under field conditions.

As illustrated in Figure 9, a relatively clear pattern of toxicity is apparent with small invertebrates being much more sensitive (i.e., having lower LC_{50} or EC_{50} values) than larger invertebrates. While somewhat speculative, it is reasonable to suggest that these differences may simply reflect differences in surface area to body weight. Smaller invertebrates have a much larger ratio of surface area to body weight and are likely to concentrate compounds more quickly than larger invertebrates. Based on the study by Naqvi et al. (1987), the relationship of body size to sensitivity holds within species, with younger (i.e., smaller) crayfish being somewhat more sensitive than adult (i.e., larger) organisms to trifluralin.

Unlike the case with fish, there is no apparent correlation between temperature and toxicity in invertebrate studies, which may be due to the lack of a single study investigating such a relationship. As discussed in Section 4.1.3.1.1, the correlation of temperature with toxicity in fish is well documented by Macek et al. (1969); however, this relationship would not have been apparent in the absence of this study, due to variability in the results of assays conducted by different investigators at different times.

As summarized in Appendix 5 (Table A5-1), several acute toxicity studies are also available on saltwater invertebrates. These studies involve both arthropods and bivalves. Only one definitive LC_{50} value is available in saltwater arthropods (i.e., 638.5 µg/L in grass shrimp), which is well within the range of LC_{50} values for freshwater invertebrates.

The endpoints in the two bioassays on saltwater bivalves are different from the endpoints in the acute toxicity studies in arthropods. The assay on bay mussel embryo/larvae indicates that mortality is comparable to that of small invertebrates (i.e., an LC_{50} of 240 µg/L); however, the EC_{50} for shell deposition is much lower (i.e., an EC_{50} of 96 µg/L from MRID 42449902 summarized in U.S. EPA-OPP 1996a). The lower EC_{50} for shell

deposition is a concern in terms of the normal development of bivalve populations. No data are available on freshwater bivalves, and the low EC_{50} for shell deposition may be regarded as the most sensitive endpoint for aquatic invertebrates. This point discussed further in the dose-response assessment for aquatic invertebrates (Section 4.3.3.3).

The early Japanese study by Hashimoto and Nishiuchi (1981) reports very high 48-hour LC_{50} values ranging from 8000 to 30,000 µg/L for three species of snails. As discussed in Sections 4.1.3.1.1 and 4.1.3.1.2, this study also reports atypically high LC_{50} values for fish and amphibians; moreover, this study was rejected by the EPA (U.S. EPA/OPP 2009a, Appendix H, p. H-26) because the study did not use control groups. Consequently, this study is not used in the hazard identification for aquatic invertebrates.

The limited information available on the toxicity of trifluralin metabolites to aquatic invertebrates is summarized in Appendix 5, Table A5-2. Based on bioassays in *Daphnia magna*, metabolite TR-6 is less toxic than trifluralin by factors of about 5.6-14 (Marino et al. 2001c) and metabolite TR-15 is less toxic than trifluralin by factors of about 14-35 (Marino et al. 2001b). One study is available on the toxicity of metabolite TR-4 in which the NOAEC for immobility in midge larvae is 2.07 mg/L with a LOAEC of about 5.2 mg/L (Henry et al. 2004a). No data are available on the acute toxicity of trifluralin to midge larvae, and comparisons to trifluralin are not possible for the TR-4 metabolite.

4.1.3.3.2. Chronic Toxicity

Information on the chronic toxicity of trifluralin to aquatic invertebrates is summarized in Appendix 5 (Table A5-3). The studies include standard life-cycle reproduction assays in *Daphnia magna* (Macek et al. 1976; Grothe and Mohr 1990), emergence studies in midge larvae (Knoch 1996a), as well as longer-term exposures in saltwater species , including Dungeness crabs (Caldwell et al. 1979), a giant crab (Gardner and Northam 1997), and a mussel, *Mytilus edulis* (Liu and Lee 1975).

The two bioassays in *Daphnia magna* use similar protocols, tested over a similar range of concentrations, and report results in mean measured concentrations. Both studies are classified by U.S. EPA/OPP (2009a) as *Acceptable*. The two studies, however, yielded markedly different results. The earlier study by Macek et al. (1976) reports a NOAEC of 2.5 µg/L, the lowest concentration tested. At higher concentrations, survival was reduced, particularly in the third generation in which no organism survived at concentrations of 25.6 or 52.7 µg/L (Macek et al., 1976, Table 17, p. 34). The later study by Grothe and Mohr (1990), however, reports an NOAEC of 50.7 µg/L, which is about 20 times greater than the NOAEC reported in the assay by Macek et al. (1976). The only difference in the two studies involves the duration of the studies. The study by Macek et al. (1976) involved an exposure period of 64 days encompassing three generations of offspring. The study by Grothe and Mohr (1990) lasted for only 21 days (the standard duration of exposure for a chronic daphnid study) and covered only one generation of offspring. Notwithstanding this difference, the study by Macek et al. (1976) does note a decrease in the number of surviving offspring in first generation by Day 21 with a NOAEC of 2.4 µg/L (i.e., the same NOAEC over the three generations and 64-day period of exposure).

Knoch (1996a) conducted a standard longer-term (28-day) study with midge larvae (benthic organisms), measuring both emergence and development in a water-sediment system. Although this study is not cited in either U.S. EPA/OPP (1996a, the RED) or in the more recent EPA ecological risk assessment, U.S. EPA/OPP (2009a), it is available at the U.S. EPA web site containing cleared reviews (http://www.epa.gov/pesticides/chemical/foia/ cleared-reviews/reviews/036101/036101.htm). While the cleared review (i.e., a Date Evaluation Record prepared by U.S. EPA/OPP) indicates that the study is classified as *Supplemental*, the description of the study in the cleared review is problematic. As indicated in Appendix 5 (Table A5-3), this study used nominal concentrations ranging from 0.25 to 8 mg/L. All but the lowest concentration substantially exceeds the solubility of trifluralin in water. In addition, the study does not provide trifluralin concentrations in sediment and only limited information on trifluralin concentrations in the water column. At nominal concentrations of 1 and 8 mg/L, the reported monitored concentrations of trifluralin in the water column are 0.0497 and 0.0495 mg/L, respectively. The reported nominal concentrations for the NOAELs and LOAELs for both emergence and development cannot be associated clearly with concentrations in the water column. Since the exposure assessment for trifluralin is based on concentrations in the water column (Section 4.2.5), the reported NOAELs and LOAELs are not directly useful in the current risk assessment and are not otherwise considered in this risk assessment.

The longer-term studies in saltwater invertebrates are also summarized in Appendix 5 (Table A5-3). These studies are from the open literature and follow a more diverse set of methods and exposure periods, compared with studies typically conducted to support pesticide registration. Nonetheless, these studies indicate that saltwater invertebrates are not more sensitive than daphnids to trifluralin. The lowest NOAEC is 10 µg/L, within the range of the chronic NOAECs in *Daphnia* (i.e., 2.5-50.7 µg/L), as discussed above. As with the acute toxicity studies in crayfish, the longer-term study by Caldwell et al. (1979) in the Dungeness crab suggests that juvenile crabs are somewhat more sensitive than adult crabs to trifluralin with NOAECs for mortality of 300 µg/L in adult crabs and 47µg/L in juvenile crabs.

Trifluralin has been used as a fungicide in the rearing of both giant crabs (*Pseudocarcinus gigas* in Gardner and Northam 1997) and giant prawn (*Penaeus monodon* in Lio-Po and Sanvictores 1986). In both applications, the longer-term therapeutic concentration of trifluralin is 10 µg/L.

Information on the toxicity of trifluralin to aquatic plants is summarized in Table 24 and illustrated in Figure 10. Additional details of these studies, as well as some other studies that do not provide definite EC_{50} values, are presented in Appendix 6.

4.1.3.4. Aquatic Plants

4.1.3.4.1. Algae

Unlike the case with aquatic invertebrates (Figure 9), the illustration of EC_{50} values for algae in Figure 10 does not lend itself to a simple interpretation, because the experimental details of the studies in algae are highly variable. There is a very broad range in the reported EC_{50} values for algae which spans a factor of about 180 [4346.9 µg a.i./L ÷ 24.3

µg a.i./L ≈ 178.88]. The reasons for this variability are not clear. Based simply on the reported EC_{50} values, *Chlorella* and *Scenedesmus* appear to be very tolerant to trifluralin. All of these studies, however, are based on assays conducted in China with an unspecified emulsifiable concentrate formulation of trifluralin (Ma and Liang 2001; Ma et al. 2002). While the most plausible explanation of the high EC_{50} values is that *Chlorella* and *Scenedesmus* are sensitive genera of algae, all of the other studies on algae were conducted using technical grade trifluralin, and the results of these studies are not directly comparable to the studies on the formulation.

In terms of the most sensitive species, the bioassay of *Scenedesmus vacuolatus* by Schmitt et al. (2000) does seem to clearly suggest that this species is highly sensitive to trifluralin. The assay by Schmitt et al. (2000) involved only a 24-hour period of exposure, and it seems reasonable to assert that longer exposures, comparable to 4- to 7-day exposures in the other algal assays summarized in Table 21 would result in a lower EC_{50} for *Scenedesmus vacuolatus*. The importance of the duration of exposure is suggested in the two bioassays on *Selenastrum capricornutum* (Adams and Cocke 1990; Fairchild et al. 1997). Both of these assays followed similar experimental procedures, and both assays were conducted at 25 °C. The only substantial difference is that the EC_{50} of 673 µg/L from the assay by Fairchild et al. (1997) was conducted over a period of 4 days and the EC_{50} of 88.7 µg/L from the assay by Adams and Cocke (1990) was conducted over a period of 7 days. The difference between the EC_{50} values from these assays is a factor of about 7.4 [673 µg/L ÷ 88.7 µg/L ≈ 7.587]. This apparent substantial impact of duration on toxicity is similar to the apparent impact of duration on the chronic studies in daphnids (Section 4.1.3.3.2). While durations of 4 to 7 days are not typically viewed as *chronic*, these durations are functionally chronic for rapidly dividing species of algae. An issue with the study by Adams and Cocke (1990) involves a very large decrease in the test concentrations over the course of the study (a decrease to <5% of the original concentrations). For this reason, the Cleared Review prepared by U.S. EPA/OPP classifies this study as invalid.

As also summarized in Appendix 6 (Table A6-1), some additional studies in algae are available. The indefinite EC_{50} of >273 µg/L in *Anabaena flos-aquae* (Hughes and Williams 1993a) is consistent with the definite EC_{50} values and suggests that *Anabaena flos-aquae* is relatively tolerant to trifluralin. The very high NOAEC of 10,000 µg/L reported by Kosinski and Merkle (1984) for mixed algal populations is a nominal concentration. This study was conducted in a container lined with plastic. It seems likely that the actual concentrations of trifluralin were much lower than the nominal concentrations; however, the trifluralin in the test water was not measured. Accordingly, this study is not directly useful in the hazard identification.

The EC_{50} of 1000 µg/L for mixed phytoplankton seems plausible, but the duration of exposure is very brief—i.e., 3 hours (Brown and Lean 1995). While this might be a reasonable period of exposure for an accidental spill into a small stream, such very short exposure periods are not specifically considered in the current risk assessment. Nonetheless, relative to the much lower EC_{50} values reported in the more sensitive species of algae, the study by Brown and Lean (1995) is consistent with the above

observations suggesting that duration is an important factor in the toxicity of trifluralin to algae.

Toxicity data in *Selenastrum capricornutum* for some of the metabolites of trifluralin are summarized in Appendix 6, Table A6-2. As with fish and aquatic invertebrates, the metabolites are much less toxic than trifluralin. Based on comparable (i.e., 96-hour) studies in trifluralin, TR-6 is less toxic by a factor of about 8 and TR-15 is less toxic by factors of about 10.

4.1.3.4.2. Aquatic Macrophytes

As summarized in Table 21 and detailed further in Appendix 6 (Table A6-3), two bioassays are available on trifluralin in macrophytes, specifically two species of *Lemna*, a 4-day EC_{50} of 170 µg/L in *Lemna minor* and a 14-day EC_{50} of 43.4 µg/L in *Lemna gibba*. Since the studies are conducted on different species of *Lemna*, the differences between the two bioassays could at least partially reflect species difference. Based on patterns seen in fish, aquatic invertebrates, and algae, however, is seems more likely that the much lower EC_{50} in the 14-day assay with *Lemna gibba* is attributable primarily to the longer period of exposure relative to the 4-day assay in *Lemna minor*.

4.1.3.5. Aquatic Microorganisms

The only information on the toxicity of trifluralin to aquatic microorganisms is the study by Aslim and Ozturk (2009) on several species of cyanobacteria. The 9-day EC_{50} values for growth and survival range from 1360 µg/L (*Chroococcus* sp) to 882,000 µg/L (*Synechocystis* sp). The lower bound EC_{50} value is comparable to the LC_{50} and EC_{50} values in tolerant or apparently tolerant species of fish, aquatic invertebrates, and algae. The upper bound concentration in tolerant cyanobacteria clearly suggests that tolerant cyanobacteria are much less sensitive than are other groups of aquatic organisms to trifluralin.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

An overview of the exposure assessments for mammals and birds is given in Worksheet G01 of the EXCEL workbook that accompanies this risk assessment. All exposure scenarios in the EXCEL workbook are based on a unit application rate of 1 lb a.i./acre, and the consequences of using different application rates are discussed in the risk characterization (Section 4.4). Forest Service risk assessments typically derive exposure assessments for direct spray, the ingestion of contaminated vegetation or prey following direct spray, as well as the ingestion of contaminated water. All of these exposure scenarios are relevant to and can be developed for pesticides applied by broadcast application methods. The current risk assessment, however, considers only the soil incorporation of trifluralin. Thus, as in the human health risk assessment, many of the standard exposure scenarios typically used for mammals and birds cannot be developed for or do not apply to soil incorporation applications of trifluralin. Also as in the exposure assessment for the human health risk assessment, section designations for the excluded scenarios are given below as a matter of convenience for individuals who regularly use many different Forest Service risk assessments—i.e., the section designations in all Forest Service risk assessments are consistent. An overview of the mammalian and avian receptors considered in the current risk assessment is given in Table 22 and these data are discussed in the following sections.

As with terrestrial animals, the exposure assessments for terrestrial plants include only a subset of the exposure scenarios for broadcast applications. Specifically, exposure scenarios associated with direct spray and spray drift are excluded for soil incorporation, and the remaining scenarios include runoff, wind erosion, and the use of contaminated irrigation water. Exposures of aquatic plants and animals to trifluralin are based on the same information used to assess the exposure to terrestrial species from contaminated water.

4.2.2. Mammals and Birds

4.2.2.1. Direct Spray

For soil incorporation applications, the direct spray of a mammal or bird is not a reasonable exposure scenario.

4.2.2.2. Dermal Contact with Contaminated Vegetation

Mammals or birds may come into contact with surfaces of treated trees; however there are no methods for estimating the magnitude of such exposures. For soil incorporation, risks associated with contacting treated vegetation are not likely to be substantial, relative to other exposure scenarios considered in the following subsections.

4.2.2.3. Ingestion of Contaminated Vegetation

For broadcast applications, standard exposure scenarios are developed for the consumption of treated vegetation, specifically the consumption of fruits (which typically have the lowest residue rates) or grasses (which typically have the highest residue rates) by several groups of mammals and birds. As discussed in Section 2.2, the anticipated use

of trifluralin in Forest Service programs involves applications to fields used to grow sunflowers as wildlife feed. As summarized in Table 13 and discussed in Section 3.2.3.6, studies are available that permit at least crude estimates of trifluralin concentrations which might occur in broadleaf vegetation and seeds.

The consumption of contaminated seeds is an obvious concern in the ecological risk assessment because trifluralin will be applied to fields used to grow sunflowers as wildlife feed. The concentration of trifluralin in seeds is calculated based on the residue rates from Table 13 in the same manner as that used in the human health risk assessment for both acute and longer-term scenarios. Details of the exposure scenarios for the consumption of seeds are given in Worksheets F04a to F04e (acute exposures) and Worksheets F10a to F10e (chronic exposures) in the EXCEL workbook that accompanies this risk assessment. Although it may be unlikely that wildlife would consume the leaves of sunflowers, this exposure scenario is also considered. Details of the exposure scenarios for the consumption of sunflower leaves are given in Worksheets F05a to F05e (acute exposures) and Worksheets F11a to F11e (chronic exposures) in the EXCEL workbook that accompanies this risk assessment.

Most Forest Service risk assessments consider the consumption of fruit rather than seeds. As noted above, however, seeds are considered as food items because this is the most likely material to be consumed by wildlife feeding on sunflowers. Thus, in the EXCEL workbook that accompanies this risk assessment, all worksheets involving the consumption of seeds (i.e., Worksheets F04a to F04e and F10a to F10e) use estimates of the caloric value for seeds as summarized in Table 23.

For both the acute and chronic exposure scenarios, the assumption is made that 100% of the diet is contaminated. This may not be a realistic assumption for some acute exposures and will probably be a rare event in chronic exposures—i.e., animals may move in and out of the treated areas. While estimates of the proportion of the diet that is contaminated could be incorporated into the exposure assessment, the estimates would be an essentially arbitrary set of adjustments.

The estimated food consumption rates by various species of mammals and birds are based on field metabolic rates (kcal/day), which, in turn, are based on the adaptation of estimates from Nagy (1987) by the U.S. EPA/OPP (1993). These allometric relationships account for much of the variability in food consumption among mammals and birds. There is, however, residual variability, which is remarkably constant among different groups of organisms (Nagy 1987, Table 3). As discussed further 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 23. Most of the specific values in Table 23 are taken from Nagy (1988) and U.S. EPA/ORD (1993).

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating trifluralin concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4). The only major differences in the estimates of exposure among the various groups of organisms considered involve the weight of the animal and the amount of water consumed. As with the estimates of food consumption, water consumption rates are well characterized in terrestrial vertebrates. The water consumption rates are based on allometric relationships in mammals and birds, as summarized in Table 22. Based on these estimates, exposure scenarios involving the consumption of contaminated water are developed for mammals and birds for accidental spills (Worksheets F02a-e), expected peak concentrations (Worksheets F06a-e), and expected longer-term concentrations (Worksheets F12a-e).

As with food consumption, water consumption in birds and mammals will vary substantially with diet, season, and many other factors; however, there are no well-documented quantitative estimates regarding the variability of water consumption by birds and mammals in the available literature. Consequently, the variability in water consumption rates of birds and mammals is not considered in the exposure assessments. As summarized in Table 12, however, the upper and lower bounds of the estimated concentrations of trifluralin in surface water vary by several orders of magnitude. Given this variability in the concentrations of trifluralin in surface water, it seems likely that a quantitative consideration of the variability in water consumption rates of birds and mammals would have a no substantial impact on the risk characterization.

4.2.2.5. Ingestion of Contaminated Fish

In addition to the consumption of contaminated vegetation, the consumption of contaminated fish is a relevant and plausible exposure pathway for trifluralin. Thus, sets of exposure scenarios are developed for an accidental spill (Worksheets F03a-b), expected peak exposures (Worksheets F09a-c), and estimated longer-term concentrations (Worksheets F13a-c). These exposure pathways are applied to 5 and 70 kg carnivores as well as a piscivorous bird.

In the ecological risk assessment, the assumption is made that fish-eating mammals or birds will consume the entire fish, and, for these exposure assessments, the whole body BCF is used. In the bluegill study used by U.S. EPA/OPP (1996a, 2009a), the whole-body BCF for trifluralin is 5674 L/kg. This bioconcentration factor is reasonably consistent with whole-body BCFs of 2090-6520 reported by Schultz and Hayton (1994). In a somewhat later study, however, Schultz and Hayton (1999) report whole-body bioconcentration factors of up to 13,000 in trout and 15,506 in bluegills. Consequently, for the ecological risk assessment, the whole-body BCF for trifluralin in fish is taken as 15,000.

As discussed in Section 3.2.3.5.3 (accidental exposure scenarios for the consumption of contaminated fish by humans), accidental spills of relatively large amounts of trifluralin could lead to concentrations in water that would cause obvious signs of toxicity in fish

and even substantial fish mortality. While mortality or gross signs of toxicity in fish reduces the likelihood of fish consumption by humans, this is not the case for wildlife. Substantial mortality in fish could lead to abnormally high rates of fish consumption by some species of mammalian wildlife.

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

As with direct spray scenarios mammals and birds (Section 4.2.2.1), the direct spray of an insect is not a likely exposure scenario for soil incorporation. While such incidental exposures might occur, this scenario is not explicitly considered in the current risk assessment on trifluralin.

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

As with terrestrial mammals and birds, terrestrial invertebrates may be exposed to trifluralin through the consumption of contaminated vegetation, specifically the leaves of treated sunflowers. Incidental exposure to other types of vegetation on treated plots cannot be ruled out. Consequently, exposure assessments are made for all four of the food items listed in Table 13, including short grass, long grass, broadleaf vegetation, and seeds. Details concerning estimated exposure levels for the consumption of contaminated vegetation by herbivorous insects are provided in Worksheets G07a, G07b, G07c, and G07d.

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).

4.2.4. Terrestrial Plants

4.2.4.1. Direct Spray

For applications involving soil incorporation, the direct spray of nontarget vegetation is not relevant and is not explicitly considered.

4.2.4.2. Off-Site Drift

For applications involving soil incorporation, limited off-site drift might occur; however, the extent of drift would be much less than that associated with foliar applications. In addition and as discussed in Section 4.1.2.5, trifluralin is less effective in foliar application than in soil applications, a factor that would reduce the impact of incidental off-site drift. Consequently, off-site drift is not explicitly considered in this risk assessment. The consequences of incidental off-site drift would probably be encompassed by considerations of runoff discussed in the following subsection.

4.2.4.3. Runoff and Sediment Loss

Exposures to terrestrial plants associated with runoff and sediment loses from the treated site to an adjacent untreated site are summarized in Worksheet G04 of the EXCEL workbook that accompanies this risk assessment.

Any pesticide can be transported from the soil at the application site by runoff, sediment loss, or percolation. Runoff, sediment loss, and percolation are considered in estimating contamination of ambient water. Only runoff and sediment loss are considered in assessing off-site soil contamination. This approach is reasonable because off-site runoff and sediment transport will contaminate the off-site soil surface and could impact non-target plants. Percolation, on the other hand, represents the amount of the herbicide that is transported below the root zone and thus may affect water quality but should not affect off-site vegetation. The GLEAMS modeling used to estimate concentrations in water provides data on loss by runoff. As with the estimates of trifluralin in surface water, runoff estimates are modeled for clay, loam, and sand at nine sites, which are representative of different temperatures and rainfall patterns (Table 9).

For trifluralin, the results of the standard GLEAMS modeling of runoff and sediment losses are summarized in Appendix 7, Table A7-1, as an effective off-site application. Note that the proportion of runoff as a fraction of the application rate will vary substantially with different types of soils as well as climates—i.e., temperature and rainfall. For the current risk assessment, the effective off-site loss as a fraction of the application rate is taken as 0.015 (0.00007 to 0.11). The central estimate is based on the average value from all 27 Gleams-Driver simulations—i.e., nine locations and three soil types per location. Similarly, the upper bound is taken as the empirical upper 95% bound from the Gleams-Driver simulations. The lower bound of 0.00007 is taken as the empirical lower 5% bound.

The amount of pesticide not washed off in runoff or sediment will penetrate into the soil column, and the depth of penetration will depend on the properties of the chemical, the properties of the soil, and the amount of rainfall. The GLEAMS model provides estimates of pesticide concentrations in soil layers of varying depths. These concentrations are output by GLEAMS in mg pesticide/kg soil (ppm). The minimum non-zero value that GLEAMS will output is 0.000001 mg/kg, equivalent to 1 nanogram/kg soil or 1 part per trillion (ppt).

The deepest penetration of trifluralin is 12 inches in clay soils, 18 inches in loam, and 24 inches in sand. As would be expected, lower penetration will occur in arid areas, relative

to soil penetration in areas with moderate to heavy rainfall. These estimates of soil penetration are reasonably consistent with field studies, with the deepest reported penetration of trifluralin into soil being about 16 inches (Yen et al. 2008).

4.2.4.4. Contaminated Irrigation Water

Unintentional direct exposure of nontarget plants is possible from the use of contaminated ambient water for irrigation, as observed by Bhandary et al. (1991) for certain herbicides. The levels of exposure associated with this scenario will depend on the pesticide concentration in the ambient water used for irrigation and the amount of irrigation water used. Concentrations in ambient water are based on the peak concentrations modeled in the human health risk assessment (Section 3.2.3.4). The amount of irrigation water used will depend on the climate, soil type, topography, and plant species under cultivation. Thus, the selection of an irrigation rate is somewhat arbitrary.

In the absence of any general approach for determining and expressing the variability of irrigation rates, the application of 1 inch of irrigation water is used in this risk assessment. Details of the calculations used to estimate the functional application rates based on irrigation using contaminated surface water are provided in Worksheet G06a of the EXCEL workbook that accompanies this risk assessment. At a unit application rate of 1 lb a.i./acre, the functional application rate associated with the use of contaminated surface water for irrigation after applications of trifluralin is about 0.00045 ($5.1x10^{-6}$ to 0.0018) lb a.i./acre.

4.2.4.5. Wind Erosion

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

For this risk assessment, the potential effects of wind erosion are estimated in Worksheet G06b. In this worksheet, it is assumed that trifluralin is incorporated into the top 5 cm of soil, which is identical to the depth of incorporation used in GLEAMS modeling (Table 10). In most Forest Service risk assessments, average soil losses are estimated to range from 1 to 10 tons/ha/year with a typical value of 5 tons/ha/year. These estimates are based on the study by Allen and Fryrear (1977) in which wind erosion is estimated to account for annual soil losses ranging from 2 to 6.5 metric tons/ha. Larney et al. (1999), however, estimates that up to 56.6 metric tons/ha may be lost from a fallow field. Since trifluralin will be applied by soil incorporation to an essentially fallow field, the higher estimate from Larney et al. (1999) is used in the current risk assessment on trifluralin. From a practical perspective, wind erosion and offsite drift of soil are likely to vary dramatically according to site conditions and weather conditions.

4.2.5. Aquatic Organisms

The plausibility of effects on aquatic species is assessed based on estimated concentrations of trifluralin in water which are identical to those used in the human health risk assessment. These values are summarized in Table 12 and discussed in Section 3.2.3.4.6.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

An overview of the specific toxicity values used in this risk assessment is given in Table 24, and the derivation of each of these values is discussed in the various subsections of this dose-response assessment. The available toxicity data support separate dose-response assessments in eight classes of organisms: terrestrial mammals, birds, terrestrial invertebrates, terrestrial plants, fish, aquatic invertebrates, aquatic algae, and aquatic macrophytes. The data on aquatic-phase amphibians is limited but a surrogate acute NOAEC can be defined for presumably tolerant species of aquatic-phase amphibians. Different units of exposure are used for different groups of organisms, depending on how exposures are likely to occur and how the available toxicity data are expressed. When possible, a range of toxicity values based on the most sensitive and most tolerant species within a given group of organisms is provided. To maintain consistency with the exposure assessment, which is necessary for the development of hazard quotients in the risk characterization, all toxicity values given in Table 23 are expressed as active ingredient.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals

As with most Forest Service risk assessments, the dose-response assessment for mammalian wildlife is based on the same studies used in the dose-response assessment for human health effects. As discussed in Section 3.3 and summarized in Table 15, the EPA bases the acute RfD on a developmental study in rats yielding an NOAEL of 100 mg/kg bw with a corresponding LOAEL 500 mg/kg bw. The chronic RfD is based on a 1-year study involving capsule administrations in dogs with a NOAEL of 2.4 mg/kg bw/day and a corresponding LOAEL of 40 mg/kg bw/day. As discussed in Section 4.1.2.1, there are no systematic differences in the toxicity of trifluralin to various groups of mammals. Consequently, the acute NOAEL of 100 mg/kg bw and the chronic NOAEL of 2.4 mg/kg bw/day are used to characterize risks associated with acute and chronic exposures, respectively, for all groups of mammals.

4.3.2.2. Birds

As discussed in Section 4.1.2.2, trifluralin is classified by the U.S. EPA as *practically nontoxic* to birds in terms of acute exposures. In acute gavage bioassays, doses of up to 2000 mg/kg bw induced signs of gross toxicity or mortality (Appendix 2, Table A1-1). Similar results were seen in acute (5-day) dietary studies at doses equivalent to about 1500-2000 mg/kg bw/day. Given this low order of toxicity, differences in the toxicity of trifluralin to different species of birds cannot be identified. As a conservative approach to the acute dose-response assessment for birds, the 5000 ppm dietary exposure from the study by Hill and Camadese (1986) may be viewed as a marginal LOAEL based on decreased food consumption in Japanese quail. A dietary exposure of 5000 ppm may also be viewed as a LOAEL in a mallard study, based on diarrhea observed in some birds (MRID 00138857 as summarized in U.S. EPA/OPP 2009). In the study by Hill and Camadese (1986), no effects were observed at a dietary exposure of 2500 ppm. As discussed in Section 4.1.2.2, this dietary exposure is estimated to correspond to a daily

dose of 750 mg/kg bw. This NOAEL is used in the current risk assessment to characterize risks to birds associated with acute exposures.

As also discussed in Section 4.1.2.2, the longer-term dietary reproduction studies in birds consistently indicate dietary NOAECs at or above about 500 ppm. While no clear differences in sensitivity are apparent between mallards and quail (the only species on which longer-term studies are available), the lowest NOAEC in any study is 452.3 ppm (MRID 40334706 as summarized in U.S. EPA-OPP 1996a), and the estimated dose associated with this dietary concentration is about 32 mg/kg bw/day. This NOAEL is used to assess risks associated with longer-term exposures in birds.

4.3.2.3. Reptiles and Amphibians (Terrestrial-Phase)

In the absence of information on the toxicity of trifluralin to reptiles and terrestrial phase-amphibians (Section 4.1.2.3), no dose-response assessment for this group of organisms can be developed.

4.3.2.4. Terrestrial Invertebrates

4.3.2.4.1. Oral Toxicity Value

As discussed in Section 4.1.2.4.1, toxicity data on honeybees are typically used in ecological risk assessments as surrogates for terrestrial insects. The direct spray of honeybees and other terrestrial insects is not explicitly considered in this risk assessment for trifluralin because the only application method under consideration involves soil incorporation (Section 4.2.3). Nonetheless, it is plausible that some herbivorous insects could consume the leaves of sunflowers on treated fields. The only oral toxicity value for any terrestrial insect is the indefinite LD_{50} of >50 µg/bee. As discussed in Section 4.1.2.4.1, a dose of 50 µg/bee corresponds to about 430 mg/kg bw. Forest Service risk assessments aim to avoid the use of LD_{50} values, definitive or indefinite. Nonetheless, for trifluralin, the dose of 430 mg/kg bw is the only available oral toxicity value for terrestrial invertebrates. Consequently, this dose is used for the risk characterization of herbivorous insects; however, this less than desirable approach has little impact on the risk assessment for trifluralin. As discussed further in Section 4.4.2.4, the dose of 430 mg/kg bw is orders of magnitude below estimated levels of exposure for herbivorous insects.

4.3.2.4.2. Soil Toxicity Values

Dose-response assessments for soil invertebrates based on concentrations of pesticides in soil are not formally developed in Forest Service risk assessments, because toxicity studies based on soil concentrations are not usually available. As noted in Sections 4.1.2.4.2 and 4.1.2.4.4, however, toxicity studies based on concentrations in soil are available for both earthworms and some soil arthropods. While these studies are not used to develop HQs, they are discussed semi-quantitatively in the risk characterization for terrestrial invertebrates (Section 4.4.2.4).

4.3.2.5. Terrestrial Plants (Macrophytes)

Although the scenarios associated with direct spray and spray drift to plants are not quantitatively considered for soil incorporation, studies on vegetative vigor are used in the exposure scenarios associated with the use of contaminated irrigation water

(Worksheet G06a) and wind erosion of contaminated soil (Worksheet G06b). As discussed in Section 4.1.2.5 and summarized in Appendix 3 (Table A3-1), the lowest NOAEL for terrestrial plants is 0.125 lb a.i./acre, which is the NOAEL for corn based on reduced plant height. This NOAEL is used in the current risk assessment for sensitive species of plants. Several tolerant species of plants, both monocots and dicots, have NOAELs of 2 lb a.i./acre based on changes in plant weight. For the dose-response assessment, however, the most sensitive endpoint is used. In the vegetative vigor assays, the most sensitive endpoint is a reduction in plant height. Based on this endpoint, both cucumber (a dicot) and wheat (a monocot) are tolerant species with a NOAEL of 0.5 lb a.i./acre.

As also discussed in Section 4.1.2.5, a Tier II seedling emergence study (MRID 43984401) is available involving the application of a 43.8% a.i. formulation of trifluralin. As detailed in Appendix 3 (Table A3-3), monocots are generally more sensitive than dicots to trifluralin, based on both EC_{25} values and NOAECs. For the dose-response assessment, only NOAECs are considered. The lowest NOAEC of 0.06 lb a.i./acre is for sorghum, which is used to assess the potential risks to sensitive species of nontarget plants. Sunflowers are the most tolerant species with an NOAEC of 2 lb a.i./acre. Since trifluralin will be applied to fields used to grow sunflowers as wildlife feed, sunflowers are a particularly relevant nontarget species, and the NOAEC of 2 lb a.i./acre is used to assess the potential impact of trifluralin applications to nontarget terrestrial plants.

4.3.2.6. Terrestrial Microorganisms

As with soil invertebrates, no formal dose-response assessment is developed for terrestrial microorganisms. As discussed further in Section 4.4.2.6, the available data on the toxicity of trifluralin to soil microorganisms is used semi-quantitatively to characterize risks to this group of organisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish

4.3.3.1.1. Acute Toxicity Values

Acute LC_{50} values for trifluralin range from 18.5 µg a.i./L to 12,000 g a.i./L (Table 18 and Appendix 4, Table A4-1). Relatively little information, however, is available on sublethal NOAECs for trifluralin. The study by Koyama (1996) provides both LC_{50} values and NOAECs in several species of saltwater fish, and the ratios of the LC_{50} values to the NOAECs range from about 2.5 to 11. These NOAECs, however, apply only to vertebral deformities and do not clearly encompass other sublethal effects. Some acute bioassays in fish report both LC_{50} values and slopes of the dose-response curve (e.g., MRID 40098001). While the slopes of the dose-response curves could be used to estimate low response rates, such estimates could be used as functional NOAECs for mortality. NOAECs for mortality, however, would not necessarily encompass other sublethal effects which might affect survival.

In the absence of useful and sensitive experimental NOAELs for sublethal toxicity, functional NOAECs can be estimated by dividing LC_{50} values by a factor of 20. This

approach reflects the U.S. EPA/OPP approach of basing risk characterizations for acute effects in aquatic organisms on LC_{50} or EC_{50} values using a level-of-concern (LOC) of 20. This approach is equivalent to dividing the LC_{50} or EC_{50} values by 20 and using a LOC of 1, the LOC that is used in all Forest Service risk assessments. Dividing the range of acute LC_{50} values by a factor of 20 leads to estimated NOAECs ranging from 0.925 to 600 µg a.i./L [18.5 µg a.i./L to 12,000 g a.i./L ÷ 20].

For the upper bound estimate of the NOAEC, the current risk assessment takes a somewhat more conservative approach. The highest LC_{50} of 12,000 µg a.i./L is from the study by Naqvi and Leung (1983) in mosquito fish, which, as illustrated in Figure 7, appears to be somewhat of an outlier—i.e., it is somewhat skewed to the right in terms of the expected sigmoidal curve. Alternatively, the LC_{50} of 2200 µg a.i./L in catfish from Johnson and Finley (1980) is used. This LC_{50} is from the U.S. Fish and Wildlife Service. As indicated in Table 18, LC_{50} values for other species from this publication are consistent with LC_{50} values reported elsewhere in the literature. Dividing this LC_{50} by 20 yields an estimated NOAEC of 110 µg/L or 0.11 mg/L [2200 µg a.i./L ÷ 20].

The lower bound estimate of the NOAEC, 0.925 µg a.i./L, is also not used directly. As discussed in the following subsection, the lower bound of the chronic NOAEC is 1.3 µg a.i./L, based on an experimental chronic NOAEC in Sheepshead minnow and supported by a NOAEC of 2.18 µg a.i./L in an egg-to-fry study in trout, a sensitive species. It is not sensible to use an estimated acute NOAEC that is below an experimental chronic NOAEC. Thus, for sensitive species of fish, the acute NOAEC is set to 1.3 µg a.i./L or 0.0013 mg a.i./L, identical to the chronic NOAEC.

4.3.3.1.2. Chronic Toxicity Values

As discussed in Section 4.1.3.1.2, two types of chronic studies are available in fish, standard development/reproduction studies (Adams et al. 1990; Macek et al. 1976; Parrish et al. 1978) and 28-day to 19-month studies on the development of vertebral dysplasia in sheepshead minnows (Couch 1984; Couch et al. 1979). The standard life-cycle reproduction studies and developmental egg-to-fry studies yield a relatively narrow range of NOAECS—i.e., from 1.3 µg/L in the life-cycle study in sheepshead minnows (Parrish et al. 1978) to 2.18 µg/L in the egg-to-fry study in rainbow trout (Adams et al. 1990). The only clear NOAEC in the study on vertebral dysplasia in sheepshead minnows is 2.7 µg/Lfrom the relatively short-term study by Couch et al. (1979). The 19-month study by Couch (1984) appears to have involved exposures that ranged from 1 to 5 µg/L over the duration of the study. This variable exposure caused adverse effects including pituitary gland pathology and abnormal bone development. Numerically, this experiment is consistent with the LOAEL of 4.8 µg/L from the standard life-cycle study in sheepshead minnows which was associated with reduced fecundity. Thus, the development/reproduction studies appear to be the most appropriate data set on which to base the longer-term dose-response assessment for fish.

The very narrow range of NOAECs in the standard longer-term studies—i.e., from 1.3 to 2.18 µg/L—is not concordant with the very wide range of acute LC_{50} values—i.e., from 18.5 µg a.i./L to 12,000 g a.i./L. Nonetheless, the chronic NOAECs do encompass both

trout and fatheads. Based on the acute LC_{50} values and as illustrated in Table 7, trout would be classified as a highly sensitive species and fatheads would be classified as a relatively tolerant species. Given that both trout and fatheads evidenced similar NOAECs in the chronic studies, there does not appear to be a compelling basis for proposing any upward adjustment to the chronic NOAECs to account for a lesser chronic toxicity in potentially tolerant species of fish. Consequently, the range of experimental chronic NOAECs is used directly to characterize risks associated with longer-term exposures to trifluralin. For fish that are sensitive to the chronic effects of trifluralin, the NOAEC of 1.3 µg/L (0.0013 mg/L) is used. For fish that are tolerant to the chronic effects of trifluralin, the NOAEC of 2.18 µg/L is rounded to 2.2 µg/L (0.0022 mg/L), and this concentration is used to assess risks in potentially tolerant species.

This dose-response assessment for chronic toxicity does not reflect acute data on groups of fish that appear to be extremely tolerant to trifluralin—i.e., cyprinids, ictalurids, and poeciliids, as illustrated in Figure 7. For these groups of fish that are extremely tolerant to trifluralin in acute exposures, an argument could be made for using ratios of acute LC_{50} values to develop a higher NOAEC for these fish. As noted above, however, there is no remarkable difference in the longer-term NOAECs for trout and fatheads. Based on acute LC_{50} values, however, trout are generally more sensitive than fatheads. Thus, it is not clear that differences in the sensitivity of fish based on acute toxicity to trifluralin would be reflected in estimates of chronic toxicity.

4.3.3.2. Amphibians (Aquatic-Phase)

As summarized in Section 4.1.3.2, very little information is available on the toxicity of trifluralin to aquatic-phase amphibians. Consequently, the dose-response assessment for this group is extremely simple. The three available LC_{50} values in the Fowler's Toad are virtually identical, about 100 µg a.i./L. No information is available on acute NOAECs and no chronic data are available.

The acute LC_{50} of 100 µg a.i./L is divided by 20 to approximate an acute NOAEC of 5 µg/L (0.005 mg/L). The rationale for this approach is identical to that discussed in Section 4.3.3.1.1 and reflects the general approach used by U.S. EPA/OPP. In the absence of information on more than one species, this estimated NOAEC is applied to tolerant species.

No chronic dose-response assessment for aquatic-phase amphibians is proposed, and potential chronic risks to this group are addressed qualitatively in the risk characterization (Section 4.4.3.2).

4.3.3.3. Aquatic Invertebrates

4.3.3.3.1. Acute Toxicity Values

As illustrated in Figure 6, aquatic arthropods appear to be less sensitive than fish or aquatic-phase amphibians to trifluralin. As illustrated in Figure 9 and summarized in Table 20, the acute LC_{50} values for aquatic arthropods range from about 250 to 26,000 µg a.i./L, spanning a factor of over 100. Based on the pattern of species sensitivity (Figure

9), small arthropods (e.g., daphnids) are clearly more sensitive than larger arthropods such as scuds, stoneflies, and crayfish to trifluralin.

As is the case with fish, very little information is available on acute NOAECs in aquatic arthropods. In a bioassay in *Daphnia magna*, Kirk et al. (1999) report an LC_{50} of 251 µg/L and a NOAEC of 130 µg/L. According to the Cleared Review (DER) for this study, the NOAEC is based on mortality and sublethal effects were not reported. The failure to report sublethal effects is not a defect in the study. When conducting bioassays on very small invertebrates, it is difficult to observe subtle signs of sublethal toxicity (e.g., changes in heart rate, grazing rate, etc.).

In the absence of NOAECs for sublethal effects, the EC_{50} values ranging from 250 to 26,000 µg a.i./L are divided by 20 to estimate NOEACs ranging from about 13 to1300 µg a.i./L [250 to 26,000 µg a.i./L ÷ 20 ≈ 12.5 to 1300 µg a.i./L].

4.3.3.3.2. Chronic Toxicity Values

As discussed in Section 4.1.3.3.2, the standard chronic reproduction bioassays in *Daphnia magna* yield disparate NOAEC—i.e., 2.5 µg a.i./L from the study by Macek et al. (1976) and 50.7 µg a.i./L in the study by Grothe and Mohr (1990). While the study by Macek et al. (1976) was conducted over a longer period of time and involved three generations of daphnids rather than one, the lower NOAEC was apparent early in the conduct of the study. Both studies appear to have been well conducted and both studies were accepted by the EPA (U.S. EPA/OPP 1996a, 2009a) Thus, the substantial differences between the NOAECs reported in these two studies may be due to factors that cannot be identified. A study in midge larvae reports a substantially higher NOAEC of 250 µg a.i./L (Knoch 1996a). As discussed in some detail in Section 4.1.3.3.2, there are issues with the design and reporting of this study, which is neither used nor cited by U.S. EPA/OPP (2009a). Consequently, the study by Knoch (1996a) is not used in the dose-response assessment.

As also discussed in Section 4.1.3.3.2, the range of chronic NOAECs in daphnids encompasses the range of chronic NOAECs in saltwater invertebrates. Consequently, the daphnid NOAECs of 2.5 and 50.7 µg a.i./L are used directly for sensitive and tolerant aquatic invertebrates. Because these NOAECs are both based on *Daphnia magna*, there is no implication of differences in species sensitivity. The range of NOAECs simply reflects differences which might be observed under a range of conditions that cannot otherwise be clarified. This limitation is discussed further in the risk characterization (Section 4.4.3.4.2).

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

As summarized in Table 21 and illustrated in Figure 10, the bioassays on algae span a very wide range and appear to reflect an essentially bimodal distribution. It is not clear, however, if these differences reflect differences in the test materials, durations of exposure, or sensitivities of the species of algae that were assayed.

The apparently tolerant species, *Chlorella* and *Scenedesmus*, were tested by Ma and coworkers (Ma and Liang 2001; Ma et al. 2002) using an unspecified 48% EC formulation of trifluralin. Since these studies were conducted in China, it is likely that a Chinese formulation of trifluralin was used. Ma and coworkers have published numerous papers on toxicity to algae, and there is no basis in terms of experimental methods for asserting that bioassays from this group of investigators should not be used. Nonetheless, their results for trifluralin using the Chinese formulation of trifluralin are clearly atypical, which may be due to components in the Chinese formulation that are not relevant to U.S. formulations. Consequently and as a conservative approach, the results from Ma and coworkers are not used in the current Forest Service risk assessment.

The next highest 4-day EC_{50} is 673 µg/L from the study in *Selenastrum capricornutum* by Fairchild et al. (1997). As discussed in Section 4.1.3.4.1, the 7-day EC_{50} of 88.7 µg/L by Adams and Cocke (1990) suggests that the higher EC_{50} from Fairchild et al. (1997) may be due to the shorter period of exposure used in the study. As discussed in Section 4.1.3.4.1 and detailed in Appendix 6 (Table A6-1), the U.S. EPA/OPP classifies the study by Adams and Cocke (1990) as invalid because of a substantial drop in the measured concentrations of trifluralin in the test media over the course of the study.

The remaining definitive EC_{50} values span a very narrow range from 24.3 to 37.9 µg a.i./L. The study by Hughes and Williams (1993c), which reports an EC_{50} of 28 µg/L in *Skeletonema costatum*, also defines an experimental NOAEC of 4.6 µg a.i./L. This EC_{50} is only modestly above the lowest reported value of 24.3 µg/L from the open literature study by Schmitt et al. (2000). The study by Hughes and Williams (1993c) is classified as Acceptable in U.S. EPA/OPP (2009a, Appendix F, p. F-5). For the current risk assessment, the experimental NOAEC of 4.6 µg a.i./L is used for sensitive species of algae.

While not illustrated in Figure 10, Hughes and Williams (1993a) report a non-definitive EC_{50} of >339 µg a.i./L in a 5-day assay with *Anabaena flos-aquae*. This study also reports an experimental NOAEC of 89 µg a.i./L, which is used to characterize risk associated with tolerant species of algae.

It is worth noting that the Cleared Reviews for the studies by Hughes and Williams (1993a,b,c) all cite issues with decreases in the concentration of trifluralin during the course of the bioassays. The Cleared Review for Hughes and Williams (1993a) contains the following hand-written comment: *Depletion of test concentrations is acceptable for trifluralin based on its chemical properties*. This appears to be a reasonable position. As detailed in Section 3.2.3.4, trifluralin will volatilize rapidly from water. The use of 5-day bioassays in algae in which the concentrations of trifluralin decreased substantially may in some respects be beneficial and better reflect the nature of exposures that may occur in the field.

4.3.3.4.2. Aquatic Macrophytes

As summarized in Section 4.1.3.4.2 and detailed in Appendix 6 (Table A6-3), the data on aquatic macrophytes consists only of two bioassays. The assay in *Lemna gibba* reports a

14-day EC_{50} of 49.7 µg a.i./L and a LOAEL of 2.53 µg a.i./L—i.e., the lowest concentration tested leaving the NOAEL undefined (Milazzo et al. 1993). The assay in *Lemna minor* reports a 4-day EC_{50} of 170 µg a.i./L and a NOAEL of 75 µg a.i./L.

For tolerant species of aquatic macrophytes, the NOAEL of 75 µg a.i./L is used directly. For sensitive species of aquatic macrophytes, the EC_{50} of 49.7 µg a.i./L is divided by a factor of 20 to approximate a NOAEL of about 2.5 µg a.i./L [49.7 µg a.i./L ÷ 20 = 2.485 µg a.i./L].

4.4. RISK CHARACTERIZATION

4.4.1. Overview

Terrestrial animals and plants exposed to trifluralin used in Forest Service Programs do not appear to be at substantial risk. Except for the consumption of contaminated fish, there is little indication that mammals or birds will be adversely affected by trifluralin. In the case of an accidental spill, the consumption of contaminated fish leads to HQs that are substantially above the level of concern. Based on expected concentrations of trifluralin in surface water, longer-term exposures involving the consumption of contaminated fish lead to modest exceedances —i.e., upper bound HQs ranging from 1.3 to 1.8 for mammals. For birds, none of the longer-term HQs exceeds the level of concern. Acute HQs based on expected concentrations of trifluralin do not exceed the level of concern for mammals or birds based either on the consumption of contaminated water or the consumption of contaminated fish. Trifluralin is an effective herbicide. Nonetheless, soil incorporation, the application method considered by the Forest Service, will limit the offsite transport of trifluralin; accordingly, substantial risks to nontarget vegetation are not anticipated. At an application rate of 2 lbs a.i./acre, the upper bound HQ of 4 suggests that there could be some damage to sensitive species of vegetation.

An accidental spill of trifluralin into a small pond could cause severe adverse effects in virtually all groups of aquatic animals and plants, including both sensitive and tolerant species. Trifluralin is highly toxic to certain species within all groups of aquatic organisms; however, certain other species within these groups are much less sensitive to trifluralin. Based on peak expected concentrations in water, tolerant species of aquatic organisms, including both animals and plants would not be adversely affected by anticipated upper bound peak or longer-term exposures. This risk characterization also applies to sensitive species in terms of longer-term exposures—i.e., all of the upper bound HQs for sensitive species are below 1 even at the maximum anticipated application rate.

Based on peak (acute) expected environmental concentrations, sensitive species of fish might be adversely affected at application rates of both 1 and 2 lbs a.i./acre with exceedance in the HQ of 1 at both the central estimates of exposure as well as the upper bounds of exposures. Similarly, there may be an impact on sensitive species of aquatic macrophytes at both the central estimate of exposure as well as the upper bound of exposure but only at the maximum anticipated application rate of 2 lbs a.i./acre.

Very little information is available on the toxicity of trifluralin to aquatic-phase amphibians. For this group, the HQs based on amphibian data suggest a potential risk only at the upper bounds of exposure. While HQs are derived based on toxicity data for amphibians, a better risk characterization may be based on the assumption that amphibians will be as sensitive as fish to trifluralin.

Aquatic invertebrates are much less sensitive than fish to trifluralin. Even at the upper bounds of exposures, there is no basis for asserting that trifluralin will have a negative impact on aquatic invertebrates.

As discussed above, most of the HQs for trifluralin which exceed a level of concern involve trifluralin concentrations likely to be found in surface water. As summarized in Table 12, an application rate of 1 lb a.i./acre can result in highly variable surface water concentrations ranging from 0.00002 to 0.0039 mg a.i./L for peak expected concentrations and from 0.000068 to 0.0006 for longer-term expected concentrations. Most of the HQs of concern are associated with peak concentrations, which span a factor of 195. This substantial variability is associated primarily with the differences in nine different sites and three soil types used in the Gleams-Driver modeling (Section 3.2.3.4.3). Thus, the upper bound HQs discussed in the risk characterization are not applicable to all sites at which trifluralin may be applied. If trifluralin is applied to areas which are not near surface water or in locations in which rainfall is low, the upper bound HQs discussed in this section may and probably will grossly overestimate risk. In such cases, site-specific or at least region-specific refinements of the Gleams-Driver modeling should be considered.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

Except for exposures associated with the consumption of contaminated fish, all HQs for mammals are substantially below the level of concern (HQ=1). Excluding fish consumption, the highest HQ is 0.05, the HQ for the consumption of contaminated water by a small mammal following an accidental spill. This HQ is below the level of concern by a factor of about 20. Consequently, considerations of application rates have no impact on the risk characterization.

For non-accidental exposures associated with the consumption of contaminated fish, the upper bound of the HQ for longer-term exposures for a large mammal approaches but does not exceed the level of concern at the unit application rate of 1 lb a.i./acre (i.e., 0.8). For a canid, the corresponding upper bound HQ is 1.2, modestly exceeding the level of concern. At the maximum application rate of 2 lbs a.i./acre, the HQs exceed the level of concern—i.e., HQs of 1.6 for a large mammalian carnivore and 2.4 for a canid. As discussed in Section 3.3.4 (dose-severity considerations), HQs in the range of >1 to 2 would be viewed as undesirable; however, there is no indication that overt signs of toxicity would be evident or that sublethal effects would occur.

For acute exposures associated with the consumption of contaminated fish based on expected (non-accidental) peak concentrations of trifluralin in water, the upper bound HQs at the unit application rate of 1 lb a.i./acre are about 0.1 for both the large mammalian carnivore and 0.2 for the canid. At the maximum anticipated application rate of 2 lbs a.i./acre, the upper bound HQs are 0.2 for the large mammalian carnivore and 0.3 for the canid. Thus, there is no basis for asserting that these acute exposures would lead to adverse effects.

In the case of an accidental spill, the HQs associated with the consumption of contaminated fish substantially exceed the level of concern for both a large mammal [HQs = 20 (0.1 to 457)] and a canid [HQs = 29 (0.1 to 658)]. The doses associated with

the upper bounds of the HQs range from about 46,000 to 66,000 mg/kg bw. As discussed in Section 3.3.4 (dose-severity relationships), the minimum lethal dose for experimental mammals is about 1250 mg/kg bw. Consequently, lethality might be observed in some sensitive species of mammals feeding on contaminated fish following an accidental spill. It is not clear, however, that mortality would be seen in carnivorous mammals that might feed on fish. As summarized in Appendix 1 (Table A1-2), Ebert et al. (1992) report no mortality in dogs following oral doses of up to 10,000 mg/kg bw; furthermore, diarrhea was the only sign of toxicity observed. As discussed in Section 4.2.2.5, however, substantial fish mortality could occur following an accidental spill of trifluralin, which could lead to abnormally high rates of fish consumption by some species of mammalian wildlife. This possibility coupled with the very high HQs for mammals associated with the consumption of contaminated fish following an accidental spill suggests that adverse effects and possibly lethal effects might be observed in piscivorous mammals in the event of an accidental spill.

Based on the above discussion of the HQs, the risk characterization for mammalian wildlife suggests that adverse effects in mammals are not likely, except in the event of an accidental spill which could cause adverse effects and perhaps severe adverse effects in piscivorous mammals could occur.

4.4.2.2. Birds

Except for the consumption of contaminated fish following an accidental spill, there is no indication that birds may be adversely affected by trifluralin. In the case of the consumption of fish following an accidental spill, the HQs for a piscivorous bird are 4 (0.02 to 102) at an application rate of 1 lb a.i./acre and 9 (0.04 to 204) at an application rate of 2 lbs a.i./acre. The upper bound HQs of 102 to 204 are associated with doses of about 76,000 to 150,000 mg/kg bw. No toxicity studies have been conducted at these doses. As discussed in Section 4.1.2.2, no definitive avian LD_{50} values for trifluralin are available. As summarized in Appendix 2 (Table A2-1), the non-definitive LD_{50} values for birds are >2,000 mg/kg bw. Hudson et al. (1984) indicate that doses of 2000 mg/kg bw are associated with only very mild ataxia. Based on this information, it seems reasonable to assert that the very high doses associated with the consumption of contaminated fish by birds following an accidental spill could result in overt signs of toxicity. Whether or not mortality might occur is not clear.

All other exposure scenarios for birds lead to HQs that are far below the level of concern. The highest non-accidental HQ at the unit application rate of 1 lb a.i./acre is 0.05 (i.e., the consumption of contaminated fish based on longer-term expected concentrations of trifluralin in water). This HQ is below the level of concern by a factor of 20, and considerations of application rates up to 2 lbs a.i./acre have no impact on the qualitative risk characterization.

4.4.2.3. Reptiles and Amphibians (Terrestrial-Phase)

No information has been identified on the toxicity of trifluralin to reptiles or terrestrial-phase amphibians (Section 4.1.2.3); accordingly, no dose-response assessment for these groups of organisms is developed (Section 4.3.2.3). In the absence of information, the

EPA assumes that toxicity data on birds are appropriate surrogates for reptiles and terrestrial-phase amphibians (U.S. EPA/OPP 2009a).

4.4.2.4. Terrestrial Invertebrates

The quantitative risk characterization for terrestrial invertebrates is limited by the available toxicity data (Section 4.3.2.4.). The toxicity value used to develop HQs is an indeterminate LD_{50} of >430 mg a.i./kg bw. This dose is used to develop HQs for the consumption of contaminated vegetation (G08b). The highest HQ is 0.0003 for the consumption of contaminated broadleaf vegetation by a herbivorous insect at the unit application rate of 1 lb a.i./acre. While there are substantial uncertainties with both the dose-response and exposure assessments, this HQ is below the level of concern by a factor of over 3000, and there is no basis for asserting that herbivorous insects are likely to be at risk from the consumption of contaminated vegetation.

Because trifluralin is applied directly to soil, potential risks to soil invertebrates are an obvious concern. Based on Gleams-Driver modeling (Section Section 3.2.3.6), the peak concentrations of trifluralin in the top 12 inches of soil are estimated at 0.31 (0.26 to 0.38) mg/kg soil (dry weight). As discussed in Section 4.1.2.4.2, the lowest reported NOAEC for trifluralin in earthworms is 28.98 mg a.i./ kg soil from the study by Hanisch and Bathelt (1994) using a European formulation of trifluralin. The upper bound concentration anticipated in soil is less than the lowest NOAEC by a factor of over 75 [28.98 mg a.i./ kg soil ÷ 0.38 mg a.i./kg soil ≈ 76.26]. Similarly and as discussed in Section 4.1.2.4.3, the NOAEC for a soil isopod in a model ecosystem is 320 mg a.i./kg soil (Staak et al. 1998). This NOAEC is greater than the maximum anticipated concentration of trifluralin in soil by a factor of over 800 [320 mg a.i./kg soil ÷ 0.38 mg a.i./kg soil ≈ 842.11]. These data indicate that adverse effects in soil invertebrates are unlikely following the soil incorporation of trifluralin at application rates to be used in Forest Service programs.

4.4.2.5. Terrestrial Plants

For broadcast applications of herbicides, adverse effects on nontarget vegetation are virtually certain. For the soil incorporation of trifluralin, however, the potential for adverse effects on nontarget vegetation is not remarkable. The highest HQs are associated with runoff from the treated site to an adjacent field. For this scenario, the HQs for sensitive species of plants are 0.3 (0.001 to 1.8) at the unit application rate of 1 lb a.i./acre (Worksheet G04). As discussed in Section 4.2.4.3, the broad range of HQs is associated with the nature of the Gleams-Driver simulations (i.e., 27 sets of simulations involving nine locations and three soil types per location). As detailed in Appendix 7 (Table A7-1), the upper bound HQs would apply to locations with relatively high rates of rainfall. In arid locations, relatively little off-site runoff is likely. At an application rate of 2 lbs a.i./acre, the upper bound HQ of 4 suggests that there could be some damage to sensitive species of vegetation. For trifluralin, however, the HQs may overestimate actual risk because trifluralin will volatilize rapidly from soil, unless steps are taken to incorporate the herbicide into the soil. Active measures to incorporate trifluralin into soil will not occur in fields adjacent to the application site.

HQs associated with the use of irrigation water contaminated with trifluralin (Worksheet G06a) and the off-site transport of trifluralin in contaminated soil due to wind erosion (Worksheet G06b) are insubstantial. The highest HQ for these scenarios is 0.008—the upper bound HQ for sensitive species of plants associated with the use of contaminated water for irrigation. While there are many uncertainties associated with these exposure scenarios, the upper bound HQ is below the level of concern by a factor of 125.

4.4.2.6. Terrestrial Microorganisms

HQs for trifluralin are not derived for terrestrial microorganisms. As discussed in Section 4.1.2.6, Dumontet and Perucci (1992) observed decreases in microbial activity (assays as soil respiration) at a concentration of 0.5 mg/kg soil. This soil concentration is only marginally above the peak concentrations 0.313 (0.263 to 0.38) mg/kg soil (dry weight) trifluralin estimated in the top 12 inches of soil based on Gleams-Driver modeling (Section 3.2.3.6). Similarly, at a concentration of 1 mg a.i./kg soil, Cullimore and McCann (1997) observed changes in species composition of soil algae. These studies suggest changes may occur in soil microorganism populations following trifluralin applications. It is not clear, however, that these changes would lead to substantial or functional impacts on soil, including gross changes in the capacity of soil to support vegetation.

4.4.3. Aquatic Organisms

The risk characterization for aquatic organisms is summarized in Worksheet G03 of the EXCEL workbook that accompanies the current risk assessment. As a convenience, this worksheet is reproduced in Table 25. As discussed above, the EXCEL workbook that accompanies the current risk assessment is based on a unit application rate of 1 lb a.i./acre. For several groups of organisms, the maximum anticipated application rate of 2 lbs a.i./acre leads to increases in the HQs that both qualitatively and quantitatively alter the risk characterization—i.e., HQs are below 1 at 1 lb a.i./acre but above 1 at 2 lbs a.i./acre. To facilitate the discussion of these instances, the HQs associated with an application rate of 2 lbs a.i./acre are presented in Table 26. This table is also based on Worksheet G03 of the EXCEL workbook that accompanies the current risk assessment but with the application rate in Worksheet A01 changed to 2 lbs a.i./acre.

As summarized in Tables 25 and 26, the risk characterization associated with the accidental spill of trifluralin into a small pond leads to HQs that substantially exceed the level of concern (HQ=1) for all groups of aquatic organisms. This is not an unusual situation for pesticides like trifluralin which are relatively toxic to aquatic organisms. The accidental spill scenario is an exposure scenario based on a standard set of assumptions used in virtually all Forest Service risk assessments; in addition, this scenario is intentionally extreme. As discussed in Section 3.2.3.4.1, the accidental spill scenario for trifluralin may be particularly extreme in that the concentrations in surface water are estimated to range from 0.23 to about 18 mg a.i./L, with a central estimate of about 4.5 mg a.i./L (Worksheet B04b). The central estimate and upper bound concentrations are substantially in excess of the solubility of trifluralin in water, which is about 0.3 mg/L. The current risk assessment makes the conservative assumption that the other ingredients in liquid formulations of trifluralin would permit these excessive concentrations to be maintained in water for a sufficient period of time for exposures to

occur. Nonetheless, the reported LC_{50} values for trifluralin range from about 0.1 to 26 mg a.i./L. The upper bound of this range is based on experimental studies in which solvents were used to reach lethal water concentrations of trifluralin. In this respect, the available acute toxicity studies on trifluralin seem appropriate for assessing the consequences of an accidental spill of trifluralin into surface water.

Based on the range of HQs for the accidental spill scenario summarized in Tables 25 and 26, it is reasonable to assert that all classes of aquatic organisms would be at risk of severe adverse effects including mortality. The only exception would be tolerant species of aquatic invertebrates, following the least severe spill modeled in the current risk assessment. The risk characterization for an accidental spill is consistent with incident reports summarized in U.S. EPA/OPP (2009a, p. 103) in which fish mortality is associated with the misuse of trifluralin. Given this uniformly severe risk characterization, the accidental spill scenario is not discussed further in the following subsections.

4.4.3.1. Fish

4.4.3.1.1. Acute Exposures

Based on expected peak concentrations of trifluralin in surface water at a unit application rate of 1 lb a.i./acre, the acute HQs for sensitive species of fish are 0.5 (0.02 to 1.7), exceeding the level of concern (HQ=1) at the upper bound concentration of trifluralin in surface water. At the maximum anticipated application rate of 2 lbs a.i./acre, the HQs for sensitive species of fish are 0.9 (0.03 to 3).

A qualitative interpretation of the HQs is limited by the experimental data on the toxicity of trifluralin to fish. As discussed in Section 4.3.3.1.1, short-term acute NOAECs based on sublethal effects in fish are not available; hence, the toxicity value for sensitive species of fish is based on the chronic NOAEL of 0.0046 mg/L. This approach is taken because the lowest LC_{50} in fish is 0.0185 mg a.i./L. If this value is divided by 20, the standard approach for estimating an acute NOAEC from an acute LC_{50}, the resulting value of about 0.001 mg a.i./L is below the chronic NOAEC. While there is strong confidence that the chronic NOAEL of 0.0046 mg/L would not cause adverse effects in acute exposures, the use of a chronic NOAEL impairs the interpretation of effects at HQs in excess of 1.

At an application rate of 2 lbs a.i./acre, the HQ of 3 is associated with a concentration in water of 0.0044 mg a.i./L. In terms of defining acute risk—i.e., the likelihood of observing acute lethal effects—the trigger of concern used by U.S. EPA/OPP is a ratio of the exposure to the acute LC_{50} that is greater than 0.5. This ratio for trifluralin—i.e., the anticipated level of exposure divided by the lowest acute LC_{50}—at an application rate of 2 lbs a.i./acre is about 0.2 [0.0044 mg a.i./L ÷ 0.0185 mg a.i./L ≈ 0.423]. Thus, using the criteria typically used by U.S. EPA/OPP, substantial mortality in sensitive species of fish would not be expected. The impact of potential sublethal effects on fish populations is unclear.

For tolerant species of fish, the risk characterization is unequivocal. At the maximum anticipated application rate of 2 lbs a.i./acre, the HQs are 0.01 (0.0004 to 0.04). The upper bound HQ is below the level of concern by a factor of 25.

4.4.3.1.2. Longer-Term Exposures

The HQs for both sensitive and tolerant species of fish are below the level of concern based on the unit application rate of 1 lb a.i./acre as well as the highest anticipated application rate of 2 lbs a.i./acre. As indicated in Table 25, the HQs for sensitive species of fish at an application rate of 1 lb a.i./acre are 0.06 (0.0002 to 0.3). At the maximum anticipated application rate of 2 lbs a.i./acre, the HQs for sensitive species of fish are 0.1 (0.0003 to 0.6). While the upper bound HQ approaches the level of concern (HQ=1), the level of concern is not exceeded and there is no basis for asserting that longer-term exposures of fish to trifluralin are likely to result in adverse effects in sensitive populations of fish.

As discussed in Section 4.3.3.1.2 and summarized in Table 24, the longer-term toxicity value for tolerant species of fish is not substantially higher than the toxicity value for sensitive species of fish. Nonetheless, the upper bound HQ associated with longer-term exposures in sensitive species of fish at the maximum application rate of 2 lb a.i./acre is 0.3, below the level of concern by a factor of about 3.

4.4.3.2. Amphibians (Aquatic-Phase)

Very little information is available on the toxicity of trifluralin to aquatic-phase amphibians (Section 4.1.3.2), and the dose-response assessment for amphibians is limited to an NOAEC that is estimated from three very similar LC_{50} values in Fowler's Toad (Section 4.1.3.2). While there is no direct basis for designating Fowler's toad as a sensitive or tolerant species, the conservative assumption is made that HQs developed from the data on Fowler's toad apply to tolerant species. Based on the very limited information on aquatic-phase amphibians, only acute HQs are developed: 0.1 (0.004 to 0.4) at a unit application rate of 1 lb a.i./acre and 0.2 (0.003 to 0.9) at the maximum anticipated application rate of 2 lbs a.i./acre.

In the absence of information on aquatic-phase amphibians, the U.S. EPA/OPP typically uses data on freshwater fish to characterize risks to aquatic-phase amphibians, and this approach is used in the recent EPA ecological risk assessment on trifluralin (U.S. EPA/OPP 2009a, p. 51). While the current Forest Service risk assessment develops HQs for amphibians based on the data on Fowler's toad, it seems appropriate to use the risk characterization on fish qualitatively to characterize risks in aquatic-phase amphibians. In other words, the limited data on amphibians suggest that their sensitivity to trifluralin is in the mid-range of fish sensitivities to trifluralin, as illustrated in Figure 6. Based on these similarities, it seems reasonable to assert that some sensitive species of aquatic-phase amphibians could be adversely affected by peak concentrations of trifluralin in water. The nature and severity of the possible effects cannot be further characterized.

4.4.3.4. Aquatic Invertebrates

4.4.3.4.1. Acute Exposures

As illustrated in Figure 6 and discussed in Section 4.1.3.3.1, aquatic invertebrates are substantially less sensitive than fish or amphibians to trifluralin, as reflected in the risk characterization. Although there is a substantial variability in the sensitivity of different species of aquatic invertebrates to trifluralin, none of the HQs reaches a level of concern (HQ=1). At the unit application rate of 1 lb a.i./acre, the upper bound HQ for sensitive species of aquatic invertebrates is 0.2. At the maximum anticipated application rate of 2 lbs a.i./acre, the upper bound HQ for sensitive species of aquatic invertebrates is 0.3.

4.4.3.4.2. Longer-Term Exposures

As with acute exposures, none of the HQs for longer-term exposures reach a level of concern (HQ=1). At the unit application rate of 1 lb a.i./acre, the upper bound HQ for sensitive species of aquatic invertebrates is 0.2. At the maximum anticipated application rate of 2 lbs a.i./acre, the upper bound HQ for sensitive species of aquatic invertebrates is 0.3. For tolerant species of aquatic invertebrates, the upper bound HQ at the maximum anticipated application rate is 0.02, below the level of concern by a factor of 50.

The only reservation with the risk characterization for longer-term exposures of aquatic invertebrates to trifluralin involves the inconsistencies in the chronic studies. As discussed in Section 4.3.3.3.2, the range of HQs for presumably tolerant and sensitive species is based on NOAECs in *Daphnia magna* of 2.5 µg a.i./L (Macek et al. 1976) and 50.7 µg a.i./L (Grothe and Mohr 1990). The reasons for the discrepancies in the NOAECs from these two studies are not apparent. While these NOAECs are used as a convention to characterize risks in presumably tolerant and sensitive species, the differences in the HQs, like the differences in the underlying HQs, cannot be ascribed to species differences but more properly reflect variability that might be seen under different, albeit undefined, conditions.

4.4.3.4. Aquatic Plants

4.4.3.4.1. Algae

As illustrated in Figure 10, the toxicity data on algae suggest a very wide range of sensitivity in algae. A discussed in Section 4.1.3.4, not all of these data are used quantitatively in the dose response assessment. Nonetheless, the range of experimental NOAECs from 0.0046 to 0.089 mg a.i./L is substantial.

For tolerant species of algae at a unit application rate of 1 lb a.i./acre, there is no indication that adverse effects would be expected with an upper bound acute HQ of 0.02 (below the level of concern by a factor of 50) and an upper bound chronic HQ of 0.002 (below the level of concern by a factor of about 250). Because of these very low HQs, the qualitative risk characterization is not impacted by the consideration of the maximum application rate of 2 lbs a.i./acre, and all of the HQs remain below the level of concern.

This risk characterization also applies to longer-term exposures of sensitive species algae, with upper bound HQs of 0.09 at an application rate of 1 lb a.i./acre and 0.2 at an

application rate of 2 lbs a.i./acre. Based on peak exposures, however, the risk characterization is sensitive to application rates. At an application of 1 lb a.i./acre, the upper bound HQ is 0.5. At an application rate of 2 lbs a.i./acre, the upper bound HQ is 1.0 – i.e. the HQ reaches but does not exceed the level of concern. Qualitatively, these HQs suggest that effects on algae are not likely to be either substantial or persistent.

4.4.3.4.2. Macrophytes

Quantitatively, the risk characterization for aquatic macrophytes is very similar to that for algae. For tolerant species of macrophytes, there is no basis for asserting that surface water concentrations of trifluralin will result in damage. The peak acute HQs are 0.03 at the unit application rate of 1 lb a.i./acre and 0.06 at the maximum anticipated application rate of 2 lbs a.i./acre. Similarly, longer-term concentrations of trifluralin do not appear to pose a risk to sensitive species of macrophytes with upper bound longer-term HQs of 0.2 at the unit application rate of 1 lb a.i./acre and 0.3 at the maximum anticipated application rate of 2 lbs a.i./acre.

For sensitive species of macrophytes, the HQs associated with peak concentrations at the unit application rate of 1 lb a.i./acre are below the level of concern – i.e., HQs of 02 (0.008 to 0.9). At the maximum application rate of 2 lb a.i./acre, the upper bound HQ is modestly above the level of concern – i.e., HQs of 0.5 (0.02 to 1.8).

While the HQs for macrophytes are similar to those for algae, the underlying toxicity data on macrophytes are less robust than the data on algae. As discussed in Section 4.3.3.4.2, only two studies are available, both of which were conducted with species of *Lemna*, and the differences in the toxicity values may reflect differences in experimental design rather than differences in sensitivity between the species of *Lemna* tested. An additional limitation in the data on macrophytes is that an experimental NOAEC for presumably sensitive species is not available.

For the presumably sensitive species—i.e., *Lemna gibba* from the study by Milazzo et al. (1993)—the experimental LOAEL is 2.53 µg a.i./L. At the unit application rate of 1 lb a.i./acre, the upper bound of the peak anticipated concentration in water is about 3.9 µg a.i./L. At the maximum anticipated application rate of 2 lbs a.i./acre, the upper bound of the peak anticipated concentration in water is about 7.8 µg a.i./L. Thus, unlike the case with algae, adverse effects in some sensitive species of aquatic macrophytes cannot be ruled out.

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.

Internet	**References obtained from various sites on the Internet.**
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SET01	**Initial TOXLINE general search – a. Tox or Kinetics [113]; b. Fate [63]; c. Anti-infective agent [9]; d: Other [4]; e: Exposure [8]; g: General [14].**
SET02	**Supplemental references from ECOTOX**
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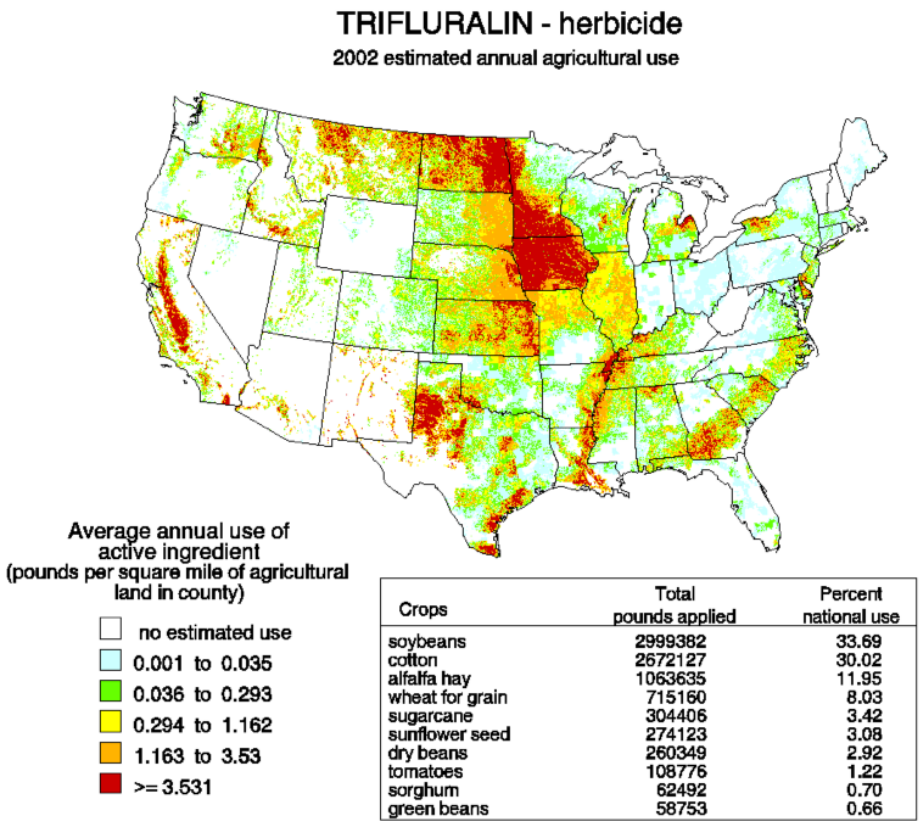


Crops	Total pounds applied	Percent national use
soybeans	2999382	33.69
cotton	2672127	30.02
alfalfa hay	1063635	11.95
wheat for grain	715160	8.03
sugarcane	304406	3.42
sunflower seed	274123	3.08
dry beans	260349	2.92
tomatoes	108776	1.22
sorghum	62492	0.70
green beans	58753	0.66

Figure 1: Estimated Agricultural Use of Trifluralin in the United States for 2002

Source: USGS(2003a)

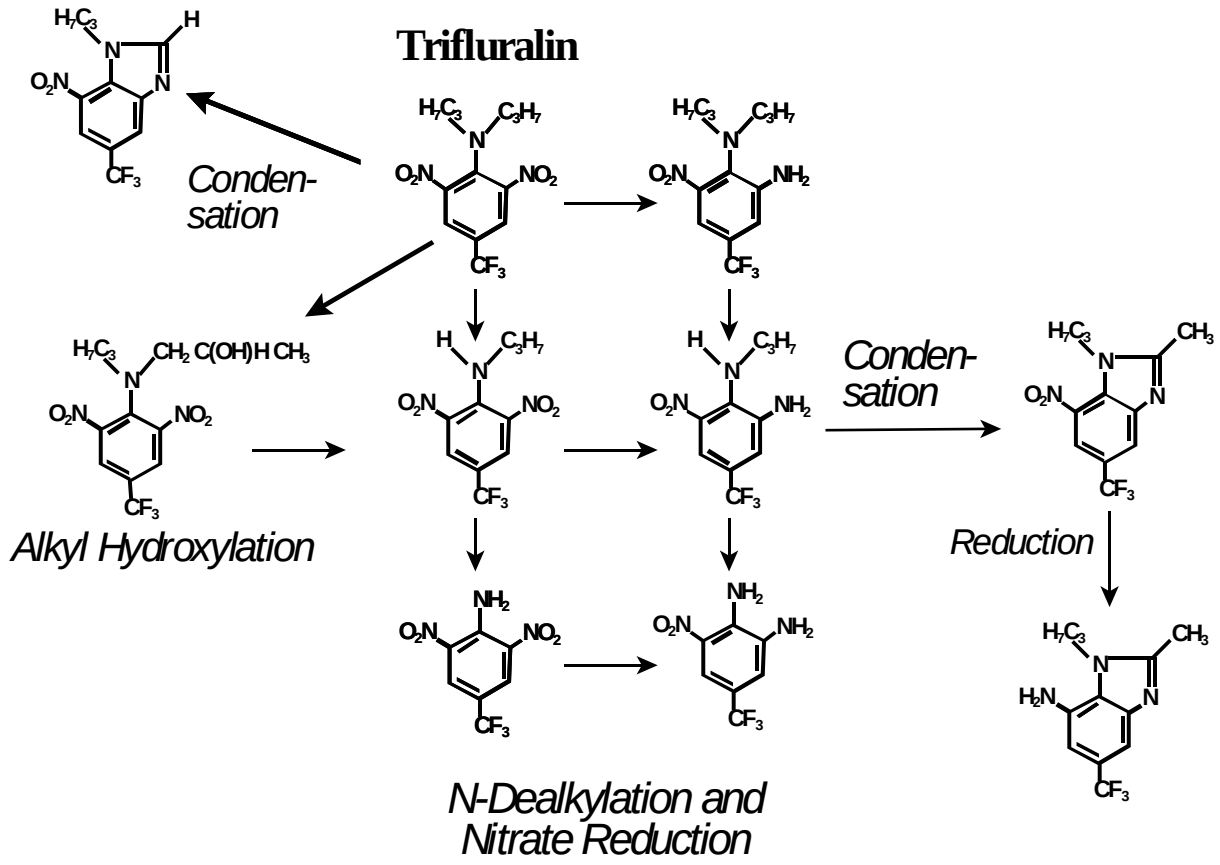


Figure 2: Partial Metabolic Pathways for Trifluralin in Rats

Modified from Figure 1 in Erkog and Menzer 1985
See Section 3.1.3.1 for discussion.

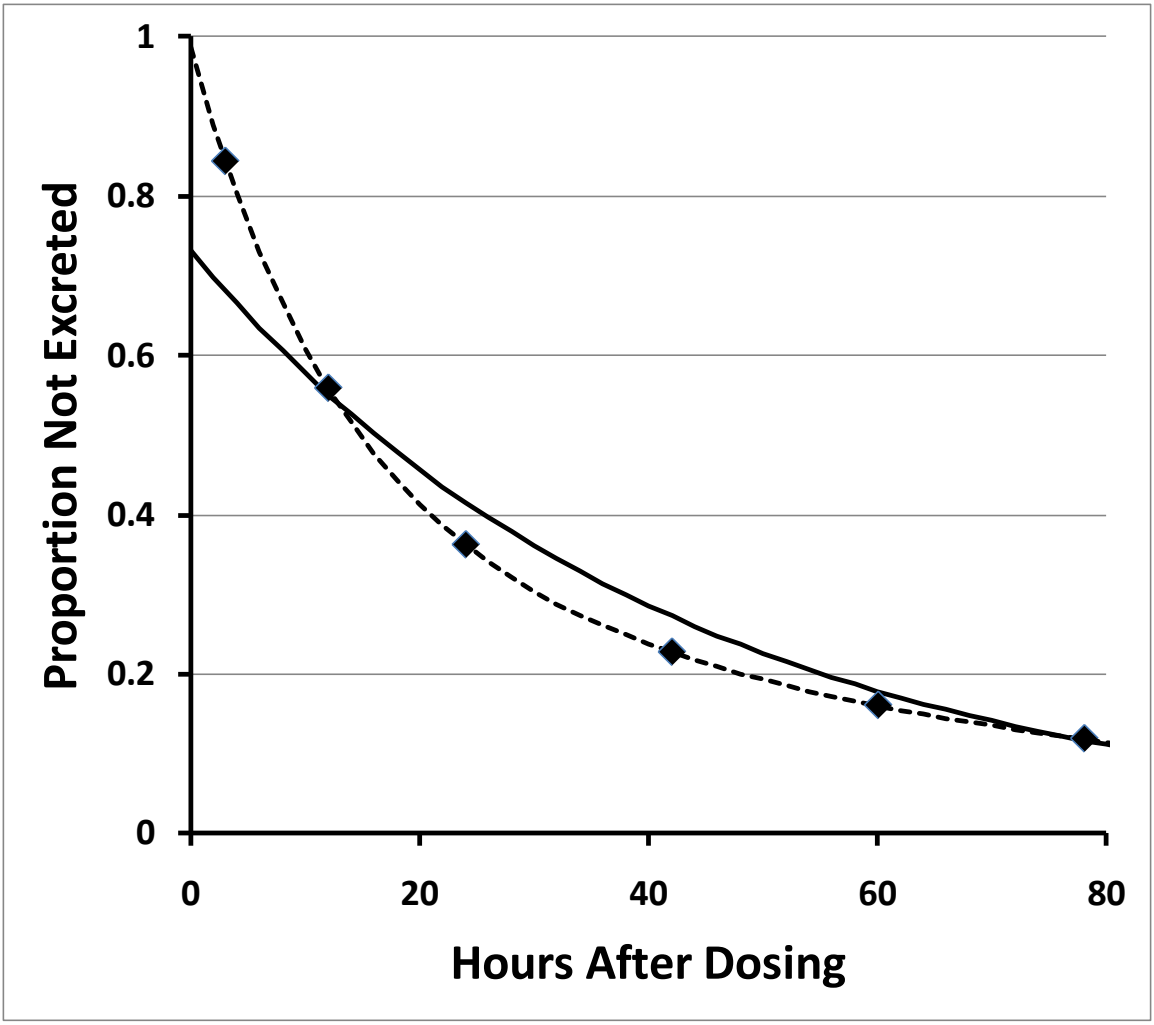


Figure 3: Excretion of Trifluralin by Rats Following An Oral Dose of 1 mg/kg bw

Data from Erkog and Menzer 1985, Table 2, 1064
See Section 3.1.3.3 for discussion.

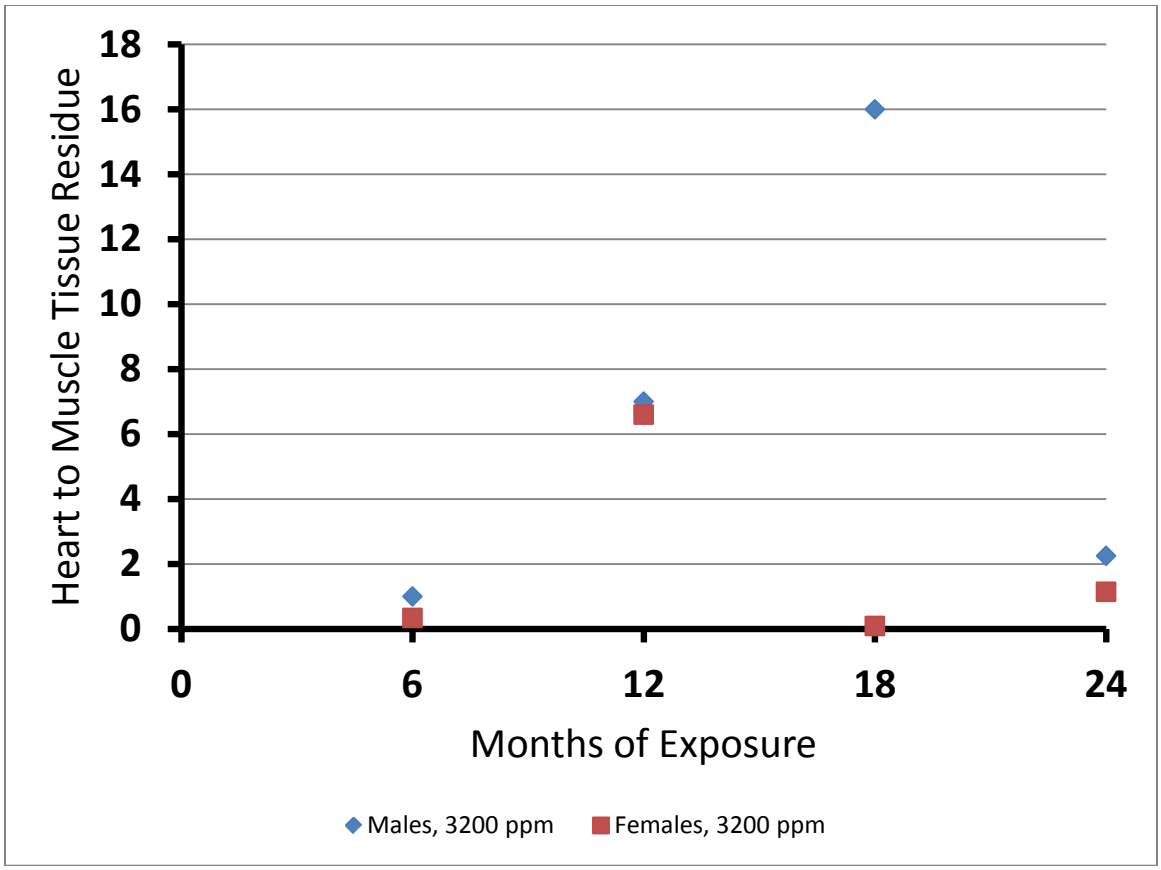


Figure 4: Trifluralin in Heart Tissue Relative to Skeletal Muscle Tissue in Rats

See Table 4 for data.
See Section 3.1.3.1 for discussion.

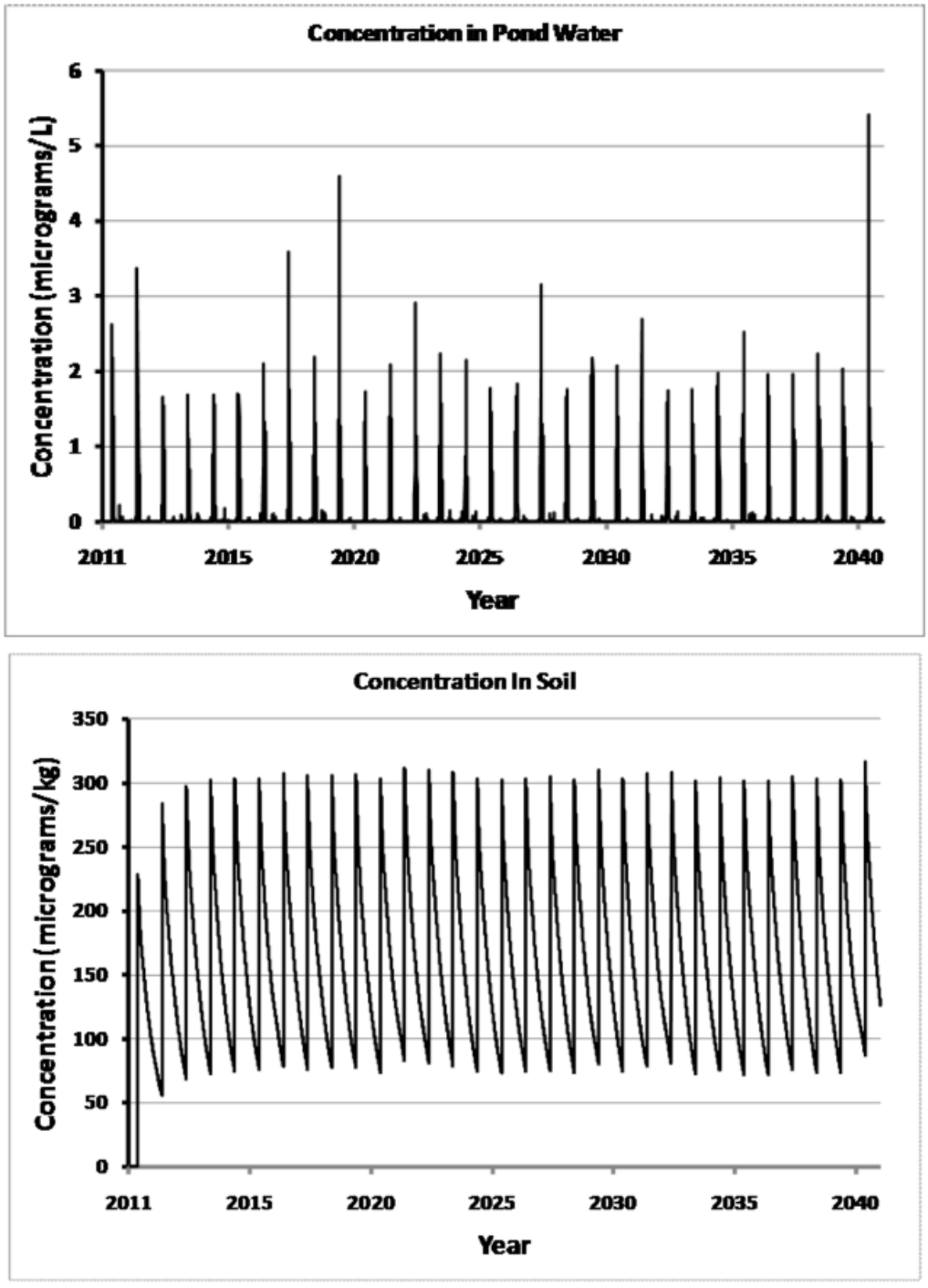


Figure 5: Simulation of 40 Years of Annual Applications of Trifluralin

The soil concentrations represent the top 12 inches of soil.
See Section 3.2.3.4.3.2 for discussion.

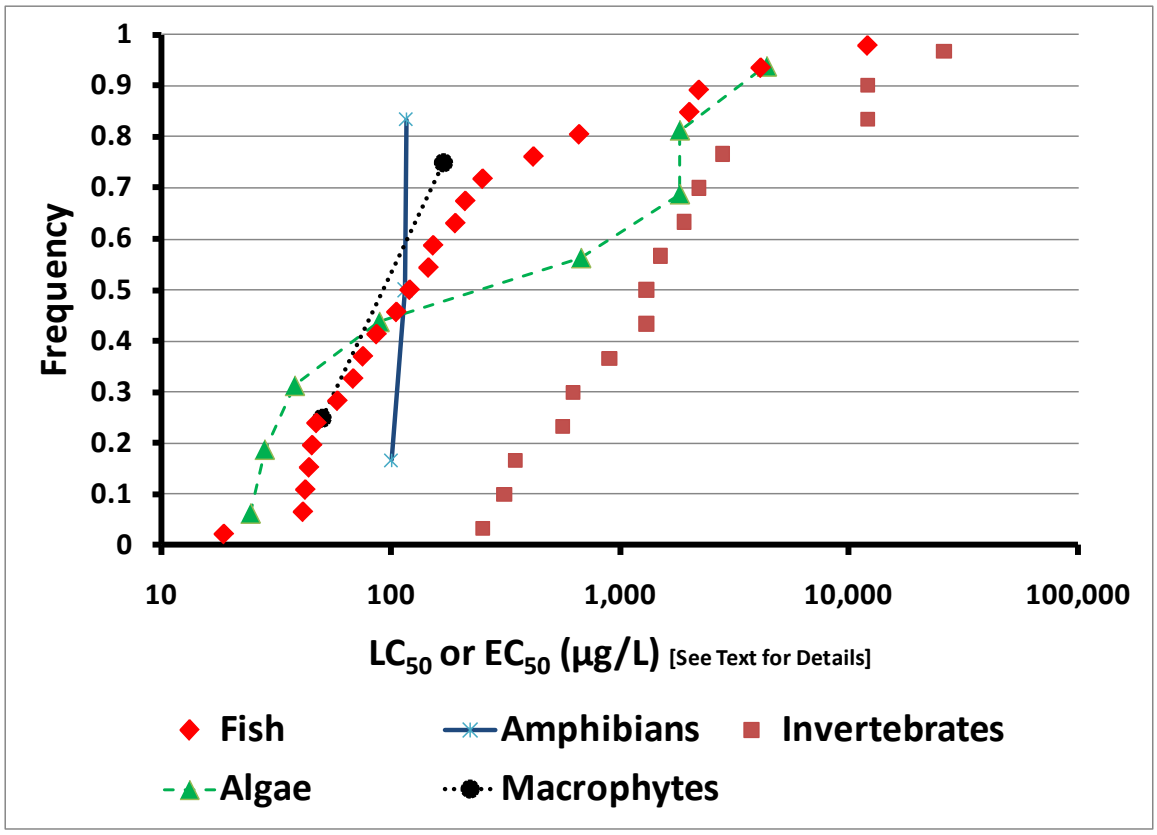


Figure 6: Overview of Acute Toxicity to Aquatic Organisms

See Section 4.1.3 for discussion and subsequent figures of additional details.

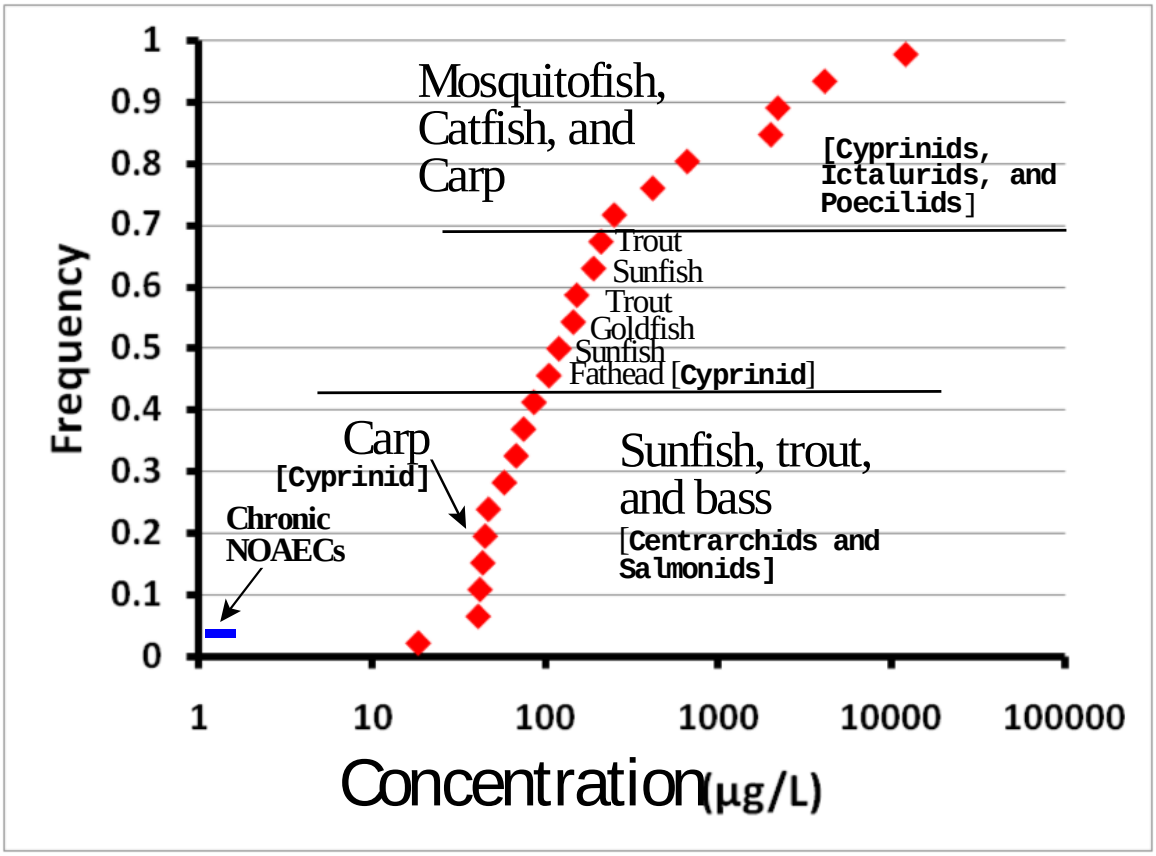


Figure 7: Fish, Acute 96-hour LC_{50}s Values and Range of Chronic NOAECs

See Table 18 for summary of data and Appendix 4 for additional details.
See Section 4.1.3.1 for discussion.

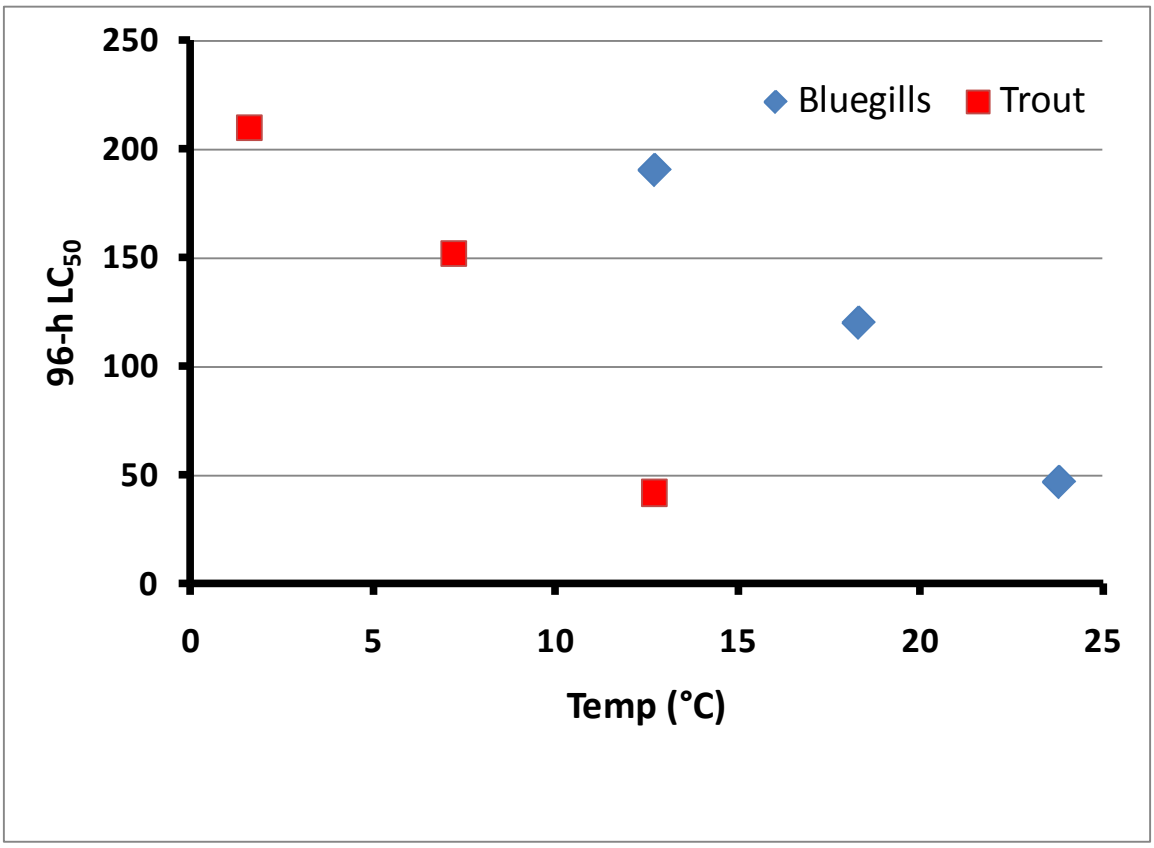


Figure 8: Impact of Temperature on Toxicity of Trifluralin to Trout and Bluegills

Data from Macek et al. (1969) as summarized in Table 18 of the current risk assessment. See Section 4.1.3.1.1 for discussion.

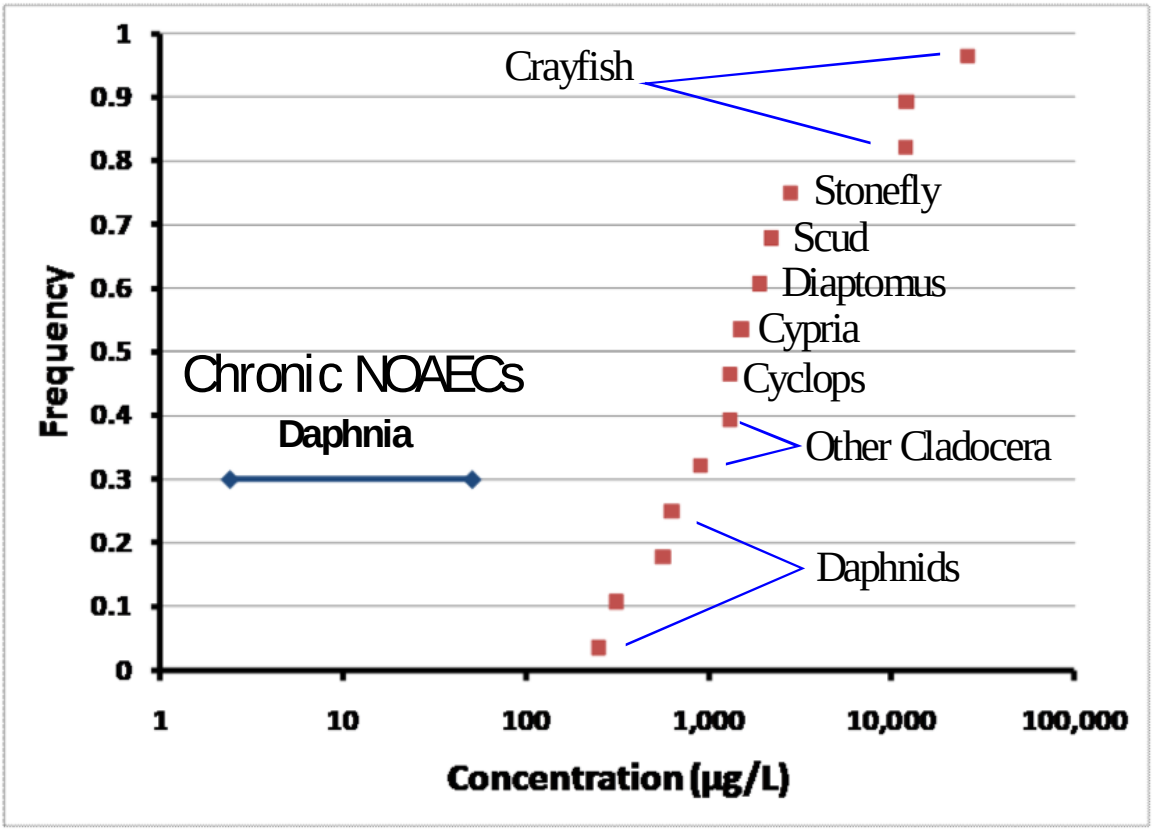


Figure 9: Freshwater Invertebrates, Acute LC_{50}s and Chronic NOAECs

See Table 20 for summary of data and Appendix 5 for additional details.
See Section 4.1.3.3 for discussion.

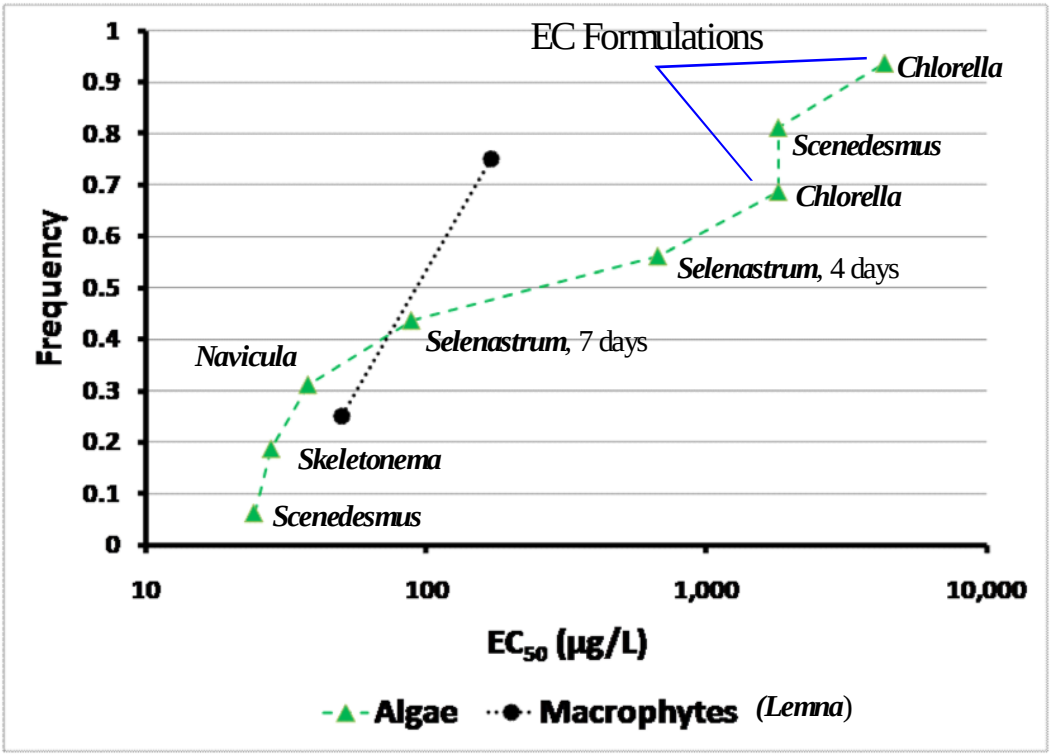


Figure 10 : Toxicity of Trifluralin to Aquatic Plants

See Table 21 for summary of data and Appendix 6 for additional details.
See Section 4.1.3.4 for discussion.

Table 1: Chemical and Physical Properties of Trifluralin

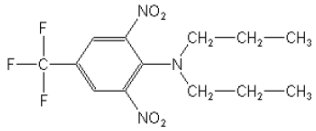
Property	Value	Reference
	Identifiers	
Common name:	Trifluralin	
IUPAC Name	α,α,α-trifluoro-2,6-dinitro-N,N-dipropyl-p-toluidine	Tomlin 2004
CAS Name	2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl) benzenamine	Tomlin 2004
CAS No.	1582-09-8	U.S. EPA/OPP 1996a
U.S. EPA/OPP Code	036101	U.S. EPA/OPP 1996a
Development Codes	L-36 352 (DowElanco); EL-152 (Lilly)	Tomlin 2004
Smiles Notation	`CCCN(CCC)c1c(cc(cc1[N+](=O)[O-])C(F)(F)F)[N+](=O)[O-]`	Tomlin 2004
Structure		
	Chemical Properties	
Boiling point	96-97 °C/24 Pa	Tomlin 2004
Henry's Law Const.	15 Pa m^3 mol^{-1}	Tomlin 2004
	1.6×10^{-4} atm-m^3 mol^{-1}	U.S. EPA/OPP 2009a
Hydrolysis	Stable at pH 5, pH 7, pH 9	U.S. EPA/OPP 2009a
	≅1030 days at 22°C, pH 7.1	Ramesh and Balasubramanian 1999
Kow	≅67,600 [Log = 4.83 (20 °C)]	Tomlin 2004
	1,000 [Log = 3]	Bacci et al. 1990; Brown and Lean 1995
	≅126,000 [Log = 5.1]	Brand and Mueller 2002
	≅186,000 [Log = 5.27]	U.S. EPA/OPP 2009a
	≅219,000 [Log = 5.34]	Connell and Schueuermann 1988
Melting Point	48.5-49 °C	Tomlin 2004
	42-49 °C	U.S. EPA/OPP 2009a
Molecular formula	$C_{13}H_{16}F_3N_3O_4$	Tomlin 2004
Molecular weight	335.3 g/mole	Tomlin 2004
	335.28 g/mole	U.S. EPA/OPP 2009a
pH		
Specific gravity	1.36 (22 °C)	Tomlin 2004
Vapor pressure	6.1 mPa (25 °C) [≅4.6×10^{-5} torr]	Tomlin 2004
	1.10×10^{-4} torr	U.S. EPA/OPP 2009a
	1.07×10^{-4} torr	Glotfelty et al. 1984
Water solubility	pH 5: 0.184 mg/L pH 7: 0.221 mg/L pH 9: 0.189 mg/L	Tomlin 2004
	0.3 mg/L	U.S. EPA/OPP 2009a
	Environmental Properties	
Bioconcentration Factor	Bluegill sunfish Edible tissue: 2041 Non-edible tissue: 9586 Whole fish: 5674	U.S. EPA/OPP 2009a, MRID 40673801
	≅5750 [Log 3.76]	Mackay 1982; Connell and Schueuermann 1988
	2280 (whole fish)	Schultz and Hayton 1993

Table 1: Chemical and Physical Properties of Trifluralin

Property	Value	Reference
	2090 to 6520 after 96 hours	Schultz and Hayton 1994
	419 to 15,506 (see discussion in Section 3.2.3.5)	Schultz and Hayton 1999
	1800 to 5800	Spacie and Hamelink 1979
Field dissipation	Half-lives of 29 to 149 days	U.S. EPA/OPP 2009a, MRIDs 41781901, 41661101, 42309101
	About 8 weeks for trifluralin. About 5 months for total C^{14}	Golab et al. 1979
	Half-lives of about 27 days	Duseja et al. 1980
	63 to 164 days	Grover et al. 1997
	54.7 days	Kim and Feagley 2002a
	94 to 129 days	Smith et al. 1988
Kd/Koc	Soil Type / Kd (L/kg) / Koc (g/mL) Sand 18.6 6,413 Sandy loam 54.8 6,748 Loam 88.3 8,457 Clay loam 155.6 13,413 Average 8,757.9	U.S. EPA/OPP 2009a, MRID 40673501
Kd	20.7 to 46.8	Mamy et al. 2008
	3.75 to 639	Pedersen et al. 1995
Koc	Mean values of 810 to 30,550	Grover et al. 1997
	875.1	Kim and Feagley 1998
	7000	Larney et al. 1999
	5542	Smith et al. 1997
	45,000 to 48,889	Tavares and Rezende 1998
	8,757.9	U.S. EPA/OPP 2009a
	Range: 6,413.3 to 13,413 90% Conf. Interval: 4,958 to 12,557	
Soil half-life, aerobic	189, 201, and 116 days	U.S. EPA/OPP 2009a, MRID 41240501
	Mean and 90% CI: 169 (91 to 246)	
	≅24 to 194 days (k_e's of 0.00357 to 0.0289 $days^{-1}$) for complete mineralization.	Farenhorst 2007
	217 days (disinfected soil/sterilization) 54 to 56 days (no disinfection)	Fenoll Serrano et al. 2010
	172 to 475 days at 10°C 58 to 108 days at 20°C 41 to 73 days at 30°C Also, more persistent in dry soils. See Section 3.2.3.4.3 for discussion.	Jolley and Johnstone
	14.2 to 25.2 days	Mamy et al. 2005
	12.9 to 27 days	Yen et al. 2008
Soil volatilization half-life	1 to 11 hours depending on wind speed, humidity, and temperature	Grass et al. 1994
Field dissipation half-life	45 days	Larney et al. 1999
	10 to 11 months (lysimeter)	Malterre et al. 1997
	41 to 475 days (shorter half-lives at higher temperature.	Jolly and John 1994
Water, Aquatic sediment half-life	Very persistent (over 1 year) due to strong sediment binding.	Greenberg et al. 2005

Table 1: Chemical and Physical Properties of Trifluralin

Property	Value	Reference
Water, Aerobic aquatic metabolism half-life	438 days: Estimated as 2x aerobic soil metabolism	U.S. EPA/OPP 2009a, Table 3.2
Water, Aqueous photolysis half-life	0.371 days	U.S. EPA/OPP 2009a, MRID 40560101
	≅0.18 days (4.4 hours)	Tagle et al. 2005
Water, metabolism anaerobic, half-life	29.5 days [59 days x 0.5, anaerobic soil half-life]	U.S. EPA/OPP 2009a, Table 3.2
Water, Aqueous dissipation half-life	0.6 to 3.2 days (mesocosm)	Laabs et al. 2007
Water, Volatilization half-life	0.5115 days (River, 1 meter deep) 11.98 days (Lake, 1 meter deep)	U.S. EPA/OPPTS 2011 (QSAR from EPI Suite)

Table 2: Representative Trifluralin Formulations

Formulation, Supplier	Composition	Application Information
Liquid Formulations (likely to be used in Forest Service programs)		
Treflan 4D, Dintec Agrichemicals, EPA No. 68156-4	Trifluralin, 43% a.i. (w/w) Liquid 4 lb a.i./gallon Petroleum distillates including naphthalene (specified as 7% in Treflan 4D).	Maximum Application Rate: 2 lb a.i./acre. Maximum rate recommended for fine soil textures. Ground or aerial broadcast 5 to 40 gallons per acre (ground) 5 to 10 gallons per acre (aerial) Specifically labeled for cottonwood trees grown for pulp.
Triflurex HFP Makhteshim Agan of NA EPA No. 66222-46	Trifluralin, 42.78 % a.i. (w/w) Liquid 4 lb a.i./gallon Aromatic hydrocarbons (49.2% w/w) Naphthalene (7 % w/w)	Maximum Application Rate: 2 lb a.i./acre. Maximum rate recommended for fine soil textures. Cumulative Annual Maximum Application rate: 4 lb a.i./acre. Ground or aerial broadcast 5 to 40 gallons per acre (ground) 5 to 10 gallons per acre (aerial) Specifically labeled for trees grown for pulp.
Granular Formulations (not likely to be used in Forest Service programs)		
Treflan 5G [1], United Horticultural Supply EPA No. 62719-98-65783	Trifluralin, 5% a.i. (w/w) Granular Kerosene, 2.8% (w/w)	Maximum Application Rate: 240 lbs formulation/acre per year (12 lb a.i./acre)[2] Ground application (rotary spreader). Not labeled for aerial application. Specifically labeled for use in Christmas tree plantations.
Treflan TR-10, Dow AgroSciences, EPA No. 62719-131	Trifluralin, 10% a.i. (w/w) Granular Clay (90%), including crystalline silica	Maximum Single and Cumulative Annual Application Rate: 2 lb a.i./acre. Labeled for ground or aerial broadcast applications.

[1] Identified with Forest Service use Fact Sheet from Information Ventures (1995).
[2] Up to 320 lb formulation/acre (16 lb a.i./acre) permitted under paved surfaces.

See Section 2.2 for discussion.

Table 3: Estimates of Dermal Permeability (Kp) from Brand and Mueller (2002)

Material	Log Kp, cm/s	Kp cm/s	Kp cm/hour
Trifluralin, 1:10	-7.11	7.7625E-08	0.000279
Trifluralin, 1:40	-7.44	3.6308E-08	0.000131
Treflan 1:10	-6.55	2.8184E-07	0.001015
Treflan 1:40	-7.02	9.5499E-08	0.000344

Log Kp values from Brand and Mueller, 2002, Table 2, p.20
See Section 3.1.3.2.2 for discussion.

Table 4: Tissue Residues in Rats During Chronic Study

Organ/ Tissue, *LOD*	Months	Dose Level (ppm or mg/kg diet)							
		Males				Females			
		0	200	800	3200	0	200	800	3200
Liver	6	<0.01	ND	ND	0.05	<0.01	ND	0.04	0.8
0.04 ppm	12	<0.01	0.04	ND	0.07	<0.03	ND	0.04	1.6
	18	<0.02	ND	ND	ND	<0.01	ND	0.04	0.3
	24				0.01				0.5
Kidney	6	<0.01	ND	0.1	7.5	<0.03	0.07	0.3	5.5
0.06 ppm	12	<0.02	ND	0.7	3.4	<0.04	ND	0.2	8.4
	18	<0.03	ND	0.2	0.6	<0.04	0.06	0.08	2.5
	24	<0.01	ND	0.06	0.4	<0.01	ND	0.3	1.7
Heart	6	<0.02	ND	ND	0.9	<0.03	ND	ND	2.9
0.06 ppm	12	<0.02	ND	ND	0.7	<0.02	ND	0.2	3.3
	18	<0.03	ND	ND	1.6	<0.02	ND	0.2	0.7
	24	<0.01	ND	<0.04	0.9	<0.01	ND	0.2	1.6
Spleen	6	<0.04	ND	ND	0.4	<0.05	ND	0.8	ND
0.09 ppm	12	<0.03	ND	ND	0.2	<0.06	ND	0.2	0.7
	18	<0.05	ND	ND	0.3	<0.04	ND	ND	1.5
	24	<0.01	ND	ND	0.3	<0.01	ND	0.1	1.4
Brain	6	<0.01	ND	ND	0.1	<0.01	ND	0.02	1.0
0.01 ppm	12	<0.01	ND	0.02	0.2	<0.01	ND	0.02	1.0
	18	<0.01	ND	0.02	0.05	<0.01	ND	0.02	0.06
	24	<0.01	ND	0.01	0.08	<0.01	0.01	0.06	0.3
Intestine	6	<0.02	0.04	0.9	11	<0.01	0.04	2.8	18
0.03 ppm	12	<0.01	0.03	1.8	8.2	<0.01	0.03	2.5	14
	18	<0.02	ND	0.9	19	<0.01	ND	2.6	32
	24	<0.01	0.08	2.2	9.1	<0.01	0.3	3.3	27
Fat	6	<0.02	0.1	1.7	45	<0.03	0.1	16	190
0.04 ppm	12	<0.01	ND	2.2	23	<0.01	0.07	6.9	100
	18	<0.01	0.1	3.4	10	<0.02	0.2	4.1	140
	24	<0.02	ND	1.9	51	<0.01	0.1	20	190
Muscle	6	<0.04	ND	0.2	0.9	<0.03	ND	0.3	8.6
0.06 ppm	12	<0.02	ND	ND	0.1	<0.03	ND	0.1	0.5
	18	<0.03	ND	ND	0.1	<0.02	ND	ND	7.8
	24	<0.01	ND	0.1	0.4	<0.01	<0.08	0.6	1.4
Blood	6	<0.01	ND		0.01	<0.01	ND	ND	0.04
0.01 ppm	12		ND	ND	0.02	<0.01	ND	ND	0.07
	18	<0.01	ND	ND	ND	<0.01	ND		0.06
	24	<0.01	ND	0.1	0.9	<0.01	ND	0.03	0.2
Carcass	6	<0.01	0.01	ND	0.4	<0.01	ND	0.2	3.0
0.01 ppm	12	<0.01	0.01	0.2	0.5	<0.01	ND	0.3	0.6
	18	<0.01	ND	0.3	1.4	<0.01	0.05	0.3	9.3
	24	<0.01	0.02	0.3	6.3	<0.01	ND	1.5	22

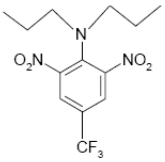
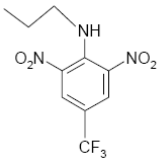
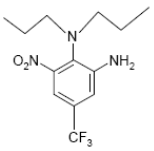
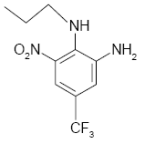
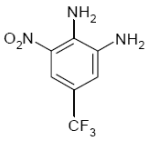
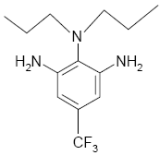
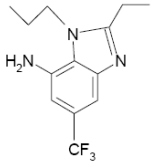
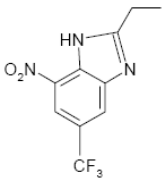
Data from Schutz and Donaubauer (1986)
See Section 3.1.3.1 for discussion.

Table 5: Summary of Developmental and Reproductive Studies

Developmental/Teratology Studies				
Species	**Doses (mg/kg bw/day)**		**Endpoint**	**Reference**
	NOAEL	**LOAEL**		
Mice		1000	Maternal and fetal mortality	Beck 1981
Rats	225 475	475 1000	Maternal, body weight Offspring, body weight	MRID 00152419 in U.S. EPA/OPP 1996a
Rats	**100**[1]	500	Maternal and fetal, signs of toxicity, delayed ossification, and wavy ribs.	MRID 00151899 in U.S. EPA/OPP 2003a,b
Rats	225 475	475 1000	Maternal: body weight Offspring: body weight	Byrd et al. 1995
Rabbits	100	225	Maternal and fetal, abortions	MRID 00152421 in U.S. EPA/OPP 1996a
Rabbits	100 225	225 500	Maternal, body weight Offspring, mortality	Byrd and Markham 1990; Byrd et al. 1995
Multigeneration Reproduction Studies				
Species	**Dietary Concentration (ppm)**		**Endpoint**	**Reference**
	NOAEL	**LOAEL**		
Rats	200	630	Decreased parental body weight. No reproductive effects	MRID 00162543 in U.S. EPA/OPP 1996a
Rats	200	650	Parental: kidney weights Offspring: reduced litter size.	Becker 1984
Rats	450	4000	Parental: decreased body weight gain, decreased ovarian weights Offspring: decreased implantation sites, litter size, and body weights.	MRID 40405007 in U.S. EPA/OPP 2003a,b.

[1] Basis for acute RfD

Table 6: Identity and Structure of Trifluralin and Metabolites

Chemical Name Toxicity summary	EPA [1] Designation	Structure
2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl) benzenamine (Trifluralin)	Parent	
2,6-dinitro-Npropyl-4-trifluromethylbenzenamine	TR-2	
α,α,α-trifluoro-5-nitro-N4,N4-dipropyl-toluene-3,4-diamine Relatively nontoxic to midge larvae (Appendix 5, Table 2). Less toxic than trifluralin to earthworms based on NOAECs (see Section 4.1.2.4)	TR-4	
α,α,α-trifluoro-5-nitro- propyltoluene-3,4-diamine	TR-5	
5-trifluoromethyl-3-nitro-1,2-benzenediamine Less toxic than trifluralin to trout by factors of 6.5 to 24. Less toxic than trifluralin to daphnids by factors of about 5.6 to 14. Less toxic to algae by factors of 8 to 61.	TR-6	
α,α,α -trifluoro-N4,N4-dipropyltoluene-3,4,5-triamine	TR-7	
7-amino-2-ethyl-1-propyl-5-(trifluoromethyl) benzimidazoles	TR-14	
2-ethyl-7-nitro-5-trifluromethylbenzimidazole Less toxic than trifluralin to trout by factors of 40 to 147. Less toxic than trifluralin to daphnids by factors of about 14 to 35. Less toxic to algae by factors of 10 to 76.	TR-15	

[1] Structure designation used in U.S. EPA (2009a).

Source: Modified from U.S. EPA/OPP (2009a), Appendix B, Table A.1.
See Section 3.1.15.1 for discussion.

Table 7: Summary of Worker Exposure Rates

Worker Group/ Application Method	Absorbed Dose Rate (mg/kg bw/day per lb applied)		
	Central	Lower	Upper
Standard Rates in Forest Service Risk Assessments			
Directed foliar	0.003	0.0003	0.01
Broadcast foliar	0.0002	0.00001	0.0009
Aerial	0.00003	0.000001	0.0001
Rates in U.S. EPA/OPP Risk Assessment of Trifluralin[1]			
Groundboom applications	$3.1x10^{-7}$		

[1] U.S. EPA/OPP 1996a, Table 1, p. 28. Ground applicator exposures, EPA Scenario VI, 0.000049 mg/kg day at an application rate of 2 lb/acre, treating 80 acres – i.e., the worker handles 160 lbs. 0.000049 mg/kg day ÷ 160 lbs a.i. = 3.06×10^{-7} mg/kg bw per lb a.i. handled.

See Section 3.2.2.1 for discussion.

Table 8: Site Characteristics and Parameters Used in Gleams-Driver Modeling

Field Characteristics	Description	Pond Characteristics	Description
Type of site and surface	Agricultural field	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 (except 0.05 for sand)	Minimum Depth	1 meter
Depth of root zone	36 inches	Maximum Depth	3 meters
Cover factor	0.15	Sediment Depth	2 centimeters
Type of clay	Mixed		
Application Date	May 1		
Surface cover	No surface depressions (plowed field)		

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

GLEAMS Crop Cover Parameters[3]	Description	Value
ICROP	Sunflowers	64
CRPHTX	Maximum height in feet.	6
DPLANT	Julian day for starting growth	140 [May 21]
DHRVST	Julian day for ending growth	290 [Oct 18]

Application, Field, and Soil Specific Factors [1]	Code[3]	Clay	Loam	Sand
Proportion applied to soil:	SOLFRC	0.99	0.99	0.99
Proportion applied to foliage:	FOLFRC	0.01	0.01	0.01
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
No. overland flow profile segments:	XFACT	1	1	1
Soil loss ratio:	CFACT	0.85	0.85	0.85
Contouring factor for overland flow profile:	PFACT	1.0	1.0	1.0
Manning's "n":	NFACT	0.01	0.01	0.01

[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 5 months before the pesticide is applied in mid-Spring.

[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 9: Precipitation, Temperature and Classifications for Standard Test Sites

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

[1] Based on composite estimation in WEPP using a latitude of 47.94 N and a longitude of -124.54 W. See SERA (2007b) for details.

Table 10: Chemical parameters used in GLEAMS modeling

Parameter	Clay	Loam	Sand	Note/Reference
Halftimes (days)				
Aquatic Sediment	730			Note 1
Foliar	3			Note 2
Soil	169 (91 to 246)			Note 3
Water	0.6 (0.4 to 3.2)			Note 4
Soil $K_{o/c}$, mL/g	8,758 (4,958 to 12,557)			Note 5
Sediment K_d, mL/g	155.6	88.3	18.6	Note 5
Water Solubility, mg/L	0.3 mg/L			Note 6
Foliar wash-off fraction	0.4			Note 7
Fraction applied to foliage	0.0			Note 8
Coefficient of Uptake	1			Note 9
Coefficient of Transformation	1			Note 10
Depth of Soil Incorporation	5 cm (≈2 inches)			Note 11

Note 1	The half-time in sediment has not been measured. A value of 2 years is selected based on Greenberg et al.2005 who estimate a half-time in aquatic sediment of over 1 year due to strong binding to sediment.
Note 2	Knisel and Davis 2000. This has minimal impact on model results because of the very low value used to application to foliage.
Note 3	Lower bound based on photolysis from MRID 41240501 as summarized in U.S. EPA/OPP (2009a). The upper bound encompasses the soil half-life for complete mineralization of 217 days from Serrano et al. (2010). Modeled with triangular distribution.
Note 4	Lower bound based on U.S. EPA/OPP 2009a half-life for aqueous photolysis used in PRZM/EXAMS modeling. Central estimate and upper bound based on microcosm simulations for aqueous dissipation half-lives from Laabs et al. (2007) in which the rapid dissipation was attributed primarily to volatilization.
Note 5	Based on values from MRID 41240501 as summarized in U.S. EPA/OPP (2009a). See Table 1 for details. K_{oc}'s modeled with triangular distribution.
Note 6	U.S. EPA/OPP 2009a, Table 3.2
Note 7	Knisel and Davis 2000. This has minimal impact on model results because of the very low value used to application to foliage.
Note 8	Trifluralin is applied to plowed fields. No deposition to plant surfaces is assumed. This is essentially identical to the approach used by U.S. EPA/OPP (2009a) which used an application efficiency of 99%.
Note 9	Plant uptake will occur and this process is central to the efficacy of trifluralin.
Note 10	Extensive soil metabolism is likely but metabolites are not modeled.
Note 11	This is identical to the depth for soil incorporation used by U.S. EPA/OPP (2009a).

Table 11: Summary of Modeled Concentrations in Surface Water

Scenario	Concentrations (ppb or µg/L)	
	Peak	**Long-Term Average**
MODELING FOR THIS RISK ASSESSMENT (µg/L per lb a.i./acre)		
Gleams-Driver		
Soil Incorporation (see Appendix 7 for details)		
Pond, Section 3.2.3.4.4	0.208 (0.004 - 1.36)	0.0074 (0.000025 - 0.04)
Stream, Section 3.2.3.4.4	2.21 (0.02 - 28.4)	0.075 (0.0002 - 0.4)
OTHER MODELING (µg/L per lb a.i./acre)		
PRZM-EXAMS		
Pond, Corn [a]	0.55	0.07 (60 day average)
Pond, Forestry [a]	0.585	0.095 (60 day average)
Monitoring Associated with Specific Applications		
Nebraska Stream [b]	0.11µg/L (maximum conc.) 0.32 µg/L per lb a.i./acre	0.01 µg/L 0.029 µg/L per lb a.i./acre
Other Monitoring Data		
California surface water monitoring database [bc]	1.5 (maximum conc.)	
Canadian streams (CCME 1999)	1.8 (maximum)	
Maas et al. 1995 (North Carolina, rural well water) [cd]	0.42 µg/L (LOD)	
Streams, Vogel and Linard 2011	0.11 µg/L (maximum)	
Sprague and Nowell 2008 (streams)	<0.2 µg/L	
Kim and Feagley 2002a (well water)	0.000026 µg/L(maximum)	
Kim and Feagley 2002b (field runoff water)	0.09 µg/L (maximum)	
U.S. EPA/OPP 1996a (summary for surface waters)	0.73 µg/L (maximum)	
Ryberg et al. 2011, NWAQA data summary [e]	≈0.0045 µg/L (peak)	

[a] U.S. EPA/OPP (2009a), See Section 3.2.3.4.4 for discussion. 2-meter deep farm pond. Forestry scenario at 2 lb a.i./acre with soil incorporation. Values normalized for an application rate of 1 lb a.i./acre. Corn (representative of sunflower fields. 1 lb a.i./acre ground application with soil incorporation.

[b] Based on an average application rate to the watershed of about 0.34 lb a.i./acre . See Section 3.2.3.4.5.1 for discussion.

[c] Monitoring from the California Department of Pesticide Regulations (http://www.cdpr.ca.gov/docs/emon/surfwtr/surfcont.htm) as summarized by U.S. EPA/OPP (2009a).

[d] Found in 1.8% of wells in rural area. Specific concentrations not given but LOD is specified as 0.42 µg/L.

[e] Ryberg et al. 2001, Figure A2-7, p. 58. Visual approximation from graph.

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

(see Section 3.2.3.4.6 for discussion)

Soil Incorporation	Water contamination rate in mg/L per lb/acre applied [a]	
	Peak	Longer-term
Central	0.0006	0.000075
Lower	0.00002	0.0000002
Upper	0.0022	0.0004

[a] 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.

Table 13: Estimated concentration factors from soil to vegetation

Food Item	Concentration in Food Item in ppm (mg/kg vegetation) per ppm in soil (mg/kg soil)		
	Central	Lower	Upper
Soil Concentration Factors			
Short grass [a]	0.0017	0.0011	0.0023
Tall grass [a]	0.0017	0.0011	0.0023
Broadleaf/forage plants [b]	0.081	0.062	0.18
Seeds [c]	0.009	0.0026	0.021

[a] Based on concentration in wheat from Cessna et al. 1988 – i.e., a range of 0.0011 to 0.0023 mg/kg wheat per mg/kg soil. The central value is taken as the average of the bounds of the range.

[b] Based on concentrations in melon leaves from Tiryaki et al. 1997 in upper canopy (lower bound), mid canopy (central estimate), and lower canopy (upper bound)

[c] Based on concentrations in fruit (melons) from Tiryaki et al. 1997: fruit skin (central estimate), fruit flesh (lower bound), and fruit seed (upper bound)

Table 14: Concentrations of Trifluralin in Mellon Tissue Following Soil Incorporation

Soil Depth	Soil ppm	
0 to 7.5 cm	0.951	
7.5 to 15 cm	0.609	
0 to 15 cm	0.780	
Plant Tissue	**Plant Tissue (ppm)**	**BCF (soil average)**
Hairy Root	1.073	1.3756
Tap Root	0.901	1.1551
Leaves, Lower	0.138	0.1769
Leaves , Mid	0.063	0.0808
Leaves, Upper	0.048	0.0615
Leaves Average	0.083	0.1064
Fruit, skin	0.007	0.0090
Fruit, flesh	0.002	0.0026
Fruit , seed	0.016	0.0205

Data from Tiryaki et al. 1997, Table 2, p. 754.
See Section 3.2.3.6 for discussion.

Table 15: Summary of Toxicity Values Used in Human Health Risk Assessment			
Duration	**Derivation of RfD**	**Reference**	**Comment**
Acute – single exposure			
NOAEL Dose	100 mg/kg bw/day	MRIDs 00151899, 00159620 and 40392310	See Section 3.3.2.
LOAEL Dose	500 mg/kg bw/day		
LOAEL Endpoint(s)	frank signs of toxicity in dams as well as increases in liver and spleen weight.		
Species, sex	Female		
Uncertainty Factor	100	U.S. EPA/OPP 2004a	
RfD	1 mg/kg bw/day		
Chronic – lifetime exposure			
NOAEL Dose	2.4 mg/kg bw/day	Adams et al. 1992, MIRD 42447001	See Section 3.3.3.
LOAEL Dose	40 mg/kg bw/day		
Species, sex	Dose, male and female		
LOAEL Endpoint(s)	decreased body weight and increased in liver and heart weight, changes in clinical chemistries.		
Uncertainty Factor	100	U.S. EPA/OPP 2004a	
RfD	0.024 mg/kg bw/day		
Carcinogenicity – lifetime exposures			
Cancer Potency Factor	0.0058 $(mg/kg\ bw/day)^{-1}$	MRID 00044337	See Section 3.3.5.
Dose Associated with a 1 in 1-millon risk	0.0017 mg/kg bw/day		
Species, sex	Rats, males and females		

Table 16: Summary of Risk Characterization for Workers

Application Rate:	1	lb a.i./acre			
Scenario	Endpoint	Hazard Quotients			Toxicity Value (mg/kg bw/day)
		Central	Lower	Upper	
Accidental/Incidental Exposures					
Contaminated Gloves, 1 min.	Toxicity	2E-03	6E-04	5E-03	**1**
Contaminated Gloves, 1 hour	Toxicity	0.1	4E-02	0.3	**1**
Spill on Hands, 1 hour	Toxicity	2E-03	4E-04	4E-03	**1**
Spill on lower legs, 1 hour	Toxicity	4E-03	9E-04	1E-02	**1**
General Exposures					
	Toxicity	1E-03	9E-04	2E-03	**0.024**
	Cancer	0.2	0.1	0.3	**0.00017**

Source: Worksheets E02 (toxicity) and E05 (carcinogenicity) in Attachment 1.
See Section 3.4.2 for discussion.

Table 17: Summary of Risk Characterization for the General Public

Application Rate:	1	lb a.i./acre			
Scenario	Receptor	Hazard Quotients			Toxicity Value (mg/kg bw/day)
		Central	Lower	Upper	
Accidental Acute Exposures (dose in mg/kg/event)					
Direct Spray of Child, whole body	Child	No exposure assessment.			
Direct Spray of Woman, feet and lower legs	Adult Female	No exposure assessment.			
Water consumption (spill)	Child	0.3	1E-02	**2**	**1**
Fish consumption (spill)	Adult Male	**21**	**1.0**	**84**	**1**
Fish consumption (spill)	Subsistence Populations	**102**	**5**	**408**	**1**
Non-Accidental Acute Exposures (dose in mg/kg/event)					
Vegetation Contact, shorts and T-shirt	Adult Female	No exposure assessment.			
Contaminated Sunflower Seeds	Adult Female	1E-05	7E-06	3E-05	**1**
Other Contaminated Vegetation	Adult Female	No exposure assessment.			
Swimming, one hour	Adult Female	2E-07	5E-09	6E-07	**1**
Water consumption	Child	5E-05	9E-07	2E-04	**1**
Fish consumption	Adult Male	3E-03	9E-05	1E-02	**1**
Fish consumption	Subsistence Populations	1E-02	4E-04	5E-02	**1**
Toxicity: Chronic/Longer Term Exposures (dose in mg/kg/day)					
Contaminated Fruit	Adult Female	No exposure assessment.			
Contaminated Vegetation	Adult Female	No exposure assessment.			
Water consumption	Adult Male	9E-05	2E-07	6E-04	**0.024**
Fish consumption	Adult Male	9E-04	2E-06	5E-03	**0.024**
Fish consumption	Subsistence Populations	7E-03	2E-05	4E-02	**0.024**
Carcinogenicity: Chronic/Longer Term Exposures (dose in mg/kg/day)					
Water consumption	Adult Male	1E-02	2E-05	8E-02	**0.00017**
Fish consumption	Adult Male	0.1	3E-04	0.7	**0.00017**
Fish consumption	Subsistence Populations	0.9	2E-03	**6**	**0.00017**

Source: Worksheets E04 (toxicity) and E05 (carcinogenicity) in Attachment 1.
See Section 3.4.3 for discussion.

Table 18: Fish, Summary of Acute Toxicity Data

Studies sorted by lowest to highest LC_{50}.

Species	Family	96 hour-LC_{50}	Reference
Bluegill sunfish [23.9 °C]	Centrarchidae	18.5	MRID 40098001
Rainbow trout [12 °C]	Salmonidae	41	Johnson and Finley 1980
Rainbow trout [12.7 °C]	Salmonidae	42	Macek et al. 1969
Rainbow trout	Salmonidae	43.6	MRID 40098001
Carp [20°C]	Cyprinidae	45	Poleksic and Karan 1999
Bluegill sunfish [23.8°C]	Centrarchidae	47	Macek et al. 1969
Bluegill sunfish	Centrarchidae	58	Johnson and Finley 1980
Bluegill sunfish [24°C]	Centrarchidae	68	Cope 1965
Largemouth bass	Centrarchidae	75	MRID 40094602
Rainbow trout [13°C]	Salmonidae	86	Cope 1965
Fathead minnow [18°C]	Cyprinidae	105	Johnson and Finley 1980
Bluegill sunfish [18.3°C]	Centrarchidae	120	Macek et al. 1969
Goldfish	Cyprinidae	145	MRID 40094602
Rainbow trout [7.2°C]	Salmonidae	152	Macek et al. 1969
Bluegill sunfish [12.7°C]	Centrarchidae	190	Macek et al. 1969
Rainbow trout [1.6°C]	Salmonidae	210	Macek et al. 1969
Bunni Fish [21 to 26 °C]	Cyprinidae	250	Mansour and Mohsen 1985
Channel catfish [22°C]	Ictaluridae	417	McCorkle et al. 1977
Carp [21 to 26 °C]	Cyprinidae	660	Mansour and Mohsen 1985
Mosquitofish [Sensitive]	Poeciliidae	2000	Fabacher and Chambers 1974
Channel catfish [22°C]	Ictaluridae	2200	Johnson and Finley 1980
Mosquitofish [Tolerant]	Poeciliidae	4100	Fabacher and Chambers 1974
Mosquitofish	Poeciliidae	12000	Naqvi and Leung 1983

See Figure 7 for illustration of data and Appendix 4 for additional details.
See Section 4.1.3.1 for discussion.

Table 19: Amphibians, Summary of Acute Toxicity Data

Species	Test Conditions	96-hour LC_{50} (µg/L)	Reference
Bufo woodhousii fouileri	Tadpoles, 15.5 °C	100 (0.08 to 0.49)	Sanders 1970
Bufo woodhousii fouileri	Tadpoles, 60.0°F[15.6 °C]	116.15	U.S. EPA/OPP 2009a, Appendix H, p. H-212
Bufo woodhousii fouileri	Tadpoles, 60.0°F[15.6 °C]	115.04 (62.0-151.0)	

Table 20: Freshwater Arthropods, Summary of Acute Toxicity Data

Studies sort by lowest to highest toxicity values.

Organism/Species	Order	Temp. °C	EC_{50}/ LC_{50} [1]	Reference
Daphnia magna	Cladocera	≈19	251	Kirk et al. 1999
Daphnia magna	Cladocera	24.5	312.42	George and Liber 2007
Daphnia magna	Cladocera	21	560	Johnson and Finley 1980
Daphnia pulex	Cladocera	15	625	Johnson and Finley 1980
Simocephalus sp.	Diplostraca/ Cladocera	15	900	Johnson and Finley 1980
Alonella sp	Cladocera	20	1300	Naqvi et al. 1985
Cyclops, *Eucyclops* sp	Cyclopoida	20	1300	Naqvi et al. 1985
Cypria sp	Ostracoda	20	1500	Naqvi et al. 1985
Diaptomus sp.	Calanoida	20	1900	Naqvi et al. 1985
Scud, *Gammarus fasciatus*	Amphipoda	21	2200	Johnson and Finley 1980
Stonefly, *Pteronarcys* sp	Plecoptera	15	2800	Johnson and Finley 1980
Crayfish, *Procambarus clarkii*[Juv.]	Decapoda	≈24	12000	Naqvi and Leung 1983
Procambarus clarkii[Juv.]	Decapoda	24	12100	Naqvi et al. 1987
Procambarus clarkii[Adult]	Decapoda	24	26000	Naqvi et al. 1987

[1] Duration for studies ranged from 48 to 96 hours. LC_{50}s for larger arthropods and EC_{50}s for immobility for smaller arthropods.

See Figure 9 for illustration of data and Appendix 5 for additional details.
See Section 4.1.3.3 for discussion.

Table 21: Acute Toxicity to Aquatic Plants

Species	Duration	Material	EC_{50} µg/L	Reference
Algae				
Scenedesmus vacuolatus	1 day	Tech.	24.3	Schmitt et al. 2000
Skeletonema costatum	5 days	Tech.	28	Hughes and Williams 1993c
Navicula pelliculosa	5 days	Tech.	37.9	Hughes and Williams 1993b
Selenastrum capricornutum	7 days	Tech.	88.7	Adams and Cocke 1990
Selenastrum capricornutum	4 days	Tech.	673	Fairchild et al. 1997
Chlorella pyrenoidosa	4 days	EC Form.	1813.4	Ma and Liang 2001
Scenedesmus obliquus	4 days	EC Form.	1813.4	Ma and Liang 2001
Chlorella vulgaris	4 days	EC Form.	4346.9	Ma et al. 2002
Macrophytes				
Lemna gibba	14 days	Tech.	49.7	Milazzo et al. 1993
Lemna minor	4 days	Tech.	170	Fairchild et al. 1997

Table 22: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

Animal	Representative Species	W[4]	Food Consumption[5]	Water Consumption	Other
MAMMALS[1]					
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]		
Canid	Fox	5,000	$0.6167\ W^{0.862}$ [Eq 3-47]		
Large Herbivorous Mammal	Deer	70,000	$1.518\ W^{0.73}$ [Eq 3-46]		
Large Carnivorous Mammal	Bear	70,000	$0.6167\ W^{0.862}$ [Eq 3-47]		
BIRDS[2]					
Small bird	Passerines	10	$2.123\ W^{0.749}$ [Eq 3-36]	$0.059\ W^{0.67}$ [Eq 3-17]	
Predatory bird	Owls	640	$1.146\ W^{0.749}$ [Eq 3-37]		
Piscivorous bird	Herons	2,400	$1.916\ W^{0.704}$ [Eq 3-38]		
Large herbivorous bird	Geese	4,000	$1.146\ W^{0.749}$ [Eq 3-37]		
INVERTEBRATES[3]					
Honey bee	*Apis mellifera*	0.000116	≈2 (1.2 to 4)[6]	Not used	SA[7]: 1.42 cm^2
Herbivorous Insects	Various	Not used	1.3 (0.6 to 2.2)	Not used	

[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] 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 4.2.2.3. and 4.2.2.3 for discussion.

Table 23: Diets: Metabolizable Energy of Various Food Commodities

Note: Only seeds and vegetation are explicitly considered for trifluralin.

Food Item	Animal Group	Caloric Value [1] (kcal/g dw)	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	
Seeds	Mammals	4.92	0.093	Water content for dicot seeds taken from U.S. EPA/OPP 1993, Table 4-2, p. 4-14.
	Birds	4.92	0.093	
Vegetation (NOS)	Mammals	2.26	0.85	
	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 dw (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 dw (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 dw x 0.51 ≈ 1.1 kcal/g dw]

[5] Based on a gross caloric value of 4.2 kcal/g dw for dicot leaves (U.S. EPA/ORD 1993, Table 4-2) and an assimilation factor for the consumption leaves by birds of 47% [4.2 kcal/g dw x 0.47 = 1.974 kcal/g dw]

Table 24: Summary of toxicity values used in ecological risk assessment

Group/Duration Organism		Endpoint	Toxicity Values (a.i.)	Reference
Terrestrial Animals				
Acute				
Mammals (all)		Developmental NOAEL	100 mg/kg bw	Section 4.3.2.1.
Birds		Acute dietary NOAEL	750 mg/kg bw	Section 4.3.2.2
Herbivorous Insects		>LD_{50} in Honey Bee	430 mg/kg bw	Section 4.3.2.4.1
Longer-term				
Mammals (all)		Chronic NOAEL	2.4 mg/kg bw/day	Section 4.3.2.1
Bird		Reproductive NOAEL	32 mg/kg/bw/day	Section 4.3.2.2.
Terrestrial Plants				
Vegetative Vigor	Sensitive	NOAEC (monocots)	0.125 lb/acre	Section 4.3.2.5
	Tolerant	NOAEC (dicots)	0.5 lb/acre	
Seedling Emergence	Sensitive	NOAEC (monocots)	0.06 lb/acre	Section 4.3.2.5
	Tolerant	NOAEC (dicots, sunflowers)	2.0 lb/acre	
Aquatic Animals				
Acute				
Amphibians	Sensitive	No data	No data	Section 4.3.3.2
	Tolerant	LC_{50} of 0.1 mg/L ÷ 20	0.005 mg/L	
Fish	Sensitive	Used chronic values	0.0013 mg/L	Section 4.3.3.1
	Tolerant	LC_{50} of 2.2 mg/L ÷ 20	0.11 mg/L	
Invertebrates	Sensitive	EC_{50} of 0.25 mg/L ÷ 20	0.013 mg/L	Section 4.3.3.3
	Tolerant	LC_{50} of 26 mg/L ÷ 20	1.3 mg/L	
Longer-term				
Amphibians	Sensitive	No data	No data	Section 4.3.3.2
	Tolerant	No data	No data	
Fish	Sensitive	Chronic NOAEC	0.0013 mg/L	Section 4.3.3.1
	Tolerant	Egg-to-fry NOAEC	0.0027 mg/L	
Invertebrates	Sensitive	Chronic NOAEC	0.0024 mg/L	Section 4.3.3.3
	Tolerant	Chronic NOAEC	0.05 mg/L	
Aquatic Plants				
Algae	Sensitive	Experimental NOAEC	0.0046 mg/L	Section 4.3.3.4.1
	Tolerant	Experimental NOAEC	0.089 mg/L	
Macrophytes	Sensitive	EC_{50} of 0.0497 mg/L÷ 20	0.0025 mg/L	Section 4.3.3.4.2
	Tolerant	Experimental NOAEC	0.075 mg/L	

Table 25: Risk Characterization for Aquatic Organisms at 1 lb a.i./acre

Exposures	Concentrations (mg/L)			
Scenario	**Central**	**Lower**	**Upper**	**Worksheet**
Accidental Spill	4.542	0.2271	18.168	B04b
Peak EEC	0.0006	0.00002	0.0022	B04a
Chronic	0.000075	0.0000002	0.0004	B04a

Receptor	Type	Hazard Quotients			Toxicity Value	Toxicity Endpoint
		Central	Lower	Upper		
Accidental Acute Exposures						
Fish	Sensitive	**3,494**	**175**	**13,975**	**0.0013**	NOAEC
	Tolerant	**41**	**2**	**165**	**0.11**	NOAEC*
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	**908**	**45**	**3,634**	**0.005**	
Invertebrate	Sensitive	**349**	**17**	**1,398**	**0.013**	NOAEC*
	Tolerant	**3**	0.2	**14**	**1.3**	NOAEC*
Macrophyte	Sensitive	**1,817**	**91**	**7,267**	**0.0025**	NOAEC*
	Tolerant	**61**	**3**	**242**	**0.075**	NOAEC
Algae	Sensitive	**987**	**49**	**3,950**	**0.0046**	NOAEC
	Tolerant	**51**	**3**	**204**	**0.089**	NOAEC
Non-Accidental Acute Exposures						
Fish	Sensitive	0.5	2E-02	**1.7**	**0.0013**	NOAEC
	Tolerant	5E-03	2E-04	2E-02	**0.11**	NOAEC*
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	0.1	4E-03	0.4	**0.005**	NOAEC*
Invertebrate	Sensitive	5E-02	2E-03	0.2	**0.013**	NOAEC*
	Tolerant	5E-04	2E-05	2E-03	**1.3**	NOAEC*
Macrophyte	Sensitive	0.2	8E-03	0.9	**0.0025**	NOAEC*
	Tolerant	8E-03	3E-04	3E-02	**0.075**	NOAEC
Algae	Sensitive	0.1	4E-03	0.5	**0.0046**	NOAEC
	Tolerant	7E-03	2E-04	2E-02	**0.089**	NOAEC
Chronic/Longer Term Exposures						
Fish	Sensitive	6E-02	2E-04	0.3	**0.0013**	NOAEC
	Tolerant	3E-02	7E-05	0.1	**0.0027**	NOAEC
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	No toxicity data.			N/A	
Invertebrate	Sensitive	3E-02	8E-05	0.2	**0.0024**	NOAEC
	Tolerant	2E-03	4E-06	8E-03	**0.05**	NOAEC
Macrophyte	Sensitive	3E-02	8E-05	0.2	**0.0025**	NOAEC*
	Tolerant	1E-03	3E-06	5E-03	**0.075**	NOAEC
Algae	Sensitive	2E-02	4E-05	9E-02	**0.0046**	NOAEC
	Tolerant	8E-04	2E-06	4E-03	**0.089**	NOAEC

Source: Worksheet G03 of the EXCEL Workbook (Attachment 1)
See Section 4.4.3 for discussion.

Table 26: Risk Characterization for Aquatic Organisms at 2 lb a.i./acre

Exposures	Concentrations (mg/L)				
	Scenario	Central	Lower	Upper	Worksheet
	Accidental Spill	9.084	0.4542	36.336	B04b
	Peak EEC	0.0012	0.00004	0.0044	B04a
	Chronic	0.00015	0.0000004	0.0008	B04a

Receptor	Type	Hazard Quotients			Toxicity Value	Toxicity Endpoint
		Central	Lower	Upper		
Accidental Acute Exposures						
Fish	Sensitive	**6,988**	**349**	**27,951**	**0.0013**	NOAEC
	Tolerant	**83**	**4**	**330**	**0.11**	NOAEC*
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	**1,817**	**91**	**7,267**	**0.005**	
Invertebrate	Sensitive	**699**	**35**	**2,795**	**0.013**	NOAEC*
	Tolerant	**7**	0.3	**28**	**1.3**	NOAEC*
Macrophyte	Sensitive	**3,634**	**182**	**14,534**	**0.0025**	NOAEC*
	Tolerant	**121**	**6**	**484**	**0.075**	NOAEC
Algae	Sensitive	**1,975**	**99**	**7,899**	**0.0046**	NOAEC
	Tolerant	**102**	**5**	**408**	**0.089**	NOAEC
Non-Accidental Acute Exposures						
Fish	Sensitive	0.9	3E-02	**3**	**0.0013**	NOAEC
	Tolerant	1E-02	4E-04	4E-02	**0.11**	NOAEC*
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	0.2	8E-03	0.9	**0.005**	NOAEC*
Invertebrate	Sensitive	9E-02	3E-03	0.3	**0.013**	NOAEC*
	Tolerant	9E-04	3E-05	3E-03	**1.3**	NOAEC*
Macrophyte	Sensitive	0.5	2E-02	**1.8**	**0.0025**	NOAEC*
	Tolerant	2E-02	5E-04	6E-02	**0.075**	NOAEC
Algae	Sensitive	0.3	9E-03	1.0	**0.0046**	NOAEC
	Tolerant	1E-02	4E-04	5E-02	**0.089**	NOAEC
Chronic/Longer Term Exposures						
Fish	Sensitive	0.1	3E-04	0.6	**0.0013**	NOAEC
	Tolerant	6E-02	1E-04	0.3	**0.0027**	NOAEC
Amphibian	Sensitive	No toxicity data.			N/A	
	Tolerant	No toxicity data.			N/A	
Invertebrate	Sensitive	6E-02	2E-04	0.3	**0.0024**	NOAEC
	Tolerant	3E-03	8E-06	2E-02	**0.05**	NOAEC
Macrophyte	Sensitive	6E-02	2E-04	0.3	**0.0025**	NOAEC*
	Tolerant	2E-03	5E-06	1E-02	**0.075**	NOAEC
Algae	Sensitive	3E-02	9E-05	0.2	**0.0046**	NOAEC
	Tolerant	2E-03	4E-06	9E-03	**0.089**	NOAEC

Source: Worksheet G03 of the EXCEL Workbook (Attachment 1) modified for 2 lb a.i./acre
See Section 4.4.3 for discussion.

Appendix 1: Toxicity to Mammals

Table A1-1: MSDS Summary of Selected Trifluralin Formulations

Data	Treflan 4D	Treflan HFP	Triflurex HFP	Treflan TR-10	Treflan 5G
Type of Formulation	Liquid	Liquid	Liquid	Granular	Granular
% a.i.	43%	43%	42.78%	10%	5%
Specified Inerts	Naphthalene, 7%	Naphthalene, amount not specified.	Aromatic hydrocarbons (49.2%) Naphthalene (7%)	Clay	Kerosene 2.8%
Specific Gravity	1.117 (literature)	1.12 (approximate)	1.1225	Not applicable.	Not available.
pH	5 (literature, aqueous 50/50)	5 to 8 (aqueous 50/50)	5.59	7.7 (50% aqueous)	7.7 (50% aqueous)
Oral LD_{50} (mg/kg bw)	Rat (M): >5,000 Rat (F): 4,013	Rat: >5,000	Rat: Between 500 and 5,000	Not determined.	Rats: 500
Dermal LD_{50} (mg/kg bw)	Rabbit: >2,000	Rabbit: >5,000	Rat:>5000	Rabbits:>2000	Rabbit: 2000
Inhalation 4-hour LC_{50} (mg/L)	Rats: >7.74	Rats (M): 5.59 Rats (F):>6.05	Rat: > 2.03	May cause irritation.	May cause irritation.
Skin Sensitization:	May cause	May cause	Not a sensitizer	Not a sensitizer	No information on MSDS
Skin Irritation:	May cause	May cause	Moderate	Not likely to cause	May cause
Eyes:	Slight eye irritation and corneal injury.	Moderate. Corneal irritation not likely.	Mild irritation	May cause with corneal injury.	Moderate

See Section 2.1 for a discussion of formulations.

Table A1-2: Acute Oral Toxicity			
Species	**Exposure**	**Response**	**Reference**
Dog, beagle, male and female, 1/dose group	Technical grade trifluralin (≥96.0% purity; N-nitrosodi-n-propylamine <0.4ppm) suspended in sesame oil.	No mortality or clinical signs of toxicity, except diarrhea LD_{50} >10,000 mg/kg bw (male and female)	Ebert et al. 1992
Mouse, NMRI, males and females, 5/dose group	Technical grade trifluralin (≥96.0% purity; N-nitrosodi-n-propylamine <0.4ppm) suspended in sesame oil.	LD_{50} 3150-5000 mg/kg bw (males) 5000 mg/kg bw (females) Minimum lethal dose 5000 mg/kg/bw (males) 3500 mg/kg bw (females)	Ebert et al. 1992
Rat	Technical grade trifluralin (NOS)	LD_{50}>5000 mg/kg –bodyweight No mortality or sublethal effects	MRID 00157486 U.S. EPA-OPP 1996a and 2009a (Appendix F)
Rat, Wistar, males, 5/dose group	Technical grade trifluralin (≥96.0% purity; N-nitrosodi-n-propylamine <0.4ppm based on information in Ebert et al. 1992); suspended in sesame oil.	LD_{50} = 1930 mg/kg bw (males) Minimum lethal dose = 1600 mg/kg/bw (1/10) NOAEC (mortality): 1250 mg/kg bw)	Hollander 1979, MRID 00153164 (males). Also summarized in Ebert et al. 1992
Voles (*Microtus canicaudus* and *Microtus ochrogaster*)	Technical grade	LC_{50} > 5,000 mg/kg bw. No signs of toxicity except depression which during the first day after dosing	Cholakis et al. 1978

Table A1-3: Acute and Subchronic Dermal Toxicity			
Species	**Exposure**	**Response**	**Reference**
ACUTE			
Rat	Dermal LD_{50}	>2000 mg/kg Category III	MRID 00157482 U.S. EPA-OPP 1996a
SUBCHRONIC			
Wistar rats	Dermal applications of trifluralin (technical grade) at 0, 40, 200, or 1000 mg/kg/day for 6 hrs/day for total of 23 applications over 31 days.	No signs of systemic toxicity. NOAE: 1000 mg/kg bw/day. Dermal irritation (sub-epidermal inflammation and ulcerations) at all but the lowest dose.	MRID 00153171 U.S. EPA-OPP 1996a and U.S. EPA/OPP 2003a
Rabbits, New Zealand White, 5 animals/sex/ dose	Technical grade (96.45%) trifluralin at 0 or 1000 mg/kg/day, 6 hours/day for 21 consecutive days.	No signs of systemic toxicity. NOAEL: 1000 mg/kg bw/day. Dermal effects: moderate to severe erythema and slight to moderate edema bleeding skin beginning at 6-12 days.	MRID 00152888, U.S. EPA/OPP 2003a
Rabbits, New Zealand White, 5 animals/sex/ dose	Trifluralin formulation (35.8% a.i.) at doses of 0, 100, 500, or 1000 mg/kg /day for 21 days.	No signs of systemic toxicity. NOAEL: 1000 mg/kg bw/day. Dermal effects: (slight to moderate erythema, edema, and/or scaling and fissuring at all doses.	MRID 41993810, U.S. EPA/OPP 2003a

Table A1-4: Acute and Subchronic Inhalation Studies			
Species	**Exposure**	**Response**	**Reference**
ACUTE			
Rat	Inhalation LC_{50}	>4.66 mg/L (4660 mg/m^3) Category III	MRID 00155261 U.S. EPA/OPP 1996a
SUBCHRONIC			
Rats, Wistar KFM-Han, 15/sex/dose	Trifluralin (99%), nose-only, 100, 300, or 1000 mg/m^3 , 6 hours/day, 5 days/week for up to 30 days (equivalent to 0, 27, 81 and 270 mg/kg/day).	NOAEL: 81 mg/kg/day LOAEL: 270 mg/kg bw/day: Increase in liver weights accompanied by liver pathology. Also an increase methemoglobin and bilirubin in females.	MRID 40392312, 00151904 U.S. EPA/OPP 2003b

Table A1-5: Skin Irritation Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbit	Acute dermal irritation	no irritation Category IV	MRID 00157485 U.S. EPA-OPP 1996a

Table A1-6: Skin Sensitization Studies			
Species	**Exposure**	**Response**	**Reference**
Guinea pig	Dermal sensitization	sensitizer	MRID 00157484 U.S. EPA-OPP 1996a

Table A1-7: Eye Irritation Studies			
Species	**Exposure**	**Response**	**Reference**
Rabbit	Eye irritation	slight irritation Category III	MRID 00157483 U.S. EPA-OPP 1996a

Table A1-8: Developmental Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Charles River rats, females	Gavage doses of trifluralin at 0, 100, 224, 475, or 1000 mg/kg/day on gestation days 6-15.	NOEL (***maternal toxicity***) = 225 mg/kg/day based on decreased weight gain and food consumption at higher doses NOEL (***developmental toxicity***) = 475 mg/kg/day based on decreased mean fetal body weight at 1000 mg/kg/day.	MRID 00152419 U.S. EPA-OPP 1996a
Dutch Belted rabbits, females	Oral (NOS) doses of trifluralin at 0, 100, 225, or 500 mg/kg/day on gestation days 6-28.	NOEL (***maternal toxicity***) = 100 mg/kg/day, based on anorexia, cachexia, and resultant abortion at higher doses. NOEL (***developmental toxicity***) = 225 mg/kg/day based on depressed fetal weight and increased number of fetal runts at higher dose. LOAEL: 225 mg/kg bw/day based on abortions. 500 mg/kg bw/day: hypoplastic thymus in some small offspring from one litter.	MRID 00152421 U.S. EPA-OPP 1996a
Mice, CD-1	1,000 mg/kg bw on Days 6-16 of gestation	Maternal mortality and increase in fetal mortality as well as skeletal abnormalities..	Beck 1981
Rabbits, females (NOS)	Gavage does of 0, 100, 225, 500, or 800 mg/kg trifluralin (NOS) on days 6-18 of gestation, followed by cesarean sections on day 28 of gestation.	NOEL (***maternal toxicity***) = 100 mg/kg, based on abortions and/or deaths in combination with decreased body weight gain and food consumption observed at the 225-, 500-, and 800-mg/kg dose levels. NOEL (***developmental toxicity***) = 225 mg/kg, based on decreased fetal viability and weight 500 mg/kg dose level. No adverse effects on fetal morphology observed at any dose level.	Byrd and Markham 1990 (*This is an abstract of a pilot study; see* ***Byrd et al. 1995*** *below for summary of the definitive developmental toxicity study*)

Table A1-8: Developmental Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Rats, Wistar	Gavage doses of 0, 20, 100, or 500 mg/kg/day on Days 7 to 16 of gestation.	NOAEL (maternal and developmental): 100 mg/kg bw/day. LOAEL (maternal and developmental): 500 mg/kg bw/day based on delayed ossification in offspring as well as increase in early resorptions. In dams, increased mortality and clinical signs of toxicity as well as decreased food consumption, body weight gain, and increased weights of liver and spleen. **Working Note: Study on which the acute RfD is based.**	MRIDs 00151899, 00159620 and 40392310, U.S. EPA/OPP 2003a,b
Dutch Belted rabbits, females, 3.45 ± 0.02 kg at initiation of study, 5 animals/treatment group	Gavage does of 0, 100, 225, or 500 mg/kg trifluralin (Eli Lilly & Co.) suspended in 10% aqueous acacia administered on days 6-18 of gestation, followed by cesarean sections on day 28 of gestation. In-life phase of study 33 days (time from first insemination to last cesarean section).	NOAEL (***maternal toxicity***) = 100 mg/kg, based on abortions and/or deaths in conjunction with anorexia and cachexia (body wasting syndrome) the 225 and 500 mg/kg dose levels. NOAEL (***developmental toxicity***) = 225 mg/kg, based on decreased fetal viability and weight at 500 mg/kg dose level. No adverse effects on fetal morphology observed at any dose level.	Byrd et al. 1995
Rats, females (NOS)	Gavage does of 0, 100, 225, 475, or 1000 mg/kg trifluralin (NOS) on days 6-15 of gestation, followed by cesarean sections on day 20.	NOEL (***maternal toxicity***) = 225 mg/kg, based on decreased body weight gain and food consumption observed at the 475- and 1000-mg/kg dose levels. NOEL (***developmental toxicity***) = 475 mg/kg, based on decreased fetal weight observed at the 1000-mg/kg dose level. No adverse effects on fetal morphology observed at any dose level.	Byrd and Markham 1990 (*This is an abstract of a pilot study; see* ***Byrd et al. 1995*** *below for summary of the definitive developmental toxicity study*)

Table A1-8: Developmental Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
CD rats, females, 3- to 4-mos, 220.8 ± 1.5g at initiation of study, 25 animals/treatment group.	Gavage does of 0, 100, 225, 475, or 1000 mg/kg trifluralin (Eli Lilly & Co.) suspended in 10% aqueous acacia administered on days 6-15 of gestation, followed by cesarean sections on day 20 of gestation. In-life phase of study 26 days (time from first insemination to last cesarean section).	NOAEL (***maternal toxicity***) = 225 mg/kg, based on decreased body weight gain and food consumption observed at the 475- and 1000-mg/kg dose levels. NOEL (***developmental toxicity***) = 475 mg/kg, based on decreased fetal weight observed at the 1000-mg/kg dose level. No adverse effects on fetal morphology observed at any dose level.	Byrd et al. 1995

Table A1-9: Reproductive Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
CD rats, males and females (NOS)	0, 200, 630, or 2000 ppm (15, 47, or 148 mg/kg/day) trifluralin in diet for 2 generations (NOS)	Reproductive NOEL >2000 ppm (i.e., 0.2% in diet). Systemic NOEL = 200 ppm (47 mg/kg/day) Systemic LOEL = 630 ppm (148 mg/kg/day) based on decreased body weight in parental rats.	MRID 00162543 U.S. EPA/OPP 1996a
Wistar KFM-Han rats, males and females (NOS)	0, 200, 650, or 2000 ppm trifluralin in diet for 2 generations (NOS). Food Consumption: DER provides data on mean food consumption (Table 3, p. 9). Slight decrease in food consumption at 2000 ppm in F0 male and female rats in Weeks 1 and 3 (≅15 g/day for females and 21 g/day for males). In general, about 20 to 24 g/day for males and 15 to 19 g/day for females. Body Weights: DER provides data on mean body weights (Table 1, p. 6). Significant decrease in female weight at highest dose -- i.e., terminal weight of 207 g relative to 221 g in controls.	NOEL (***reproductive and developmental toxicity***) = 200 ppm (10 mg/kg/day). LOEL (NOS) = 650 ppm (32.5 mg/kg/day) based on decreased weanling body weights at 650 and 2000 ppm and reduced litter sizes at the highest dose level. LOEL (***parental***) = 200 ppm (10 mg/kg/day based on increased relative kidney weight at all dose levels tested. Renal lesions and increased relative liver weights observed at 650 and 2000 ppm dose levels. Also at 2000 ppm, relative thymus weights were decreased (p<=0.05) 15-16% in the Fl males and females. relative testes weights were increased 8% (each) in both F1 litters. U.S. EPA-OPP 2009a (Appendix F) *Using standard laboratory rat weights, the NOAEC = 200 mg/kg-diet can be converted to a NOAEL = 10 mg/kg-bwt.*	Becker 1984; MRID 00151901 00151902 00151903 Also summarized in U.S. EPA-OPP 1996a and U.S. EPA-OPP 2009a (Appendix F)

Table A1-9: Reproductive Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Rats, CD(CRL) rats (25/sex/dose)	Trifluralin (97.3% a.i.), dietary concentrations of 0, 50, 450, or 4000 ppm. Dose equivalencies: Males: 0, 3.9, 35, 295 mg/kg/day Females: 0, 4.7, 42, 337 mg/kg/day	Endpoints Parental: NOAEL= 450 ppm LOAEL= 4000 ppm, decreased body weights, body weight gains, food consumption, and food efficiency in males and females of both parental generations; decreased ovary weights in both parental generations; colon distension in the F1 males; and uterine atrophy in the females of both generations. Offspring: NOAEL= 450 ppm LOAEL= 4000 ppm, decreased pup weight in F1a litters, decreases in implantation sites and litter size	MRID 40405007, U.S. EPA/OPP 2003a,b. Not cited or summarized in RED or CRLF analyses.

Table A1-10: Subchronic and Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Rats, Fischer 344	0.005, 0.02, 0.08, 0.32, or 0.64% trifluralin in the diet for 90 days	NOEL = 0.005% (50 ppm or 2.5 mg/kg/day) LOEL = 0.2% (10 mg/kg/day) based on increased hyaline droplet formation in cortical cells, increased total protein excretion, and changes in urine color and clarity. Many of the observed effects were reversible during 6-week recovery period.	MRID 40138301 U.S. EPA-OPP 1996a Additional details in Usher 1986.
Rats, Wistar	0, 800, 2000, or 5000 ppm trifluralin in the diet for 90 days	NOEL = 800 ppm (40 mg/kg/day, lowest dose tested), based on decreased relative liver and pituitary gland weights at all dose levels tested.	MRID 00151906 U.S. EPA-OPP 1996a
Beagle dogs, 4 per sex per dose group. BW: ≅6.3 kg males and 5.37 kg females.	Trifluralin (99.8%) by capsule at doses of 0, 0.75, 2.4, or 40 mg/kg/day for 1 year.	NOAEL = 2.4 mg/kg/day LOAEL = 40 mg/kg/day based on decreased body weight; decreased red cells and hemoglobin levels, increased thrombocyte, methemoglobin, cholesterol, and triglyceride levels, and increased liver weight. Decrease in absolute heart weights and the ratio of heart to brain weight. No indication of histopathological changes in heart tissue. **Working Note: Study on which the U.S. EPA/OPP 2004a chronic RfD is based.**	Adams et al. 1992, MIRD 42447001 U.S. EPA-OPP 1996a
Beagle dogs	Dietary doses of 0, 30, 150, or 750 ppm for 1 year. Based on measured food consumption, the dietary concentrations corresponded to 0, 0.75, 3.75, and 18.75 mg/kg/day	NOEL = 30 ppm (0.75 mg/kg/day, LDT) LOEL = 150 ppm (3.75 mg/kg/day) based on increases in liver weight and methemoglobin At 750 ppm, effects included decreased weight gain, decreased RBC, increased methemoglobin, increased serum lipids, triglycerides, and cholesterol. **Working Note: Study on which the early chronic RfD was based (Ghali 1994; U.S. EPA/ORD 1993).**	MRID 00151908, 00159618 U.S. EPA/OPP 1996a and U.S. EPA/OPP 2003a,b, 2004

Table A1-10: Subchronic and Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
Fischer 344 rats, males and females (NOS)	Dietary doses of 0, 813, 3250, or 6500 ppm for 2 years. Equivalent doses of 0, 41, 163 and 325 mg/kg/day.	325 mg/kg/day (HDT) caused significant increases of combined malignant and benign urinary bladder tumors in females. Increased incidence of carcinomas of the renal pelvis observed in males in all dose groups. Increased incidence of thyroid gland follicular cell tumors (adenomas and carcinomas combined) observed in males (dose groups not specified). Carcinogenicity Classification: **Group C**: possible human carcinogen. U.S. EPA/OPP 1996a derived a cancer potency factor of 0.0077 $(mg/kg/day)^{-1}$. A somewhat lower cancer potency factor of 0.00579 $(mg/kg\ bw/day)^{-1}$ is derived by U.S. EPA/OPP 2003b.	MRID 00044337 U.S. EPA/OPP 1996a; U.S. EPA/OPP 2003a
Wistar rats (NOS)	*Presumably* dietary doses of 0, 200, 800, or 3200 ppm.	NOAEL: 200 ppm (≅10 mg/kg bw) LOEL = 800 ppm (40 mg/kg/day) based on decreased body weight. Significant decrease in absolute mean prostate weight in high does males and absolute heart weight in mid- and high-dose females. Significant increase in relative heart weight in males and females considered to be related to decreased body weight and not considered to be compound related.	Schutz and Donaubauer 1986, MRID 00162458 U.S. EPA-OPP 1996a
$B6C3F_1$ mice, males and females (NOS)	Trifluralin (NOS), contaminated with N-nitroso-di-n-propylamine, at 0, 2375, or 5000 ppm for 78 weeks.	N-nitroso-di-n-propylamine (contaminant) considered to be the cause of liver carcinomas, alveolar-bronchiolar adenomas, and squamous-cell carcinomas of the forestomach in the female mice.	U.S. EPA-OPP 1996a summary of Jaeger (1986), not otherwise referenced.
$B6C3F_1$ mice (NOS)	Trifluralin at 0, 563, 2250, or 4500 ppm for 2 years.	No tumors due to test compound.	MRID 00044338 U.S. EPA-OPP 1996a

Table A1-10: Subchronic and Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
NMRI mice	Purified trifluralin (NOS) at 0, 50, 200, or 800 ppm for 2 years.	Systemic NOEL: 50 ppm (7.5 mg/kg/day) in males 200 ppm (30 mg/kg/day) in females Increased liver weights in males at 200 and 800 ppm (30 and 120 mg/kg/day) and at 800 ppm in females. Significant increase in heart/body and heart/brain weight ratios for the 50 ppm males at 104 weeks. Not considered to be compound related. No notation of damage to heart tissue. Note: US EPA/OPP 1996a concludes that mouse carcinogenicity bioassays show that trifluralin did not induce increases in tumor incidence.	Suter et al. 1987, MRID 00158935 40392313 Summarized in U.S. EPA-OPP 1996a and U.S. EPA/OPP 2003b
Osborne-Mendel rats, 50 animals per sex per control and dose groups	Dietary, 8000 and 412S ppm for male rats, 7917 and 4125 ppm for female rats. 78 weeks of dietary exposure with 33 weeks of additional observation. Food consumption data not reported. Note: Summary by U.S. EPA/OPP (2003b) indicates that the test compound was contaminated with dipropylnitrosamine at concentrations of 84 to 88 ppm.	No impact on tumor development. No effect on heart tissue in males. In females, pathologic changes to the myocardium in 2/50 (4%) control animals and 1/12 (8%) females in both the low and high doses. Not significant based on the Fisher Exact test (p=0.481756).	NTP 1978

Table A1-10: Subchronic and Chronic Oral Toxicity Studies			
Species	**Exposure**	**Response**	**Reference**
B6C3F1 Mice, 50 animals per sex per dose group with 20 per sex in controls.	Dietary, 3744 and 2000 ppm for male mice, and 5l92 and 2740 ppm for female mice 78 weeks of dietary exposure with 12 weeks of additional observation. Food consumption data not reported. Note: Summary by U.S. EPA/OPP (2003b) indicates that the test compound was contaminated with dipropylnitrosamine at concentrations of 84 to 88 ppm.	Female Mice: Significant increase in hepatocellular carcinoma (0/20, 12/47, and 21/44 of the control, low dose, and high dose, respectively). Increase in squamous-cell carcinomas of the stomach (rare tumor but response not statistically significant) No pathologic changes noted in circulatory tissue.	NTP 1978

Appendix 2: Toxicity to Birds

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

Species	Exposure	Response	Reference
Northern bobwhite	Technical grade trifluralin (96.7% a.i.)	LD_{50} >2000 mg/kg	MRID 00137573 U.S. EPA-OPP 1996a
Bobwhite quail (*Colinus virginianus*) Acceptable	Trifluralin (96.7% a.i.) NOS	No mortality or signs of toxicity LD_{50} >2000 mg/kg Classification: practically nontoxic	MRID 00137573 (Cochrane et al. 1983; Hudson et al. 1984) U.S. EPA-OPP 2009 (Appendix F)
Mallard duck	Technical grade trifluralin (96.7% a.i.)	LD_{50} >2000 mg/kg	Hudson et al. 1984 U.S. EPA-OPP 1996a
Mallard duck (*Anas platyrhynchos*) Acceptable	Trifluralin (96.7% a.i.) NOS	No mortality LD_{50} >2000 mg/kg Very mild ataxia Classification: practically nontoxic	Hudson et al. 1984 U.S. EPA-OPP 2009 (Appendix F)
Pheasant (NOS) Acceptable	Trifluralin (96.7% a.i.) NOS	No mortality LD_{50} >2000 mg/kg Very mild ataxia. Classification: practically nontoxic	Hudson et al. 1984 U.S. EPA-OPP 2009 (Appendix F)

Table A2-2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference
Northern bobwhite	Technical grade trifluralin (99.96% a.i.)	LD_{50}: >5000 mg/kg diet (about >1500 mg/kg bw)	MRID 00138857 U.S. EPA-OPP 1996a
Bobwhite quail (*Colinus virginianus*) Acceptable	Trifluralin (99.96% a.i.) NOS in diet	No mortality or signs of toxicity LC_{50} >5000 mg/kg diet (about >1500 mg/kg bw) Classification: practically nontoxic	MRID 00138858 (Emerson and Kehr 1983) U.S. EPA-OPP 2009 (Appendix F)
Mallard duck	Technical grade trifluralin (99.96% a.i.)	LD_{50}: >5000 mg/kg (about >2000 mg/kg bw)	MRID 00138858 U.S. EPA-OPP 1996a
Mallard duck (*Anas platyrhynchos*) Acceptable	Trifluralin (99.96% a.i.) NOS	No mortality; some birds evidenced diarrhea observed at 5000 mg/kg-diet levels on days 6-8; food consumption unaffected by treatment. LC_{50} >5000 mg/kg diet (about >1500 mg/kg bw) Classification: practically nontoxic	MRID 00138857 (Emerson and Kehr 1983) U.S. EPA/OPP 2009 (Appendix F)
Japanese Quail (*Coturnix japonica*), 15 birds/concentration	5-day dietary exposure at 2500 and 5000 ppm	No signs of toxicity. Substantial decrease in food consumption at 5000 ppm on Day 1. Less remarkable decrease on later days. Assuming typical food consumption for quail (≈0.3 kg food/kg bw), the NOAEL of 2500 ppm would be about 750 mg/kg bw. The LOAEL would be <1500 mg/kg bw.	Hill and Camadese 1986

See Section 4.1.2.2 for discussion. Typical food consumption rates for acute dietary studies are taken as 0.4 kg food/kg bw for mallards and 0.3 kg food/kg bw from SERA (2007c).

Table A2-3: Reproductive Toxicity Studies in Birds			
Species	**Exposure**	**Response**	**Reference**
Mallard duck (*Anas platyrhynchos*)	Trifluralin (99.6% a.i.) NOS	NOAEC: = 50 mg a.i./kg –diet LOAEC: >50 mg a.i./kg-diet *Although there were increased cracked eggs at 50 ppm, it was a small increase (2.4%) and deemed biologically insignificant based on information from other avian reproduction studies using trifluralin* (EPA/OPP 2009a, page F-9)	Beavers and Fink 1978, MRID 00131132 Commentary from U.S. EPA-OPP 2009a (Appendix F)
At 5 mg/kg-diet, there was a statistically significant reduction in the percentage of eggs not cracked ("eggs not cracked/eggs laid") at the highest test concentration of 50 mg/kg-diet. This effect was relatively small (98.8, 99.7, and 97.0% eggs not cracked/eggs laid in the control, 5 mg/kg-diet, and 50 mg/kg-diet groups, respectively). This effect was not observed in any of the other chronic bird studies including those that had test concentrations up to 1000 mg/kg-diet (MRID 403347-04 and 403347-06). After evaluating the size of the effect and the full suite of avian reproduction studies conducted for trifluralin, EFED determined that the reduction in the percentage of eggs cracked in this study (MRID 00131132) was not biologically significant, and the study NOAEC should be established at 50 mg/kg-diet (the highest concentration tested).			
Northern bobwhite (*Colinus virginianus*)	Trifluralin (99.6% a.i.) NOS	NOAEC = 50 mg a.i./kg-diet (highest test concentration) Endpoints affected: none. *The NOAEC was established at 50 mg/kg-diet (the highest test concentration), as no significant effects were observed for any of the reported endpoints. Although this study was classified as Acceptable, there is concern for the validity of the study as the overall percentage of cracked eggs was high (9.7% of eggs laid in controls). EPA guidance for bobwhite quail reproduction studies states that typically only 0.6 – 2.0% of eggs laid are cracked*. (EPA/OPP 2009a, page F-9).	Beavers and Fink 1978, MRID 00131134 U.S. EPA-OPP 2009a (Appendix F)

Table A2-3: Reproductive Toxicity Studies in Birds

Species	Exposure	Response	Reference
Mallard duck	Technical grade trifluralin (96.0% a.i.)	NOAEC: 910.5 ppm (≈64 mg/kg bw) LOAEC: Not determined No endpoints affected by treatment.	MRID 40334704 U.S. EPA-OPP 1996a
Mallard duck (*Anas platyrhynchos*)	Trifluralin (96.0% a.i.) NOS	NOAEC: 500 mg a.i./kg-diet (≈35 mg/kg bw) LOAEC: 1000 mg a.i./kg-diet (≈70 mg/kg bw) Endpoints affected: decreased eggshell thickness, 14-day survival, and decrease body weight in males at 1000 ppm (highest test concentration.	MRID 40334704 (Beavers et al. 1987) U.S. EPA/OPP 2009a (Appendix F)
Northern bobwhite	Technical grade trifluralin (96.0% a.i.)	NOAEC: 452.3 ppm (≈32 mg/kg bw) LOAEC: 910.5 ppm (≈64 mg/kg bw) based on cracked eggs as a percentage of eggs laid.	MRID 40334706 U.S. EPA-OPP 1996a
Northern bobwhite (*Colinus virginianus*)	Trifluralin (96.0% a.i.) NOS	NOAEC = 500 mg a.i./kg-diet (≈35 mg/kg bw) LOAEC = 1000 mg a.i./kg-diet (≈70 mg/kg bw) Endpoints affected: increased number of eggs cracked at 1000 ppm (highest concentration tested)	MRID 40334706 (Beavers et al. 1987) U.S. EPA-OPP 2009a (Appendix F)

See Section 4.1.2.2 for discussion. Typical food consumption rates for dietary reproduction studies are taken as 0.07 kg food/kg bw for mallards and bobwhites from SERA (2007c).

Appendix 3: Toxicity to Terrestrial Plants

Table A3-1: Vegetative Vigor Bioassays

Species	Exposure	Response			Reference
Monocots (see column 3)	95% a.i. at 0.0, .125, 0.25, 0.50, 1.0, and 2.0 lb a.i./acre. Observation at 14 days after treatment.	**Species**	**EC_{25} (lb a.i./acre)**	**NOAEL (lb a.i./acre)**	Waldrup 1990b, MRID 41934503. Also summarized in U.S. EPA-OPP 1996a
		Height			
		Corn	1.47	0.125	
		Onion	1.45	0.25	
		Wheat		0.5	
		Sorghum	2.648	0.25	
		Weight			
		Corn	1.09	0.5	
		Onion	N.D.	2.0	
		Wheat	N.D.	2.0	
		Sorghum	N.D.	2.0	
Dicots (see column 3)	95% a.i. at 0.0, 0.125, 0.25, 0.50, 1.0, and 2.0 lb a.i./acre. Observation at 14 days after treatment.	**Species**	**EC_{25} (lb a.i./acre)**	**NOAEL (lb a.i./acre)**	Waldrup 1990b, MRID 41934503. Also summarized in U.S. EPA-OPP 1996a
		Height			
		Soybean	N.D.	0.25	
		Sunflower	2.276	0.25	
		Cotton	2.267	0.25	
		Cucumber	0.800	0.50	
		Cabbage	2.644	0.25	
		Radish	0.936	0.25	
		Weight			
		Soybean	N.D.	2.0	
		Sunflower	N.D.	2.0	
		Cotton	N.D.	2.0	
		Cucumber	0.796	0.25	
		Cabbage	N.D.	2.0	
		Radish	1.23	0.5	

N.D.: Not determined

Working Note for Table A3-1: The U.S. EPA/OPP DER reanalyzed the data reported by the investigators and there are minor differences between the reported values in the study and the results of the EPA reanalysis. All values above are based on the EPA reanalysis.

Table A3-2: Seed Germination Bioassays

Species	Exposure	Response	Reference
Onion (monocot)	95% a.i. (NOS)	NOAEL: 0.13 lb a.i./acre LOAEL: 0.25 lb a.i./acre EC_{25}: 0.33 lb a.i./acre EC_{50}: 4.3 lb a.i./acre	Schwab 1993, MRID 42695601 U.S. EPA-OPP 1996a
Cabbage (dicot)	95% a.i. (NOS)	NOAEL: 2 lb a.i./acre LOAEL: Not determined EC_{25}: 4 lb a.i./acre EC_{50}: >4 lb a.i./acre	Schwab 1993, MRID 42695601 U.S. EPA-OPP 1996a
Monocots (see column 3 for species)	Technical grade trifluralin (95.7% purity), Tier 1 Assay at 24 ppm soil (equivalent to 8 lb a.i./acre).	**Species** / **% Germination** Corn 100% Onion 8% Wheat 100% Sorghum 71%% Working Note: EPA estimates of germination for some species were less than the estimates from the study authors. Values above are from the EPA reanalysis.	Waldrup 1990a, MRID 41934501
Dicots (see column 3)	Technical grade trifluralin (95.7% purity), Tier 1 Assay at 24 ppm soil (equivalent to 8 lb a.i./acre).	**Species** / **% Germination** Soybean 100% Sunflower 100% Cotton 100% Cucumber 100% Cabbage 35% Radish 100% Working Note: EPA estimates of germination for some species were less than the estimates from the study authors. Values above are from the EPA reanalysis.	Waldrup 1990a, MRID 41934501

Table A3-3: Tier II Seedling Emergence.

Data for Trifluralin (Treflan HEP) 43.8% purity

Crop	Species	NOAEL (lb a.i./acre)	EC_{25} (lb a.i./acre)	Most Sensitive Endpoint	Reference
Monocot	Corn	0.13	0.17	Shoot fresh weight	MRID 43984401 (Hansen et al. 1996) U.S. EPA-OPP 2009a (Appendix F)
	Sorghum	0.06	0.09	Shoot fresh weight	
	Onion	0.50	0.74	Shoot fresh weight	
	Wheat	0.13	0.21	Shoot fresh weight	
Dicot	Cotton	NA	NA	Invalid results: soil medium detrimental to plant growth	
	Cabbage	0.50	0.78	Shoot fresh weight	
	Radish	1.0	2.4	Shoot fresh weight	
	Cucumber	0.13	0.19	Shoot fresh weight	
	Soybean	1.0	1.3	Shoot fresh weight	
	Sunflower	2.0	4.0	Shoot fresh weight	

For this study, an incorporated application was simulated by spraying the material into a rotating cement mixer filled with soil. This soil was used to provide the top two 2 inches of soil in each treatment pot.

Appendix 4: Toxicity to Fish

Table A4-1: Acute Toxicity of Trifluralin to Fish

Species	Exposure	Response	Reference
Bunni Fish (*Barbus sharpeyi*) [Cyprinid family, tropical]	44.5% EC formulation not otherwise specified (investigators from Egypt and Iraq), 21 to 26 °C	96-h LC_{50}: 250 µg a.i./L	Mansour and Mohsen 1985
Bluegill sunfish	Technical grade trifluralin (95.9% a.i.)	96-h LC_{50} = 58 µg a.i./L Toxicity Category: very highly toxic Identical value cited in Leblanc 1984. Working Note: This study is cited by U.S. EPA-OPP 1996a and referenced to Johnson and Finley (1980)but this value has not been located in Johnson and Finley (1980).	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Bluegill sunfish	Trifluralin (95.9% a.i.) under static conditions for 96 hours, 23.9 °C	96-h LC_{50} = 18.5 µg a.i./L 95%CI (16-19.7) Probit slope = 23.94 Toxicity Category: very highly toxic	MRID 40098001 U.S. EPA-OPP 2009a (Appendix F)
Bluegill sunfish	Technical grade (NOS), 75°F (24°C)	96-h LC_{50} = 68 µg a.i./L	Cope 1965
Bluegill sunfish	96 hours, technical grade	**Temperature, °C** / **LC_{50} (µg a.i./L)** 24 hours / 96 hours 12.7: 540 (460-640) / 190 (160-230) 18.3: 360 (300□430) / 120 (100-140) 23.8: 130 (110-150) / 47 (40-55) Standard direct relationship of toxicity to temperature.	Macek et al. 1969
Carp (*Cyprinus carpio*)	44.5% EC formulation not otherwise specified (investigators from Egypt and Iraq), 21 to 26 °C	96-h LC_{50}: 660 µg a.i./L	Mansour and Mohsen 1985

Appendix 4: Toxicity to Fish *(continued)*

Table A4-1: Acute Toxicity of Trifluralin to Fish

Species	Exposure	Response	Reference
Carp (*Cyprinus carpio*)	Trifluralin (99%), 20 °C	96-h LC_{50}: 45 µg a.i./L Sublethal effects in 14-day exposures: 5 µg/L: no effects reported on gill, kidney or liver pathology. 10 µg/L: hyperplasia of gill tissue 20 µg/L: more pronounced hyperplasia of gills. Vacuolization of hepatocytes. Degenerative changes in kidney tissue.	Poleksic and Karan 1999
Carp (NOS)	Technical grade, NOS. 48 hours. Temperature specified as 20-28 °C.	48-hour LC_{50}: 1,000 µg/L	Hashimoto and Nishiuchi 1981
Channel catfish	Technical grade trifluralin (95.9% a.i.), 22 °C	LC_{50} = 2200 µg a.i./L Toxicity Category: moderately toxic **Not used in U.S. EPA/OPP 2009a due to insufficient experimental data.** **Cited in Leblanc 1984. The above LC_{50} is not a typo. Study classified as Supplemental by U.S. EPA/OPP (1996a, p. 32)**	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Channel Catfish (*Ictalurus punctatus*), fingerlings	Purity not specified.	96-h LC_{50}: 417 µg a.i./L	McCorkle et al. 1977
Fathead minnow	Technical grade trifluralin (95.9% a.i.), 18 °C	96-h LC_{50} = 105 µg a.i./L Toxicity Category: highly toxic **Not used in U.S. EPA/OPP 2009a.**	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Goldfish	Technical grade trifluralin (46% a.i.)	96-h LC_{50} = 145 µg a.i./L Toxicity Category: highly toxic **Not used in U.S. EPA/OPP 2009a due to insufficient experimental data.**	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Goldfish	Technical grade, NOS. 48 hours. Temperature specified as 20-28 °C.	48-hour LC_{50}: 850 µg/L	Hashimoto and Nishiuchi 1981
Largemouth bass	Technical grade trifluralin (95.9% a.i.)	96-h LC_{50} = 75 µg a.i./L Toxicity Category: very highly toxic **Not used in U.S. EPA/OPP 2009a due to insufficient experimental data.** **Summarized in Leblanc 1984.**	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Medaka	Technical grade, NOS. 48 hours. Temperature specified as 20-28 °C.	48-hour LC_{50}: 430 µg/L	Hashimoto and Nishiuchi 1981

Appendix 4: Toxicity to Fish *(continued)*

Table A4-1: Acute Toxicity of Trifluralin to Fish

Species	Exposure	Response	Reference
Mosquitofish (*Gambusia affinis*)	Technical grade, 24-hour exposures	24-h LC_{50}s Sensitive: 2,000 µg/L Tolerant: 4,100 µg/L	Fabacher and Chambers 1974
Mosquitofish (*Gambusia affinis*)	Technical grade, 24-hour exposures. Source and purity not reported.	24-h LC_{50}: 28,000 µg/L 96-h LC_{50}: 12,000 µg/L	Naqvi and Leung 1983
Pond loach	Technical grade, NOS. 48 hours. Temperature specified as 20-28 °C.	48-hour LC_{50}: 350 µg/L	Hashimoto and Nishiuchi 1981
Rainbow trout	Technical grade trifluralin (95.9% a.i.), 12 °C	LC_{50} = 41 µg a.i./L Toxicity Category: very highly toxic	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Rainbow trout	Trifluralin (95.9% a.i.) under static conditions for 96 hours, 12 °C	LC_{50} = 43.6 µg a.i./L 95%CI (32.7-58.1) Probit slope = 4.16 Toxicity Category: very highly toxic	MRID 40098001, U.S. EPA-OPP 2009a (Appendix F)
Rainbow trout	Technical grade (NOS), 55°F (13°C)	96-h LC_{50} = 86 µg a.i./L	Cope 1965
Rainbow trout	96 hours, technical grade	**Temperature, °C** / **LC_{50} (µg a.i./L)**: **24 hours** / **96 hours** 1.6: **3.8??** (270-375) / 210 (182-240) 7.2: 239 (196-267) / 152 (132-175) 12.7: 98 (85-113) / 42 (38-46) **Working Note: The value for 1.6 °C for 24 hours is clearly incorrect.**	Macek et al. 1969

Appendix 4: Toxicity to Fish *(continued)*

Table A4-1: Acute Toxicity of Trifluralin to Fish

Species	Exposure	Response	Reference
Several species of marine fish (see column 3)	96 hours with assays for mortality and vertebral deformity. Japanese formulation (Sionogi Chern. Ind.Ltd.) containing a solvent and emulsifier (NOS)	See nested table below	Koyama 1996
Sheepshead minnow (*Cyprinodon variegates*)	Technical grade trifluralin (99% a.i.)	LC_{50} = 190 ppb Toxicity Category: highly toxic	Parrish et al. 1978, MRID 42449901 U.S. EPA-OPP 1996a

Species	Conc. (µg/L)		
	LC_{50}	Vertebral deformities	
		NOEC	**LOEC***
Yellowtail	<5	>71	>71
Flounder	56	20	30
Black sea bream	>56	7	19
Longchin body	120	12	23
Girella	110	23	31
Red Sea brean, Large	26	<13	<13
Red Sea brean, Medium	22	8	16
Red Sea brean, Small	21	<6	<6
Mullet	32	3	5
Grunt	33	12	19
Herring	<5	9	13
Jacoperver	>74	>74	>74

Working Note: The authors appear to express results in a.i. but this is not explicitly stated in publication.

*The NOECs are only for vertebral deformities and not for general sublethal effects. Ratios of definite LC_{50}s to NOAEC are about 2.5 to 11.

Table A4-2: Acute Toxicity of Trifluralin Metabolites to Fish			
Species	**Exposure**	**Response**	**Reference**
Rainbow trout	**TR-6** Metabolite, 96-hours, temperature not specified in summary by Hartless and Pease (2010)	96-h LC_{50}: 0.991 mg/L NOAEC: 0.858 mg/L (mortality) NOAEC: 0.299 mg/L (sublethal) Working Note: Trout LC_{50}s for trifluralin range from about 41 µg/L to 152 µg/L. This metabolite is less toxic by factors of about 6.5 to 24.	MRID 47807001 as summarized in Hartless and Pease 2010
Rainbow trout	**TR-15** Metabolite at 0, 1.04, 1.73, 2.84, 4.69, 7.77, and 13.0 mg a.i./L. 12.8-13.5°C, 96-hours.	96-h LC_{50}: 6.04 mg/L NOAEC: 4.69 mg/L (mortality) NOAEC: 1.04 mg/L (sublethal) Sublethal adverse effects included partial or complete loss of equilibrium, lethargy, erratic swimming, excess fluid in body cavity and immobility Working Note: Trout LC_{50}s for trifluralin range from about 41 µg/L to 152 µg/L. This metabolite is less toxic by factors of about 40 to 147.	Marino et al. 2001a, MRID 47807002 Also summarized in Hartless and Pease 2010

Table A4-3: Longer-term Toxicity to Fish

Species	Exposure	Response	Reference
Fathead minnow	Full Life Cycle (35 weeks): trifluralin (97% a.i.) under (mean-measured) flow-through conditions	NOAEC = 1.9 µg/L LOAEC = 5.1 µg/L Affected endpoint: survival	Macek et al. 1976, MIRD 05008271 U.S. EPA-OPP 2009a (Appendix F)
Rainbow trout (early life stage, NOS)	48 Days (early life-stage) Trifluralin (99.86% a.i.) under measure flow-through conditions	NOAEC = 2.18 µg/L LOAEC = 4.23 µg/L Affected endpoints: reduction in larval fish length (3.5%) relative to negative control) reduction in bodyweight (8.8% relative to negative control)	Adams et al. 1990, MIRD 41386202 U.S. EPA-OPP 2009a (Appendix F)
Sheepshead minnow (*Cyprinodon variegates*)	19 Months 0 or 1 to 5 µg/L trifluralin (NOS) in flowing seawater. Working Note: Table 1 of paper indicates concentrations of 1 to 5 mg/L and not 1 to 5 µg/L. This appears to be a typographical error in Table 1. The concentrations appear to have varied from 1 to 5 µg/L. Separate exposure groups are not discussed in paper.	Treatment-related histopathological changes to the pituitary gland along with abnormal bone development (vertebral dysplasia).	Couch 1984
Sheepshead minnow (*Cyprinodon variegates*), zygotes	28 Days Average measured concentrations of 0, 1.2, 2.7, 5.5, 20, or 31 µg/L trifluralin (NOS) in flowing seawater (i.e., throughout early development)	NOEAC: 2.7 µg/L Adverse Effects: 5.5 to 31 µg/L, Treatment-related extreme vertebral dysplasia. Working Note: The presumptive NOAEC of 2.7 µg/L is not explicitly noted in paper but is inferred from the discussion.	Couch et al. 1979
Sheepshead minnow (*Cyprinodon variegates*), early life stages (zygotes up to 51 days) and adults	51 Days exposure, depurated for 41 days Average measured concentration of 16.6 µg/L trifluralin (NOS) in flowing seawater	Treatment-related vertebral dysplasia, which was more pronounced than in fish exposed for 28 days.	Couch et al. 1979
Sheepshead minnow (*Cyprinodon variegates*)	166 Days (full life cycle) Technical grade (99%). Concentrations of 1.3, 4.8, 9.6, 17.7., and 34.1 µg/L.	NOAEC: 1.3 µg/L LOAEC: 4.8 µg/L, reduced fecundity. LOAEC: 9.6 µg/L, reduced growth and hatch. Frank effect: 17.7 µg/L, parental mortality.	Parrish et al. 1978

Appendix 5: Toxicity to Aquatic Invertebrates

Table A5-1: Acute Toxicity of Trifluralin to Aquatic Invertebrates

Species	Exposure	Response	Reference
FRESHWATER			
Alonella sp. (Cladocera)	48-hour, 20 °C, source and purity of trifluralin not specified	48-h LC_{50}: 1,300 µg/L	Naqvi et al. 1985
Cypria sp. (Ostracod)	48-hour, 20 °C, 48-hour, source and purity of trifluralin not specified	48-h LC_{50}: 1,500 µg/L	Naqvi et al. 1985
Daphnia magna (Cladocera)	Technical grade trifluralin (95.9% a.i.) , 96-hours, 21°C.	EC_{50} = 560 ppb Toxicity Category: highly toxic Also summarized in Leblanc 1984	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Daphnia magna (Cladocera)	Trifluralin (97.1% a.i.) for 48 hours, 19.4 to 19.9°C. Mean measured concentrations of 0, 6.7, 38, 67.7, 130, 239, and 438 µg/L	NOAEC = 130 µg/L (mortality) EC_{50} = 251 µg/L 95% CI = 219 to 288 DER Classification: Supplemental (see below) Note from Hartless and Pease 2010: Poor husbandry caused loss of two daphnids during the test (lost during transfer to renewal test solutions). This study is scientifically sound and is classified as Supplemental.	Kirk et al. 1999, MRID 47807007 Marino 2009a, MIRD 47939001 (response to EPA comments) Also summarized in U.S. EPA-OPP 2009 (Appendix F)
Daphnia magna (Cladocera)	Source and purity not specified, 48 hours exposure, 24.5 0±.5 °C.	LC_{50} = 312.42 µg/L	George and Liber 2007
Daphnia pulex (Cladocera)	Technical grade trifluralin (95.9% a.i.) , 96-hours, 15 °C.	EC_{50} = 625 µg/L Toxicity Category: highly toxic	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a

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

Table A5-1: Acute Toxicity of Trifluralin to Aquatic Invertebrates			
Species	**Exposure**	**Response**	**Reference**
Diaptomus sp. (Calanoida)	48-hour, 48-hour, 20 °C, source and purity of trifluralin not specified	48-h LC_{50}: 1,900 µg/L	Naqvi et al. 1985
Eucyclops sp. (Cyclopoida)	48-hour, 48-hour, 20 °C, source and purity of trifluralin not specified	48-h LC_{50}: 1,300 µg/L	Naqvi et al. 1985
Scud, *Gammarus fasciatus* (Amphipoda)	Technical grade trifluralin (95.9% a.i.) , 96-hours, 21 °C.	LC_{50} = 2200 ppb Toxicity Category: moderately toxic	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Procambarus clarkii (Crayfish, Decapoda)	Technical grade, 96-hour exposure, 23 to 25 °C. Source and purity not reported.	LC_{50}: 12,000 µg/L (juvenile) NOEC (mortality): 3,000 µg/L	Naqvi and Leung 1983
Procambarus clarkii (Crayfish, Decapoda)	Technical grade, 96-hour exposure. 24±3°C, source and purity not reported.	LC_{50}: 23,800 µg/L (adult) LC_{50}: 12,100 µg/L (juvenile)	Naqvi et al. 1987
Pteronarcys sp. (stonefly, Plecoptera)	Technical grade trifluralin (95.9% a.i.), 96-hours, 15 °C.	LC_{50} = 2800 ppb Toxicity Category: moderately toxic	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
Simocephalus sp. (Cyclops, Diplostraca)	Technical grade trifluralin (95.9% a.i.) , 96-hours, 15 °C	EC_{50} = 900 ppb Toxicity Category: highly toxic	Johnson and Finley 1980, MRID 40094602 U.S. EPA-OPP 1996a
SALTWATER			
Mytilus edulis (Mytiloida)	Specified as Treflan (99% trifluralin). 96-hour exposure, 18.1 °C	EC_{50} (attachment)= 350 µg/L	Liu and Lee 1975
Mysid (NOS)	Trifluralin (NOS) for 96 hours	LC_{50} >136 µg/L Note: According to EPA/OPP 2009a, this study is "*unreviewed*".	MRID 43662001 (Nimmo et al. 1981) U.S. EPA-OPP 2009a (Appendix F)
Grass shrimp	Trifluralin (96.4% a.i.) under flow-through conditions	LC_{50} = 638.5 µg/L 95% CI = 471-974.1 Probit slope = 3.48 NOAEL ≤138 µg/L Toxicity Category: highly toxic	MRID 40674801 EPA-OPP 2009a (Appendix F)

Table A5-2: Acute Toxicity of Trifluralin Metabolites to Aquatic Invertebrates			
Species	**Exposure**	**Response**	**Reference**
Chironomus riparius	**TR-4** Metabolite	NOAEC: 2.07 mg/L (visual immobility) LOAEC: 5.195 mg/L Working Note: No corresponding data on trifluralin.	Henry et al. 2004a, MRID 47807012
Daphnia magna	**TR-6** Metabolite: Mean measured concentrations of 0, 0.775, 1.26, 2.04, 3.51, 5.52, and 8.07 mg a.i./L.	LC_{50}: 3.52 mg/L NOAEC: 0.755 mg/L (visual immobility) NOAEC: 2.04 mg/L (Fisher's Exact Test for immobility) Working Note: Trifluralin LC_{50}s in daphnids range from 251 µg/L to 625 µg/L (see Table A5-1). Metabolite is less toxic than trifluralin by factors of about 5.6 to 14.	Marino et al. 2001c, MRID 47807004 Also summarized in Hartless and Pease 2010
Daphnia magna	**TR-15** Metabolite: 0, 1.56, 2.73, 4.56, 7.65, 12.6, and 19.3 mg a.i./L.	LC_{50}: 8.91 mg/L NOAEC: 2.73 mg/L (visual immobility) NOAEC: 7.65 mg/L (Fisher's Exact Test for immobility) Working Note: Trifluralin LC_{50}s in daphnids range from 251 µg/L to 625 µg/L (see Table A5-1). Metabolite is less toxic than trifluralin by factors of about 14 to 35.	Marino et al. 2001b, MRID 47807003 Also summarized in Hartless and Pease 2010

Table A5-3: Longer-term Toxicity to Aquatic Invertebrates			
Species	**Exposure**	**Response**	**Reference**
FRESHWATER			
Daphnia magna	Life cycle (64 days) test: trifluralin (97% a.i.) under flow-through conditions. 19 ±1 °C. Mean measured concentrations from 2.4 to 52.7 µg/L.	NOAEC = 2.4 µg/L LOAEC = 7.2 µg/L Endpoint affected: survival Classified by U.S. EPA/OPP 2009a as Acceptable.	Macek et al. 1976, MRID 05008271 U.S. EPA-OPP 2009a (Appendix F)
Daphnia magna	Life cycle test (21 days): trifluralin (99.86% a.i.) under mean measured static renewal conditions. 20 °C. Concentrations from 1.57 to 50.7 µg/L.	NOAEC = 50.7 µg/L Endpoint(s) affected: none. Cleared Review Classification: Guideline. Classified by U.S. EPA/OPP 2009a as Acceptable	Grothe and Mohr 1990, MRID 41386201 U.S. EPA-OPP 2009 (Appendix F)
Midge, *Chironomus riparius* (Dipteran)	28 days, Nominal concentrations of 0.25, 0.5, 1.0, 2.0, 4.0, and 8.0 mg/L. Nominal concentrations of 1 and 8 mg/L vs monitored concentration of 0.0497 at 1 mg/L and 0.0495 mg/L at 8 mg/L in water column. Pore water not measured.	Nominal Concentrations Emergence: NOAEC: 2,000 µg/L LOAEC 4,000 µg/L EC_{50}: 6.900 µg/L Development rate: NOAEC: 250 µg/L LOAEC: 500 µg/L DER Classification: Supplemental Working Note: The above concentrations all appear to be nominal. These are not meaningful for the water column. Note also that the higher nominal concentrations substantially exceed the water solubility – i.e., ≈0.3 mg/L.	Knoch 1996a, MRID 47807013 This study is not cited or discussed in either U.S. EPA/OPP 1996a or 2009a. Cleared review available and study is classified as *Supplemental*.
ESTUARINE and MARINE			
Dungeness crab, (*Cancer magister*), zoeae stage	70 days Technical grade, exposure period up to 70 days	26 µg/L : no remarkable impact on survival relative to untreated or acetone controls. 220 µg/L: Virtually complete mortality by Day 10.	Caldwell et al. 1979
Dungeness crab, (*Cancer magister*), juvenile stage	80 days Technical grade	47 µg/L : no remarkable impact on survival relative to untreated or acetone controls. 590 µg/L: Marginal increase in mortality relative to acetone controls after Day 40.	Caldwell et al. 1979
Dungeness crab, (*Cancer magister*), adults	80 days Technical grade	Up to 300 µg/L : no remarkable impact on survival relative to untreated or acetone controls.	Caldwell et al. 1979

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

Table A5-3: Longer-term Toxicity to Aquatic Invertebrates			
Tasmanian giant crab, (*Pseudocarcinus gigas*), newly hatched larvae, 50/concentration	115 days Technical grade trifluralin at 0.001, 0.003, 0.01, 0.03, or 0.1 mg/kg for 115 days in indefinite baths. Purpose of study was to screen chemicals for prophylactic treatment of epibiotic fouling and fungal mycosis.	Toxic effects (NOS) on larvae were observed at 30 µg/L NOEL = 10 µg/L	Gardner and Northam 1997
Mytilus edulis (mussel), larvae	26 days Specified as Treflan (99% trifluralin). 48 hours at concentrations of 24, 48, 96, and 192 µg/L. Observation period of 26 days.	Complete inhibition of metamorphosis at 192 µg/L. No larvae at two higher concentrations survived to 26 days. Delayed metamorphosis at two lower concentrations.	Liu and Lee 1975
Mytilus edulis (mussel)	10 to 20 days Specified as Treflan (99% trifluralin). 10 to 20 days at concentrations of 24 to 192 µg/L.	No effect on shell length at concentrations up to 192 µg/L. Either no effect or increase in larval size.	Liu and Lee 1975
Mytilus edulis (mussel), 30 day old larvae	40 days Specified as Treflan (99% trifluralin). 20, 40, 80, and 160µg/L for 40 days.	Decrease in larval survival relative to controls but not concentration related. Increased in rate of metamorphosis but effect appears related to solvent (acetone).	Liu and Lee 1975

Appendix 6: Toxicity to Aquatic Plants

Table A6-1: Toxicity of Trifluralin to Algae

Species	Exposure	Response	Reference
Anabaena flos-aquae Tier II	97.92% a.i. for 5 days	Original DER values (prior to 2009) EC_{50} >339 µg/L NOAEC = 89 ppb LOAEC: 162 ppb **Modified DER values**: EC_{50} >273 µg/L NOAEC = 273 µg/L	Hughes and Williams 1993a, MRID 42834103 U.S. EPA-OPP 2009a (Appendix F) U.S. EPA-OPP 1996a
Chlorella pyrenoidosa	48% EC formulation, 4 days	EC_{50}: 1.8134 mg/L (appears to be in units of a.i) Note units: mg/L	Ma and Liang 2001
Chlorella vulgaris	48% EC formulation, 4 days	EC_{50}: 4.3469 mg a.i./L (clearly in units of a.i.) Note units: mg/L	Ma et al. 2002
Mixed algal populations in artificial streams	Nominal concentrations of 0, 0.1, 1, and 10 mg/kg (≅mg/L)	No impact on algal populations. Half-life in stream of 51 minutes, probably due to strong adsorption. Working Note: Exposures cannot be meaningfully assessed. Seems likely that there was strong adsorption to plastic liner of artificial streams. Study is only marginally relevant.	Kosinski and Merkle 1984
Mixed lake phytoplankton	3 hour exposure period. Exposures appear to be expressed as a.i.	1,000 µg/L: 50% inhibition of carbon uptake	Brown and Lean 1995
Navicula pelliculosa Tier II Supplemental	97.92% a.i., Nominal Concentrations of 0, 6.35, 12.7, 25.3, 50.6, 101, and 202µg/L for 5 days.	Original DER values (prior to 2009) IC_{50} = 15.3 µg/L 95% CI = 6.7, 34.7 µg/L NOAEC = NA LOAEC: 7.7 µg/L (measured) **Modified DER values**: IC_{50} = 37.9µg/L 95% CI = 19.3, 74.3 µg/L NOAEC = <6.01 µg/L IC_{05} = 7.9 µg/L	Hughes and Williams 1993b, MRID 42834102 U.S. EPA-OPP 2009a (Appendix F) U.S. EPA-OPP 1996a
Scenedesmus obliquus	48% EC formulation, 4 days	EC_{50}: 1.8134 mg/L (appears to be in units a.i.) Note units: mg/L	Ma and Liang 2001

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

Table A6-1: Toxicity of Trifluralin to Algae

Species	Exposure	Response	Reference
Scenedesmus vacuolatus	24-hours, purity specified only as >97 to >99%.	log EC50: -7.14 mol/L or -1.14 µM/L or 24.3 µg/L	Schmitt et al. 2000
Selenastrum capricornutum (Tier II study) Acceptable	99.86% a.i. for 7 days. 25 °C	Original DER values (prior to 2009) IC_{50} = 7.52 µg/L NOAEC = 5.37 µg/L **Modified DER values**: IC_{50} = 88.7 µg/L 95% CI = 59.4. 132.4 µg/L NOAEC <10 µg/L IC_{05} = 35.7 µg/L Working Note: EPA/OPP 2009a expresses concern about validity of study because the author reported "Low levels of trifluralin were detected in control solutions at test termination due to contamination on glassware used at the end of the study for biomass determinations." The Cleared Review for this study indicates that the study is invalid because the concentrations decreased by over 95% during the assay.	Adams and Cocke 1990, MRID 41934502 U.S. EPA-OPP 2009a (Appendix F) U.S. EPA-OPP 1996a
Selenastrum capricornutum	Technical trifluralin (NOS) under static conditions for 96 hours, 25 °C.	96-hour EC_{50} = 673 µg/L 95% CI = 594-751 µg/L NOEC = 150 µg/L LOEC = 300 µg/L	Fairchild et al. 1997
Skeletonema costatum (Tier II) Acceptable	97.92% a.i. for 5 days	Original DER values (prior to 2009) IC_{50} = 28 µg/L 95% CI = 24.2. 32.5 µg/L NOAEC = 4.6 µg/L **Modified DER values**: IC_{50} = 21.9 µg/L 95% CI = 18.8. 25.50µg/L NOAEC =14 µg/L	Hughes and Williams 1993c, MRID 42834101 U.S. EPA-OPP 2009a (Appendix F) U.S. EPA-OPP 1996a

Table A6-2: Toxicity of Trifluralin Metabolites to Algae

Species	Exposure	Response	Reference
Selenastrum capricornutum	**Metabolite TR-6** at 0, 0.065, 0.156, 0.300, 0.613, 1.17, 2.40,4.79, and 5.56 mg /L for 96 hours	**End Point** / **Response (mg/L)**: Cell Density: EC_{50} 5.4, NOAEC 0.156; Biomass: EC_{50} 4.6, NOAEC <0.065; Growth Rate: EC_{50} >5.56, NOAEC 0.156 Note from Hartless and Pease (2010): The reviewer's analysis detected a significant effect ($p<0.05$) of the solvent on algal cell density and biomass parameters and noted that the fit of the Bruce-Versteeg model to the data for cell density and biomass was poor and not representative of the raw data. Neither a NOAEC nor an IC_{05} could be established for this parameter. Reported results can be used qualitatively in risk characterization but cannot be used quantitatively for risk estimation. Working Note: EC_{50}s for trifluralin in this species range from 88.7 µg/L to 673 µg/L. This metabolite is less toxic by factors of about 8 to 61.	Henry et al. 2002a, MRID 47807006.
Selenastrum capricornutum	**TR-15** Metabolite at 0.0586, 0.112, 0.272, 0.467, 0.952, 1.89, 7.29, and 11.5 mg a.i./L for 96 hours.	**End Point** / **□esponse (mg/L)**: Cell Density: EC_{50} 6.7, NOAEC 1.89; Biomass: EC_{50} 6.7, NOAEC 0.952; Growth Rate: EC_{50} 9.3, NOAEC 1.89 Working Note: EC_{50}s for trifluralin in this species range from 88.7 µg/L to 673 µg/L. Based on the most sensitive endpoint, this metabolite is less toxic by factors of about 10 to 76.	Marino et al. 2001d, MRID 47807005 Also summarized in Hartless and Pease 2010

Table A6-3: Toxicity to Macrophytes

Species	Exposure	Response	Reference
Lemna gibba (Tier II study) Supplemental	14 Days Technical grade, 95% a.i. Initial measured concentrations of 2.53, 5.91, 12.9, 25.3, 45.5, and 91.3 µg/L. Static renewal. 14-day period of exposure. Because of instability of compound, all concentrations below the limit of detection by Day 3.	Original DER values (prior to 2009) EC_{50} = 43.5 µg/L 95% CI = 4.16-454.7 µg/L NOAEC = <2.53 µg/L (lowest test concentration) **Modified DER values**: EC_{50} = 49.7 µg/L 95% CI = 4.16, 53.6 µg/L NOAEC = <2.53 µg/L IC_{05} = 14.7 µg/L	Milazzo et al. 1993, MRID 42834104 Summarized in U.S. EPA-OPP 1996a and in U.S. EPA-OPP 2009a (Appendix F)
Lemna minor	96 Hours Technical trifluralin (NOS) under static conditions for 96 hours. Biomass estimates based on measurement of frond numbers at 48, 72, and 96 hours.	96-hour EC_{50} = 170 µg/L 95% CI = 10-330 µg/L NOEC = 75 µg/L LOEC = 150 µg/L	Fairchild et al. 1997

Appendix 7: Results of Gleams-Driver Modeling

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.00033 (0 - 0.006)	0 (0 - 0.00284)	0 (0 - 0)
Dry and Temperate Location	0.0006 (0 - 0.0043)	1.53E-05 (0 - 0.00228)	0 (0 - 0.0016)
Dry and Cold Location	0.0033 (0.00162 - 0.0063)	0.0024 (0.00112 - 0.005)	0.0047 (0.00221 - 0.0094)
Average Rainfall and Warm Location	0.0148 (0.0065 - 0.04)	0.009 (0.00266 - 0.028)	0.0006 (0 - 0.007)
Average Rainfall and Temperate Location	0.0113 (0.0055 - 0.0256)	0.0069 (0.00228 - 0.0183)	0.00316 (0.00101 - 0.0071)
Average Rainfall and Cool Location	0.0096 (0.0038 - 0.0222)	0.0062 (0.00232 - 0.0186)	0.0057 (0.00249 - 0.0115)
Wet and Warm Location	0.0287 (0.0125 - 0.05)	0.0221 (0.0083 - 0.05)	0.00259 (0.0005 - 0.0111)
Wet and Temperate Location	0.0235 (0.0106 - 0.041)	0.014 (0.0056 - 0.0301)	0.00118 (0.000147 - 0.0059)
Wet and Cool Location	0.077 (0.051 - 0.101)	0.069 (0.044 - 0.093)	0.084 (0.059 - 0.11)
		Average of Central Values:	0.01484
		25th Percentile of Lower Bounds:	0.0000735
		Maximum Value:	0.11
		Summary of Values:	0.0148 (0.0000735 - 0.11)

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.35 (0.31 - 0.38)	0.312 (0.272 - 0.34)	0.312 (0.273 - 0.34)
Dry and Temperate Location	0.35 (0.302 - 0.38)	0.309 (0.267 - 0.34)	0.309 (0.267 - 0.34)
Dry and Cold Location	0.33 (0.293 - 0.37)	0.292 (0.259 - 0.32)	0.293 (0.259 - 0.32)
Average Rainfall and Warm Location	0.34 (0.301 - 0.37)	0.299 (0.265 - 0.33)	0.299 (0.265 - 0.33)
Average Rainfall and Temperate Location	0.33 (0.295 - 0.36)	0.295 (0.26 - 0.32)	0.296 (0.26 - 0.32)
Average Rainfall and Cool Location	0.33 (0.293 - 0.36)	0.293 (0.259 - 0.32)	0.293 (0.259 - 0.32)
Wet and Warm Location	0.33 (0.292 - 0.36)	0.289 (0.259 - 0.316)	0.292 (0.259 - 0.32)
Wet and Temperate Location	0.33 (0.292 - 0.36)	0.291 (0.259 - 0.32)	0.294 (0.259 - 0.32)
Wet and Cool Location	0.33 (0.291 - 0.35)	0.288 (0.257 - 0.313)	0.287 (0.256 - 0.311)
		Average of Central Values:	0.3097
		25th Percentile of Lower Bounds:	0.259
		Maximum Value:	0.38
		Summary of Values:	0.31 (0.259 - 0.38)

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.118 (0.103 - 0.128)	0.104 (0.091 - 0.113)	0.104 (0.091 - 0.113)
Dry and Temperate Location	0.117 (0.101 - 0.127)	0.103 (0.089 - 0.112)	0.103 (0.089 - 0.112)
Dry and Cold Location	0.111 (0.098 - 0.122)	0.097 (0.086 - 0.107)	0.098 (0.086 - 0.107)
Average Rainfall and Warm Location	0.113 (0.1 - 0.123)	0.1 (0.088 - 0.108)	0.1 (0.088 - 0.109)
Average Rainfall and Temperate Location	0.112 (0.098 - 0.121)	0.098 (0.087 - 0.107)	0.099 (0.087 - 0.107)
Average Rainfall and Cool Location	0.111 (0.098 - 0.12)	0.098 (0.086 - 0.106)	0.098 (0.086 - 0.106)
Wet and Warm Location	0.109 (0.097 - 0.119)	0.096 (0.086 - 0.105)	0.097 (0.086 - 0.106)
Wet and Temperate Location	0.11 (0.097 - 0.119)	0.097 (0.086 - 0.106)	0.098 (0.086 - 0.107)
Wet and Cool Location	0.109 (0.097 - 0.118)	0.096 (0.086 - 0.104)	0.096 (0.085 - 0.104)
		Average of Central Values:	0.1034
		25th Percentile of Lower Bounds:	0.086
		Maximum Value:	0.128
		Summary of Values:	0.103 (0.086 - 0.128)

Trifluralin Soil Incorporation

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

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

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.25 (0 - 3.4)	0 (0 - 2.14)	0 (0 - 0)
Dry and Temperate Location	0.3 (0 - 2.81)	0.016 (0 - 1.82)	0 (0 - 1.57)
Dry and Cold Location	1.06 (0.5 - 2.22)	1 (0.5 - 2.39)	2.72 (1.47 - 4.8)
Average Rainfall and Warm Location	4.4 (1.78 - 16.9)	3.7 (1 - 19.4)	0.21 (0 - 1.77)
Average Rainfall and Temperate Location	3.16 (1.04 - 9)	2.41 (0.6 - 9)	0.9 (0.5 - 1.96)
Average Rainfall and Cool Location	2.03 (0.8 - 9.8)	1.57 (0.5 - 9.6)	1.04 (0.5 - 2.22)
Wet and Warm Location	6.7 (2.6 - 21.5)	6.9 (1.79 - 28.4)	0.6 (0.09 - 4.1)
Wet and Temperate Location	3.4 (1.48 - 9.4)	2.78 (0.9 - 10.8)	0.26 (0.04 - 1.42)
Wet and Cool Location	5.3 (3.3 - 10.7)	4.9 (2.58 - 11.4)	4 (2.96 - 6.7)
		Average of Central Values:	2.21
		25th Percentile of Lower Bounds:	0.02
		Maximum Value:	28.4
		Summary of Values:	2.21 (0.02 - 28.4)

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.0027 (0 - 0.04)	0 (0 - 0.017)	0 (0 - 0)
Dry and Temperate Location	0.004 (0 - 0.028)	0.00011 (0 - 0.013)	0 (0 - 0.007)
Dry and Cold Location	0.029 (0.014 - 0.06)	0.021 (0.01 - 0.04)	0.04 (0.02 - 0.06)
Average Rainfall and Warm Location	0.12 (0.06 - 0.25)	0.06 (0.018 - 0.15)	0.0016 (0 - 0.011)
Average Rainfall and Temperate Location	0.11 (0.06 - 0.19)	0.05 (0.02 - 0.11)	0.021 (0.008 - 0.04)
Average Rainfall and Cool Location	0.09 (0.04 - 0.16)	0.05 (0.02 - 0.1)	0.03 (0.017 - 0.05)
Wet and Warm Location	0.22 (0.11 - 0.4)	0.13 (0.06 - 0.26)	0.006 (0.0012 - 0.02)
Wet and Temperate Location	0.16 (0.1 - 0.25)	0.08 (0.04 - 0.14)	0.003 (0.0004 - 0.013)
Wet and Cool Location	0.3 (0.25 - 0.4)	0.26 (0.19 - 0.3)	0.23 (0.18 - 0.27)
		Average of Central Values:	0.0748
		25th Percentile of Lower Bounds:	0.0002
		Maximum Value:	0.4
		Summary of Values:	0.075 (0.0002 - 0.4)

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.03 (0 - 0.4)	0 (0 - 0.4)	0 (0 - 0)
Dry and Temperate Location	0.05 (0 - 0.25)	0.0019 (0 - 0.28)	0 (0 - 0.26)
Dry and Cold Location	0.14 (0.07 - 0.3)	0.14 (0.06 - 0.4)	0.4 (0.17 - 1.09)
Average Rainfall and Warm Location	0.31 (0.17 - 0.8)	0.3 (0.12 - 1)	0.06 (0 - 0.4)
Average Rainfall and Temperate Location	0.27 (0.12 - 0.5)	0.27 (0.1 - 0.7)	0.2 (0.08 - 0.5)
Average Rainfall and Cool Location	0.21 (0.09 - 0.6)	0.21 (0.08 - 1)	0.23 (0.09 - 0.6)
Wet and Warm Location	0.3 (0.14 - 0.8)	0.4 (0.13 - 1.12)	0.1 (0.023 - 0.5)
Wet and Temperate Location	0.18 (0.1 - 0.3)	0.18 (0.1 - 0.4)	0.04 (0.008 - 0.14)
Wet and Cool Location	0.4 (0.26 - 0.7)	0.5 (0.31 - 1)	0.7 (0.4 - 1.36)
		Average of Central Values:	0.2082
		25th Percentile of Lower Bounds:	0.004
		Maximum Value:	1.36
		Summary of Values:	0.208 (0.004 - 1.36)

Trifluralin Soil Incorporation

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.0003 (0 - 0.006)	0 (0 - 0.0029)	0 (0 - 0)
Dry and Temperate Location	0.0006 (0 - 0.003)	0.000014 (0 - 0.002)	0 (0 - 0.0013)
Dry and Cold Location	0.004 (0.0018 - 0.007)	0.0027 (0.0012 - 0.006)	0.005 (0.0026 - 0.01)
Average Rainfall and Warm Location	0.014 (0.007 - 0.022)	0.007 (0.0024 - 0.015)	0.0004 (0 - 0.0026)
Average Rainfall and Temperate Location	0.013 (0.007 - 0.022)	0.007 (0.0031 - 0.013)	0.004 (0.0016 - 0.008)
Average Rainfall and Cool Location	0.01 (0.005 - 0.018)	0.006 (0.0028 - 0.014)	0.006 (0.0028 - 0.009)
Wet and Warm Location	0.015 (0.01 - 0.021)	0.01 (0.006 - 0.017)	0.001 (0.00017 - 0.0028)
Wet and Temperate Location	0.011 (0.008 - 0.016)	0.006 (0.003 - 0.01)	0.0004 (0.00005 - 0.0016)
Wet and Cool Location	0.026 (0.02 - 0.03)	0.024 (0.019 - 0.03)	0.026 (0.02 - 0.04)
		Average of Central Values:	0.00739
		25th Percentile of Lower Bounds:	0.000025
		Maximum Value:	0.04
		Summary of Values:	0.0074 (0.000025 - 0.04)