SERA TR-056-17-04b

Chlorsulfuron
Human Health and Ecological Risk Assessment
FINAL REPORT

Submitted to:
Dr. Harold Thistle
USDA Forest Service
Forest Health Technology Enterprise Team
180 Canfield St.
Morgantown, WV 26505
Email: hthistle@fs.fed.us

USDA Forest Service Contract: **AG-3187-C-12-0009**
USDA Forest Order Number: **AG-3187-D-15-0077**
SERA Internal Task No. 56-**17**

Submitted by:
Patrick R. Durkin
Syracuse Environmental Research Associates, Inc.
8125 Solomon Seal
Manlius, New York 13104

E-Mail: **SERA_INC@msn.com**
Home Page: **www.sera-inc.com**

November 23, 2016

Table of Contents

LIST OF TABLES vi
LIST OF FIGURES vi
LIST OF APPENDICES vii
ACRONYMS, ABBREVIATIONS, AND SYMBOLS viii
COMMON UNIT CONVERSIONS AND ABBREVIATIONS xi
CONVERSION OF SCIENTIFIC NOTATION xii
EXECUTIVE SUMMARY xiii
1. INTRODUCTION 1
1.1. Chemical Specific Information 1
1.2. General Information 2
2. PROGRAMS DESCRIPTION 5
2.1. Overview 5
2.2. Chemical Description and Commercial Formulations 5
2.4. Application Methods 7
2.4. Mixing and Application Rates 7
2.5. Use Statistics 8
3. HUMAN HEALTH 11
3.1. HAZARD IDENTIFICATION 11
3.1.1. Overview 11
3.1.2. Mechanism of Action 11
3.1.3. Pharmacokinetics and Metabolism 12
3.1.3.1. Metabolism and Distribution 12
3.1.3.2. Dermal Absorption 13
3.1.3.2.1. First-Order Dermal Absorption 13
3.1.3.2.2. Zero-Order Dermal Absorption 14
3.1.3.3. Excretion 15
3.1.4. Acute Oral Toxicity 16
3.1.5. Subchronic or Chronic Systemic Toxic Effects 17
3.1.6. Effects on Nervous System 19
3.1.7. Effects on Immune System 19
3.1.8. Effects on Endocrine System 20
3.1.9. Reproductive and Developmental Effects 21
3.1.9.1. Developmental Studies 21
3.1.9.2. Reproduction Studies 22
3.1.10. Carcinogenicity and Mutagenicity 23
3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes) 23
3.1.11.1. Skin Irritation 24

3.1.11.2. Skin Sensitization 24
3.1.11.3. Ocular Effects 24
3.1.12. Systemic Toxic Effects from Dermal Exposure 24
3.1.13. Inhalation Exposure 25
3.1.14. Adjuvants and Other Ingredients 26
3.1.14.1. Other Ingredients 26
3.1.14.2. Adjuvants 27
3.1.15. Impurities and Metabolites 27
3.1.15.1. Metabolites 27
3.1.15.2. Impurities 28
3.1.16. Toxicological Interactions 28
3.2. EXPOSURE ASSESSMENT 29
3.2.1. Overview 29
3.2.2. Workers 29
3.2.2.1. General Exposures 29
3.2.2.2. Accidental Exposures 30
3.2.3. General Public 31
3.2.3.1. General Considerations 31
3.2.3.1.1. Likelihood and Magnitude of Exposure 31
3.2.3.1.2. Summary of Assessments 32
3.2.3.2. Direct Spray 32
3.2.3.3. Dermal Exposure from Contaminated Vegetation 33
3.2.3.4. Contaminated Water 33
3.2.3.4.1. Accidental Spill 33
3.2.3.4.2. Accidental Direct Spray/drift for a Pond or Stream 34
3.2.3.4.3. GLEAMS Modeling 34
3.2.3.4.4. Other Modeling Efforts 36
3.2.3.4.5. Monitoring Data 37
3.2.3.4.6. Concentrations in Water Used for Risk Assessment 38
3.2.3.5. Oral Exposure from Contaminated Fish 39
3.2.3.6. Dermal Exposure from Swimming in Contaminated Water 40
3.2.3.7. Oral Exposure from Contaminated Vegetation 40
3.3. DOSE-RESPONSE ASSESSMENT 42
3.3.1. Overview 42
3.3.2. Chronic RfD 42
3.3.3. Acute RfD 43

3.3.4. Surrogate RfD for Occupational Exposures 43
3.3.5. Dose-Severity Relationships 44
3.4. RISK CHARACTERIZATION 45
3.4.1. Overview 45
3.4.2. Workers 46
3.4.3. General Public 46
3.4.4. Sensitive Subgroups 48
3.4.5. Connected Actions 48
3.4.6. Cumulative Effects 49
4. ECOLOGICAL RISK ASSESSMENT 50
4.1. HAZARD IDENTIFICATION 50
4.1.1. Overview 50
4.1.2. Terrestrial Organisms 50
4.1.2.1. Mammals 50
4.1.2.2. Birds 51
4.1.2.3. Reptiles and Amphibians (Terrestrial Phase) 52
4.1.2.4. Terrestrial Invertebrates 53
4.1.2.5. Terrestrial Plants (Macrophytes) 54
4.1.2.5.1. General Considerations 54
4.1.2.5.2. Toxicity Data 55
4.1.2.5.3. Resistance 57
4.1.2.6. Terrestrial Microorganisms 58
4.1.3. Aquatic Organisms 59
4.1.3.1. Fish 59
4.1.3.2. Amphibians (Aquatic Phase) 60
4.1.3.3. Aquatic Invertebrates 60
4.1.3.4. Aquatic Plants 61
4.1.3.4.1. Algae 62
4.1.3.4.2. Aquatic Macrophytes 63
4.2. EXPOSURE ASSESSMENT 65
4.2.1. Overview 65
4.2.2. Mammals and Birds 65
4.2.2.1. Direct Spray 66
4.2.2.2. Dermal Contact with Contaminated Vegetation 66
4.2.2.3. Ingestion of Contaminated Vegetation or Prey 66
4.2.2.4. Ingestion of Contaminated Water 67
4.2.2.5. Consumption of Contaminated Fish 68

4.2.3. Terrestrial Invertebrates 68
4.2.3.1. Direct Spray and Drift 68
4.2.3.2. Ingestion of Contaminated Vegetation or Prey 69
4.2.4. Terrestrial Plants 69
4.2.4.1. Direct Spray 70
4.2.4.2. Off-Site Drift 70
4.2.4.3. Runoff and Soil Mobility 71
4.2.4.4. Contaminated Irrigation Water 71
4.2.4.5. Wind Erosion 72
4.2.5. Aquatic Organisms 73
4.3. DOSE-RESPONSE ASSESSMENT 74
4.3.1. Overview 74
4.3.2. Toxicity to Terrestrial Organisms 75
4.3.2.1. Mammals 75
4.3.2.2. Birds 76
4.3.2.3. Reptiles and Amphibians (Terrestrial Phase) 76
4.3.2.4. Terrestrial Invertebrates 76
4.3.2.5. Terrestrial Plants (Macrophytes) 77
4.3.2.6. Terrestrial Microorganisms 77
4.3.3. Aquatic Organisms 78
4.3.3.1. Fish 78
4.3.3.2. Amphibians 78
4.3.3.3. Aquatic Invertebrates 79
4.3.3.4. Aquatic Plants 79
4.3.3.4.1. Algae 79
4.3.3.4.2. Macrophytes 80
4.4. RISK CHARACTERIZATION 81
4.4.1. Overview 81
4.4.2. Terrestrial Organisms 82
4.4.2.1. Mammals 82
4.4.2.2. Birds 83
4.4.2.3. Reptiles and Amphibians (Terrestrial Phase) 84
4.4.2.4. Terrestrial Invertebrates 84
4.4.2.5. Terrestrial Plants 84
4.4.2.5.1. Direct Spray and Spray Drift 84
4.4.2.5.2. Soil Exposures by Runoff 85

4.4.2.5.3. Contaminated Irrigation Water 86
4.4.2.5.4. Wind Erosion 87
4.4.2.6. Terrestrial Microorganisms 87
4.4.3. Aquatic Organisms 88
4.4.3.1. Fish 88
4.4.3.2. Amphibians 88
4.4.3.4. Aquatic Invertebrates 88
4.4.3.4. Aquatic Plants 89
4.4.3.4.1. Algae 89
4.4.3.4.2. Macrophytes 89
5. REFERENCES 91

LIST OF TABLES

Table 1: Summary of Open Literature Most Relevant to Risk Assessment 117
Table 2: Chemical and Physical Properties 118
Table 3: Designated and Representative Formulations 122
Table 4: Regional Summary of Chlorsulfuron Use by the Forest Service from 2000 to 2004... 123
Table 5: Summary of LD_{50} values for chlorsulfuron and chlorsulfuron formulations 124
Table 6: Directed Foliar Applications - Derivation of Worker Exposure Rates 125
Table 7: Ground Broadcast Applications - Derivation of Worker Exposure Rates 126
Table 8: Aerial Applications - Derivation of Worker Exposure Rates 127
Table 9: Precipitation, Temperature and Classifications for Standard Test Sites 128
Table 10: Input Parameters for Fields and Waterbodies Used in Gleams-Driver Modeling..... 129
Table 11: Chemical parameters used in Gleams-Driver modeling 130
Table 12: Summary of Modeled Concentrations in Surface Water 131
Table 13: Concentrations in surface water used in this risk assessment 132
Table 14: Estimated residues in food items per lb a.i. applied 133
Table 15: Summary of toxicity values used in human health risk assessment 134
Table 16: Terrestrial Nontarget Animals Used in Ecological Risk Assessment 135
Table 17: Diets: Metabolizable Energy of Various Food Commodities 136
Table 18: Summary of toxicity values used in ecological risk assessment 137

LIST OF FIGURES

Figure 1: Lower Bound Estimated Agricultural Use of Chlorsulfuron for 2012 138
Figure 2: Upper Bound Estimated Agricultural Use of Chlorsulfuron for 2012 139
Figure 3: Environmental Metabolites of Chlorsulfuron 140
Figure 4: Relative Sensitivities of Monocots and Dicots 141
Figure 5: Summary of EC_{50} values in phytotoxicity assays by Jettner et al. (1999) 142
Figure 6: Definitive EC_{50} values for algae 143
Figure 7: Comparison of Toxicity to Freshwater Macrophytes and Freshwater Algae 144

LIST OF APPENDICES

Appendix 1: Toxicity to mammals. 145
Appendix 2: Toxicity to birds 169
Appendix 3: Toxicity to Terrestrial Invertebrates. 172
Appendix 4: Toxicity to Terrestrial Plants 174
Appendix 5: Toxicity to fish. 184
Appendix 6: Toxicity to aquatic invertebrates 187
Appendix 7: Toxicity to Aquatic Plants 189
Appendix 8: Gleams-Driver Modeling 198
Appendix 9: EPA Surface Water Models 206

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
AEL	adverse-effect level
a.e.	acid equivalent
a.i.	active ingredient
a.k.a.	also known as
a.s.	active substance
ALS	acetolactate synthase
APHIS	Animal and Plant Health Inspection Service
ATSDR	Agency for Toxic Substances and Disease Registry
ASAE	American Society of Agricultural Engineers
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
CI	confidence interval
cm	centimeter
CNS	central nervous system
COC	crop oil concentrates
DAA	days after application
DAT	days after treatment
DER	data evaluation record
d.f.	degrees of freedom
EC	emulsifiable concentrate
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
ECOTOX	ECOTOXicology (database used by U.S. EPA/OPP)
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
g	gram
GLP	Good Laboratory Practices
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient
HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IRED	Interim Reregistration Eligibility Decision
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram

$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
LR_{50}	50% lethal response [EFSA/European term]
m	meter
M	male
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MSO	methylated seed oil
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
NIOSH	National Institute for Occupational Safety and Health
NIS	nonionic surfactant
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
N.R.	not reported
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
SDS	safety data sheet
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
T.G.I.A.	Technical grade active ingredient

TRED	Tolerance Reassessment Eligibility Decision
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
VMD	volume median diameter (for droplet size distributions)
WHO	World Health Organization
WWSA	Weed Science Society of America

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

This risk assessment updates a previous USDA Forest Service risk assessment on chlorsulfuron. Chlorsulfuron is used for pre-emergent and post-emergent control of many grasses and broadleaf weeds in both agricultural and non-agricultural applications. While no formulations of chlorsulfuron are labeled explicitly for forestry applications, some formulations are labeled for non-crop sites, including rights-of-way. The Forest Service has indicated that chlorsulfuron is generally used in Forest Service programs for pre- and post-emergent control of noxious and invasive weeds in rangelands, pastures, and along right-of-ways. The most common methods of ground application for chlorsulfuron involve backpack (selective foliar) and boom spray (broadcast foliar) operations. The Forest Service does not use aerial applications for chlorsulfuron. Nonetheless, both of the formulations of chlorsulfuron considered explicitly in this risk assessment are labeled for aerial applications, and aerial applications are included in this risk assessment in the event the Forest Service wishes to consider this application method. For this risk assessment, the typical application rate of 0.0625 lb a.i./acre is used because this is the maximum labelled application rate for rangeland.

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

For both workers and members of the general public, none of the exposure scenarios exceed the level of concern even at the upper bounds of estimated exposures. Mild irritation to the skin and eyes can result from relatively high levels of exposure to chlorsulfuron. From a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling chlorsulfuron. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

Chlorsulfuron is an effective and potent herbicide likely to cause adverse effects on some nontarget terrestrial and aquatic plant species, unless measures are taken to limit exposure. For terrestrial plants, the dominant factor in the risk characterization is the potency of chlorsulfuron, relative to the application rate. The typical application rate considered in this risk assessment, 0.0625 lb a.i./acre, is above the NOAEC in vegetative vigor (direct spray) assays by a factor greater than 78,000 for sensitive species and 56 for tolerant species. If chlorsulfuron is applied directly to either sensitive or tolerant species, adverse effects in the exposed plants are virtually certain. The HQs associated with drift are also substantial, particularly for sensitive species. At a distance of 900 feet downwind, the HQs for sensitive species are 24 to 969 for fine droplet applications and 24 to 250 for coarse droplet applications, depending on the application method. The HQs associated with soil exposures are also substantial but less than those associated with direct deposition. For runoff, the HQs are 11 (0.000007 to 460) for sensitive species and 0.5 (0.0000003 to 19) for tolerant species. For the use of contaminated irrigation water, the HQs are 2212 (0.02 to 23,364) for sensitive species and 1.6 (0.00001 to 17) for tolerant species. The wide range of HQs reflects the wide range of conditions used in the GLEAMS-Driver modeling to estimate runoff and chlorsulfuron concentrations in surface water. The HQs associated with wind erosion of contaminated soil are 5 (1.1 to 11) for sensitive species and 0.004 (0.0.0008 to

0.008) for tolerant species. The product labels for the formulations designated by the Forest Service specifically note potential hazards to terrestrial vegetation associated with the use of contaminated water for irrigation and with the transport by wind of contaminated soil.

For aquatic plants, risks to sensitive species of macrophytes are greater than risks to sensitive species of algae. For sensitive species of aquatic macrophytes, the acute HQ is 33 with a range of 0.001 to 172 and the longer-term HQ is 17 with a range of 0.0004 to 99. For acute exposures in algae, the acute HQ is 0.8 with a range of 0.00003 to 4 for sensitive species but below the level of concern for tolerant species. For tolerant species of both macrophytes and algae, all longer-term HQs are below the level of concern.

Just as there is little doubt that chlorsulfuron may adversely affect some plant species, there is no clear basis for suggesting that effects on terrestrial or aquatic animals are likely or would be substantial. Adverse effects in mammals, birds, terrestrial insects, and microorganisms are not likely at the typical application rate of 0.0625 lb a.i./acre. One study suggests that latent/sublethal chlorsulfuron toxicity to one plant species could result in adverse reproductive effects in one species of beetle that consumes the leaves of the affected plant. This appears to be a highly specific plant-insect interaction that is not confirmed in publications by other groups of researchers.

The risk characterization for aquatic animals is relatively simple and unambiguous. Chlorsulfuron appears to have a very low potential to cause any direct adverse effects in aquatic animals. All of the upper bounds of the HQs for aquatic animals are extremely low, ranging from 0.0001 (acute exposures in tolerant fish) to 0.002 (acute exposures to sensitive aquatic invertebrates).

While the risk characterization for chlorsulfuron focuses on the potential for direct toxic effects, there is also a potential for indirect effects in virtually all groups of nontarget organisms. Alterations in vegetation following the application of any effective herbicide, including chlorsulfuron, could alter vegetation in ways that may be beneficial to some species and detrimental to others. The magnitudes of these indirect effects are likely to vary over time. If algae are adversely affected by chlorsulfuron, cumulative impacts on aquatic invertebrates and fish could be detrimental due to a decrease in available food and habitat modification. In the event of an accidental spill, oxygen depletion due to decaying vegetation could be detrimental to many aquatic animals.

1. INTRODUCTION

1.1. Chemical Specific Information

This document provides human health and ecological risk assessments on the use of chlorsulfuron in Forest Service vegetation management programs. This risk assessment updates a previous USDA Forest Service risk assessment on chlorsulfuron (SERA 2004a).

The previous Forest Service risk assessment was completed just before the release of the U.S. EPA Reregistration Eligibility Decision (RED) and related documents (U.S. EPA/OPP 2005a,b) on chlorsulfuron. In addition to the EPA documents for the RED, chlorsulfuron is currently under registration review by the U.S. EPA/OPP. The U.S. EPA registration review program operates on a 15-year cycle, and the registration review for chlorsulfuron is scheduled to be completed by 2018 (U.S. EPA/OPP 2013a). While the final registration review documents are not available, several relevant risk assessments and related reviews are available from the U.S. EPA/OPP's Health Effects Division (U.S. EPA/OPP/HED 2002a, 2012a, 2013a, 2015a) and Ecological Fate and Environmental Effects Division (U.S. EPA/OPP/EFED 2004a,b, 2012a, 2015a,b).

In the previous Forest Service risk assessment (SERA 2004a), full copies of the studies submitted to the U.S. EPA in support of the registration of chlorsulfuron were kindly provided by the U.S. EPA Office of Pesticide Programs. The U.S. EPA/OPP no longer provides full copies of registrant studies for risk assessments conducted in support of activities outside of U.S. EPA/OPP. Consequently, only summaries of the registrant studies from SERA (2004a) are included in the current Forest Service risk assessment. Nonetheless, additional summaries from EPA in the form of Data Evaluation Records (DERs) were obtained from EPA web sites as specified at the start of Section 5 (References). DERs are discussed further in Section 1.2. In the interest of transparency, information on registrant studies based either on copies of full studies or DERs is cited in the standard author/date format, supplemented by the MRID number. Information taken only from EPA documents is cited using the MRID number and a reference to the EPA document in which the information is summarized.

The U.S. EPA/OPP often reevaluates studies during the preparation of a RED or registration review, and the values used in the current risk assessment reflect the more recent risk assessment documents from EPA (cited above). Any substantial discrepancies between the summaries of the registrant studies from the previous Forest Service risk assessment and the summaries in the more recent EPA documents are discussed in the text of the current risk assessment as appropriate.

Updates of the open literature on chlorsulfuron were conducted using TOXLINE (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TOXLINE) and ECOTOX (http://cfpub.epa.gov/ecotox/). As summarized in Table 1, most of the newer literature relates to effects on or resistance in terrestrial plants. The focus on terrestrial plants is common for herbicides that do not appear to have substantial effects on other groups of nontarget organisms.

Other relevant studies were identified through reviews and risk assessments in the open literature (e.g., EFSA 2008; ENSR 2005; European Commission 2010; FAO/WHO 2003; HSDB 2006).

Generally, these reviews are used only to identify published studies to ensure adequate coverage of the literature. Information taken from reviews and used directly in this risk assessment (e.g., unpublished studies) is specifically noted in the text.

1.2. General Information

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

This is a technical support document which addresses some specialized technical areas. Nevertheless an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2014a). The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. As with the previous risk assessment, no attempt is made to encompass all studies. The primary focus is on studies that directly impact the assessment of potential risks. The level of detail in study summaries presented in the appendices and the discussions in chapters 2, 3, and 4 of the risk assessment are intended to be sufficient to support an independent review of the risk analyses.

As noted in Section 1.1, studies submitted by registrants in support of the registration of chlorsulfuron are used extensively in this risk assessment. In any risk assessment based substantially on registrant-submitted studies, the Forest Service is sensitive to concerns of potential bias. The general concern might be expressed as follows:

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

This concern is largely without foundation. While any study (published or unpublished) can be falsified, concerns with the design, conduct and reporting of studies submitted to the U.S. EPA for pesticide registration are minor. The design of the studies submitted for pesticide registration is based on strict guidelines for both the conduct and reporting of studies. These guidelines are developed by the U.S. EPA and not by the registrants. Full copies of the guidelines for these studies are available at http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm. Virtually all studies accepted by the U.S. EPA/OPP are conducted under Good Laboratory Practices (GLPs). GLPs are an elaborate set of procedures which involve documentation and independent quality control and quality assurance that substantially exceed the levels typically seen in open literature publications. As a final point, the EPA reviews each submitted study for adherence to the relevant study guidelines. These reviews most often take the form of Data Evaluation Records (DERs). While the nature and complexity of DERs varies according to the nature and complexity of the particular studies, each DER involves an independent assessment of the study to ensure that the EPA Guidelines are followed and that the results are expressed accurately. In

many instances, the U.S. EPA/OPP will reanalyze raw data from the study as a check or elaboration of data analyses presented in the study. In addition, each DER undergoes internal review (and sometimes several layers of review). The DERs prepared by the U.S. EPA form the basis of EPA risk assessments and, when available, DERs are used in Forest Service risk assessments.

Despite the real and legitimate concerns with risk assessments based largely on registrant-submitted studies, data quality and data integrity are not substantial concerns. The major limitation of risk assessments based substantially on registrant-submitted studies involves the nature and diversity of the available studies. The studies required by the U.S. EPA are based on a relatively narrow set of criteria in a relatively small subset of species and follow standardized protocols. The relevance of this limitation to the current risk assessment on chlorsulfuron is noted in various parts of this risk assessment as appropriate.

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

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

Some of the calculations, however, are cumbersome. For those calculations, an EXCEL workbook (i.e., sets of EXCEL worksheets) is included as an attachment to this risk assessment, as discussed further in Section 2.4. The worksheets in this workbook provide the detail for the estimates cited in the body of the document. Documentation for the use of this workbook is presented in SERA (2016a).

The EXCEL workbook is an integral part of the risk assessment. The worksheets contained in the workbook are designed to isolate the numerous calculations from the risk assessment narrative. In general, all calculations of exposure scenarios and quantitative risk characterizations are derived and contained in the worksheets. In these worksheets as well as in the text of this risk assessment, risks are characterized using the hazard quotient (HQ), the ratio of the estimated exposure to a toxicity value, typically a no adverse effect level or concentration (i.e., NOAEL or NOAEC). While the HQs are calculated in the EXCEL workbook, both the rationale for the calculations and the interpretation of the hazard quotients are contained in this

risk assessment document. Details of the general use of HQs in Forest Service risk assessments are given in SERA (2014a).

2. PROGRAMS DESCRIPTION

2.1. Overview

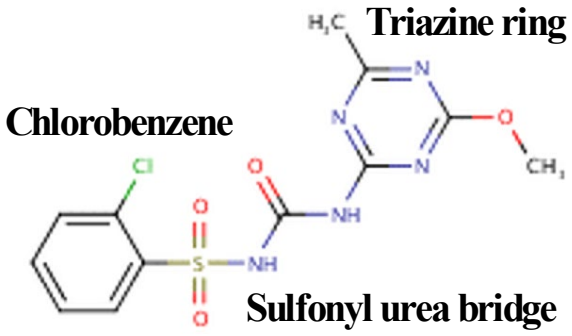
Chlorsulfuron is used for pre-emergent and post-emergent control of many grasses and broadleaf weeds in both agricultural and non-agricultural applications. While no formulations of chlorsulfuron are labeled explicitly for forestry applications, some formulations are labeled for non-crop sites, including rights-of-way. The Forest Service has indicated that chlorsulfuron is generally used in Forest Service programs for pre- and post-emergent control of noxious and invasive weeds in rangelands, pastures, and along right-of-ways. Two formulations of chlorsulfuron as the sole active ingredient are labelled for rights-of-way and rangeland: Chlorsulfuron 75 and Telar XP. These formulations are explicitly considered in the current risk assessment. Both formulations are dry flowables that contain 75% (w/w) chlorsulfuron.

The most common methods of ground application for chlorsulfuron involve backpack (selective foliar) and boom spray (broadcast foliar) operations. The Forest Service does not use aerial applications for chlorsulfuron. Nonetheless, both of the formulations of chlorsulfuron considered explicitly in this risk assessment are labeled for aerial applications, and aerial applications are included in this risk assessment in the event the Forest Service may wish to consider this application method. For this risk assessment, the typical application rate of 0.0625 lb a.i./acre is used because this is the maximum application rate for rangeland. An application rate up to 0.25 lb a.i./acre (the highest labelled rate for any formulation of chlorsulfuron) is considered in the risk characterization (Section 3.4); however, this high rate would be atypical of Forest Service applications.

The amounts of chlorsulfuron used in agricultural and forestry related applications are reasonably well documented. While forestry related uses of chlorsulfuron may be predominant in some locations, the agricultural uses of chlorsulfuron appear to be much greater than forestry related uses.

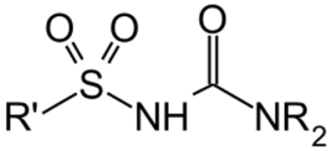
2.2. Chemical Description and Commercial Formulations

Chlorsulfuron is the common name for 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl] benzenesulfonamide. Chlorsulfuron is essentially a chlorobenzene ring linked to a triazine ring (with methyl [-CH_3] and methoxy [-OCH_3] substituents) by a sulfonyl urea bridge:



Selected chemical and physical properties of chlorsulfuron are summarized in Table 2. Chlorsulfuron has been registered in the United States since 1982 and was originally developed by E. I. du Pont de Nemours Co. (Patent US 4127405, Tomlin 2004).

Chlorsulfuron is a member of the sulfonyl urea herbicides, a large class of herbicides with the following general structure:



Other sulfonyl urea herbicides used by the Forest Service and for which Forest Service risk assessments are available include metsulfuron methyl (SERA 2004b) and sulfometuron methyl (SERA 2004c).

As with the previous risk assessment, no formulations of chlorsulfuron are explicitly labelled for forestry applications; nonetheless, several formulations are labeled for non-crop sites including rights-of-way. The Forest Service has indicated that chlorsulfuron is generally used in Forest Service programs for pre- and post-emergent control of noxious and invasive weeds in rangelands, pastures, and along right-of-ways. These uses are essentially identical to the uses of chlorsulfuron covered in the previous Forest Service risk assessment (SERA 2004a). The previously conducted Forest Service risk assessment covers three formulations: Telar DF, Glean FC, and Corsair, all from DuPont. These formulations appear to have been discontinued or at least the formulation names have been changed. The formulation names covered in the previous risk assessment are no longer listed at label sites (e.g., http://www.cdms.net/Label-Database; http://iaspub.epa.gov/apex/pesticides/f?p=PPLS:1).

For the current risk assessment, the Forest Service has designated two formulations: Chlorsulfuron 75 and Telar XP. Both of these formulations are labelled for weed control on non-crop sites including rangeland and rights-of-way. An overview of these formulations is given in Table 3, and these formulations are explicitly considered in the current risk assessment. Both of these formulations are dry flowables that contain 75% chlorsulfuron (w/w).

The formulations given in Table 3 are not intended to be exclusive. Other formulations of chlorsulfuron are available commercially (e.g., 34 active formulations listed by Kegley et al. 2004), and new formulations of chlorsulfuron may become available at some point in the future. The Forest Service may elect to use any formulation of chlorsulfuron registered for applications relevant to forestry. If other formulations are used in Forest Service programs, attempts should be made to identify information on the inerts in the formulations as well as the toxicity of the formulations to ensure that the formulation under consideration is comparable to the formulations explicitly designated in Table 3. Material Safety Data Sheets (MSDSs) or Safety Data Sheets (SDSs) for formulations will contain some information on the toxicity of the formulation and/or ingredients in the formulation and additional information may be available from manufacturers or suppliers. For clarity, it should be noted that SDSs are a more recent formatting of information that was typically included in MSDSs (e.g., https://www.msdsonline.com/blog/compliance-education/2012/08/20/from-msds-to-sds). Both

MSDSs and SDSs are still in common use. As discussed by NAS (2013, p. 120), standard acute mammalian toxicity studies on formulations are required by the U.S. EPA. These studies are typically summarized on MSDS/SDSs.

Some formulations of chlorsulfuron are available as mixtures with other herbicides—e.g., sulfometuron methyl in Landmark XP, sulfentrazone and sulfometuron methyl in Cimarron Plus and Throttle XP, aminocyclopyrachlor in Perspective, and metsulfuron methyl in both Chisum and Report Extra. As with all Forest Service risk assessments as well as the EPA risk assessments cited in Section 1 for reregistration and registration review, applications of different active ingredients as a formulation mixture or tank mixture are not considered in the current risk assessment. Pesticide mixtures can be considered at the program-specific level using a utility in the most recent version of WorksheetMaker (SERA 2016a).

2.4. Application Methods

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

Both formulations of chlorsulfuron listed in Table 3 are labeled for ground and aerial applications. The Forest Service generally avoids aerial applications. Accordingly, the Forest Service indicated specifically that chlorsulfuron applications in Forest Service programs or projects will be most commonly applied in ground applications using boom sprayers (broadcast foliar applications) or backpack sprayers (directed foliar applications). Nonetheless, and consistent with the previous risk assessment on chlorsulfuron (SERA 2004a), aerial applications are covered by this updated risk assessment in the event that the Forest Service elects to consider aerial applications.

As discussed in Section 1.3, this risk assessment is accompanied by an EXCEL workbook that details the exposure scenarios for chlorsulfuron and the hazard quotients associated with the various exposure scenarios. While the utility used to create the EXCEL workbook generally covers only a single application method per workbook (SERA 2011a), the workbook that accompanies this risk assessment is customized to cover the three application methods considered in this risk assessment—i.e., directed foliar (backpack) and broadcast foliar applications by ground or aerial methods.

2.4. Mixing and Application Rates

As summarized in Table 3, the maximum application rate for the formulations of chlorsulfuron related to forestry uses is 0.14 lb a.i./acre. As detailed on the product labels for these formulations, recommended application rates vary with the species of weed to be controlled and site-specific factors such as soil pH. More generally, the maximum application rate for rangeland is 0.0625 lb a.i./acre. The maximum application rate for any formulation is 0.25 lb a.i./acre for ornamentals and turf (U.S. EPA/OPP 2004a, p. 3, Table 1; U.S. EPA/OPP 2012a, p. 6).

As summarized in Table 4 and discussed further in Section 2.5 (Use Statistics), the average application rate for chlorsulfuron in Forest Service programs from 2000 to 2004 is 0.053 lb

a.i./acre, which is probably representative of typical Forest Service uses on rangeland or rights-of-way. As also summarized in Table 4, the highest application rates used by the Forest Service are about 0.25 lb a.i./acre. The minor exceedances (e.g., up to 0.273 lb a.i./acre) probably reflect rounding of either total pounds applied or numbers of acres treated.

The previous Forest Service risk assessment on chlorsulfuron (SERA 2004a) uses 0.056 lb a.i./acre as the application rate for the workbook released with the risk assessment and considers application rates up to 0.25 lb a.i./acre in the risk characterizations for human health and ecological effects. The EXCEL workbook released with this updated risk assessment uses the application rate of 0.0625 lb a.i./acre—i.e., the maximum application rate for rangeland—for the development of hazard quotients used in the risk characterization. As with the previous risk assessment, application rates up to 0.25 lb a.i./acre are considered in the risk characterization, although this application rate probably will not be used regularly in Forest Service programs or projects.

In addition to application rates, application volumes, meaning the number of gallons of pesticide solution applied per acre, have an impact on the estimates of potential risk. The extent to which a formulation of chlorsulfuron is diluted prior to application primarily influences dermal and direct spray scenarios, both of which depend on 'field dilution' (i.e., the concentration of chlorsulfuron in the applied spray). In all cases, the higher the herbicide concentration (i.e., equivalent to the lower dilution of the herbicide), the greater the risk. As summarized in Table 4, the recommended application volumes for chlorsulfuron formulations range from 10 to 300 gallons/acre for ground applications and 3 to 300 gallons per acre for aerial applications.

In the EXCEL workbooks that accompany this risk assessment, the range of application volumes is taken as 3 to 300 gallons per acre to encompass the application volumes that could be used in both aerial and ground applications—i.e., 3 gallons per acre is the lower bound for aerial applications and 300 gallons per acre is the upper bound for ground applications (Table 4). The central estimate of the application volume is taken as 10 gallons/acre (i.e., the lower bound of the application volume for ground applications). The dilution volumes used in the workbooks are intended only to encompass the ranges of the chlorsulfuron concentrations in field solutions that might be used in Forest Service programs.

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

2.5. Use Statistics

Forest Service risk assessments attempt to characterize the use of a pesticide in Forest Service programs relative to the use of the pesticide in agricultural applications. Forest Service pesticide use reports up to the year 2004 are available on the Forest Service web site (http://www.fs.fed.us/foresthealth/pesticide/reports.shtml). While these use reports may not reflect current or future use, the reports are the most recent information posted by the Forest Service.

Applications of chlorsulfuron by the Forest Service or their cooperators are summarized in Table 4 for years 2000 to 2004. Chlorsulfuron applications by the Forest Service occurred

primarily in the north to mid central areas of the U.S.—i.e., Region 1 (Northern), Region 2 (Rocky Mountain Region), and Region 4 (Intermountain Region). One minor (1.5 lbs) application occurred in Region 5 (Pacific Southwest Region). The total Forest Service use of about 5500 lbs corresponds to an average annual use of about 1100 lbs with an average application rate across all regions of about 0.053 lb a.i./acre. This average application rate is virtually identical to the average application rate of 0.056 lb a.i./acre from the previous Forest Service risk assessment (SERA 2004a). The average application rate for Region 1 (0.088 lb a.i./acre) and Region 2 (0.067 lb a.i./acre) are similar and greater than the application rate for Region 4 (0.022 lb a.i./acre). The maximum application rate used in any Forest Service application is reported as 0.273 lb a.i./acre (i.e., Region 4, Forest 2, in 2004). As noted in Table 4, some application rates from Region 4 are censored because the data appear to be errors in reporting.

Information on the agricultural use of pesticides is compiled by the U.S. Geological Survey (USGS 2015). The agricultural use of chlorsulfuron in 2012 (the most recent year for which data are available) is estimated from about 60,000 lbs (Figure 1) to somewhat greater than 90,000 lbs (Figure 2). The greatest use of chlorsulfuron is in the central United States running from Kansas to Texas and eastwards to western Mississippi with an additional cluster of substantial use in the Carolinas. Based on use data by crop (also summarized in Figure 1 and Figure 2), chlorsulfuron is currently used largely on wheat. Over the period from 1992 to 2012, the annual agricultural use of chlorsulfuron has been variable with upper bound use estimates ranging from about 45,000 lbs in 2001 to greater than 120,000 lbs in 1995 with a slight tendency of decreasing use over time.

Detailed pesticide use statistics are compiled by the state of California. The use statistics from California for 2013, the most recent year for which statistics are available, indicate that a total of 3149.04 lbs of chlorsulfuron was applied in California (CDPR 2015, p. 255). The major use related to forestry applications is 2501.04 lbs applied to rights-of-way, which accounts for about 80% [2501.04 lbs ÷ 3149.04 ≈ 0.79422] of the total use in California for 2013. CDPR (2015, p. 255) does not provide estimates of acreage treated for all chlorsulfuron applications to rights-of-way but does note that 6.23 pounds was applied to 255.42 acres of rights-of-way for an average application rate of about 0.023 lb a.i./acre [6.23 lbs ÷ 255.42 acres ≈ 0.023384]. This average application rate of 0.023 lb a.i./acre is virtually identical to the average rate of 0.022 lb a.i./acre from Forest Service Region 4, as summarized in Table 4. The use data from California indicates that forestry related applications are the predominant use of chlorsulfuron in California. As discussed above and illustrated in Figure 1 and Figure 2, the agricultural uses of chlorsulfuron in California are minimal. Thus, the predominant use of chlorsulfuron in forestry related applications in California is not likely to hold in other parts of the country where agricultural uses of chlorsulfuron are substantial—e.g., the central to southern/southeastern areas of the United States.

As part of the registration review for chlorsulfuron discussed in Section 1.1, the Biological and Economic Analysis Division (BEAD) of U.S. EPA/OPP (2012a) conducted a use analysis of chlorsulfuron. Consistent with the above discussion, U.S. EPA/OPP (2012a) notes that the average annual use of chlorsulfuron in the United States is about 50,000 lbs with an average

application rate of 0.01 lbs a.i./acre (U.S. EPA/OPP 2012a, p. 2) with applications to wheat accounting for more than 95% of the total use (U.S. EPA/OPP 2012a, Figure 3).

While forestry related uses of chlorsulfuron may be predominant in some locations, the agricultural uses of chlorsulfuron appear to be much greater than forestry related applications within the United States as a whole. This is a common pattern in pesticides which partly reflects, the larger areas of crop cultivation relative to forestry management—i.e., about 613 million acres for agriculture (http://www.epa.gov/agriculture/ag101/landuse.html) relative to 193 million acres of forests managed by the Forest Service (http://www.fs.fed.us/documents/USFS_An_Overview_0106MJS.pdf) and the more intensive use of pesticides in agriculture relative to forestry.

3. HUMAN HEALTH

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

In experimental mammals, the acute oral LD_{50} for chlorsulfuron in rats is greater than 5000 mg/kg, which indicates a low order of toxicity. Acute exposure studies of chlorsulfuron and chlorsulfuron formulations give similar results, indicating that formulations of chlorsulfuron are not more toxic than chlorsulfuron alone. The most common signs of acute, subchronic, and chronic toxicity are weight loss and decreased body weight gain. The only other commonly noted effects are changes in various hematological parameters and general gross pathological changes to several organs. None of these changes, however, suggests specific target organ toxicities. Appropriate tests provide no evidence that chlorsulfuron presents any reproductive risks or causes malformations or cancer. Results of all mutagenicity tests on chlorsulfuron are negative. The inhalation toxicity of chlorsulfuron is not well documented in the literature; however, the results of a single acute inhalation study indicate that chlorsulfuron produces local irritant effects. Chlorsulfuron is mildly irritating to the eyes and skin, but does not produce sensitizing effects following repeated dermal exposure.

Limited information is available on the toxicokinetics of chlorsulfuron. Chlorsulfuron does not appear to concentrate or be retained in tissues following either single or multiple dose administration. Chlorsulfuron exhibits first order elimination kinetics, with an estimated half-life in rats of < 6 hours. In all mammalian species studied, chlorsulfuron and its metabolites are extensively and rapidly cleared by a combination of excretion and metabolism. The primary excretory compartment for chlorsulfuron and its metabolites is the urine, with smaller amounts excreted in the feces. Most of the chlorsulfuron excreted in urine is in the form of the parent compound. Studies on the toxicity of chlorsulfuron metabolites have not been conducted.

As discussed in the exposure assessment, skin absorption is the primary route of exposure for workers. Data regarding the dermal absorption kinetics of chlorsulfuron are not available in the published or unpublished literature. For this risk assessment, estimates of dermal absorption rates, both zero order and first order, are based on quantitative structure-activity relationships. These estimates of dermal absorption rates are used in turn to estimate the amounts of chlorsulfuron that might be absorbed by workers, and the estimated rates of dermal absorption are used with the available dose-response data to characterize risk. The lack of experimental data regarding dermal absorption of chlorsulfuron adds substantial uncertainties to this risk assessment. Uncertainties in the rates of dermal absorption, although they are substantial, can be estimated quantitatively and are incorporated in the human health exposure assessment.

3.1.2. Mechanism of Action

The mechanism of action for the phytotoxicity of chlorsulfuron and other sulfonylurea herbicides is well understood. As discussed further in Section 4.1.2.5, the sulfonyl urea herbicides act by inhibiting acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids (i.e., valine, leucine, and isoleucine), all of which are essential for plant growth (e.g., Blair and Martin 1988; Brown 1990). The mechanism of action for chlorsulfuron and other sulfonylurea herbicides in mammals, however, is not well characterized.

U.S. EPA/OPP (2015a, p.4) cites the paper by Joutel et al. (1996) as indicating that …*humans do have an ALS enzyme*. Joutel et al. (1996), however, note that a gene identified in a fetal brain cDNA library encodes a putative protein similar to ALS. As noted by Duggleby et al. (2000), vectors for this presumed ALS did not yield a soluble protein with ALS activity. In any event, there is no indication that chlorsulfuron or other sulfonylurea herbicides act in humans or other vertebrates via an inhibition of ALS or similar enzymes.

Apart from the sulfonylureas used as herbicides, there is a class of other sulfonylureas that are used in the management of type II diabetes. These sulfonylureas act by blocking ATP-sensitive potassium channels of pancreatic beta cells resulting in an increase in the release of endogenous insulin (Archer et al. 2013; Kalra and Gupta 2015; Kalra et al. 2015; Melander et al. 1989). A notable side-effect for these sulfonylurea drugs is hypoglycemia, which is a reduction in blood glucose to undesirable levels (Bodmer et al. 2008). Some antidiabetic sulfonylurea drugs may also reduce the hepatic extraction of insulin and reduce blood cholesterol and serum triglycerides (Melander et al. 1989). As discussed in subsequent sections of this risk assessment, there is no indication that chlorsulfuron has an influence on blood glucose, cholesterol, or triglycerides.

Sulfonamides are a class of antibiotic drugs that may augment the hypoglycemic effects of some sulfonylurea antidiabetic drugs. Exposures to some sulfonamides are associated with the development of hemolytic anemia (i.e., a lysis or destruction of blood cells that results in a decreased number of red blood cells) in humans (Dickerman 1981; Issaragrisil et al. 1997). A single case report, discussed further in Section 3.1.16, also noted a potentiation of a sulfonylurea used for the control of diabetes with a sulfonamide antibiotic.

Sulfometuron methyl, another sulfonylurea herbicide, has been associated with hemolytic anemia (SERA 2004c); however, this effect has not been observed consistently with chlorsulfuron. As discussed further in Section 3.1.5, a decrease in hematocrit was observed in one chronic study in dogs (Atkinson 1991, MRID 41862601) but not in longer-term studies in rats (Wood et al. 1980b, MRID 00031419; Wood et al. 1981a, MRID 00086003).

3.1.3. Pharmacokinetics and Metabolism

3.1.3.1. Metabolism and Distribution

Two types of metabolism are considered in Forest Service risk assessments—i.e., *in vivo* mammalian metabolites, which are discussed in this section, and environmental metabolites, which are discussed in Section 3.1.15.1. For both types of metabolites, the primary concern is whether toxic metabolites need to be considered quantitatively in the risk assessment. For some pesticides (e.g., the formation of malaoxon from malathion), this is an important consideration. For chlorsulfuron, however, toxic metabolites are not a major concern.

For pesticide registration, the U.S. EPA/OPP generally requires a relatively standard metabolism study in rats in which the compound is administered orally or by a combination of oral and intravenous routes (U.S. EPA/OPPTS 1998a). A relatively detailed summary of one such study (MRID 42540701) is provided in an EPA review (U.S. EPA/OPP/HED 2002b, pp. 16-19). In the acute phase of this study, rats (five/group/sex) were administered gavage doses of ^{14}C-chlorsulfuron (labelled in the pyridine ring) at single oral doses of 25 or 250 mg/kg bw. In the repeated dose phase, rats were dosed with non-labelled chlorsulfuron at 25 mg/kg bw/day for 14

days and then administered a single gavage dose of labelled chlorsulfuron at either 25 or 250 mg/kg bw. Chlorsulfuron was rapidly absorbed with the highest concentrations found in the blood and liver. Chlorsulfuron was also rapidly excreted in all dose groups with no substantial differences based on sex, dose, or number of exposures. Most chlorsulfuron was excreted in the urine (58-72%) with lesser amounts excreted in the feces (20-35%) and very little excreted in the air as CO_2 (<0.08%). As discussed further in Section 3.1.3.3, most of the administered dose (93-96%) was excreted by 3 days after dosing. As with other sulfonylurea herbicides (e.g., Zheng et al. 2008), the major metabolic pathway involved contraction of the sulfonyl urea bridge, oxidation, and hydroxylation.

As discussed further in Section 3.1.15.1, U.S. EPA reviewed the *in vitro* metabolites of chlorsulfuron and determined that tolerances should be based on the parent compound. In other words, a toxic metabolite requiring quantitative consideration was not identified.

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 chlorsulfuron is likely to be absorbed from the skin surface.

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

3.1.3.2.1. First-Order Dermal Absorption

Dermal absorption studies are not covered or summarized in the reviews available from U.S. EPA, the European community, or other reviews listed in Table 1. The lack of dermal absorption studies is explicitly noted in the toxicology chapter on chlorsulfuron prepared by the Office of Pesticide Programs' Health Effects Division which states: *Since no dermal absorption data are available, toxicity by the dermal route will be considered to be equivalent to toxicity by the oral route of exposure* (U.S. EPA/OPP/HED 2002b, p. 17). This approach is maintained in the most recent EPA human health risk assessment (U.S. EPA/OPP/HED 2015a, p. 8). The most recent review from the European Food Safety Authority also states that 100% dermal absorption is assumed …*in the absence of experimental values* (EFSA 2008, p. 3).

The Forest Service typically defers to the EPA unless there is a compelling reason to do otherwise. Conversely, in the absence of experimental data on first-order dermal absorption

rates for a pesticide, Forest Service risk assessments typically use quantitative structure activity relationships (QSAR), as detailed in SERA (2014a, Section 3.1.3.2.2). Based on the extensive literature on the dermal absorption of pesticides (e.g., Durkin et al. 1995; Thongsinthusak et al. 1999), including a review of U.S. EPA/OPP data on dermal absorption of pesticides (Zendzian 2010), 100% dermal absorption is seldom a realistic assumption. As noted in (WHO 2006, p. 4), the assumption of 100% dermal absorption may be useful as a screening tool but … *more realistic estimate of the extent of dermal absorption is provided by a consideration of the physicochemical properties of the chemical and the vehicle*.

As discussed in Section 3.1.4, definitive oral LD_{50} values for chlorsulfuron are in the range from 1363 mg/kg bw (oral LD_{50} in guinea pigs from Hall and Dashiell 1980) to greater than 7000 mg/kg bw (definitive LD_{50} values in rats from Hinckle and Dashiell 1980, MRID 00031407). As discussed in Section 3.1.12, the only dermal toxicity data on chlorsulfuron are from studies in rabbits that report only indefinite LD_{50} values of >3400 mg/kg bw for technical grade chlorsulfuron (Edwards 1979a,b,c). Although limited, these data reinforce the supposition that the assumption of 100% dermal absorption would overestimate exposure to chlorsulfuron.

As discussed in SERA (2014a, Section 3.1.3.2.2), the QSAR method typically used in Forest Service risk assessments is based exclusively on dermal absorption data from studies in humans involving numerous chemicals, including pesticides. As detailed in Worksheet B03b of attachment to this risk assessment, the QSAR method yields estimated dermal absorption rate coefficients for chlorsulfuron of about 0.00018 (0.000035–0.00089) $hour^{-1}$, using a K_{ow} value of 0.1 and a molecular weight of 357.8 (Table 2). Both the K_{ow} and the molecular weight for chlorsulfuron are in the range of values used in the development of the QSAR algorithm—i.e., K_{ow} values ranging from 0.0015 to 3,000,000 and in the range of 60 to 400 g/mole. Note that the values given in Worksheet B03b are rounded to two significant places in Worksheet B01, and these rounded values are used in the exposure assessments.

The current Forest Service risk assessment uses the above estimates of the first-order dermal absorption rate coefficients based on the QSAR algorithm from SERA (2014a, Section 3.1.3.2.2). As discussed further in Section 3.4 (Risk Characterization), the use of these rates leads to conclusions consistent with those of EPA in that none of the exposure scenarios for dermal absorption exceeds the level of concern (HQ=1).

3.1.3.2.2. Zero-Order Dermal Absorption

Exposure scenarios involving the assumption of zero-order dermal absorption require an estimate of dermal permeability (K_p) in units of cm/hour. As with first-order absorption rate coefficients, no experimental data are available on the dermal permeability rate of chlorsulfuron. In the absence of experimental data, Forest Service risk assessments generally use a QSAR algorithm developed by the EPA (U.S. EPA/ORD 1992, 2007). This approach is discussed in further detail in SERA (2014a, Section 3.1.3.2.1). As with the algorithm for estimating the first-order dermal absorption rate constant, the EPA algorithm is based on molecular weight and K_{ow} values (U.S. EPA/ORD 1992, 2007). The molecular weight and K_{ow} values used to estimate the K_p are identical to those used to estimate the first-order dermal absorption rate constants (i.e., a K_{ow} value of 0.1 and a molecular weight of 357.8 as summarized in Table 2). The EPA algorithm is derived from an analysis of 95 organic compounds with K_{ow} values ranging from about 0.0056 to 309,000 and molecular weights ranging from approximately 30 to 770 (U.S. EPA/ORD 1992,

2007). These ranges of K_{ow} values and molecular weights encompass the estimates of the corresponding values for chlorsulfuron.

Details of the implementation of the algorithms are given in Worksheet B03a in the EXCEL workbooks for chlorsulfuron (Attachments 1). Using the EPA algorithm results in an estimated dermal permeability (K_p) of about 0.0000023 (0.00000079 to 0.0000069) cm/hour. As with the first-order rates, the values given in Worksheet B03a are rounded to two significant places in Worksheet B01, and these rounded values are used in the exposure assessments.

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

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

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

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

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

The elimination of chlorsulfuron was studied in rats (Hawkins et al. 1989, Hunt 1981, Shrivastava 1979), goats (Han 1981f, Lee 1992b, Plowchalk 1994), cows (Slates and Moore 1981), and hens (Bodden and Rhodes1994, Rhodes 1995). Chlorsulfuron exhibits first order elimination kinetics, with an estimated half-life in rats of < 6 hours (Shrivastava 1979). In all mammalian species studied, chlorsulfuron and its metabolites are extensively and rapidly cleared by a combination of excretion and metabolism. The primary excretory compartment for chlorsulfuron and its metabolites is the urine, with smaller amounts excreted in the feces. Most of the chlorsulfuron excreted in urine is in the form of the parent compound (Hunt 1981, Plowchalk 1994). In lactating goats and cows, <0.25% of the administered dose was excreted in milk (Lee 1992b, Plowchalk 1994, Slates and Moore 1981). Chlorsulfuron does not appear to be eliminated in expired air (Hawkins et al. 1989). In goats, chlorsulfuron administered on treated wheat foliage exhibited similar excretion and metabolism patterns as chlorsulfuron administered directly to goats (Han 1981g).

Based on first-order elimination kinetics (e.g., Goldstein et al. 1974, p. 302), the proportion remaining in the body (*M*) by a given time (*t*) is:

$$M = e^{-kt} \quad \text{(Eq. 3)}$$

Rearranging to solve for *k*, the first-order excretion rate coefficient,

$$k = -\ln(M) \div t \quad \text{(Eq. 4)}$$

Based on metabolism study in rats discussed in Section 3.1.3.1, chlorsulfuron is rapidly eliminated (93-96% of the administered dose) within 3 days. Taking *M* as 1-0.945 (i.e., one minus the average of the range of 0.93 to 0.96) and *t* as 3 days, the first-order elimination rate (*k*) is about 0.967 day^{-1} [-ln(1-0.945)÷3 days ≈ 0.967 day^{-1}]. Based on the plateau principle, the steady-state body burden for chlorsulfuron following daily dosing (i.e., t*=1 day) would be a factor of about 1.6 [1 ÷ (1-$e^{-0.967}$)] higher than the body burden following a single dose. In other words, daily doses of chlorsulfuron should not lead to substantial accumulations in mammals over prolonged periods of exposure.

3.1.4. Acute Oral Toxicity

Standard acute oral toxicity studies are typically used to determine LD_{50} values—i.e., the treatment dose estimated to be lethal to 50% of the animals. LD_{50} values are not used directly to derive toxicity values as part of the dose-response assessment in Forest Service risk assessments. LD_{50} values as well as other measures of acute toxicity discussed in the following sections are used by the U.S. EPA/OPP to categorize potential risks. U.S. EPA/OPP uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response). Details of the EPA system of categorization are detailed in SERA (2014a, Table 4) as well as in U.S. EPA/OPP (2015b, Table 1), the label review manual.

As summarized in Table 5 and detailed further in Appendix 1 (Table A1-1), standard acute oral toxicity studies were conducted in rats. One of the acute toxicity studies in rats involved technical grade chlorsulfuron (Trivits 1979, MRID 00031406). Based on the acute oral LD_{50} values of about 5500 mg/kg bw in male rats and 6300 mg/kg bw in female rats, U.S. EPA/OPP/HED (2015a, p. 20) classifies chlorsulfuron as Category IV for acute oral toxicity.

As summarized in Table 5 and detailed further in Appendix 1 (Table A1-1), two registrant-submitted studies are available on chlorsulfuron formulations—i.e., one study on a 80% a.i. formulation and the other on a 75% a.i. dry flowable formulation. In terms of LD_{50} values in units of mg a.i./kg bw, the LD_{50} values for the 80% a.i. formulation are somewhat higher than the LD_{50} values for technical grade chlorsulfuron in both male and female rats (Hinckle and Dashiell 1980, MRID 00031407). This, however, is not the case for the 75% a.i. dry flowable formulation (Dashiell and Hinckle 1981, MRID 00083958) for which the LD_{50} values are lower than the corresponding LD_{50} values by a factor of about 2.3 in male rats [5268 ÷ 2290 ≈ 2.3004] and about 3.6 in female rats [5978 ÷ 1656 ≈ 3.61].

As summarized in Table 2, both of the formulations specified for use by the Forest Service are 75% dry flowable formulations—i.e., Chlorsulfuron 75 from Alligare LLC and Telar XP from DuPont. It is not clear that either of these formulations was used in the study by Hinckle and Dashiell (1980). As summarized in Table 5, the material safety data sheet (MSDS) for

Chlorsulfuron 75 specifies an LD_{50} of >5000 mg/kg bw but does not indicate if the toxicity value refers to the formulation or chlorsulfuron. As also summarized in Table 5, the safety data sheet (SDS) for Telar XP specifies an LD_{50} of >2000 mg/kg. Again, the MSDS does not explicitly indicate if the LD_{50} is for the formulation or chlorsulfuron.

As discussed further in Section 3.1.14 (Adjuvants and Other Ingredients), the acute oral toxicity data on technical grade chlorsulfuron and the 75% a.i. dry flowable formulation suggest that inerts might contribute to the toxicity of the formulation. Given the limited nature of the data—i.e., only single bioassay in rats on the a.i. and the formulation as well as the lack of clarity in the relation of the 1980 study to current formulations—the assessment of the role of inerts is speculative at best.

The acute toxicity data on chlorsulfuron also includes an acute oral LD_{50} in guinea pigs and an acute intraperitoneal LD_{50} in rats. As summarized in Appendix 1 (Table A1-1), both of these LD_{50} values are below the LD_{50} value for the 75% a.i. dry flowable formulation—i.e., 1363 mg a.i./kg bw for oral LD_{50} in guinea pigs and 1450 mg a.i./kg bw for the intraperitoneal LD_{50} in rats. While the lack of replicate studies limits an interpretation of the data, both of these studies as well as the oral studies discussed above appear to have been conducted by the same groups of investigators. The lower intraperitoneal LD_{50} relative to the oral LD_{50} probably reflects virtually complete absorption and increased body burden following intraperitoneal injection, relative to oral dosing. The LD_{50} in guinea pigs suggests that these mammals may be more sensitive than rats to the acute oral toxicity of chlorsulfuron.

Qualitative assessments of toxicity were also made in all acute toxicity studies. Clinical signs of toxicity include weight loss, diarrhea, weakness, wet and stained peritoneal area, lethargy, and humped posture. Non-specific, gross pathological changes in several organs were also observed and were similar for chlorsulfuron and chlorsulfuron formulations. These are rather general signs of toxicity commonly observed in acute lethal studies and do not clearly suggest a mode of toxicity.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

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

The subchronic and chronic toxicity studies on chlorsulfuron are summarized in Appendix 1, Table A1-2. All of the subchronic and chronic studies involve submissions to the U.S. EPA's Office of Pesticide Programs (U.S. EPA/OPP) in support of the registration of chlorsulfuron. No studies were identified in the open literature. Based on recent EPA reviews and risk assessments (as specified in Table 1), no new studies on subchronic and chronic toxicity in mammals have been submitted to U.S. EPA/OPP in support of the registration review of chlorsulfuron. As specifically noted in the most recent EPA human health risk assessment, additional toxicology studies are not required for chlorsulfuron (U.S. EPA/OPP/HED 2015a, p. 4).

As discussed in Section 3.1.9.2, the two-generation reproduction study in rats conducted by Mylchreest (2005) is the only new repeated dose toxicology study in mammals submitted to EPA since the previous Forest Service risk assessment (SERA 2004a. Thus, all of the studies summarized in Appendix 1, Table A1-2, are taken from the previous Forest Service risk assessment (SERA 2004a) with updated information (primarily estimates of mg/kg bw/day doses from dietary studies) taken from U.S. EPA/OPP/HED (2015a). As discussed in Section 1.1, the study summaries in Appendix 1, Table A1-2, are based on full studies received from the EPA for the preparation of the previous Forest Service risk assessment. These full studies, however, were not available for the preparation of the current updated Forest Service risk assessment.

As summarized in Appendix 1, Table A1-2, there are two chronic exposure studies in rats (Wood et al. 1980a, Wood et al. 1981a), two chronic exposure studies in dogs (Atkinson 1991, Schneider et al. 1980), and three chronic exposure studies in mice (Smith et al. 1980, Wood et al. 1980b, Wood et al. 1981b). Subchronic and chronic exposure studies involving reproductive performance assays were also conducted in rats (Alvarez 1991a, Rodgers et al. 1978, Wood 1980, Wood et al. 1981a) and rabbits (Alvareez 1991b, Hoberman 1980) and are discussed further in Section 3.1.9.

Similar adverse effects are observed following both subchronic and chronic exposure to chlorsulfuron. The most sensitive effects for chlorsulfuron in mammals are weight loss and decreased weight gain. The current U.S. EPA RfD (Section 3.3.2) is based on a 2-year feeding study in male and female rats (80 rats/sex/dose) in which chlorsulfuron was administered at dietary concentrations that resulted in daily doses of 5, 25, or 125 mg/kg/day (Wood et al. 1981a). In this study, a slight (but not statistically significant) decrease in body weight was observed in male rats in the 25 mg/kg/day group and statistically significant decreases in body weight and body weight gain were observed in the 125 mg/kg/day group. At the 125 mg/kg bw/day dose, the decrease in body weight was accompanied by a decrease in food conversion efficiency.

In addition to weight loss and decreased weight gain, dose-related hematological effects were observed in mice (Smith et al. 1980), and dogs (Schneider et al. 1980) after subchronic exposure and in rats (Wood et al. 1980a) and dogs (Atkinson 1991) after chronic exposure. In female dogs, increases in lymphocytes and eosinophils were observed following exposure to chlorsulfuron for 26 weeks (Schneider et al .1992), and increased lymphocyte counts and decreased neutrophilic granulocytes are noted in a chronic exposure study in mice (Smith et al. 1980). Results of these studies are discussed in more detail in Section 3.1.7 (Effects on Immune System).

Chronic exposure of male rats to 25 or 125 mg/kg/day for 52 weeks resulted in changes that were suggestive of treatment-induced reticulocytosis; however, these effects were not observed during the second year of this study (Wood et al. 1981a). Effects were not observed in male rats at lower doses or in female rats at any dose. Similar effects were reported in male dogs exposed to 375 mg/kg/day (Atkinson et al. 1991). No gross or histopathological changes were observed in organs of rats exposed to up to 125 mg/kg/day chlorsulfuron (95% a.i.) for 2 years (Wood et al. 1981a) or in mice exposed to chlorsulfuron (95% a.i.) at doses up to 250 mg/kg/day for 2 years (Wood et al. 1981b).

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 developed a battery of assays to test for neurotoxicity (Group E in U.S. EPA/OCSPP 2015), 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.

As summarized in Appendix 1, reports of lethargy or weakness are reported in chlorsulfuron acute toxicity studies (Trivits 1979, MRID 00031406; Hinckle and Dashiell 1980, MRID 00031407; Dashiell and Hinckle 1981, MRID 00083958; Hinckle 1979, MRID 00031410). These reports, however, do not implicate chlorsulfuron as a direct neurotoxicant. As summarized in its most recent human health risk assessment, the EPA waived the standard requirements for acute and chronic assays for neurotoxicity and notes that there is … *no concern for neurotoxicity* (U.S. EPA/OPP/HED 2015a, p. 6-7). This assessment is also reflected in the review of chlorsulfuron by the European Food Safety Authority (EFSA 2008, p. 14). In the absence of any clear indication that chlorsulfuron has a specific impact on nervous system function, the current Forest Service risk assessment concurs with the assessments from EPA and EFSA.

3.1.7. Effects on Immune System

There are various methods for assessing the effects of chemical exposure on immune responses, including assays of antibody-antigen reactions, changes in the activity of specific types of lymphoid cells, and assessments of changes in the susceptibility of exposed animals to resist infection from pathogens or proliferation of tumor cells. Typical subchronic or chronic animal bioassays involve morphological assessments of the major lymphoid tissues, including bone marrow, major lymph nodes, spleen and thymus (organ weights are sometimes measured as well), and blood leukocyte counts. These assessments can detect signs of inflammation or injury indicative of a direct toxic effect of the chemical on the lymphoid tissue. Changes in morphology of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected. Additional details on standard assays for effects of immune function are given in SERA (2014a, Section 3.1.7).

Only two long-term exposure studies, one in dogs and the other in mice, report effects that could be interpreted as an impact on immune system function. In a subchronic study in dogs, Schneider et al. (1980; MRID 00031420) note an increase in lymphocytes and eosinophils at dietary concentrations of 500 and 2500 ppm in male dogs. Similarly, a subchronic study in mice notes decreases in neutrophilic granulocytes but an increase in lymphocytes at high dietary concentrations (5000 or 7500 ppm) of chlorsulfuron. This effect, however, was observed only in females (Smith et al. 1980, MRID 00031421). Similar effects are not reported in several other chronic and subchronic studies in rats, mice, and dogs as detailed in Appendix 1, Table A1-2.

In a review of the toxicology data on chlorsulfuron (U.S. EPA/OPP/HED 2015a, p. 6), the EPA waives the requirement for specific immunotoxicity studies for chlorsulfuron. In addition, the EPA reviewed the toxicity data on chlorsulfuron and 14 other sulfonylurea herbicides and stated a minimal concern for immunotoxicity:

> *The overall weight of evidence (WOE) suggests that these chemicals do not target the immune system. There were some effects on hematology, clinical chemistry, and histopathological alterations in immune-related tissues; but these effects generally were observed in the presence of toxicity in other organs and were not considered major effects.*
>
> U.S. EPA/OPP/HED 2013a, p. 3

In the absence of specific immunotoxicity studies on chlorsulfuron, the current Forest Service risk assessment defers to the judgement cited in U.S. EPA/OPP/HED (2013a, 2015a), and immunotoxicity is not identified as an endpoint of primary concern for chlorsulfuron.

3.1.8. Effects on Endocrine System

Assessments of the direct effects of chemicals on endocrine function are most often based on mechanistic studies on estrogen, androgen, or thyroid hormone systems (i.e., assessments on hormone synthesis, hormone receptor binding, or post-receptor processing). The EPA developed an Endocrine Disruptor Screening Program that is being applied to pesticides as well as other chemicals (U.S. EPA/OPP 2016). As of August, 2016, the EPA had posted the results of Tier 1 screening assays for 21 chemicals and issued requests for additional data for many other chemicals, including pesticides (https://www.epa.gov/ingredients-used-pesticide-products/endocrine-disruptor-screening-program-tier-1-assessments). To date, chlorsulfuron is not among the chemicals screened by EPA, nor has the EPA issued data requests for chlorsulfuron. While the most recent EPA human health risk assessment discusses the Endocrine Disruptor Screening Program, it does not provide specific comments on or evaluations of chlorsulfuron (U.S. EPA/OPP/HED 2015a, pp. 8-9). An earlier review of chlorsulfuron by EPA indicated that …*EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for chlorsulfuron* (U.S. EPA/OPP/HED 2012a, p. 5); however, additional information on this request has not been identified.

In addition, inferences concerning the potential for endocrine disruption can sometimes be made from responses seen in standard toxicity tests—i.e., changes in the structure of major endocrine glands (i.e., the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis) or changes in growth rates. Effects on organs associated with endocrine function may be secondary to other toxic effects. Thus, in the absence of information on specific endocrine mechanisms, pathological changes in endocrine tissues do not necessarily indicate a direct effect on endocrine function. Additional details on the evaluation of chemicals on endocrine function are given in SERA (2014a, pp. 44-46).

As noted in Section 3.1.1., a variety of sulfonylurea drugs reduce blood glucose by stimulating the release of insulin from pancreatic B cells. Studies investigating the effects of chlorsulfuron on insulin release or metabolism were not identified in the literature. As noted in Appendix 1, Table A1-2, both weight loss and reduced body weight gain were observed in animals treated

with chlorsulfuron; however, changes in food conversion efficiency are not reported in most standard subchronic or chronic studies. The only exception is the chronic feeding study in rats which notes a decrease in food conversion efficiency at the high dose group—i.e., 125 mg/kg bw/day (Wood et al. 1981a, MRID 00086003). Decreased pituitary and thyroid weights, not considered treatment-related, were observed in male dogs exposed to chlorsulfuron (~95% a.i.) for 26 weeks (Schneider et al. 1980). Based on an evaluation of these standard subchronic and chronic studies, U.S. EPA/OPP/HED (2002, p. 6) concludes: *No effects were observed on the endocrine system*.

Signs of adverse effects on the endocrine system may also be reflected in reproductive impairment. As discussed in Section 3.1.9.2 and summarized in Appendix 1, Table A1-3, a multigeneration reproduction study (Mylchreest 2005) has been submitted to the EPA since the publication of the Reregistration Eligibility Decision (RED) for chlorsulfuron (U.S. EPA/OPP 2005a). While this study does not report an impact on reproductive parameters, a decrease in food conversion efficiency (82-91% of controls) was observed in males and females in the high dose-group (456 mg a.i./kg bw/day for males and 591 mg a.i./kg bw/day for females). The EPA review of this study in the DER (i.e., Mylchreest 2005, p. 18) characterizes the effect in males as *slight* and the effect in females as *transient*. Although this study is cited in the most recent human health risk assessment for chlorsulfuron (U.S. EPA/OPP/HED 2015a, p. 21), the impact on food conversion efficiency is not noted or discussed. While effects on the endocrine system can be associated with decreases in food conversion efficiency (e.g., Sohlstrom et al. 1998), the sporadic observations of decreased food conversion efficiency in one chronic study and one reproduction study cannot be used as a basis to conclude that chlorsulfuron is an endocrine disruptor.

3.1.9. Reproductive and Developmental Effects

3.1.9.1. Developmental Studies

Developmental studies are used to assess the potential of a compound to cause malformations and signs of toxicity during fetal development. These studies typically entail gavage administration of the chemical compound to rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required by the EPA for the registration of pesticides, and specific protocols are established by EPA for developmental and reproduction studies (U.S. EPA/OPPTS 2000).

As summarized in Appendix 1, Table A1-3, four developmental studies are available on chlorsulfuron, two studies in rabbits (Alvarez 1991b, MRID 41983101; Hoberman 1980, MRID 00083945) and two studies in rats (Alvarez 1991a, MRID 41976406; Rogers et al. 1978, MRID 00031424).

As discussed further in Section 3.3.2 (Acute RfD), the most recent EPA human health risk assessment uses the study by Alvarez (1991b) as the basis for the acute dose-response assessment for human health effects (U.S. EPA/OPP/HED 2015a, p. 8). In the study by Alvarez (1991b), no adverse effects on dams or the developing fetus were noted at gavage doses of 25 or 75 mg/kg bw/day. At 200 mg/kg bw/day, the only adverse effects noted were decreases in maternal body weights (Maternal LOAEL, Developmental NOAEL). At 400 mg/kg bw/day, adverse developmental effects included an increase in fetal soft tissue malformations and

decreases in fetal body weights. Based on the study in rats by Alvarez (1991a), rats are somewhat less sensitive than rabbits with a rat maternal NOAEL of 165 mg/kg bw/day and a fetal/developmental NOAEL of 500 mg/kg bw/day.

The earlier studies by Hoberman (1980) and Rogers et al. (1978) are not cited or summarized in the more recent EPA human health documents (U.S. EPA/OPP/HED 2002a, 2012a, 2015a) or in assessments from the European literature (EFSA 2005; FAO/WH) 2003). These older studies were obtained and summarized in the previous Forest Service risk assessment on chlorsulfuron (SERA 2004a). In the absence of EPA evaluations, the studies from Hoberman (1980) and Rogers et al. (1978) are included for the sake of completeness but are not otherwise used in the current Forest Service risk assessment.

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 exposing one or more parental (P_i) generations 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). In the case of chlorsulfuron, the reproduction study (discussed below) involved the generation of two groups of offspring from the P_1 generation—i.e., F_{1a} and F_{1b} offspring—with the F_{1a} offspring acting as the P_2 generation to produce a F_2 offspring. During these types of studies, standard observations for gross signs of toxicity are made. Additional observations often include the length of the estrous cycle, assays on sperm and other reproductive tissue, and number, viability, and growth of offspring. Typically, the EPA requires one acceptable multi-generation reproduction study for pesticide registration (U.S. EPA/OPPTS 2000). When reproduction studies suggest that reproductive endpoints are more sensitive than endpoints from chronic toxicity studies, multigeneration reproduction studies can form the basis for the chronic RfD.

As summarized in Appendix 1, Table A1-3, three multigeneration reproduction studies in rats were submitted to EPA: Mylchreest (2005 MRID 46493201), Wood et al. (1981a, MRID 00086003), and Wood (1980, MRID 00031423). The studies by Wood et al. (1981a) and Wood (1980) appear to be submissions of the same study. This is a rather unusual study in that it was conducted as part of a standard 2-year chronic study in rats. As discussed in U.S. EPA/OPP/HED (2015a, p. 20-21), the EPA classifies the 2-year feeding study in rats as *Acceptable/Guideline* but classifies the multigeneration reproduction study as *Unacceptable/Non-guideline*. While a DER for this study is not available, a detailed discussion of the study is provided in U.S. EPA/OPP/HED (2002b, p. 14) which lists several study deficiencies based on current EPA standards although the study had …*conformed to the old guideline requirements*.

The more recent 2-generation reproduction study by Mylchreest (2005) is classified by EPA as Acceptable/Guideline, and a DER for this study is available. No effects on reproductive parameters were noted at any dose level, and the NOAEL for reproductive effects is classified as 7500 ppm (mg a.i./kg diet), the highest dose tested, which corresponded to doses of about 500 mg a.i./kg bw/day. The only parental effect noted is decrease in adult body weight with a parental NOAEL of 2500 ppm, which corresponds to doses of about 150 mg a.i./kg bw/day. This parental NOAEL is substantially above the chronic NOAEL of 5 mg/kg bw/day and chronic

LOAEL of 25 mg/kg bw/day from the 2-year feeding study in rats (Wood et al. 1981a, MRID 00086003). Thus, the multigeneration reproduction study is not used in the dose-response assessment for chronic exposures (Section 3.3.3). Based on the lack of endpoints associated with reproductive effect, the EPA notes that there is no indication that chlorsulfuron causes reproductive toxicity (U.S. EPA/OPP/HED 2015a, p. 7).

3.1.10. Carcinogenicity and Mutagenicity

In terms of a quantitative significance to the human health risk assessment, carcinogenicity is an issue only if the data are adequate to support the derivation of a cancer potency factor. A cancer potency factor is typically derived based on a dose-related increase in malignant tumors from a chronic toxicity study in mammals which encompasses a significant portion of the test animals' lifespan.

As summarized in Appendix 1, Table A1-2, and discussed in Section 3.1.5, standard chronic toxicity/carcinogenicity bioassays were conducted in mice (Wood et al. 1981b, MRID 00090030) and rats (Wood et al. 1981a, MRID 00086003). No evidence of carcinogenic activity was found in either study. In addition, a standard battery of mutagenicity assays, summarized in Appendix 1, Table A1-8, gives no indication of mutagenic or genotoxic activity. Based on these studies, the EPA concludes that chlorsulfuron is … "*not likely to be carcinogenic to humans"; therefore, cancer risk is not a concern* (U.S. EPA/OPP/HED 2015a, p. 3). This assessment is also consistent with the determination in FAO/WHO (2003, p. 23) that chlorsulfuron …*is not carcinogenic or mutagenic*.

The only reservation with the classification of chlorsulfuron as non-carcinogenic is expressed in the evaluation of chlorsulfuron by the European Food Safety Authority (ESFA, 2008). This review summarizes a study (without a full reference/citation) indicating that a dose of 104 mg/kg bw/day of chlorsulfuron was associated with an increase in the incidence of testicular tumors in rats. The study is not described in detail but the following evaluation is offered:

> *In the absence of any mechanistic data indicating the opposite, the increased incidence of unilateral testicular interstitial cell tumours was considered relevant for the risk assessment, leading to the proposed classification Carcinogen Category 3, R40 (Limited evidence of a carcinogenic effect).*
>
> EFSA, 2008, p. 12

The above evaluation is provided in the interest of transparency. The Forest Service defers to U.S. EPA on the classification of the carcinogenicity of pesticides. In the absence of additional details and a concurrence from EPA, the EPA assessment discussed above takes precedence over the assessment from EFSA (2008).

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

As with acute oral toxicity, the U.S. EPA/OPP requires acute assays for skin irritation, skin sensitization, and eye irritation and uses a ranking system for responses ranging from Category I (most severe response) to Category IV (least severe response) for skin and eye irritation. Skin sensitization is classified simply as occurring or not occurring. For each type of assay, the EPA has developed standard protocols (U.S. EPA/OCSPP 2015).

3.1.11.1. Skin Irritation

Based on a standard skin irritation assay with technical grade chlorsulfuron, U.S. EPA/OPP/HED (2015a, p. 20, MRID 46449006) classifies chlorsulfuron as Category IV in terms of primary skin irritation. As summarized in Appendix 1, Table A1-4, other skin irritation assays with technical grade chlorsulfuron are available in rabbits (Henry and Dashiell 1980, MRID 00031416) and guinea pigs (Goodman 1976, MRID 00031417), all of which support this assessment. In addition, studies of a 75% dry flowable formulation in rabbits (Dashiell and Silber 1980b, MRID 00083961) and guinea pigs (Dashiell and Silber 1981, MRID 00083962) also support the assessment that this chlorsulfuron formulation is not a primary skin irritant. As discussed in Section 3.1.4, it is not clear that earlier studies on 75% dry flowable formulations were conducted on the exact 75% dry flowable formulation proposed in the current Forest Service risk assessment (i.e., Table 3). Nonetheless, the MSDS for Chlorsulfuron 75 indicates that the formulation is only a mild skin irritant (Alligare LLC 2010). Similarly, the SDS for Telar XP indicates that this formulation is not a skin irritant (DuPont Crop Protection 2015).

3.1.11.2. Skin Sensitization

The most recent EPA human health risk assessment indicates that chlorsulfuron is not a skin sensitizer (U.S. EPA/OPP 2015a, p. 20, MRID 46449007). As summarized in Appendix 1, Table A1-4, this assessment is supported by an earlier study on technical grade chlorsulfuron (Goodman 1976, MRID 00031417) as well as a study on a 75% a.i. dry flowable formulation (Dashiell and Silber 1981, MRID 00083962). This assessment is also reflected in the MSDS for Chlorsulfuron 75 (Alligare LLC 2010) and the SDS for Telar XP (DuPont Crop Protection 2015).

3.1.11.3. Ocular Effects

As with skin irritation (Section 3.1.11.1), the U.S. EPA classifies chlorsulfuron as Category IV for eye irritation (U.S. EPA/OPP/HED 2015a, p. 20, MRID 46449005). As summarized in Appendix 1, Table A1-5, earlier studies note transient eye irritation for an 80% a.i. formulation (Silber 1980, MRID 00031415) as well as a 75% a.i. dry flowable formulation (Dashiell and Silber 1980a, MRID 00083959). The MSDS for Chlorsulfuron 75 indicates that the formulation may cause slight eye irritation (Alligare LLC 2010), and the SDS for Telar XP indicates that this formulation is not an eye irritant (DuPont Crop Protection 2015).

Based on the available information, minimal eye irritation might be associated with exposures to some formulations of chlorsulfuron; however, there is no basis for asserting that serious eye damage would be likely.

3.1.12. Systemic Toxic Effects from Dermal Exposure

Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared to an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies. Thus, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which chlorsulfuron is likely to be absorbed from the surface of the skin. As discussed in Section 3.1.3.2.1 (First-Order Dermal Absorption), the toxicity studies on dermal absorption are particularly important in the current risk assessment because both the U.S. EPA/OPP/HED (2015a, p. 8) and the European Food Safety Authority (EFSA 2008, p. 3) use the assumption of 100% dermal absorption; whereas, the current Forest

Service risk assessment uses QSAR methods which suggest much lower rates of dermal absorption.

The available dermal toxicity studies on chlorsulfuron are summarized in Appendix 1, Table A1-6 and consist of one study on technical grade chlorsulfuron (Edwards 1979a,b,c) as well as a study on an 80% a.i. formulation (Silber and Dashiell 1980, MRID 00031412) and a study on a 75% a.i. dry flowable formulation (Dashiell and Ashley 1980a,b). As noted in Table A1-6, it appears that each of the studies on technical grade chlorsulfuron and the 75% a.i. dry flowable formulation were submitted to EPA multiple times—i.e., three submissions for the study on the a.i. and two submissions for the study on the 75% a.i. dry flowable formulation. For the sake of clarity, it is noted that multiple submissions are not unusual and may reflect responses by registrants to queries or comments from the EPA. While the EPA sometimes requires repeated dose studies on pesticides, this requirement was waived for chlorsulfuron (U.S. EPA/OPP 2007a, p. 2; U.S. EPA/OPP/HED 2015a, p. 6).

All of the acute dermal toxicity studies on chlorsulfuron yield indefinite LD_{50} values—i.e., an LC_{50} value could not be calculated because insufficient mortality was induced at the highest dose assayed. For technical grade chlorsulfuron, the indefinite LD_{50} is >3400 mg a.i./kg bw. Based on this indefinite dermal LD_{50}, U.S. EPA/OPP/HED (2015a, p. 20) classifies chlorsulfuron as Category III for acute dermal toxicity. The classification of chlorsulfuron as Category III rather than Category IV is not a reflection of any presumed dermal toxicity. As discussed in SERA (2014a, Section 3.1.4 and Table 4), the EPA classifies a compound as Category IV only if the dose used in the study was >5000 mg/kg bw. For the two formulations, the indefinite LD_{50} is >2000 mg a.i./kg bw. The only signs of systemic toxicity reported in these studies are sporadic weight loss and diarrhea, which are not clearly associated with treatment.

3.1.13. Inhalation Exposure

The U.S. EPA typically requires short-term (single 4-hour exposure) inhalation toxicity studies in rats (U.S. EPA/OPPTS 1998b) and may require a subchronic inhalation toxicity study in rats to support pesticide registration. As with the dermal studies, the EPA has waived the requirement for the subchronic inhalation toxicity assay (U.S. EPA/OPP 2007; U.S. EPA/OPP/HED 2015a, p. 6). As summarized in Appendix 1, Table A1-7, a single acute inhalation study on technical grade chlorsulfuron was submitted to EPA. As with other types of assays, it appears that this study was submitted on multiple occasions with differing citations and MRID numbers. Citing Ferenz (1980b, MRID 00086825), U.S. EPA/OPP/HED (2015a, p. 20) uses the inhalation LC_{50} of 5.9 mg/L to classify chlorsulfuron as Category IV (the least toxic ranking) for acute inhalation toxicity. The only effect observed in this study was irritation of the nasal passages.

As summarized in Table 2 and noted by U.S. EPA/OPP/EFED (2012a, p. 12), chlorsulfuron has a low vapor pressure (2.3×10^{-11} torr at 25°C) and significant volatilization into air is not anticipated. Thus, significant exposures via inhalation are unlikely.

3.1.14. Adjuvants and Other Ingredients

3.1.14.1. Other Ingredients

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

The identities of inerts in pesticide formulations are generally considered trade secrets and need not be disclosed to the general public. Nonetheless, all inert ingredients as well as the amounts of the inerts in the formulations are disclosed to and reviewed by the U.S. EPA as part of the registration process. Some inerts are considered potentially hazardous and are identified as such on various lists developed by the federal government and state governments. Material Safety Data Sheets (MSDS) or Safety Data Sheets (SDS) sometimes specify inerts used in pesticide formulations. U.S. EPA/OPP (2015b, p. 5-13) encourages but does not generally require expanded inert statements on product labels which specifically identify the inert ingredients in the product. One notable exception, however, involves petroleum distillates including xylene or xylene range solvents that are part of the formulation and at a concentration of ≥10%. In this case, the product label must contain the following statement: *Contains petroleum distillates, xylene or xylene range aromatic solvents* (U.S. EPA/OPP 2015b, p. 5-7). None of the product labels for the representative formulations of chlorsulfuron listed in Table 3 indicates that these formulations contain petroleum distillates.

The only inert specified on the SDS for Telar XP is *modified lignin sulfonate salt*, which is present at 5-10% of the formulation. No other details or descriptors (e.g., CAS number) are provided. The entries for modified lignin sulfonate salt are listed at the EPA's InertFinder web site (https://iaspub.epa.gov/apex/pesticides/f?p=INERTFINDER:1:::NO:1::). As noted in Section 1.1, the CBI files were accessed in the preparation of the previous Forest Service risk assessment on chlorsulfuron (SERA 2004a), and information on the inerts in the formulations covered in the previous Forest Service risk assessment were reviewed. The formulations covered in the current Forest Service risk assessment, however, are different from those covered in the current Forest Service risk assessment. As discussed in Section 3.1.4 and summarized in Table 5 of the current Forest Service risk assessment, the acute oral LD_{50} values for a 75% a.i. formulation of chlorsulfuron are somewhat lower than those for technical grade chlorsulfuron—i.e., by a factor of about 2.3 in male rats and about 3.6 in female rats, which may suggest that inerts in the 75% a.i. formulation contribute to the acute toxicity of the formulation. Nonetheless, no remarkable differences between chlorsulfuron and the 75% a.i. formulation are noted based on skin and eye irritation (Section 3.1.11) and dermal toxicity (Section 3.1.12). While these comparisons are noted for the sake of completeness, the relationship of the 75% a.i. formulation tested in the 1980s to the formulations currently designated by the Forest Service (Table 3) is unclear.

3.1.14.2. Adjuvants

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

The product labels for representative formulations of chlorsulfuron (Table 2) indicate that surfactants should be used to improve efficacy at least for postemergence control. The labels do not recommend specific surfactants and do not address the amount of surfactants that should be used. In the absence of more specific information, no further assessment can be made concerning the use of surfactants in applications of chlorsulfuron.

3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

Two types of metabolites may be considered in a risk assessment, *in vivo* metabolites and environmental metabolites. *In vivo* metabolites refer to the compounds formed within the animal after the pesticide has been absorbed, and these metabolites are discussed in Section 3.1.3.1. Under the assumption that metabolism is similar among different species of mammals, the toxicity of *in vivo* metabolites is generally encompassed by *in vivo* toxicity studies in mammals. Environmental metabolites refer to compounds that may be formed in the environment by a number of different biological or chemical processes, including breakdown in soil or water or breakdown by sunlight (photolysis). These metabolites are not necessarily encompassed by *in vivo* toxicity studies in mammals. If environmental metabolites are more toxic than the parent compound, they may be considered explicitly in a risk assessment.

The environmental metabolites of chlorsulfuron are reviewed in detail by U.S. EPA/OPP/EFED (2012a, pp. 101-114). An overview of the metabolism of chlorsulfuron taken from the EPA review is given in Figure 3 of the current Forest Service risk assessment. Chlorsulfuron undergoes a variety of metabolic transformations including cleavage of the sulfonylurea bridge and triazine ring, hydroxylation, and o-dealkylation. As discussed further in Section 4.1 (hazard identification for the ecological risk assessment), the metabolites of chlorsulfuron are not more toxic to ecological receptors, particularly algae, than the parent compound. Data on the toxicity of the metabolites of chlorsulfuron to mammals are not detailed in the EPA human health risk assessments (U.S. EPA/OPP/HED 2002b, 2012a, 2015a). U.S. EPA/OPP/HED (2012a, p.12) indicates that *…chlorsulfuron does not appear to produce a toxic metabolite produced by other substances which have tolerances in the U.S.* This statement is relevant to the assessment of cumulative effects, as discussed further in Section 3.4.6. The EPA determined that only the parent compound (i.e., chlorsulfuron) needs to be addressed *…as a residue of concern for risk assessment* (U.S. EPA/OPP/HED 2015a, p. 4). While the European Food Safety Authority (EFSA 2008a, p. 61) raises concern for two metabolites (i.e., triazine amine and chlorosulfonamide), EPA assessed these and other metabolites and specifically classifies them as compounds that are not of concern for terrestrial vertebrates (U.S. EPA/OPP/EFED 2012a, Table 8, p. 28).

3.1.15.2. Impurities

The impurities in chlorsulfuron are not addressed in either the published literature or the EPA documents on chlorsulfuron (Table 1). As summarized in Appendix 1 as well as other appendices to this risk assessment, the purity of technical grade chlorsulfuron is typically characterized as about 95%. The remainder of the material may be viewed as impurities.

Registrants disclose the nature of impurities in their technical grade material to the U.S. EPA; however, the identities of the impurities are not disclosed to the public, because that information may provide insight into the manufacturing process, which is considered proprietary and is protected under FIFRA (Section 10). Proprietary information on the identities of impurities in technical grade chlorsulfuron was not available for the preparation of the current Forest Service risk assessment.

To some extent, concern for impurities in technical grade chlorsulfuron is reduced because most of the existing toxicity studies were conducted with the technical grade product. Thus, any toxic impurities present in the technical grade product are likely to be encompassed by the available toxicity studies on the technical grade product.

3.1.16. Toxicological Interactions

No information is available on the toxicological interactions of chlorsulfuron with other compounds in mammals. In general, compounds with similar mechanisms of action are considered to have additive toxicity (e.g., NAS 2013). Based on this premise, the U.S. EPA/OPP/EFED (2015a) has jointly considered the phytotoxicity of 22 sulfonyl urea herbicides. This approach, however, is not relevant to the human health risk assessment because the available data on other sulfonylurea herbicides do not support the assessment of a common mechanism of action in mammals (U.S. EPA/OPP/HED 2015a, p. 13). Consequently, no generalizations can be proposed for the potential of other compounds to interact with chlorsulfuron in mammals.

The product labels for both Chlorsulfuron 75 and Telar XP note that these formulations should not be applied as a tank mixture with DuPont Hyvar X-L herbicide, a 21.9% formulation of the lithium salt of bromacil. The rationale for this cautionary note is not given on the product labels, and mixtures of chlorsulfuron and bromacil are not discussed in the most recent EPA human health and ecological risk assessments (U.S. EPA/OPP/HED 2015a; U.S. EPA/OPP/EFED 2004a, 2012a). Publications on the joint toxicity of chlorsulfuron and bromacil were not identified in the open literature (as of August 29, 2016).

Tucker and Hirsch (1972) cite an incident in which chlorpropamide, a sulfonylurea drug administered for the control of diabetes may have been potentiated by co-exposure to sulfisoxazole, a sulfonamide drug used as an antibacterial agent. This incident, however, does not support generalizations concerning the interactions of sulfonylurea herbicides with sulfonamides.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

The details of the exposure assessments used in the current risk assessment are specified in Attachment 1. This workbook contains a set of worksheets that detail each exposure scenario discussed in this risk assessment as well as summary worksheets for both workers (Worksheet E01) and members of the general public (Worksheet E03). Documentation for these worksheets is presented in SERA (2016a). All exposure assessments are conducted assuming an application rate of 0.0625 lb a.i./acre (Section 2).

Worker exposures are modeled for backpack spray, broadcast ground spray, and aerial spray. In non-accidental scenarios involving the normal application of chlorsulfuron, central estimates of exposure for workers are approximately 0.000027 mg/kg/day for backpack applications, 0.00021 mg/kg/day for ground broadcast applications, and 0.00015 mg/kg bw/day for aerial spray. The upper bound of the prediction intervals for worker exposures is approximately 0.00045 mg/kg/day for backpack applications and 0.01 mg/kg/day for ground and aerial broadcast applications. As discussed further in Section 3.4, these exposure estimates are below the level of concern.

For the general public (Worksheet E03), acute non-accidental exposure levels associated with a single application of chlorsulfuron range from negligible (e.g., $\approx 9 \times 10^{-14}$ mg/kg/day) to about 0.08 mg/kg bw. As with most exposure assessments involving foliar applications of pesticides, the highest levels of exposure are associated with the consumption of contaminated vegetation (i.e., upper bound dose of up to about 0.08 mg/kg bw/day). The lowest exposure levels are associated with swimming in contaminated water (i.e., upper bound doses of about 8×10^{-8} mg/kg bw/day). For the accidental exposure scenarios, the greatest exposure levels are associated with the consumption of contaminated water by a small child following an accidental spill, for which the upper bound dose is about 0.2 mg/kg bw.

3.2.2. Workers

3.2.2.1. General Exposures

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

In Table 14 of SERA (2014b), three reference chemicals with corresponding worker exposure rates are given for directed foliar applications with differing first-order dermal absorption rate coefficients (k_a values)—i.e., glyphosate (k_a = 0.00041 hour^{-1}), 2,4-D (k_a = 0.00066 hour^{-1}), and triclopyr BEE (k_a = 0.0031 hour^{-1}). As discussed in Section 3.1.3.2.1 of the current risk assessment, the central estimate of the first-order dermal absorption rate coefficient for chlorsulfuron is 0.00018 hour^{-1}. This rate coefficient for chlorsulfuron is a factor of about 2 less than the corresponding coefficient for glyphosate, the reference pesticide with the lowest k_a [0.00041 hour^{-1} ÷ 0.00018 hour^{-1} = 2.2777…]. A factor of 20 involves only minor extrapolation, and glyphosate is used as the reference chemical for directed foliar applications. For directed foliar applications, the application of the methodology from SERA (2014b) is detailed in Table 6

of the current risk assessment. The rates given in Table 6 are rounded to one significant digit and are used in Worksheet C01a of Attachment 1 (i.e., the EXCEL workbook that accompanies this risk assessment) to estimate exposures for workers involved in directed foliar applications.

As also summarized in Table 14 of SERA (2014b), only one reference chemical, 2,4-D, is available for ground broadcast and aerial applications, and the first-order dermal absorption rate coefficient for 2,4-D is taken as 0.00066 $hour^{-1}$. This first-order dermal absorption rate coefficient is below the corresponding value for chlorsulfuron by a factor of about 4 [0.00066 $hour^{1} \div 0.00018\ hour^{-1} \approx 3.666\ldots$]. While the application of dermal adjustment factors is optional in the SERA (2014b) methodology, the dermal adjustment factor is used in this risk assessment of chlorsulfuron since the level of extrapolation is modest. The application of the methodology from SERA (2014b) is detailed in Table 7 (ground broadcast applications) and Table 8 (aerial applications). As with the estimated occupational exposure rates for directed foliar applications, the estimates from Table 7 and Table 8 are rounded to one significant place and used in Worksheet C01b (ground broadcast applications) and Worksheet C01c (aerial applications) in Attachment 1.

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

3.2.2.2. Accidental Exposures

Since dermal exposure is generally the predominant route of exposure for pesticide applicators (Ecobichon 1998; van Hemmen 1992), accidental dermal exposures are considered quantitatively in all Forest Service risk assessments. The two types of dermal exposures modeled in the risk assessments include direct contact with a pesticide solution and accidental spills of the pesticide onto the surface of the skin. In addition, two exposure scenarios are developed for each of the two types of dermal exposure. The estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Both sets of exposure scenarios are summarized in Worksheet E01 of the EXCEL workbook that accompanies this risk assessment—i.e., Attachment 1. Additionally, Worksheet E01 references other worksheets in which the calculations of each exposure assessment are detailed.

Exposure scenarios involving direct contact with solutions of chlorsulfuron are characterized either by immersion of the hands in a field solution for 1 minute or wearing pesticide contaminated gloves for 1 hour. The assumption that the hands or any other part of a worker's body will be immersed in a chemical solution for a prolonged period of time may seem unreasonable; however, it is possible that the gloves or other articles of clothing worn by a worker may become contaminated with pesticide. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in the solution. In both cases, the chemical concentration in contact with the skin and the resulting dermal absorption rate are essentially constant. For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. For these types of exposures, the rate of absorption is estimated based on a zero-order dermal absorption rate (K_p). Details regarding

the derivation of the K_p value for chlorsulfuron are provided in Section 3.1.3.2.2. The amount of the pesticide absorbed per unit time depends entirely on the concentration of the chemical in solution. This concentration is highly variable depending on the application method and also on the dilution volumes, as discussed in Section 2.4. These exposure scenarios are detailed in Worksheets C02a (1-minute exposure) and C02b (60-minute exposure).

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

3.2.3. General Public

3.2.3.1. General Considerations

3.2.3.1.1. Likelihood and Magnitude of Exposure

The likelihood that members of the general public will be exposed to chlorsulfuron in Forest Service programs will vary considerably, depending on the application method and the site of application. If chlorsulfuron is applied in or near recreational areas, like campgrounds, picnic areas, and trails, exposure is plausible for members of the general public, particularly in the event of broadcast applications. Conversely, members of the general public are not likely to be exposed to chlorsulfuron applied in remote areas.

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

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

In addition to this upper bound MEI value, the Extreme Value approach used in this risk assessment provides a central estimate of exposure as well as a lower bound on exposure. While not germane to the assessment of upper bound risk, the use of the central estimate and especially

the lower bound estimate is not intended to lessen concern. To the contrary, the central and lower estimates of exposure are used to assess the feasibility of mitigation—e.g., protective measures to limit exposure. If lower bound exposure estimates exceed a level of concern, this is strong indication that the pesticide cannot be used in a manner that will lead to acceptable risk.

3.2.3.1.2. Summary of Assessments

The exposure scenarios developed for the general public are summarized in Worksheet E03 of the EXCEL workbook (Attachment 1) that accompanies this risk assessment. The details regarding the assumptions and calculations used in these assessments are given in the worksheets in the EXCEL workbook (Worksheets D01–D10).

For chlorsulfuron, a standard set of exposure assessments used in all Forest Service risk assessments for broadcast applications is considered. As summarized in Worksheet E03 of Attachment 1, the kinds of exposure scenarios developed for the general public include acute accidental, acute non-accidental, and longer-term or chronic exposures. The accidental exposure scenarios assume that an individual is exposed to the compound of concern either during or shortly after its application. Non-accidental exposures involve dermal contact with contaminated vegetation as well as the consumption of contaminated fruit, vegetation, water, or fish. The longer-term or chronic exposure scenarios parallel the acute exposure scenarios for the consumption of contaminated fruit, water, or fish. All of the non-accidental exposure scenarios are based on levels of exposure to be expected following an application of chlorsulfuron at 0.0625 lb a.i./acre, as discussed in Section 2 (Program Description).

The nature of the accidental exposure scenarios is intentionally extreme. The non-accidental, acute exposure scenarios are intended to be conservative but plausible, meaning that it is not unreasonable to assume that the magnitude of exposures in the non-accidental exposure scenarios could occur in the routine use of chlorsulfuron. This interpretation does not extend to the longer-term exposure scenarios. The longer-term exposure scenarios are based on the assumption that an individual consumes contaminated vegetation, or fruits, or water from a treated area every day over a prolonged period of time. Albeit unlikely, this exposure scenario cannot be ruled out completely. As discussed further in Section 3.4.3, this is an important consideration in the interpretation of hazard quotients associated with longer-term exposures to contaminated vegetation.

3.2.3.2. Direct Spray

Direct spray scenarios for members of the general public are modeled in a manner similar to accidental spills for workers (Section 3.2.2.2). In other words, it is assumed that the individual is sprayed with a field solution of the compound and that some amount of the compound remains on the skin and is absorbed by first-order kinetics. Two direct spray scenarios are given, one for a young child (D01a) and the other for a young woman (D01b).

For the young child, it is assumed that a naked child is sprayed directly during a broadcast application and that the child is completely covered with pesticide (i.e., 100% of the surface area of the body is exposed). This exposure scenario is intentionally extreme. As discussed in Section 3.2.3.1.1, the upper limits of this exposure scenario are intended to represent the *Extreme Value* of exposure for the *Most Exposed Individual* (MEI).

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

For the direct spray scenarios, assumptions are made regarding the surface area of the skin and the body weight of the individual, as detailed in Worksheet A03 of the attachments. The rationale for and sources of the specific values used in these and other exposure scenarios are provided in the documentation for WorksheetMaker (SERA 2016a) and in the methods document for preparing Forest Service risk assessments (SERA 2014a).

3.2.3.3. Dermal Exposure from Contaminated Vegetation

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

No data are available on dermal transfer rates for chlorsulfuron. This is not a severe limitation in this risk assessment. As detailed in Durkin et al. (1995), dermal transfer rates are reasonably consistent for numerous pesticides, and the methods and rates derived in Durkin et al. (1995) are used as defined in Worksheet D02. U.S. EPA/OPP/HED (2015a, p. 13) indicates specifically that dislodgeable residue studies for chlorsulfuron were waived. In the absence of data on dislodgeable residues for chlorsulfuron, a default dislodgeable residue rate of 0.1 of the nominal application rate is used for this exposure scenario.

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

3.2.3.4. Contaminated Water

3.2.3.4.1. Accidental Spill

The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill of a field solution into a small pond. The calculation of the concentration of chlorsulfuron in water following the spill is given in Worksheet B04b, and the estimate of the dose to a small child is given in Worksheet D05 of the attachment to this risk assessment. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation is considered.

Since this exposure scenario is based on assumptions that are somewhat subjective and highly variable, the scenario may overestimate exposure. The actual chemical concentrations in the water will vary according to the amount of compound spilled, the size of the water body into

which it is spilled, the time at which water consumption occurs relative to the time of the spill, and the amount of contaminated water that is consumed. All Forest Service risk assessments assume that the accidental spill occurs in a small pond with a surface area of about one-quarter of an acre (1000 m^2) and a depth of 1 meter. Thus, the volume of the pond is 1000 m^3 or 1,000,000 liters.

For applications of chlorsulfuron, a spill volume of 100 gallons with a range of 20 to 200 gallons is used to reflect plausible spill events. These spill volumes are used in all Forest Service risk assessments involving terrestrial applications of liquids. The chlorsulfuron concentrations in the field solution are also varied to reflect the plausible range of concentrations in field solutions—i.e., the material that might be spilled—using the same values as in the accidental exposure scenarios for workers (Section 3.2.2.2). Based on these assumptions, the estimated nominal concentration of chlorsulfuron in a small pond ranges from about 0.002 to about 2 mg/L with a central estimate of about 0.3 mg/L as detailed in Worksheet B04b.

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

These scenarios involve the accidental direct spray or incidental spray drift to a small pond and a small stream. The exposure scenarios involving drift are less severe but more plausible than the accidental spill scenario described in the previous section. The drift estimates are based on AgDrift, as detailed in SERA (2014a, Section 3.2.3.4.2). The direct spray and drift scenarios are detailed in Worksheet B04c (small pond) and Worksheet B04d (small stream). As would be expected, the concentrations for direct spray are far below the concentrations associated with the accidental spill—i.e., about 0.007 mg/L for a small pond and 0.006 mg/L for a small stream. Also, as expected, the concentrations associated with drift are much lower. Using a distance of 25 feet down wind as an example, the concentrations in a small pond and a small stream are about 0.00006 to 0.0015 mg/L, depending on the application method.

3.2.3.4.3. GLEAMS Modeling

The Forest Service developed a program, Gleams-Driver, to estimate expected peak and longer-term pesticide concentrations in surface water. Gleams-Driver serves as a preprocessor and postprocessor for GLEAMS (Knisel and Davis 2000). GLEAMS is a field scale model developed by the USDA/ARS and has been used for many years in Forest Service and other USDA risk assessments (SERA 2007a, 2011b).

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

Table 9 provides an overview of the locations used in the Gleams-Driver modeling. These locations are standard sites used in Forest Service risk assessments for Gleams-Driver simulations and are intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool) (SERA 2007a). The characteristics of the fields and bodies of water used in the simulations are summarized in Table 10. For each location, simulations were conducted using clay (high runoff, low leaching potential), loam (moderate runoff and leaching potential), and sand (low runoff, high leaching potential) soil textures. For each combination of location and soil, Gleams-Driver was used to simulate pesticide losses to

surface water from 100 modeled applications at a unit application rate of 1 lb a.i./acre, and each of the simulations was followed for a period of about 1½ years post application. Note that an application rate of 1 lb a.i./acre is used as a convention in all Forest Service risk assessments in order to avoid rounding limitations in GLEAMS outputs and are referred to water contamination rates (WCR), concentrations in water associated with an application rate of 1 lb/acre. In the workbooks that accompany this risk assessment, the WCRs are converted to expected concentrations by multiplying the WCRs by the anticipated application rate of 0.0625 lb a.i./acre as discussed in Section 2 (Program Description).

Table 11 summarizes the chemical-specific values used in Gleams-Driver simulations. For the most part, the chemical properties used in the Gleams-Driver simulations are based on the parameters used by the Environmental Fate and Effects Division (EFED) of the U.S. EPA's Office of Pesticides Programs modeling for the chlorsulfuron drinking water assessment (U.S. EPA/OPP/EFED 2002a). One substantial difference between the EPA and GLEAMS-Driver modeling involves estimates of variability. The EPA modeling is typically based on either central estimates or upper bound (90th percentile) input parameters. Following the Extreme Value approach discussed in Section 3.2.3.1.1, the input parameters for the GLEAMS-Driver modeling are based on estimates of variability either as ranges or confidence intervals when estimates of variability are available. For chlorsulfuron, the estimates of variability are made for soil half-life, soil binding (K_{oc}), and sediment binding (K_d). In the GLEAMS-Driver simulations, the central estimates with lower and upper bounds are implemented as triangular distributions (SERA 2007a). In the current risk assessment, most of the model input values are based on the environmental fate studies submitted to the U.S. EPA by registrants, standard values for GLEAMS modeling recommended by Knisel and Davis (2000), and studies from the open literature. The notes to Table 11 indicate the specific sources of the chemical properties used in the GLEAMS modeling effort. The most substantial deviations of inputs used in the current risk assessment from the modeling inputs used by EPA include estimates of the variability in soil and sediment binding (K_{oc} and K_d values). Another difference between the EPA and GLEAMS-Driver runs involves half-lives in aquatic sediment. As discussed in Section 3.2.3.4.4, some EPA models accommodate a zero degradation rate. This is not the case with GLEAMS which requires half-lives rather than degradation rates. Consequently, the GLEAMS-Driver inputs for the half-life in aquatic sediment is set at 7300 days (i.e., about 20 years).

GLEAMS requires estimates of foliar half-life and foliar washoff fraction. These inputs are not used by EPA models. Knisel and Davis (2000) report a foliar half-life of 30 days for chlorsulfuron. Experimental details supporting this half-life as well as estimates of variability are not provided in Knisel and Davis (2000). Based on an analysis for 41 pesticides, Juraske et al. (2008) proposes a simple approximation for estimating either dislodgeable foliar residues or total residues based on soil half-lives: plant surface half-lives can be estimated as the soil half-life divided by 4, and the half-life of total residues can be estimated as the soil half-life divided by 16. Although these relationships are not intuitive, they are well-supported by the analysis offered by Juraske et al. (2008) and a summary of the soil and vegetation half-lives for a far greater number of pesticides (Knisel and Davis 2000) suggests that soil half-lives are usually much greater than foliar half-lives. As summarized in Table 11, a soil half-life of 80 days with a range of 17.3 to 299 days is used for Gleams-Driver modeling. The central estimate of 80 days is identical to the aerobic soil metabolism half-life used by U.S. EPA/OPP/EFED (2002a, p. 75)

for the drinking water assessment of chlorsulfuron. The upper and lower bounds are based on a registrant submitted study (MRID 00035275) as detailed in Table 1. Rather than estimating total residue half-lives as one-sixteenth of the soil half-lives, as recommended by Juraske et al. (2008), the current risk assessment takes a more conservative approach and divides the soil half-lives by 4. Thus, the half-lives for total residues on contaminated vegetation or fruit are taken as 20 days with a range of 4 to 75 days [80 (17.3-299) days ÷ 4 = 20 (4.325 to 74.75) days].

More rapid dissipation of chlorsulfuron may occur in some tolerant species of plants. Fanke et al. (2014, Table 1, p. 8594) have reported shorter dissipation half-times of 0.3 (0.07 to 1.27) days for chlorsulfuron. These estimates appear to be based on the study by Cotterman and Saari (1992, Table 2, p. 187), who report half-lives of 1 to 13 hours (i.e., about 0.04 to 0.5 day) in excised roots and stems of ryegrass seedlings (*Lolium rigidum*) following the methods of Chrisopher et al. (1992). Half-lives of 2-3 hours (i.e., about 0.083 to 0.125) have been reported in wheat based on absorbed residues in wheat leaves (Sweetser et al. 1980). In site-specific analyses, these shorter half-lives for chlorsulfuron in tolerant species of vegetation could be considered in a refined modeling effort if chlorsulfuron was being applied to highly tolerant species of plants – i.e. plants which may rapidly metabolize chlorsulfuron.

Table 12 summarizes the concentrations of chlorsulfuron modeled in surface water by GLEAMS-Driver. Details of the GLEAMS-Driver simulations are detailed in Appendix 8. The specific concentrations of chlorsulfuron in surface water used in the exposure assessments for the current risk assessment are discussed in Section 3.2.3.4.6, following a comparison of the GLEAMS-Driver simulations with surface water models used by EPA (Section 3.2.3.4.4).

The most striking features of the GLEAMS-Driver modeling are the substantially higher estimated longer-term concentrations in a small pond relative to a small stream. These differences are common for compounds such as chlorsulfuron which are persistent in sediments but not strongly bound to sediments—i.e., low K_d values. In the stream system, the chlorsulfuron is flushed downstream (outside of the modelled area) by stream flow due to the low binding to stream sediment. In the pond model, the pond water is not flushed by water flow and the sediment is a sink which contributes, albeit to a limited extent, to the persistence in and, hence, high concentrations of the pesticide in the pond over time.

3.2.3.4.4. Other Modeling Efforts

Along with the GLEAMS-Driver modeling, Table 12 summarizes the results of the application of two EPA Tier 1 screening models to estimate concentrations of chlorsulfuron in surface water (FIRST) and ground water (PRZM-GW). FIRST (*F*QPA *I*ndex *R*eservoir *S*creening *T*ool) is a Tier I (i.e., screening level) model developed by the EPA for estimating concentrations of pesticides in surface water (U.S. EPA/OPP 2008). PRZM-GW (Pesticide Root Zone Model for Ground Water) is a Tier 1 model developed by the EPA in conjunction with Canada's Pesticide Management Regulatory Authority to estimate concentrations of pesticides in groundwater (https://archive.epa.gov/epa/pesticide-science-and-assessing-pesticide-risks/sci-grow-description.html). The inputs and outputs for these Tier 1 models are detailed in Appendix 9.

Table 12 also summarizes the EPA application of FIRST modeling for the drinking water assessment of chlorsulfuron (U.S. EPA/OPP/EFED 2002a) as well as PRZM/EXAMS modeling conducted for the Reregistration Eligibility Decision for chlorsulfuron (U.S. EPA/OPP/EFED

2004a). The U.S. EPA/OPP typically models pesticide concentrations in water at the maximum labeled rate. In Table 12, the modeling results reported in U.S. EPA/OPP/EFED (2002a, p. 77) are normalized to an application rate of 1 lb/acre so that the results are comparable to the GLEAMS-Driver modeling.

Since FIRST is a reservoir model (i.e., a lentic rather than lotic body of water), comparisons between FIRST and GLEAMS-Driver are based on the GLEAMS-Driver pond modeling. Based on the central estimates of exposure, the estimated concentrations from FIRST are similar to those for GLEAMS-Driver using loam soils. The peak central estimate from FIRST is 99.3 µg/L versus an estimated peak concentration from GLEAMS-Driver using a loam soil texture of 97.4 µg/L (Table 12). The peak concentrations from PRZM/EXAMS (Tier 2) modeling are somewhat unusual in that they exceed the estimates from the FIRST (Tier 1) model. Nonetheless, the upper bound estimates from GLEAMS-Driver (i.e., 320 to 660 µg/L) encompass the highest estimate from PRZM/EXAMS (i.e., 274 µg/L).

The longer-term estimate from FIRST is 34.9 µg/L versus an estimated longer-term concentration from GLEAMS-Driver of 49 µg/L using a loam soil texture. The ranges from the GLEAMS-Driver modeling (e.g., 0.004-410 µg/L per lb/acre for peak concentrations in loam soils), however, are much greater than those from the FIRST modeling (i.e., 90.3 to 102.9 µg/L per lb/acre). Broader ranges from the GLEAMS-Driver modeling relative to the FIRST model are commonly noted in Forest Service risk assessments and reflect the broader range of input values used in the GLEAMS-Driver modeling, the number and diversity of locations and soil types used in the GLEAMS-Driver modeling, and the large number of simulations conducted in the GLEAMS-Driver modeling relative to the FIRST or PRZM/EXAMS modeling.

As summarized in Table 13, PRZM-GW estimated concentrations of chlorsulfuron in groundwater are substantially below those estimated by GLEAMS-Driver and the FIRST model. Concentrations of chlorsulfuron in groundwater are not specifically used in Forest Service risk assessments; hence, the results from PRZM-GW are noted only for the sake of completeness in terms of covering models commonly used by EPA.

3.2.3.4.5. Monitoring Data

The monitoring data on chlorsulfuron are sparse. U.S. EPA/OPP/EFED (2002a) summarizes a study (not specifically referenced) in which chlorsulfuron was detected in less than 5% of 71 streams and was not detected in any of 25 wells at a limit of detection of 1 µg/L. USGS (2014) indicates that chlorsulfuron was not detected in two sampled wells (LOD = 0.0017 µg/L) but was detected in 1 of 43 samples of drinking water at a concentration of 0.0028 µg/L.

In terms of evaluating the surface water modeling efforts discussed in the previous sections, the most useful monitoring studies are those that associate monitored concentrations of a pesticide in water with defined applications of the pesticide—e.g., applications at a defined application rate to a well-characterized field. When available, such studies can provide a strong indication of the plausibility of modeled concentrations of a pesticide in surface water. In the absence of such monitoring data, the modelled estimates discussed in Sections 3.2.3.4.3 and 3.2.3.4.4 cannot be further evaluated.

3.2.3.4.6. Concentrations in Water Used for Risk Assessment

The modeled surface water concentrations of chlorsulfuron used in the current risk assessment are summarized in Table 13. The concentrations are specified as water contamination rates (WCRs)—i.e., the concentrations in water expected at a normalized application rate of 1 lb a.i./acre, converted to units of ppm or mg/L per lb a.i./acre. In Table 12, the summary of all of the modeling efforts, units of exposure are expressed as ppb or µg/L, as a matter of convenience. In Table 13, however, ppb is converted to mg/L (ppm), because 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.

As summarized in Table 13, the peak WCRs are taken as 0.125 (0.000004 to 0.66) mg a.i./L. The central estimate is based on the average of the peak concentrations among all soil types given in Table 12 – i.e., 124.9 µg/L – rounded to three significant places. The lower and upper bounds of the peak concentrations are taken as the lowest and highest concentrations among all of the soil types – i.e., the lower bound of 0.004 µg/L for loam soils and the upper bound of 660 µg/L for sand.

As also summarized in Table 13, the longer-terms WCRs are taken as 0.0636 (0.0000016 to 0.38) mg a.i./L) mg/L. As with the peak WCRs, the central estimate is based on the average of the longer-term concentrations among all soil types given in Table 12 – i.e., 63.6 µg/L. The lower and upper bounds of the longer-term concentrations are taken as the lowest and highest concentrations among all of the soil types – i.e., the lower bound of 0.0016 µg/L for loam soils and the upper bound of 380 µg/L for sand.

The water contamination rates are entered in Worksheet B04Rt in the attachments to this risk assessment. The values in Worksheet B04Rt are linked to the appropriate scenario-specific worksheets in the EXCEL workbook and are adjusted to the application rate entered in Worksheet A01—i.e., 0.0625 lb a.i./acre in the workbook released with this risk assessment. In the worksheet associated with contaminated surface water (i.e., Worksheet B04a), the application rate is multiplied by the water contamination rates to estimate the expected concentrations of chlorsulfuron in surface water.

As discussed previously and summarized in Table 12, the Gleams-Driver simulations of the small pond provide the highest estimates of chlorsulfuron concentrations in surface water, and the central estimates from GLEAMS-Driver are reasonably consistent with the central estimates from the Tier I modeling using FIRST. As detailed in Section 3.2.3.4.3, the GLEAMS-Driver simulations encompass a much broader range of soils and locations with a concomitant increase in the range of modelled values. Consequently, the Gleams-Driver simulations serve as the primary basis for the water concentrations of chlorsulfuron used in the current risk assessment.

As noted in 3.2.3.4.5, monitoring data on concentrations of chlorsulfuron in surface water are not available to assess the plausibility of the modeling. While the Gleams-Driver estimates are reasonably consistent with U.S. EPA/OPP modeling (Section 3.2.3.4.4), the lack of appropriate monitoring data adds uncertainty to this risk assessment.

As with all uses of GLEAMS-Driver in Forest Service risk assessments, the estimated concentrations of chlorsulfuron in water cover a substantial range. For example and as summarized in Table 13, the estimated peak concentrations range from 0.000004 to 0.66 mg/L per lb a.i. applied. This range spans a factor of over 150,000 [0.66 ÷ 0.000004 = 165,000]. This variability is typical of composite summaries of GLEAMS-Driver simulations in Forest Service risk assessments and reflects the wide range of conditions used in the GLEAMS-Driver modeling (Section 3.2.3.4.3). In region-specific or site-specific assessments, consideration should be given to the more detailed summaries of the modeling simulations in Appendix 8 or to conducting site-specific assessments to reflect local conditions (see SERA 2016a, Section 3.3.4).

3.2.3.5. Oral Exposure from Contaminated Fish

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

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

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

Generally, bioconcentration factors for the edible portion of fish (i.e., muscle) are used in the human health risk assessment under the general assumption that humans do not consume offal. As discussed in U.S. EPA/OPP/EFED (2012a, p. 10), the low octanol water partition coefficient for chlorsulfuron suggests that this pesticide will not bioconcentrate in fish or other aquatic organisms. As summarized in Table 2, BCFs are reported for bluegill sunfish (BCFs of <1 in edible tissue) and channel catfish (1.5 in edible tissue). In the exposure assessment for humans, a BCF of 1 is used for acute exposures and a BCF of 1.5 is used for longer-term exposures. As noted in Section 4.2.2.5, the BCFs for whole fish are used in the exposure assessments for mammalian and avian wildlife—i.e., a BCF of 1 for acute exposures and a BCF of 12 for longer-term exposures. As discussed in the risk characterizations for human health (Section 3.4) and ecological effects (Section 4.4), all exposure assessments for the consumption of contaminated fish are substantially below the level of concern (HQ=1).

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

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

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

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

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

3.2.3.7. Oral Exposure from Contaminated Vegetation

Although none of the Forest Service applications of chlorsulfuron will involve crop treatment, Forest Service risk assessments typically include standard exposure scenarios for the acute and longer-term consumption of contaminated vegetation. Two sets of exposure scenarios are provided: one for the consumption of contaminated fruit and the other for the consumption of contaminated vegetation. These scenarios are detailed in Worksheets D03a (fruit) and D03b (vegetation) for acute exposure and Worksheets D04a (fruit) and D04b (vegetation) for chronic exposures.

The pesticide contamination on fruit and vegetation is estimated using the empirical relationships between application rate and concentration on different types of vegetation (Fletcher et al. 1994). The rates provided by Fletcher et al. (1994) are based on a reanalysis of data originally compiled by Hoerger and Kenaga (1972) and represent estimates of pesticide concentration in different types of vegetation (mg chemical/kg vegetation) after an application at a normalized rate of 1 lb a.e./acre. Although the EPA human health risk assessments do not consider this exposure scenario, the residue rates recommended by Fletcher et al. (1994) are used by U.S. EPA/OPP in their ecological risk assessment of chlorsulfuron (U.S. EPA/OPP 2004a, p. 67).

The residue rates recommended by Fletcher et al. (1994) are given in Table 14 of the current Forest Service risk assessment. Fletcher et al. (1994) and Hoerger and Kenaga (1972) provide only central and upper bound estimates of residue rates. Accordingly, the lower bound estimates in Table 14 are made under the assumption that the ratio of the central estimate to the upper

bound estimate is identical to the ratio of the lower bound estimate to the central estimate (i.e., the variability is lognormal).

For longer-term exposures, the time-weighted-average exposure is estimated using the initial pesticide concentration and its half-life on vegetation (Worksheet D04a and D04b). These worksheets accommodate a central estimate and the lower and upper bounds on the half-life. In these worksheets, the half-lives are identical to those used in the Gleams-Driver modeling, as summarized in Table 11. For longer-term exposure scenarios associated with the consumption of broadleaf vegetation, the likelihood and plausibility of such exposures will be low for herbicides like chlorsulfuron which are toxic to broadleaf vegetation, as considered further in Section 3.4.3 (risk characterization for members of the general public).

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

An overview of the dose-response assessment for the human health effects is given in Table 15. Following standard practices in Forest Service risk assessments, RfDs are adopted from the values proposed by U.S. EPA/OPP. In terms of study selection, the EPA dose-response assessment is unchanged from the previous Forest Service risk assessment on chlorsulfuron (SERA 2004a). The EPA, however, reduced the uncertainty factor used to derive both the acute and chronic dose-response assessment from 300 to 100 in response to the submission of an acceptable study on reproductive toxicity. The surrogate acute RfD is 0.75 mg/kg bw based on a developmental NOAEL of 75 mg/kg bw/day and an uncertainty factor of 100. The chronic RfD is 0.05 mg/kg bw/day based on a NOAEL of 5 mg/kg bw/day from a standard chronic feeding study in rats and an uncertainty factor of 100. Dose-severity relationships, although taken into consideration, do not have a substantial impact on the risk assessment because neither the acute nor chronic RfDs is exceeded in any of the exposure assessments.

3.3.2. Chronic RfD

The most recent EPA human health risk assessment derives a chronic RfD of 0.05 mg/kg bw/day (U.S. EPA/OPP/HED 2015a, p. 8), based on a NOAEL of 5 mg/kg bw/day in rats from the 2-year feeding study by Wood et al. (1981a, MRID 00086003), as discussed in Section 3.1.5 and summarized in Appendix 1, Table A1-2. The NOAEL is associated with a LOAEL of 25 mg/kg bw/day based on a decrease in body weight. As also summarized in Appendix 1, Table A1-2, the chronic NOAEL of 5 mg/kg bw/day in rats is below the corresponding NOAEL of 108 mg/kg bw/day in mice (Wood et al. 1981b, MRID 00090030) and 60.6 mg/kg bw/day in dogs (Atkinson 1991, MRID 41862601). In addition, the chronic NOAEL in rats is below the lowest NOAEL from the multigenerational reproduction study in rats—i.e., 151mg/kg/day for parental male rats from the study by Mylchreest (2005, MRID 46493201), as summarized in Appendix 1, Table A1-3. The chronic rat NOAEL of 5 mg/kg bw/day is divided by an uncertainty factor of 100—a factor of 10 for species-to-species extrapolation multiplied by a factor of 10 for potentially sensitive individuals in the human population—to derive the RfD of 0.05 mg/kg bw/day.

This chronic RfD of 0.05 mg/kg bw/day is identical to the chronic RfD originally posted on the U.S. EPA's Agency-wide Integrated Risk Information System (U.S. EPA 1987). As noted in the previous Forest Service risk assessment (SERA 2004a), U.S. EPA/OPP previously accepted the study selection and NOAEL from U.S. EPA (1987) but elected to use an uncertainty factor of 300 rather than 100 (U.S. EPA/OPP 2002b, p. 27). As discussed in Section 3.1.9.2, the additional uncertainty factor of 3 reflects the assessment by U.S. EPA/OPP that the then current multigenerational reproduction study by Wood et al. (1981a, MRID 00086003) was unacceptable. As also discussed in Section 3.1.9.2, U.S. EPA/OPP reviewed the more recent multigenerational reproduction study by Mylchreest (2005, MRID 46493201) and classified this study as *Acceptable/Guideline* (U.S. EPA/OPP/HED 2015a, p. 21). Thus, the original and standard uncertainty factor of 100 was reinstated by EPA.

The European regulatory literature recommends a somewhat higher Acceptable Daily Intake (AID) of 0.2 mg/kg bw/day (European Commission 2010, p. 3; EFSA 2008, p. 22). This higher toxicity value is noted for the sake of completeness but is not otherwise considered in the current risk assessment. As discussed above, the chronic RfD from U.S. EPA/OPP/HED 2015a, p. 8) is

well documented and is based on the most sensitive endpoint in the most sensitive species. Consequently, the current Forest Service risk assessment defers to U.S. EPA/OPP.

3.3.3. Acute RfD

The U.S. EPA/OPP sometimes derives acute RfDs for pesticides. For chlorsulfuron, however, the EPA did not derive an acute RfD for the general population. The rationale for not doing so is as follows: *No appropriate endpoint attributable to a single dose was identified including developmental toxicity studies in rats and rabbits.* (U.S. EPA/OPP/HED (2015a, Table 4.3.1, p. 8). The recent risk assessment by the European Food Safety Authority reaches essentially the same conclusion: *The meeting of experts agreed that the setting of an ARfD is not needed for chlorsulfuron based on its toxicological profile of low acute toxicity* (EFSA 208, p. 16). Similarly, the WHO has classified chlorsulfuron as ...*Unlikely to present acute hazard in normal use* (FAO/WHO 2003, p. 21; IPCS/WHO 2010, p. 67).

As detailed in Section 3.2, several accidental and non-accidental exposure scenarios typically used in Forest Service risk assessments are developed for chlorsulfuron. All of these exposure assessments involve exposure for a single day or during a single incident. In the absence of an acute RfD associated with a single day or single incident exposure, the current Forest Service risk assessment uses the approach developed by EPA for short-term incidental exposures (1-30 days). The U.S. EPA/OPP/HED (2015a, Table 4.3.1, p. 8) assesses such short-term incidental exposures using the NOAEL of 75 mg/kg bw/day from a developmental study in rabbits (i.e., Alvarez 1991b, MRID 41983101, as summarized in Appendix 1, Table A1-3). In applying this NOAEL to risk characterization, the EPA uses a Margin of Exposure (MOE) of 100, which is based on a factor of 10 for extrapolating from animals to humans multiplied by a factor of 10 considering sensitive subgroups in the human population. This approach is fundamentally equivalent to using a short-term RfD of 0.75 mg/kg bw. In the absence of an acute RfD, the short-term surrogate RfD of 0.75 mg/kg bw is used in the current Forest Service risk assessment to characterize risks associated with acute exposures.

The above approach is obviously conservative because this acute toxicity value is based on a repeated dose developmental study but is applied to single-day exposure scenarios. As discussed further in the risk characterization (Section 3.4), this approach has no substantial impact on the risk assessment, because none of the acute exposure scenarios exceeds the level of concern.

3.3.4. Surrogate RfD for Occupational Exposures

The U.S. EPA/OPP sometimes derives toxicity values for workers that are different from the acute and longer-term toxicity values used for the general public, which is not the case for chlorsulfuron. For characterizing risks associated with occupational exposures, the U.S. EPA/OPP/HED (2005a, Table 4.3.2, p. 8) uses the NOAEL of 75 mg/kg bw/day and a margin of exposure of 100—i.e., essentially equivalent to using the surrogate acute RfD of 0.75 discussed in the previous section. The European Food Safety Authority (2008, p. 16) recommends a modestly lower acceptable operator exposure level (AOEL) of 0.43 mg/kg bw/day.

Forest Service risk assessments typically assume that a worker will apply a pesticide over the course of a season—i.e., several months. Consequently, chronic RfDs rather than surrogate acute RfDs are not typically used in the risk characterization for workers, unless there is a need to elaborate the risk characterization. As discussed further in the risk characterization for

workers (Section 3.4.2), this is not the case for chlorsulfuron because none of the exposure scenarios exceeds the level of concern (HQ=1).

3.3.5. Dose-Severity Relationships

Forest Service risk assessments sometimes consider dose-severity relationships to more fully characterize potential risks in exposure scenarios where the doses exceed the acute or chronic RfDs. For chlorsulfuron, this consideration is not relevant because even at the upper bounds of exposure, none of the estimated doses in the exposure scenarios for workers or members of the general public exceeds the RfDs (Section 3.4).

Notwithstanding the above, a brief and minimal consideration of dose-severity relationships can be based on the ratios of the LOAEL to the corresponding NOAEL for the acute and chronic RfDs. As summarized in Table 15, these ratios are about 2.7 for the acute RfD [200 mg/kg bw/day ÷ 75 mg/kg bw/day = 2.666…] and 5 for the chronic RfD [25 mg/kg bw/day ÷ 5 mg/kg bw/day]. In both cases, the LOAELs are based on nonspecific and relatively mild effects—i.e., decreases in body weight and body weight gain.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

In both the human health and ecological risk assessments, the quantitative expression of the risk characterization is the hazard quotient (HQ), the ratio of the anticipated dose or exposure to the RfD (human health) or no-observed-effect level or concentration (ecological effects) using 1 as the level of concern—i.e., an HQ of < 1 is below the level of concern. For the human health risk assessments the toxicity values are a surrogate acute RfD of 0.75 mg/kg bw/day and a longer-term RfD of 0.05 mg/kg bw/day (Table 15). The HQs for workers (Worksheet E02) and members of the general public (Worksheet E04) are summarized in Attachment 1. All HQs given in Attachment 1 are based on the anticipated application rate of 0.0625 lb a.i./acre. Higher application rates, up to the maximum labeled rate of 0.25 lb a.i./acre, are considered for exposure scenarios that approach a level of concern (HQ=1). For both workers and members of the general public, none of the exposure scenarios exceed the level of concern even at the upper bounds of estimated exposures.

The highest HQ for workers is 0.2—i.e., the upper bound HQ for workers applying chlorsulfuron in ground or aerial broadcast applications. The upper bound exposures for workers are based on extremely conservative 95% upper prediction intervals. The HQs are linearly related to application rates. For the upper bound HQs to reach a level of concern, the application rate would need to be about 0.3 lb a.i./acre[0.0625 lb a.i./acre ÷ 0.2 = 0.3125 lb a.i./acre], which exceeds the maximum labelled rate. Mild irritation to the skin and eyes can result from exposure to relatively high levels of exposure to chlorsulfuron. From a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling chlorsulfuron. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

For members of the general public, the highest upper bound HQs in each category of exposure scenarios are 0.3 (accidental exposures), 0.1 (acute non-accidental exposures), and 0.7 (longer-term exposures). As with the worker exposure assessments, exposure assessments for members of the general public are conservative, particularly at the upper bounds of the estimates. This is particularly true for the longer-term HQ of 0.7, which is associated with the upper bound exposure scenario for the consumption of contaminated vegetation. Vegetation treated with an effective herbicide will likely show signs of damage, and it does not seem reasonable to assume that an individual would consume the vegetation over a prolonged period of time. Notwithstanding this reservation, an application rate of about 0.09 lb a.i./acre would lead to an HQ that reaches the level of concern (HQ=1), and the application rate of 0.09 lb a.i./acre is within the labelled rates for chlorsulfuron. If this or a higher application rate is used in specific Forest Service programs, measures should be considered to mitigate longer-term exposures from the consumption of contaminated vegetation by members of the general public.

For both workers and members of the general public, the relatively benign risk characterizations are consistent with the most recent human health risk assessments from EPA.

3.4.2. Workers

The highest HQ for workers is 0.2, the upper bound HQ for workers involved in ground and aerial broadcast applications. This HQ is below the level of concern (HQ=1) by a factor of 5. Note that the accidental HQs are lower than the HQs for general exposures. As discussed in Section 3.2.2.2, all of the accidental exposure scenarios for workers involve dermal exposures. As discussed in Section 3.1.3.2.1, the estimated first-order dermal absorption rates for chlorsulfuron are 0.00018 (0.000035–0.00089) $hour^{-1}$. As also discussed in Section 3.1.3.2.1, the U.S. EPA/OPP/HED (2015a, p. 8) assumes 100% dermal absorption; however, this assumption does not seem reasonable and is not adopted in the current Forest Service risk assessment.

The upper bound HQ of 0.2 is based on an application rate of 0.0625 lb a.i./acre. For workers, all exposures are linearly related to the application rate. Thus, the level of concern (HQ=1) would be reached at an application rate of about 0.3 lb a.i./acre [0.0625 lb a.i./acre ÷ 0.2 = 0.3125 lb a.i./acre]. As discussed in Section 2.1, the highest labelled rate for any formulation of chlorsulfuron is 0.25 lb a.i./acre. Although the use of this highest application rate is not anticipated in Forest Service applications, the use of higher labelled application rates would not have an impact on the qualitative risk characterization—i.e., all HQs would be below 1.

The risk characterization for workers given in the current Forest Service risk assessment is consistent with the risk characterizations for workers given in the EPA's most recent occupational and residential exposure and risk assessment (U.S. EPA/OPP/HED 2002a, p. 2) as well as the EPA's most recent human health risk assessment in support of the registration review of chlorsulfuron (U.S. EPA/OPP/HED 2015a, p. 14). The highest risk estimate from EPA is a margin of exposure of 360, which corresponds to an HQ of 0.36 using EPA's recommended margin of exposure of 100 (U.S. EPA/OPP/HED 2015a, p. 15). This equivalent HQ of 0.36 is similar to the upper bound HQ of 0.2 derived in the current Forest Service risk assessment.

As discussed in Section 3.1.11, chlorsulfuron can cause mild irritation to eyes and skin. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, effects on the eyes or skin are likely to be the only overt effects as a consequence of mishandling chlorsulfuron. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of chlorsulfuron.

3.4.3. General Public

The HQs for the general public associated with exposures to chlorsulfuron are summarized in Worksheet E04 of Attachment 1. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the surrogate acute RfD of 0.75 mg/kg/day for acute/short-term exposure scenarios and the chronic RfD of 0.05 mg/kg/day for chronic or longer term exposures. At an application rate of 0.0625 lb a.i./acre, none of the HQs for members of the general public exceed the level of concern for accidental, acute non-accidental, or longer-term exposure scenarios. The highest HQs in each exposure scenario category are 0.3 (accidental exposures), 0.1 (acute non-accidental exposures), and 0.7 (longer-term exposures).

For accidental scenarios, the highest HQ of 0.3 is associated with the consumption of contaminated water following an accidental spill. As discussed in Section 3.2.3.4.1, this

exposure scenario involves the accidental spill of up to 200 gallons of a field solution of chlorsulfuron at a concentration of 2.5 mg a.i./L (Worksheet B04b). As discussed in Section 2.4, the concentration of 2.5 mg a.i./L is associated with the lowest application volume of 3 gallons/acre, which is used only in aerial applications. Based on this relatively extreme exposure assessment, the upper bound HQ of 0.3 suggests that accidental spills are not likely to exceed the level of concern unless the spill is substantially more extreme than that used in the current risk assessment. Notwithstanding this assessment, the mitigation of any accidental exposure to chlorsulfuron or any other pesticide is clearly prudent.

The highest upper bound non-accidental HQs of 0.1 for acute exposure and 0.7 for longer-term exposures are both associated with the consumption of contaminated vegetation. As discussed in the exposure assessment for these scenarios (Section 3.2.3.7), the acute scenario should not be viewed as extreme, at least for broadcast applications. Nonetheless, the HQ of 0.1 suggests that the level of concern (HQ=1) would be reached only at an application rate of 0.625 lb a.i./acre, which is in excess of the maximum labelled rate of 0.25 lb a.i./acre (Section 2.4). The HQ of 0.7 for longer-term exposures should be viewed as extreme, particularly for herbicides. The exposure assessment assumes that an individual will consume contaminated vegetation over a prolonged period of time (i.e., 90 days). As discussed in SERA (2014a, Section 3.2.3.7, pp. 66-68), vegetation treated with an effective herbicide will likely show signs of damage and it does not seem reasonable to assume that an individual would consume the vegetation over a prolonged period of time. Nonetheless, the Forest Service has determined that such exposures cannot be ruled out. For this longer-term exposure scenario, an application rate of about 0.09 lb a.i./acre [0.0625 lb a.i./acre ÷ 0.7 ≈ 0.08929 lb a.i./acre] would lead to an HQ that reaches the level of concern (HQ=1). The application rate of 0.09 lb a.i./acre is within the labelled rates for chlorsulfuron. If this or a higher application rate is used in specific Forest Service programs, measures should be considered to mitigate longer-term exposures from the consumption of contaminated vegetation by members of the general public.

The relatively benign risk characterization for members of the general public is consistent with the risk characterization in the most recent human health risk assessment from EPA. The lowest margin of exposure (corresponding to the highest risk) derived by EPA is 6400 (U.S. EPA/OPP/HED 2016a, Table 6.1.1, p. 12). Based on the relationship of EPA's margin of exposure (MOE) to the HQ (SERA 2014a, p. 74), the MOE of 6000 corresponds to an HQ of about 0.2 [1 ÷ (6,400 ÷ 100) = 0.15625]. Based on EPA's dietary and drinking water exposure, the highest ratio of exposure to the chronic RfD is 0.14, which corresponds to an HQ of 0.14 (U.S. EPA/OPP/HED 2015a, Table 5.3, p. 11).

Each of the HQs summarized in Worksheet E04 involves a single exposure scenario. In some cases, individuals could be exposed by more than one route, and, in such cases, risk can be quantitatively characterized by simply adding the HQs for each exposure scenario. For chlorsulfuron, considerations of multiple exposure scenarios have little impact on the risk assessment. For example, based on the upper bounds of the HQs for all accidental and acute exposures developed in the current risk assessment for a young woman (i.e., direct spray on the lower legs, staying in contact with contaminated vegetation, eating contaminated fruit and contaminated vegetation, drinking contaminated water, and consuming contaminated fish at rates characteristic of subsistence populations), the total HQ would be about 0.13 [0.001 + 0.0001 +

0.02 + 0.1 + 0.006 + 0.0006 = 0.1277]. Similarly, for all of the chronic exposure scenarios, all of which involve a young woman, the addition of all HQs (i.e., the consumption of contaminated fruit and vegetation, contaminated water, and contaminated fish at rates characteristic of subsistence populations) leads to a combined HQ of about 0.82 [0.1 + 0.7 + 0.02 + 0.0008 = 0.8208].

3.4.4. Sensitive Subgroups

For exposures to almost any chemical, there is particular concern for children, women who are pregnant or may become pregnant, the elderly, or individuals with any number of different diseases. Nonetheless, the available information on chlorsulfuron does not identify subgroups in the human population that might be atypically sensitive to exposure. Under the Food Quality Protection Act (FQPA), the EPA is required to consider populations that might be at increased risk to pesticide exposures including considerations of reproductive effects, pre- and post-natal toxicity, and neurological effects. Each of these effects is considered in Section 3.1. Consistent with the current risk assessment, the EPA determined that these endpoints do not justify quantitative changes in the dose-response assessment (U.S. EPA/OPP/HED 2016a, p. 7).

As indicated in Section 3.1.5, the most sensitive effect of chlorsulfuron in mammals appears to be weight loss. Exposure to chlorsulfuron may also result in alterations in hematological parameters. There is no indication, however, that individuals with pre-existing diseases of the hematological system or metabolic disorders would be particularly sensitive to chlorsulfuron exposure.

3.4.5. Connected Actions

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions as actions which occur in close association with the action of concern; in this case, the use of a pesticide (40 CFR 1508.25, https://www.gpo.gov/fdsys/granule/CFR-2010-title40-vol32/CFR-2010-title40-vol32-sec1508-25). Actions are considered to be connected if they: (i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously, and (iii) Are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this assessment of chlorsulfuron, "connected actions" include actions or the use of other chemicals which are necessary and occur in close association with use of chlorsulfuron.

As discussed in Section 3.1.14.1, chlorsulfuron formulations contain other ingredients (i.e., *inerts*). Based on comparisons of toxicity studies on chlorsulfuron and a 75% a.i. formulation conducted in the 1980s, the formulation was somewhat more toxic in terms of acute oral toxicity (Section 3.1.3) but not in terms of skin and eye irritation (Section 3.1.11) and dermal toxicity (Section 3.1.12). Given the low HQs associated with both accidental and non-accidental exposure scenarios (Section 3.4.3) and the generally conservative assumptions on which these HQs are based (Section 3.2.3.1.1), there does not appear to be a plausible basis for suggesting that inerts will have an impact on the risk characterization for potential human health effects.

As discussed in Section 3.1.14.2, chlorsulfuron may be applied with a surfactant; nonetheless, specific surfactants are not recommended on the product labels. Furthermore, the impact of surfactants on the toxicity of chlorsulfuron is not addressed in the available information, and as

noted in the previous Forest Service risk assessment (SERA 2004a), the impact of surfactants on the toxicity of chlorsulfuron was not identified in the FIFRA files (i.e., confidential business information) on chlorsulfuron.

3.4.6. Cumulative Effects

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

The most recent EPA human health risk assessment on chlorsulfuron does determine whether other pesticides may have cumulative effects with chlorsulfuron.

> *Although the SUs* [sulfonyl urea herbicides] *share some chemical and toxicological characteristics, the toxicological database does not support a testable hypothesis for a common mechanism of action.*
>
> U.S. EPA/OPP/HED 2015a, p. 13.

As discussed further in Section 4.4.2.5 (risk characterization for terrestrial plants), chlorsulfuron shares a common mechanism of phytotoxicity with other sulfonyl urea herbicides; however, this detail does not have an impact on the assessment of cumulative effects for the human health risk assessment.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Chlorsulfuron and other sulfonylurea herbicides act by inhibiting acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids that are essential for plant growth. Standard bioassays on terrestrial plants submitted to EPA in the support of the registration of chlorsulfuron indicate that dicots are somewhat more sensitive than monocots. What is most striking is that the differences in species sensitivity within dicots and monocots appear to be greater than the differences between dicots and monocots in general. Members of the Triticeae tribe (e.g., wheat and barley) appear to be among the most tolerant monocots. As with many herbicides, the development of resistance in terrestrial plants is an issue of concern. Resistance appears to develop in plants primarily through mutations in the ALS receptor. Plant tolerance may develop through the induction of a cytochrome P450, which is involved in the metabolism and detoxification of chlorsulfuron in terrestrial plants.

The data on aquatic macrophytes are more limited than the data on terrestrial plants, with all but one study involving monocots. The data on algae are robust and indicate that freshwater algae are generally more sensitive than saltwater algae. Macrophytes are clearly more sensitive than algae. In terms of EC_{50} values for growth inhibition in sensitive species, macrophytes are more sensitive by a factor of about 46. For tolerant species, macrophytes are more sensitive than algae by a factor greater than 150,000.

Chlorsulfuron is much less toxic to animals than plants. Based on acute toxicity data, the EPA classifies chlorsulfuron as *Practically Nontoxic* to mammals, birds, honeybees, fish, and aquatic invertebrates. No data are available on the toxicity of chlorsulfuron to reptiles or amphibians. In both mammals and birds, the primary signs of chronic toxicity are weight loss or decreased body weight gain. Similarly, reduced growth is the most sensitive sign of toxicity in longer-term studies with fish. Only one longer-term study in aquatic invertebrates is available—i.e., a standard reproduction assay in *Daphnia magna*—and the only sign of toxicity observed was a decrease in the number of offspring.

4.1.2. Terrestrial Organisms

4.1.2.1. Mammals

As summarized in Appendix 1 and discussed in the human health risk assessment (Section 3.1), several standard toxicity studies in experimental mammals were conducted and submitted to the EPA as part of the registration process for chlorsulfuron. All of these studies, which are used in the human health risk assessment to identify the potential toxic hazards in humans associated with exposures to chlorsulfuron, can also be used to identify potential toxic effects in mammalian wildlife. No field studies are available on the direct or indirect impact of chlorsulfuron on mammalian wildlife.

The mechanism of action for chlorsulfuron in mammals is not well characterized (Section 3.1.2). The most common and consistent signs of acute, subchronic, and chronic toxicity of chlorsulfuron in mammals are weight loss and decreased body weight gain. The only other

commonly noted effects are changes in various hematological parameters and general gross pathological changes to several organs. None of these changes, however, suggest specific target organ toxicities.

While human health risk assessments typically focus on the most sensitive species as a surrogate for humans, the ecological risk assessment is concerned with differences in toxicity among species. The available information on the acute oral toxicity in mammals is inadequate to clearly assess differences in sensitivity among species. As discussed in Section 3.1.3 and summarized in Appendix 1, Table A1-1, most acute oral LD_{50} studies have been conducted on rats. Based on the LD_{50} of 5545 mg a.i./kg bw in male rats (Trivits 1979, MRID 00031406), the EPA classifies technical grade chlorsulfuron as Category IV—i.e., practically nontoxic in terms of acute oral toxicity) (U.S. EPA/OPP/HED 2015a, p. 20; U.S. EPA/OPP/EFED 2012a, p. 22). The only available study on technical grade chlorsulfuron conducted with guinea pigs cites an LD_{50} of 1363 mg a.i./kg bw (Hall and Dashiell 1980, MRID 00031408). This study suggests that guinea pigs may be more sensitive than rats to chlorsulfuron in terms of acute oral toxicity; however, any generalizations are tenuous in the absence of corroborating data.

Subchronic and chronic toxicity studies on chlorsulfuron were conducted with dogs, mice, and rats, and developmental studies were conducted with rats and rabbits. Based on the chronic toxicity studies, rats are clearly the most sensitive species with a chronic NOAEL of 5 mg a.i./kg bw/day and a corresponding LOAEL of 25 mg a.i./kg bw/day based on decreased body weights (Wood et al. 1981a, MRID 00086003). Mice are markedly less sensitive with a chronic NOAEL of 108 mg a.i./kg bw/day and a corresponding LOAEL of 750 mg a.i./kg bw/day, again based on decreased body weights, (Wood et al. 1981b, MRID 00090030). Dogs appear to be intermediate in sensitivity with a chronic NOAEL of 60.6 mg a.i./kg bw/day and a corresponding LOAEL of 215 mg a.i./kg bw/day, based on decreased body weight gain and changes in hematological parameters (Atkinson 1991, MRID 41862601). Note that this pattern of sensitivities—i.e., rats > dogs > mice—does not suggest a systematic relationship between body weight and sensitivity to chlorsulfuron.

In terms of developmental toxicity, rabbits are somewhat more sensitive than rats. In rabbits, the most sensitive endpoint is maternal toxicity with a NOAEL of 75 mg a.i./kg bw/day and LOAEL of 200 mg a.i./kg bw/day, based on decreased body weight (Alvarez 1991b, MRID 41983101). In rats, the most sensitive endpoint is also maternal toxicity with a NOAEL of 165 mg a.i./kg bw/day and a corresponding LOAEL of 500 mg a.i./kg bw/day, based on decreased body weight and an increase in overt signs of toxicity (Alvarez 1991a, MRID 41976406). Any potential and general systematic differences among species cannot be identified because developmental studies are available on only two species.

4.1.2.2. Birds

As summarized in Appendix 2, standard sets of toxicity studies—i.e., acute gavage studies (Appendix 2, Table A2-1), acute dietary studies (Appendix 2, Table A2-2), and reproduction studies (Appendix 2, Table A2-3)—were submitted to the U.S. EPA/OPP in support of the registration of chlorsulfuron. These are standard assays and test species usually required by the EPA for pesticide registration. All of these studies are summarized in the previous Forest Service risk assessment on chlorsulfuron (SERA 2004a), and no other or more recent toxicity studies in birds are summarized in the recent EPA ecological risk assessments of chlorsulfuron

(U.S. EPA/OPP/EFED 2012a, 2015a). Furthermore, the open literature does not include avian toxicity studies or field studies conducted with chlorsulfuron.

The chlorsulfuron literature does not include definitive gavage LD_{50} or dietary LC_{50} values for birds. The gavage studies in birds report an indefinite LD_{50} of >5000 mg a.i./kg bw in both bobwhite quail (Hinkle and Twigg 1980, MRID 00035263) and mallard ducks (Hinkle and Bristol 1980, MRID 00035264). As discussed in Section 4.1.2.1, the lowest definitive LD_{50} values for mammals are 5545 mg a.i./kg bw in rats and 1363 mg a.i./kg bw in guinea pigs. These limited data suggest that birds may be somewhat less sensitive than mammals to the acute toxic effects of chlorsulfuron. As with mammals, the EPA classifies chlorsulfuron as *Practically Nontoxic* to birds (U.S. EPA/OPP/EFED 2012a, p. 22).

In terms of longer-term toxicity, comparisons between mammals and birds are somewhat confounded based on differences in the scope and duration of the available studies. In birds, the lowest longer-term toxicity values are from the standard reproduction study in bobwhite quail which yielded a NOAEL of about 24.5 mg a.i./kg bw/day with a corresponding LOAEL of 135 mg a.i./kg bw/day, based on decreased body weight. The comparable study in mammals is the reproduction study in rats by Mylchreest (2005, MRID 46493201) which yielded a parental NOAEL of about 155 mg a.i./kg bw/day with a LOAEL of about 456 mg a.i./kg bw/day, based on decreased body weight. From this comparison, birds appear to be somewhat more sensitive than mammals; however, the comparison is compromised by differences in the duration of exposure—i.e., up to about 107 days in the study in rats and 154 days in the study in quail. Studies covering a significant fraction of the lifespan of birds are not available. For mammals, the most sensitive longer-term toxicity study is the 2-year (approximate lifespan) study in rats which yielded a NOAEL of 5 mg a.i./kg bw/day with a corresponding LOAEL of 25 mg a.i./kg bw/day, based on decreased body weight (Wood et al. 1981a, MRID 00086003). While this NOAEL is substantially below the lowest NOAEL in birds—i.e., 24.5 mg a.i./kg bw, as discussed above—a comparison of sensitivities seems inappropriate given the substantial differences in the durations of the reproduction study in quail (154 days) and the chronic study in rats (≈730 days).

While quantitative comparisons of sensitivities between mammals and birds are difficult, decreases in body weight are the primary signs of toxicity noted in toxicity studies on both mammals and birds.

4.1.2.3. Reptiles and Amphibians (Terrestrial Phase)

There is no information regarding the toxicity of chlorsulfuron to reptiles or terrestrial phase amphibians (i.e., amphibians in a life-stage where they are predominantly on land) in the open literature or in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a). Neither the compendia published by Pauli et al. (2000) nor the open literature include toxicity studies that address the effects of chlorsulfuron on reptiles or terrestrial phase amphibians.

Risks to terrestrial phase amphibians are addressed in the most recent EPA ecological risk assessment on chlorsulfuron (U.S. EPA/OPP/EFED 2012a). Following standard practice at EPA, birds are used as surrogates for terrestrial phase amphibians and reptiles, in the absence of data on these groups of organisms (U.S. EPA/OPP/EFED 2012a, p. 22). A concern with the use of birds as a surrogate for amphibians involves the permeability of amphibian skin to pesticides

and other chemicals. While no data are available on the permeability of amphibian skin to chlorsulfuron, Quaranta et al. (2009) note that the skin of the frog *Rana esculenta* is much more permeable to several pesticides than pig skin and that these differences in permeability are consistent with differences in the structure and function of amphibian skin, relative to mammalian skin.

4.1.2.4. Terrestrial Invertebrates

The honey bee is the standard test organism for assessing the potential effects of pesticides on terrestrial invertebrates, and the EPA typically requires an acute contact study with the technical grade pesticide for pesticides that may be applied to foliage. The most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, p. 19) reports an indefinite LD_{50} of >25 µg a.i./bee in a standard contact toxicity study in bees (MRID 42129902). Based on this assay, the EPA classifies chlorsulfuron as *Practically Nontoxic* to bees. Typical body weights for worker bees range from 81 to 151 mg (Winston 1987, p. 54). Taking 116 mg as an average body weight, a dose of 25 µg a.i./bee corresponds to about 216 mg a.i./kg bw [0.025 mg a.i. ÷ 0.000116 kg ≈ 215.517 mg a.i./kg bw]. This indefinite LD_{50} in bees is below the definitive LD_{50} values in experimental mammals (≈ 1000 to 5000 mg a.i./kg bw as summarized in Appendix 1, Table A1-1) and the indefinite LD_{50} values for birds (>5000 mg a.i./kg bw as summarized in Appendix 2, Table A2-1). Because all of the LD_{50} values are indefinite, the sensitivity of the honeybee relative to mammals and birds cannot be assessed.

As summarized in Appendix 3, Table A3-1, a modest open literature is available on the toxicity of chlorsulfuron to terrestrial arthropods. No significant change in mortality rate was observed in first-instar larva of *Gastrophysa polygoni* directly sprayed with chlorsulfuron at exposure levels ranging from 0 - 1.2 mg a.i./cm^2. In a 6-day feeding study in which *Gastrophysa polygoni* larvae were fed leaves treated with chlorsulfuron applied at a rate corresponding to 0.0014lb a.i./acre, no change in weight of larvae was observed (Kjaer and Elmegaard 1996). Survival and development of *Gastrophysa polygoni* was also assessed by placing eggs on *Polygonum convolvuvus* 2 days after plants were sprayed with sublethal doses of chlorsulfuron (Kjaer and Elmegaard 1996). Survival from egg hatch to the last stage of metamorphosis was significantly decreased by chlorsulfuron applied to the host plant at rates of 0.0012 and 0.0024 lb a.i./acre, with first- and second-instar larvae showing the most marked effects (Kjaer and Elmegaard 1996). Although mortality was unaffected for larvae on plants treated with 0.00028 and 0.00060 lb/acre, delayed development was observed at these exposure levels. The mechanism of action of chlorsulfuron in insects is unclear. As discussed further in 4.1.2.5, chlorsulfuron inhibits cytochrome P450 in plants but has only a minimal effect of cytochrome P450 in the housefly (Scott 1996).

The potential for indirect effects on insects via direct effects on plants is evaluated in a study by Kjaer and Heimbach (2001). This study assesses the relationship between chlorsulfuron treated plants and insect survival and growth using the specific insect:plant pairs *Pieris brassicae:Brassica napa* (large white butterfly:oilseed rape) and *Gastrophysa polygoni:Polygonum convolvulus* (beetle:black-bindweed). No significant effects on survival or growth were observed for either insect:plant pair when plants were treated with chlorsulfuron for 4 consecutive days at a rate ranging from 0.025 to 0.8 g a.i./ha (≈0.00002 to 0.0007 lb a.i./acre).

In addition to the studies on terrestrial arthropods, two studies are available on the toxicity of chlorsulfuron to beneficial nematodes—i.e., pathogens to pest insects, and these studies are summarized in Appendix 3, Table A3-2. An early study by Rovesti and Desco (1990) found no adverse effects, including effects on pathogenicity to a wax moth, in two species of nematodes (i.e., *Steinernema carpocapsae* and *Steinernema feltiae*) at test concentrations of up to 10,000 mg/L. This paper, however, presents no detailed data on the responses (e.g., mortality rates) specific to chlorsulfuron and does not specify the source and nature of the chlorsulfuron (i.e., a.i. vs formulation). More recently, Gutierrez et al. (2008) conducted assays on two populations of *Steinernema feltiae*—i.e., a commercial strain and a strain isolated from a natural host, *Bibio hortulanus* (i.e., a species of March fly). At the single assay concentration of 150 mg a.i./L from an unspecified Glean formulation, only 11.8% mortality was noted in the commercial strain; however, 42% mortality was noted in the natural strain. Both of the *Steinernema* species assayed by Rovesti and Desco (1990) were isolated from natural sources—i.e., soil for *Steinernema feltiae* and as a species of wax moth for *Steinernema carpocapsae*. The only obvious experimental design difference between the two studies is the duration of exposure—i.e., 72 hours in the study by Rovesti and Desco (1990) and 48 hours in the study by Gutierrez et al. (2008). This modest difference in duration would not seem to account for the apparent differences in the sensitivities of *Steinernema feltiae* in these two studies.

4.1.2.5. Terrestrial Plants (Macrophytes)

4.1.2.5.1. General Considerations

Chlorsulfuron and other sulfonylurea herbicides act by inhibiting acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids (i.e., valine, leucine, and isoleucine), all of which are essential for plant growth (e.g., Blair and Martin 1988; Brown 1990). The central role of ALS inhibition to the phytotoxicity of chlorsulfuron is illustrated in that the phytotoxic effects of chlorsulfuron can be blocked by supplying branched-chain amino acids prior to chlorsulfuron exposure (Bestman et al. 1990). The inhibition of ALS leads to secondary effects including the accumulation in plants of amino acids (Bestman et al. 1990), pyruvate (Gaston et al. 2003), quinate (Orcaray et al. 2010), sugars (Bestman et al. 1990; Zabalza et al. 2004) and hydroxycinnamic acids (Orcaray et al. 2011). The extent to which the accumulation of these compounds represents primary toxicological effects or effects secondary to phytotoxicity is unclear.

Chlorsulfuron may be absorbed through both roots and foliage. As discussed further in Section 4.1.2.5.2 and illustrated in the study by Al-Khatib (1992a), foliar absorption appears to be somewhat more effective (when expressed in terms of application rate) than soil exposures. Following foliar application, chlorsulfuron is transported both above and below the treated area, at least in sunflowers (Anderson et al. 2010). The major signs of toxicity in plants include chlorosis, abnormal leaf growth, and reductions in normal development and reproduction (Felsot et al. 1996; Fletcher et al. 1996; U.S. EPA/OPP/EFED 2004a). Chlorsulfuron will induce and is metabolized by one or more plant cytochrome P450s, mixed function oxidases involved in the detoxification of xenobiotics as well as endogenous toxicants (Werck-Reichhart et al. 2000). At least in a species of annual grass (*Lolium rigidum*), sublethal doses of 2,4-D will induce cytochrome P450 and antagonize the toxicity of chlorsulfuron. This protective effect can be blocked by malathion, a known inhibitor of plant cytochrome P450 (Han et al. 2013). As

discussed further Section 4.1.2.5.3, cytochrome P450 may play a role in some plant species in the development of resistance or at least tolerance to chlorsulfuron.

4.1.2.5.2. Toxicity Data

The testing requirements for the effects of herbicides on terrestrial plants are relatively rigorous since terrestrial vegetation is the typical target group for herbicides. The testing requirements of U.S. EPA involve bioassays of several species of dicots and monocots for seedling germination and emergence (soil exposures) as well as vegetative vigor (foliar exposures). The standard toxicity studies on terrestrial plants include post-emergent assays for preemergence assays for seedling emergence (Appendix 4, Table A4-1) and vegetative vigor (Appendix 4, Table A4-2). Summaries of these studies are taken from the EPA ecological risk assessment in support of the reregistration for chlorsulfuron (U.S. EPA/OPP/EFED 2004a) and the most recent EPA ecological risk assessment of chlorsulfuron (U.S. EPA/OPP/ EFED 2012a).

As with other groups of organisms covered in the current risk assessment, differences in species sensitivities are a primary concern. The studies submitted to EPA are exceptionally useful in assessing differences in sensitivity in that they are conducted by the same group of investigators using consistent bioassay methods. As summarized in Appendix 4 (Tables A4-1 and A4-2), two sets of studies are available. The most recent study (MRID 46361801) is summarized only briefly in EPA documents with a focus on the most sensitive species of monocots and dicots. This study yields the lowest toxicity value for dicots and is discussed further in the dose-response assessment (Section 4.3.2.5). Because of the lack of detail on toxicity values for other species, however, this study is not considered further in comparisons of species sensitivities.

A full copy of the standard vegetation vigor and seedling emergence assay by McKelvey and Kuratle (1992, MRID 42587201) was available in the preparation of the previous Forest Service risk assessment on chlorsulfuron (SERA 2004a) and is also summarized in detail in the EPA ecological risk assessment in support of the RED for chlorsulfuron (U.S. EPA/OPP/ EFED 2004a). Figure 4 illustrates the species sensitivity distributions in both seedling emergence and vegetative vigor assays from the study by McKelvey and Kuratle (1992). The use of species sensitivity distributions is detailed in SERA (2014a, Section 4.3.5). As illustrated in Figure 4, chlorsulfuron may be viewed as a selective pesticide in that differences in the toxicity of chlorsulfuron vary among species by about 2 orders of magnitude in the seedling emergence assays and about 3 orders of magnitude in the vegetation vigor assay. The toxicity values for vegetative vigor are left-shifted relative to the values for seeding emergence indicating that foliar applications are somewhat more effective than soil applications when expressed in units of lb a.i./acre. While dicots are generally more sensitive than monocots, the difference between monocots and dicots is less than the range of toxicities within either group. Taking the vegetation vigor assays as an example, the difference between the most sensitive species of monocot (corn) and dicot (soybean) is a factor of about 2 [0.000044 lb a.i./acre ÷ 0.0000193 lb a.i./acre ≈ 2.28]. For dicots, the difference between the most sensitive species (soybean) and most tolerant species (cucumber), however, is a factor of over 300 [0.006125 lb a.i./acre ÷ 0.0000193 lb a.i./acre ≈ 317.4]. Similarly for monocots, the difference between the most sensitive species (corn) and most tolerant species (wheat) is a factor of about 130 [0.005813 lb a.i./acre ÷ 0.000044 lb a.i./acre ≈ 132.1].

As illustrated in Figure 5, similar relationships are evident in the open literature publication by Jettner et al. (1999). This is a somewhat unusual study involving hydroponic exposures of 15 bioassays with various species of dicots and 17 bioassays with various species of monocots. The Jettner et al. (1999) study is summarized in Appendix 4, Table A4-3 and details of EC_{50} values illustrated in Figure 5 are given in Appendix 4, Table A4-4. As with the EPA studies illustrated in Figure 4, generally, dicots appear to be only somewhat more sensitive than monocots. Differences within monocots and dicots are substantial, particularly for the monocots. For dicots, the difference between the most sensitive species (lucerne) and least sensitive species (cowpea) is a factor of about 13 [2.42 µg/L ÷ 0.19 µg/L ≈ 12.7]. For monocots, the differences are much greater—i.e., a factor of about 222 between the most sensitive species (a cultivar of corn) and the least sensitive species (wheat) [102 µg/L ÷ 0.46 µg/L ≈ 221.7]. Note that wheat is the most tolerant monocot in both the standard phytotoxicity study by McKelvey and Kuratle (1992) as well as the hydroponic assay by Jettner et al. (1999). As discussed by Sweetser et al. (1980), the tolerance of wheat to chlorsulfuron is probably due to the rapid metabolism and detoxification of chlorsulfuron in wheat. Also notable is that the greater variability within the monocots, relative to variability within the dicots, in the study by Jettner et al. (1999) is associated primarily with members of Triticeae tribe—i.e., triticale, barely, and wheat—as well as one member of the Poeae tribe (i.e., oats). Most of the other monocots in the study by Jettner et al. (1999) are cultivars of corn and sorghum, members of the Andropogoneae tribe. This relationship is also consistent with the vegetation vigor assay by McKelvey and Kuratle (1992) in which corn was the most sensitive monocot assayed.

Several other toxicity assays in plants published in the open literature are summarized in Table A4-3 and field studies are summarized in Table A4-5. While Forest Service risk assessments will generally defer to EPA in the selection of toxicity values for the dose-response assessment (Section 4.3), credible studies from the open literature are considered if the studies suggest a level of sensitivity or tolerance not encompassed by the standard studies submitted to EPA. None of the open literature studies, however, report toxicity values below those from the toxicity studies used by EPA. Obrigawitch et al. (1998) reviews numerous field studies involving applications of chlorsulfuron. In these field studies, the lowest application rate associated with adverse effects in onions, a sensitive species in the vegetative vigor assay, is reported as 0.1 g/ha (Obrigawitch et al. 1998, Table 1, p. 207). This LOEC corresponds to an application rate of 0.0001 kg/ha or 0.0000892 lb/acre and is very close to the EC_{25} value of 0.0000368 for plant height but substantially above the EC_{25} of 0.0000044 lb a.i./acre for shoot weight in the onion noted by McKelvey and Kuratle (1992, MRID 42587201). Based on the results of field studies using foliar application, as detailed in Appendix 4, Table 4-5, cherries appear to be the most sensitive species, with adverse effects observed at application rates as low as 0.000023 lbs/acre (Bhatti et la. 1995).

Two studies report atypically high levels of tolerance to chlorsulfuron. As summarized in Appendix 4, Table A4-3, the highest reported NOEC from a greenhouse vegetative vigor assay is 0.14 lb/acre for Crested wheat, Russian wild rye, Bermuda grass and alkali sacaton (Davison et al 1987). As summarized in Appendix 4, Table A4-5, a slightly higher NOEL of 0.16 lb/acre is reported in a field study of wine grapes (Moore and Elliott 1989). While these studies are noted for the sake of completeness, they are inconsistent with the other toxicity studies on the effect of

chlorsulfuron on terrestrial plants and grossly inconsistent with the studies reviewed by EPA. Consequently, these studies are not used quantitatively in the current risk assessment.

4.1.2.5.3. Resistance

The inhibition of ALS is exhibited by other classes of herbicides including imidazolinones, pyrimidinylthio-benzoates, and triazolopyrimidines (Fan et al. 2005). The sulfonylurea herbicides share a common mechanism of phytotoxicity, and 22 sulfonylurea herbicides are considered as a class in an ecological risk assessment for phytotoxicity (U.S. EPA/OPP/EFED 2015a). As reviewed by Mallory-Smith and Retzinger (2003), chlorsulfuron and other ALS inhibitors are categorized as Class 2 herbicides under the system used by the Weed Science Society of America (WWSA) and as Class B herbicides under the system used by the Herbicide Resistance Action Committee (HRAC). As with many herbicides, resistance is an issue in maintaining the efficacy of sulfonylurea herbicides, and HRAC resistance classifications are used as a guide to reduce the potential for resistance in long-term vegetation management programs. As summarized in Appendix 4, Table A4-5, field studies note resistance to chlorsulfuron in target weed species (Adamczewski et al. 2009; Cirujeda and Taberner 2010).

The major mechanism for resistance appears to be mutations in the ALS receptor (e.g., Hamouzova et al. 2014; Han et al. 2012; Saari et al. 1990). Another mechanism of resistance may involve the induction of cytochrome P450. As discussed above, cytochrome P450 is involved in the metabolism of chlorsulfuron, and enhanced metabolism is associated with tolerance to chlorsulfuron exposures in plants (U.S. EPA/OPP/EFED 2004a, p. 1). The enhanced metabolism of chlorsulfuron is associated with the development of resistance in several species of plants (Busi et al. 2011; Cotterman and Saari 1992; Han et al. 2013; Wen-Sheng et al. 2006; Xiang et al. 2005). Resistance based both on decreased ALS sensitivity as well as increased metabolism of chlorsulfuron has been documented in some species (Christopher et al. 1992). As would be expected in the case of genetic resistance in a population of plants, some plant species can propagate resistant populations through seed dispersal (prickly lettuce, *Lactuca serriola*, Lu et al. 2007) or pollen dispersal (common windgrass, *Apera spica-venti*, Adamczewski et al. 2009). In terms of the magnitude of resistance, the highest resistance factor encountered in the literature is a factor of 320.4 based on EC_{50} values for the inhibition ALS activity in a study on corn poppies (Kaloumenos et al. 2011). In a whole plant bioassay, reported resistance factors are lower—e.g., a factor of 18 in sunflowers (Kolkman et al. 2004) and 5.3 to 5.6 in resistance cultivars of tobacco (Slavov et al. 2005).

Some studies indicate that plants resistant to chlorsulfuron also display cross-resistance to other sulfonylurea urea herbicides (e.g., Ashworth et al. 2014; Kaloumenos et al. 2011; Saari et al. 1990). Somewhat surprisingly, however, cross-resistance to both chlorsulfuron and glyphosate were observed in two dicots—i.e., a species of wild radish (*Raphanus raphanistrum*) [Order Brassicales] (Ashworth et al. 2014) and *Bassia scoparia* [Order Caryophyllales] (Varanasi et al. 2015). Cross-resistance to glyphosate and chlorsulfuron, however, was not observed in a species of rockcress (*Arabidopsis* sp.) [Order Brassicales] (Jander et al. 2003). A possible link between cross-resistance to both chlorsulfuron and glyphosate is suggested in the study by Xiang et al. (2005) which notes that wheat cytochrome P450 monooxygenase is involved in the metabolism of chlorsulfuron and that glyphosate is an inhibitor of a wheat cytochrome P450 (isozyme CYP71C6v1). As discussed in Section 4.1.2.5.1, pre-treatment of plants with 2,4-D (an auxin herbicide) has been associated with an increased tolerance in a species of grass to chlorsulfuron

(Han et al. 2013). No cross-resistance to 4-chloro-2-ethylphenoxyacetate (a.k.a., MCPA, another auxin) and chlorsulfuron was observed in hemp-nettle (Weinberg et al. 2006).

4.1.2.6. Terrestrial Microorganisms

The U.S. EPA does not typically require studies that evaluate the effects of herbicides on soil microorganisms. As summarized in the previous Forest Service risk assessment (SERA 2004a), one study (Julis 1980, MRID 00035277) regarding the effect of technical grade chlorsulfuron on terrestrial microorganisms was submitted to the EPA. This study is cited but not discussed in U.S. EPA/OPP/EFED (2012a) and is neither cited nor discussed in the ecological risk assessment in support of the RED for chlorsulfuron (U.S. EPA/OPP/EFED 2004a). The study by Julis (1980) notes growth reduction in some single-species cultures of fungi at concentration of 1 mg a.i./L. Julis (1980) notes that in soil cultures, there were no effects on populations of soil bacteria and fungi at concentrations of up to 100 mg a.i./kg soil.

Field and field simulation studies (i.e., soil exposures) are consistent with the study by Julis (1980) indicating only minimal effects on soil microorganisms. Nitrification and soil dehydrogenase activity were assessed in three soil types (sandy, clay, and organic) obtained from fields sprayed with 4 and 12 g a.i./ha [≈ 0.0035 and 0.01 lb a.i./acre] for two growing seasons (Junnila et al. 1994). In sandy soil, a small, but statistically significant reduction in soil nitrification was observed 1day after chlorsulfuron application; however, decreases in soil nitrification were not observed in sandy soil at any time throughout the 2-year study. Small increases in soil nitrification were observed in clay soil at the end of the first growing season and in organic soil at the end of the second growing season. These effects could be due to factors other than direct toxicity to microorganisms, such as the death of weeds. In sandy soil, dehydrogenase activity was inhibited at the end of the first growing season for the highest application rate. More recently, both Ahtiainen et al. (2003) and Wang et al. (2010) observed no effects on soil microorganisms in soil assays at concentrations of up to 500 mg a.i./kg soil (i.e., soil respiration in the study by Ahtiainen et al. 2003) or 50 mg a.i./kg soil (microbial activities and microbial biomass in the study by Wang et al. 2010). In a separate field application, Ahtiainen et al. (2003) observed only a transient increase in soil nitrification following an application of Glean 20 DF at 0.02 kg/ha (≈0.018 lb a.i./acre).

Laboratory studies also indicate a lack of remarkable toxicity in terrestrial microorganisms. Results of laboratory (Belai and Oros 1996, Julis 1980, Rapisard 1981a) and field studies (Julis 1980, Junnila et al. 1994) show that chlorsulfuron is only mildly toxic to terrestrial microorganisms. The laboratory study by Belai and Oros (1996) indicates that growth was inhibited in only three of 17 fungal species exposed to 0.1 µmol/agar plate (35.8 µg a.i./plate) of chlorsulfuron. In a laboratory study using silt loam, incubation of soil treated with 0.1 to 10 ppm chlorsulfuron had no effect on the ability of microorganisms to degrade cellulose and protein (Rapisarda 1981a). The only definitive toxicity value in a standard laboratory assay is an EC_{50} (bacterial grow) of 60 mg a.i./L in a culture media bioassay by Ahtiainen et al. (2003).

As discussed in the previous section, chlorsulfuron is a potential inhibitor of plant branched-chain amino acid biosynthesis. This effect, however, was not observed in an assay on *Mycobacterium avium*, a human and animal pathogen that can lead to tuberculosis in immune-compromised individuals (Zohar et al. 2003).

At least under laboratory culture conditions, two species of fungi can degrade chlorsulfuron—i.e., *Aspergillus niger* (Boschin et al. 2003) and *Talaromyces flavus* (Song et al. 2013). As summarized in Table 2, soil microorganisms can degrade chlorsulfuron with half-lives in the range of about 20 to 300 days.

4.1.3. Aquatic Organisms

4.1.3.1. Fish

As summarized in Appendix 5 (Table A5-1), acute bioassays are available on technical grade chlorsulfuron in bluegill sunfish, channel catfish, fathead minnows, and rainbow trout, all of which are freshwater fish, and one species of marine fish, (i.e., sheepshead minnow). An acute bioassay on brown trout using a formulation is also available (Grande et al. 1994, MRID 45202909). In addition and as summarized in Appendix 5, Table A5-2, two early life-sages studies are available, one in fathead minnow (Pierson 1991, MRID 41976405) and the other in sheepshead minnow (MRID 41976401). Except for the early life-stage study in sheepshead minnow, full copies of all of the studies were available in the conduct of the previous Forest Service risk assessment (SERA 2004a).

The study by Grande et al. (1994, MRID 45202909), which is an open literature study submitted to EPA and assigned an MRID number, was conducted in Norway using a 75% a.i. Glean formulation. This study is cited in the most recent EPA ecological risk assessment (U.S. EPA/OPP/EFED 2012a, p. 56) but is not summarized or discussed. The significance of the study by Grande et al. (1994) is that it reports the only definitive LC_{50} for chlorsulfuron—i.e., 40 mg a.i./L—with a NOAEC of 30 mg a.i./L. All reported LD_{50} values for technical grade chlorsulfuron are indefinite with reported LD_{50} values ranging from >50 mg a.i./L (channel catfish, Smith 1979d, MRID 00035261) to >980 mg a.i./L (sheepshead minnow, Ward and Boeri 1991a, MRID 41976401). Based on an LC_{50} of >300 mg a.i./L (bluegill sunfish, Smith 1979a, MRID 00035258), the EPA classifies chlorsulfuron as Practically Nontoxic to fish (U.S. EPA/OPP/EFED 2012a, p. 19).

As the only available study on a formulation of chlorsulfuron, Grande et al. (1994) is important in that it suggests that materials in the Glean formulation other than chlorsulfuron may have contributed to the toxicity of the formulation. Occasionally, toxicity data on formulations are available on the Material Safety Data Sheets (more currently designated as simply Safety Data Sheets). This is not the case for chlorsulfuron. As also summarized in Appendix 5, the MSDS for Chlorsulfuron 75 (Alligare LLC 2010) gives indefinite LC_{50} values for fish that are identical to the LC_{50} values summarized in EPA documents. The SDS for Telar XP (DuPont 2015) gives some LC_{50} values that cannot be directly linked to studies summarized by EPA; nonetheless, the SDS clearly designates the LC_{50} values for fish as values for technical grade chlorsulfuron rather than the Telar XP formulation. While the study by Grande et al. (1994) could be viewed with concern, this study was conducted over 20 years ago with a formulation that is not being considered by the Forest Service (Table 3). Furthermore, this study was conducted in Norway, and the relationship of the formulation used in the study to formulations currently used in the United States is unclear.

Based on the indefinite LC_{50} of >300 mg a.i./L, the U.S. EPA/OPP/EFED (2012a, p. 19) classifies technical grade chlorsulfuron as *Practically Nontoxic* to bluegill sunfish. As

summarized in SERA (2014a, Table 16), this classification is given to pesticides with acute LC_{50} values for aquatic organisms of >100 mg a.i./L. Based on this value, all of the indefinite LC_{50} values for technical grade chlorsulfuron would be used to classify chlorsulfuron as *Practically Nontoxic* except for LC_{50} of >50 mg a.i./L in channel catfish (Smith 1979d, MRID 00035261) which would be used to classify chlorsulfuron as *Slightly Toxic* to catfish on an acute basis. An obvious issue with use of the classification system used by EPA when applied to indefinite LC_{50} values is that these values simply reflect the highest concentration assayed. In other words, an indefinite LC_{50} of >50 mg a.i./L cannot viewed as indicating twice the potency of an indefinite LC_{50} of >100 mg a.i./L. In the absence of definitive LC_{50} values, assessments of relative potency cannot be made.

Two early life-stage studies, one in rainbow trout and the other in sheepshead minnow) are reported for technical grade chlorsulfuron (Appendix 5, Table A5-2). As noted above, the summary of the early life-stage study on rainbow trout in Appendix 5 is based on access to the full study (Pierson 1991, MRID 41976405) during the preparation of the previous Forest Service risk assessment (SERA 2004a). A much briefer summary of the study in sheepshead minnow is given in U.S. EPA/OPP/EFED (2012a, p. 91). Based on a NOAEC of 32 mg a.i./L with a corresponding LOAEC of 66 mg a.i./L for reduced length, rainbow trout appear to be more sensitive than sheepshead minnow in which no effects were noted up to the maximum concentration assayed—i.e., 980 mg a.i./L. A concern with the study in sheepshead minnow, however, is that the MRID number used to identify this study is MRID 41976401. This MRID number is attributed by U.S. EPA/OPP/EFED (2012a, p. 56) to the same study used for the acute LC_{50}. This study is cited in the current Forest Service risk assessment as Ward and Boeri (1991a). A chronic assay was not identified in the review of the full study by Ward and Boeri (1991a) during the preparation of the previous Forest Service risk assessment. Another concern with this chronic value is that the value is not listed in the summary table in U.S. EPA/OPP/EFED (2012a, p. 19). From a practical perspective, issues with the credibility of the chronic NOAEC of 980 mg a.i./L in sheepshead minnow has little impact on the current Forest Service risk assessment because this NOAEC is not a sensitive endpoint. As discussed further in Section 4.3.3.1 (dose-response assessment for fish), the reported NOAEC is not used in the current risk assessment.

4.1.3.2. Amphibians (Aquatic Phase)

As with terrestrial phase amphibians, toxicity data are not available for aquatic phase amphibians. The EPA risk assessments (Table 1) on chlorsulfuron do not cite any registrant-submitted studies on aquatic phase amphibians; moreover, the lack of toxicity data on aquatic phase amphibians extends to the open literature and the compendia of amphibian toxicity studies by Pauli et al. (2000). As noted in the most recent EPA ecological assessment on chlorsulfuron (U.S. EPA/OPP/EFED 2012a, p. 21), the EPA uses fish as a surrogate for aquatic phase amphibians.

4.1.3.3. Aquatic Invertebrates

Information on the toxicity of chlorsulfuron to aquatic invertebrates is summarized in Appendix 6, Table A6-1 for acute toxicity and Table A6-2 for chronic toxicity. Acute toxicity data are available on two species of freshwater invertebrates—i.e., *Daphnia magna*, *Daphnia pulex*—and two species of estuarine/marine invertebrates—i.e., *Mysidopsis bahia* (an arthropod) and *Crassostrea virginica* (the Eastern oyster). Except for the open literature publication by

Hessen et al. (1994), all of the available studies are submissions to the EPA in support of the registration of chlorsulfuron. With the exception of one study on the Eastern oyster (MRID 42328601), all of the studies submitted to EPA and summarized in Appendix 6 were included in the previous Forest Service risk assessment (SERA 2004a), and complete copies of these studies were available in the preparation of the previous Forest Service risk assessment. All of the available acute and chronic toxicity studies involve technical grade chlorsulfuron. No toxicity studies on chlorsulfuron formulations have been identified and no formulation studies are summarized in the MSDS for Chlorsulfuron 75 (Alligare LLC 2010) or the SDS for Telar XP (DuPont 2015).

Unlike the case with fish, several of the acute toxicity studies on aquatic invertebrates report definitive LC_{50} or EC_{50} values. Based on the EC_{50} of 370.9 mg a.i./L in *Daphnia magna* (Goodman 1979, MRID 00035262), U.S. EPA/OPP/EFED (2012a, p. 19) classifies chlorsulfuron as *Practically Nontoxic* to this freshwater invertebrate. For daphnids and other small crustaceans, EC_{50} values are based on immobility. Based on an LC_{50} of 89 mg a.i./L in *Mysidopsis bahia*, a mysid shrimp, the U.S. EPA/OPP/EFED (2012a, p. 19) classifies chlorsulfuron as *Slightly toxic* to this saltwater invertebrate. Bioassays of the Eastern oyster yielded definitive EC_{50} values of 376 mg a.i./L (Ward and Boeri 1991c, MRIDs 41976403 and 42328601). EC_{50} values for mollusks are based on the inhibition of shell growth. Using the standard classification scheme from U.S. EPA discussed in the previous section and detailed in SERA (2014a, Table 16), chlorsulfuron would be classified as *Practically Non-toxic* to this saltwater mollusk. Note that the study by Ward and Boeri (1991c) has two different MRID numbers that report slightly different toxicity values. This commonly occurs when the EPA reanalyzes toxicity studies and requests clarifications of the study from a registrant. In any event and as with fish, chlorsulfuron is not highly toxic to aquatic invertebrates in terms of acute toxicity.

Only one chronic study is available—a standard reproduction study in *Daphnia magna* (Ward and Boeri 1989, MRID 41976404; Hutton 1992, MRID 42309701). This study has two MRID numbers and was submitted twice to EPA to clarify a minor discrepancy in the original submission. Again, this is not an uncommon occurrence. This study is noteworthy in that the NOAEC of 20 mg a.i./L and LOAEL of 36 mg a.i./L are substantially below the acute LC_{50} of 370.9 mg a.i./L in this species (Goodman 1979, MRID 00035262). As discussed further in Section 4.4.3.4, however, this circumstance has little practical impact on the current risk assessment because the anticipated levels of exposure are far below the chronic NOAEC in all exposure scenarios including the accidental spill.

The open literature publication by Wei et al. (1999) indicates that the metabolites of chlorsulfuron as well as other sulfonylurea herbicides had no significant toxicity to *Daphnia magna* in 24-hour assays. The publication, however, does not provide details of the bioassays.

4.1.3.4. Aquatic Plants

Chlorsulfuron is listed as a toxic chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act. Due to the toxicity of chlorsulfuron to algae and aquatic macrophytes, the EPA recently denied a petition to delist chlorsulfuron (U.S. EPA/OPP 2013b). As detailed in the following sections, this decision is supported by both registrant studies and the open literature on the toxicity of chlorsulfuron to algae and aquatic macrophytes.

4.1.3.4.1. Algae

Information on the toxicity of chlorsulfuron to algae is summarized in Appendix 7, Table A7-1. The available literature includes several standard studies submitted to EPA in support of the registration for chlorsulfuron as well as a robust open literature.

EC_{50} values based on various measures of growth inhibition indicate a substantial variability in the sensitivity of different species of algae as well as substantial variability within with some species. The most sensitive species is *Synechococcus leopoliensis*, a freshwater blue-green algae, with a reported EC_{50} of 0.0161 mg a.i./L. The most tolerant species is *Porphyridium cruentum*, a marine species of red algae. Both of these EC_{50} values are from the study by Nystrom et al. (1999) which assayed acute toxicity in 17 species of freshwater algae and 20 species of marine algae. This type of study is useful in characterizing sensitivity among species because the assays are conducted by the same group of investigators under identical experimental conditions. The study by Nystrom et al. (1999) is summarized in Appendix 7, Table A7-1. Details of this study are given in Table A7-2 and illustrated in Figure 6. Figure 6 illustrates the data for freshwater and saltwater algae in the form of species sensitivity distributions similar to those in Section 4.1.2.5.2 and discussed in SERA (2014a, Section 4.3.5). Based on this reasonably robust data set, freshwater algae are generally more sensitive than saltwater algae except at the upper extremes of species tolerance. Based on the most sensitive species from each group, freshwater algae are more tolerant than saltwater algae by a factor of about 111 [1.79 mg a.i./L ÷ 0.016 ≈ 111.111…]. Based on the most tolerant species from each group, freshwater algae are more tolerant than saltwater algae by a factor of only about 1.3 [358.87 mg a.i./L ÷ 275.5 ≈ 1.303].

The U.S. EPA risk assessments on chlorsulfuron (specified in Table 1) do not cite the study by Nystrom et al. (1999), and this study is not included in EPA's database on ecotoxicology studies (ECOTOX 2016). The most sensitive species of algae identified by the EPA (U.S. EPA/ OPP/EFED 2012a, Table 7, p. 20) is *Selenastrum capricornutum* based on an EC_{50} of 0.05 mg a.i./L from that study by Blasberg et al. (1991, MRID 42186801). As also summarized in Appendix 7, four studies in the open literature report higher EC_{50} values for this species—i.e., in ascending order, 0.123 mg a.i./L (Fairchild et al. 1997), 0.7 mg a.i./L (Abdel-Hamid 1996), 0.8 mg a.i./L (Kalliquist and Romstad 1994), and 2.4 mg a.i./L (Nystrom et al. 1999). While the value from Fairchild et al. (1997) is only a factor of about 2.5 higher than the value used by EPA, the other toxicity values for *Selenastrum capricornutum* are higher by factors of about 14 to 50.

Multiple EC_{50} values are also available on four species of *Chlorella*, a genus of freshwater green algae—i.e., 0.41 mg a.i./L for *C. pyrenoidosa* (Wei et al. 1998), 54.0 mg a.i./L for *C. saccharophila* (Sabater and Carrasco 1997), 75.5 mg a.i./L for *C. vulgaris* (Carrasco and Sabater 1997), and 43.3 mg a.i./L for *C. emersonii* (Nystrom et al. 1999). All of these studies are from the open literature and the values are all reasonably consistent except for the EC_{50} from Wei et al. (1998) which is below the other EC_{50} values by factors of about 105 [43.3 mg a.i./L ÷ 0.41 mg a.i./L ≈ 105.61] to over 180 [75.5 mg a.i./L ÷ 0.41 mg a.i./L ≈ 184.15]. The greater variability within a genus relative to the differences within a single species (i.e., *Selenastrum capricornutum* as discussed above) seems sensible. Nonetheless, the interspecies and inter-genus variabilities are noteworthy and add uncertainty to the risk assessment as discussed further in Section 4.3.3.4.1.

As also summarized in Appendix 7, Table A7-1, one mesocosm study involving a mixed phytoplankton population is available (Kalliquist et al. 1994). In this study, one lake enclosure each was treated with initial nominal chlorsulfuron concentrations of 0.001, 0.01, or 0.1 mg a.i./L and two untreated enclosures served as controls. No effects were noted at 0.001 mg a.i./L. At 0.1 mg a.i./L, algal biomass (assayed as chlorophyll-a) was decreased substantially over the 16-day observation period. At 0.01 mg a.i./L, a decrease in biomass was noted on Day 2 but recovered by Day 7. At both 0.001 and 0.01 mg a.i./L, algal biomass was slightly higher than controls by Day 16. As discussed further in Section 4.3.3.4.1 (dose-response assessment for algae), the clear NOAEL of 0.01 mg a.i./L is consistent with the most sensitive NOAEL in algae—i.e., 0.0094 mg a.i./L from the study in *Selenastrum capricornutum* by Blasberg et al. 1991, MRID 42186801).

Based on toxicity data summarized in both U.S. EPA/OPP/EFED (2012a, Table I1, pp. 111-112) and the open literature publication by Wei et al. (1998), the toxicity of the degradation products of chlorsulfuron is much less toxic than chlorsulfuron itself. The EPA assessment is based toxicity values estimated from structure-activity relationships. The assessment from Wei et al. (1998), however, is based on bioassays using *Chlorella pyrenoidosa*.

4.1.3.4.2. Aquatic Macrophytes

Information on the toxicity of chlorsulfuron to aquatic macrophytes is summarized in Appendix 7, Table A7-3. Toxicity data are available on three species of monocots covering three genera—i.e., three species of *Lemna* (*L. minor*, *L. gibba*, and *L. paucicostata*), *Hydrilla verticillata*, and *Potamogeton pectinatus*—as well as one species of dicot, *Myriophyllum aquaticum*. As summarized in Table A8-4, EC_{50} values are available in five species, including *Lemna gibba, Myriophyllum aquaticum, Lemna minor, Potamogeton pectinatus, and Lemna paucicostata* in order of decreasing sensitivity. While these studies are not strictly comparable because they were conducted over differing periods of exposure—i.e., 4 to 28 days—and were conducted by different investigators, the variability in the EC_{50} values is modest, only a factor of about 5 [0.0018 mg a.i./L ÷ 0.00035 mg a.i./L ≈ 5.14].

The variability in the EC_{50} values for macrophytes is trivial relative to the variability in the reported EC_{50} values for algae. For example, the EC_{50} values in freshwater algae from the study by Nystrom et al. (1999), as discussed in the previous section, vary by a factor of over 17,000 [275.5 mg a.i./L ÷ 0.016 mg a.i./L ≈ 17,218]. More significantly and as illustrated in Figure 7, freshwater macrophytes are substantially more sensitive than are freshwater algae to chlorsulfuron, based on a comparison of the EC_{50} values from the study by Nystrom et al. (1999) to the EC_{50} values in macrophytes. Based on the most sensitive species of freshwater algae and aquatic macrophytes, macrophytes are more sensitive by a factor of about 46 [0.016 mg a.i./L ÷ 0.00035 mg a.i./L ≈ 45.71]. Based on the most tolerant species of freshwater algae and aquatic macrophytes, macrophytes are more sensitive by a factor of over 150,000 [275.5 mg a.i./L ÷ 0.0018 mg a.i./L ≈ 153,055].

Aquatic macrophytes are also much more sensitive based on NOAECs. The lowest reported NOAEC in algae is 0.0094 mg a.i./L from the study in *Selenastrum capricornutum* by Blasberg et al. (1991, MRID 42186801). For aquatic macrophytes, the lowest reported NOAEC is 0.00024 mg a.i./L, which is below the NOAEC for algae by a factor of nearly 40 [0.0094 mg

a.i./L ÷ 0.00024 mg a.i./L ≈ 39.1666…]. This ratio may underestimate the differences between algae and macrophytes in that the Anderson (1985b) study reports an LOAEC in *Hydrilla verticillata* of 0.0001 mg a.i./L, which is below the lowest NOAEC for algae by a factor of 94.

Unlike the case with algae, no mesocosm or field studies are available on aquatic macrophytes. Nonetheless, as discussed further in Section 4.4.3.4 (risk characterization for aquatic plants), risks to aquatic macrophytes appear to be greater than risks to algae.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

A standard set of exposure assessments for terrestrial and aquatic organisms is provided in the EXCEL workbook for chlorsulfuron (Attachment 1). All exposure assessments are based on an application rate of 0.0625 lb a.i./acre as discussed in Section 2.4. This is a custom workbook that considers aerial, ground broadcast (high boom and low boom), and backpack applications.

Exposure assessments are detailed in Worksheet G01a for mammals and in Worksheet G01b for birds. For both mammals and birds, the highest exposure scenarios are associated with the consumption of contaminated vegetation. For acute exposure scenarios, the highest estimated dose for a small mammal is about 19.8 mg a.i./kg bw, the upper bound dose for the consumption of contaminated short grass. The comparable dose for a small bird is about 107 mg a.i./kg bw. For longer-term exposure scenarios, the maximum doses are also associated with the consumption of short grass—i.e., about 18.2 mg a.i./kg bw/day for a small mammal and 44.9 mg a.i./kg bw/day for a small bird.

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

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion, and the use of contaminated irrigation water. The highest exposures for terrestrial plants are associated with direct spray and spray drift. Nonetheless, as discussed in the risk characterization, runoff and sediment losses are also significant sources of potential exposure for terrestrial plants in sites that may favor runoff, particularly sites with predominantly clay soils and high rates of precipitation. Potential exposures involving the use of contaminated water for irrigation or the off-site transport of chlorsulfuron contaminated soils by wind are also potentially significant routes of exposure.

Exposures of aquatic plants and animals to surface water contaminated with chlorsulfuron are based on essentially the same information used to assess exposure to contaminated water by terrestrial species.

4.2.2. Mammals and Birds

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

4.2.2.1. Direct Spray

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

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

4.2.2.2. Dermal Contact with Contaminated Vegetation

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

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

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

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

The initial concentrations of chlorsulfuron on contaminated food items are based on the U.S. EPA/OPP (2001) adaptation of the residue rates from Fletcher et al. (1994), as summarized in Table 13. The methods of estimating the peak and time-weighted average concentrations of chlorsulfuron in vegetation are identical to those used in the human health risk assessment (Section 3.2.3.7). As summarized in Table 14, fruit and short grass comprise the food commodities with the lowest pesticide residue rates (fruit) and the highest pesticide residue rates (short grass). Tall grass and broadleaf forage plants are estimated to have intermediate residue rates. For each of these four types of vegetation, both acute and longer-term exposure scenarios

are developed, as summarized in Worksheet G01a for mammals and Worksheet G01b for birds of Attachment 1.

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

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

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

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

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating chlorsulfuron concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4.6). The only major differences in the exposure estimates concern the body weight of and the quantity of water consumed by the mammal or bird. Like food consumption rates, water consumption rates, which are well characterized in terrestrial vertebrates, are based on allometric relationships in mammals and birds, as summarized in Table 17. The exposure assessments for mammals and birds are detailed in Worksheets F02a-f (accidental spill), Worksheets F08a-f (peak concentrations), and Worksheets F16a-f (longer-term concentrations) in Attachment 1 of this risk assessment.

Like food consumption, water consumption in birds and mammals varies substantially with diet, season, and many other factors; however, quantitative estimates regarding the variability of water

consumption by birds and mammals are not well documented in the available literature and this variability is not considered in the exposure assessments. Nevertheless, as summarized in Table 13, the upper and lower bound estimates of chlorsulfuron concentrations in surface water vary substantially (i.e., by a factor of 165,000 for acute exposures [0.66 ÷ 0.000004 ≈ 165,000] and a factor of over 230,000 for chronic exposures [0.38 ÷ 0.0000016 ≈ 237,500]). Given this degree of variability in the estimated concentrations of chlorsulfuron in surface water, it is unlikely that a quantitative consideration of the variability in water consumption rates of birds and mammals would have a substantial impact on the risk characterization.

In addition, as discussed further in Section 4.4.2.1 (risk characterization for mammals) and Section 4.4.2.2 (risk characterization for birds), exposures associated with the consumption of contaminated surface water are far below the level of concern (HQ=1). For example, the highest HQ for mammals or birds is 0.0007—i.e., the upper bound of the longer-term HQ for a small mammal consuming contaminated water from Worksheet 02a. This HQ is below the level of concern by a factor of over 1400 [1 ÷ 0.0007 ≈ 1428.57]. Consequently, even extreme variations on the consumption of contaminated water by mammals or birds would have no impact on the risk characterization for these nontarget organisms.

4.2.2.5. Consumption of Contaminated Fish

In addition to the consumption of contaminated vegetation, insects, and other terrestrial prey (Section 4.2.2.3), the consumption of contaminated fish by piscivorous species is a potentially significant route of exposure to chlorsulfuron. Exposure scenarios are developed for the consumption of contaminated fish after an accidental spill (Worksheets F03a-c), expected peak exposures (Worksheets F011a-c), and estimated longer-term concentrations (Worksheets F17a-c). These exposure scenarios are applied to 5 and 70 kg carnivorous mammals as well as a 2.4 kg piscivorous bird. The 70 kg carnivorous mammal is representative of an immature brown bear (*Ursus arctos*), a large mammal that actively feeds on fish (Reid 2006). As summarized in Table 16, the 5 kg mammal is representative of a fox, and the 2.4 kg bird is representative of a heron.

Chlorsulfuron exposure levels associated with the consumption of contaminated fish depend on the chlorsulfuron concentration in water and the bioconcentration factor for chlorsulfuron in fish. The concentrations of chlorsulfuron in water are identical to those discussed in Section 4.2.2.4. As discussed in Section 3.2.3.5, chlorsulfuron does not bioconcentrate substantially in fish. As summarized in Table 2, whole fish bioconcentration factors of 1 for acute exposures and 12 for longer-term exposures based on the study by Han (1981c, MRID 00086820). These bioconcentration factors are used for all exposure scenarios involving the consumption of contaminated fish by mammalian or avian wildlife.

4.2.3. Terrestrial Invertebrates

4.2.3.1. Direct Spray and Drift

Estimated levels of exposure associated with broadcast terrestrial applications of chlorsulfuron are detailed in Worksheet G09 of Attachment 1 (i.e., the EXCEL workbook for chlorsulfuron). In Attachment 1, Worksheet G09 is a custom worksheet which includes aerial, ground broadcast (high boom and low boom), and backpack applications.

As discussed in Section 4.1.2.4, honeybees are typically used by the U.S. EPA as a surrogate for other terrestrial insects (e.g., U.S. EPA/OPP/EFED 2012a). Honeybee exposures are modeled in the current risk assessment as a simple physical process based on the application rate and surface area of the bee. The surface area of the honeybee (1.42 cm^2) is based on the algorithms suggested by Humphrey and Dykes (2008) for a bee with a body length of 1.44 cm.

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

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

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

4.2.3.2. Ingestion of Contaminated Vegetation or Prey

As discussed in Section 4.1.2.4, toxicity values for chlorsulfuron in honeybees or other species of insects are not available. Accordingly, a formal exposure assessment is not developed for the consumption of contaminated vegetation by terrestrial invertebrates. Nonetheless, as discussed in Section 4.1.2.4 and summarized in Appendix 3, Table A3-1, studies are available on effects in insects exposed to plants treated with chlorsulfuron. These studies are discussed further in Section 4.4.2.4 (risk characterization for terrestrial invertebrates).

4.2.4. Terrestrial Plants

Generally, the primary hazard to nontarget terrestrial plants associated with the application of most herbicides is unintended direct deposition or spray drift. In addition, herbicides may be transported off-site by percolation, runoff, or movement of contaminated soil particles by wind. As noted in Section 4.1.2.5 (Hazard Identification for Terrestrial Plants) and discussed further in Section 4.3.2.5 (Dose-Response Assessment for Terrestrial Plants), the phytotoxicity data on chlorsulfuron are sufficient to interpret risks associated with these exposure scenarios. Consequently, exposure assessments are developed for each of these exposure scenarios, as detailed in the following subsections. These exposure assessments are detailed in Worksheet G04 (runoff), Worksheet G05 (direct spray and drift), Worksheet G06a (contaminated irrigation water), and Worksheet G06b (wind erosion) for directed or broadcast foliar applications in Attachment 1.

4.2.4.1. Direct Spray

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

4.2.4.2. Off-Site Drift

Estimates of off-site drift are modeled using AgDRIFT. These estimates are summarized in Worksheets G05a and G05b of the EXCEL workbook that accompanies this risk assessment (Attachments 1). These are custom worksheets that include estimates of drift for aerial, ground broadcast, and backpack applications.

The drift estimates used in the current risk assessment are based on AgDRIFT (Teske et al. 2002) using Tier 1 analyses for aerial and ground broadcast applications. The term *Tier 1* is used to designate relatively generic and simple assessments which can be viewed as plausible upper limits of drift.

In Worksheet G05a, aerial drift estimates are based on Tier 1 analyses using ASAE Fine to Medium drop size distributions. Tier 1 estimates of drift for ground broadcast applications are modeled using both low boom and high boom options in AgDRIFT. For both types of applications, the values are based on very fine to fine drop size distributions and the 90th percentile values from AgDRIFT. The use of small droplet sizes in Worksheet G05a is intended to generate extremely conservative estimates of drift that would not be anticipated in typical Forest Service applications.

In Worksheet G05b, aerial drift estimates are based on Tier 1 analyses using ASAE Coarse to Very Coarse droplet size distributions (VMD ≈ 440 µm), and the ground broadcast applications are based on ASAE fine to medium coarse drop size distributions (VMD ≈ 340 µm). The product labels for all formulations of chlorsulfuron explicitly state that drift management is best achieved by using …*the largest droplets that provide sufficient coverage and control*.

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

The values for drift used in the current risk assessment should be regarded as generic estimates similar to the water concentrations modeled using GLEAMS (Section 3.2.3.4.3). Actual drift will vary according to a number of conditions—e.g., the topography, soils, wind speed, turbulence, droplet size distribution, carrier, and the pesticide formulation.

4.2.4.3. Runoff and Soil Mobility

Terrestrial plant exposures associated with runoff and sediment losses from the treated site to an adjacent untreated site are summarized in Worksheet G04 of the EXCEL workbook for chlorsulfuron (Attachment 1).

Any pesticide can be transported from the soil at the application site by runoff, sediment loss, or percolation. Runoff, sediment loss, and percolation are considered in estimating contamination of ambient water (Section 3.2.3.4). Only runoff and sediment loss are considered in assessing off-site soil contamination. This approach is reasonable because off-site runoff and sediment transport will contaminate the off-site soil surface and could have an impact on non-target plants. Percolation, on the other hand, represents the amount of herbicide transported below the root zone, which may affect water quality but does not affect off-site vegetation, except if the contaminated water is used for irrigation, as discussed further in Section 4.2.4.3. As with the estimates of chlorsulfuron in surface water, estimates of runoff and sediment losses are modeled for clay, loam, and sand at nine sites that represent different temperatures and rainfall patterns as specified in Table 9.

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

For chlorsulfuron, the results of the standard GLEAMS modeling of runoff and sediment losses are summarized in Appendix 8. Clearly, the amount of runoff and sediment loss will vary substantially with different types of climates—i.e., temperature and rainfall—as well as soils, with no runoff or sediment loss anticipated in predominantly sandy soils. The input parameters used to estimate runoff and sediment losses are identical to those used in the Gleams-Driver modeling for concentrations of chlorsulfuron in surface water as discussed in Section 3.2.3.4 and summarized in Table 10 (site characteristics) and Table 11 (chemical-specific input parameters).

The runoff for chlorsulfuron as a proportion of the application rate is taken as 0.0012 (0.00000000076 to 0.05). As detailed in Appendix 8, Table A8-1, this estimated runoff is taken as the average of values for clay and loam soils rounded to two significant places. The lower bound is the lowest non-zero value for predominantly sandy soil textures. The upper bound of 0.05 is the maximum value modelled at any site – i.e., the upper bound of offsite loss for clay soil textures in wet and cool locations.

4.2.4.4. Contaminated Irrigation Water

The scenario for the use of contaminated water for irrigation is standard in Forest Service risk assessments. The exposure levels associated with this scenario depend on the pesticide concentration in the ambient water used for irrigation and the amount of irrigation water used. Concentrations in ambient water are based on the peak concentrations modeled in the human health risk assessment, as discussed in Section 3.2.3.4.6 and summarized in Table 13.

The amount of irrigation used will depend on the climate, soil type, topography, and plant species under cultivation. Thus, the selection of a representative irrigation rate is somewhat

problematic. In the absence of any general approach for determining and expressing the variability of irrigation rates, the application of 1 inch of irrigation water with a range of 0.25 to 2 inches is used in this risk assessment. These are standard assumptions used in all Forest Service risk assessments (SERA 2014a). 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 for chlorsulfuron (Attachment 1).

While the labels and/or EPA documents for some herbicides specifically state that water potentially contaminated with herbicides should not be used for irrigation, no such language has been identified for chlorsulfuron. Nonetheless, the product labels for the representative formulations of chlorsulfuron explicitly considered in this risk assessment (Table 3) indicate that applications should be made in a manner that does not allow chlorsulfuron to move into irrigation or drainage ditches. Concerns with the contamination of irrigation water with chlorsulfuron are also expressed by U.S. EPA/OPP/EFED (2012a, p. 30-31). As discussed further in Section 4.4.2.5.3, this cautionary language is clearly justified. As with drift estimates, application-specific modifications to the generic assumptions used in Worksheet G06a should be used if irrigation water might be contaminated with chlorsulfuron.

4.2.4.5. Wind Erosion

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

For this risk assessment, the potential effects of wind erosion are estimated in Worksheet G06b Attachment 1. In Worksheet G06b, it is assumed that chlorsulfuron is incorporated into the top 1 cm of soil, which is identical to the depth of incorporation used in GLEAMS modeling (Table 11). Average soil losses are estimated to range from 1 to 10 metric tons/ha/year with a central estimate of 5 tons/ha/year. These estimates are based on the results of agricultural field studies which found that wind erosion may account for annual soil losses ranging from 2 to 6.5 metric tons/ha (Allen and Fryrear 1977).

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

losses due to wind erosions following pesticide applications under forest canopies or heavily vegetated areas are likely to be much less than the estimates used in this risk assessment.

In any event, the higher offsite losses reported by Larney et al. (1999) are comparable to exposures associated with offsite drift at distances of about 50 feet from the application site following low boom and high boom ground broadcast applications (Worksheet G05a). All of the estimates for wind erosion and offsite drift are likely to vary dramatically according to site conditions and weather conditions.

The product labels for the representative formulations of chlorsulfuron explicitly considered in the current risk assessment (Table 3) provide cautionary language concerning exposures associated with wind erosion. In addition, the U.S. EPA/OPP/EFED (2004a, p. 4) notes the potential for the movement of chlorsulfuron contaminated soils by wind. As discussed further in Section 4.4.2.5.4, wind erosion may have an impact on sensitive species of terrestrial plants, based on the exposure assumptions used in the current Forest Service risk assessment. If chlorsulfuron is applied to sites in which the transport of chlorsulfuron in contaminated soils seems plausible, attempts to refine the exposure assessment to reflect site-specific conditions are warranted.

4.2.5. Aquatic Organisms

The concentrations of chlorsulfuron in surface water used to estimate exposures for aquatic species are identical to those used in the human health risk assessment, as discussed in Section 3.2.3.4.6 and summarized in Table 13.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

The toxicity values used in the ecological risk assessment are summarized in Table 18. The derivation of each of these values is discussed in the subsections below. The available toxicity data support separate dose-response assessments in eight classes of organisms: terrestrial mammals, birds, terrestrial invertebrates (contact exposure only), terrestrial plants, fish, aquatic invertebrates, aquatic algae, and aquatic macrophytes. No dose-response assessment can be developed for reptiles or for terrestrial or aquatic phase amphibians. Different units of exposure are used for different groups of organisms, depending on the nature of exposure and the way in which the toxicity data are expressed. To maintain consistency with the exposure assessment, which is necessary for the development of hazard quotients (HQs) in the risk characterization, all toxicity values given in Table 18 are expressed as active ingredient (a.i.).

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

For terrestrial mammals, the acute dose response assessment is based on the same data as the human health risk assessment (i.e., a NOAEL of 75 mg a.i./kg bw for developmental effects in rabbits which is applied to acute exposures and a chronic NOAEL in rats of 5 mg a.i./kg bw/day which is applied chronic exposures). The acute NOAEL for birds is taken as 300 mg a.i./kg bw from an acute dietary study in quail. The chronic NOAEL for birds (i.e., 24.5 mg a.i./kg bw/day) is based on a reproduction study in quail. For terrestrial invertebrates, the dose response assessment is based on a contact assay in honeybees which reports an indefinite LD_{50} of about 216 mg a.i./kg bw. It is not clear if this indefinite LD_{50} approximates a NOAEL or a dose associated with partial but less than 50% mortality. This uncertainty is addressed further in the risk characterization.

Chlorsulfuron is used primarily for the pre-emergent (soil treatment) and post-emergent (foliar treatment) control of grasses (monocots) and broadleaf weeds (dicots). In general, dicots are somewhat more sensitive than monocots to chlorsulfuron but variations within each group (i.e., monocots and dicots) exceed the apparent differences between these two groups. For foliar exposures, NOAELs for sensitive and tolerant species are 0.0000008 lbs a.i./acre (rape, dicot) and 0.000163 lbs a.i./acre (sorghum, monocot), respectively. For soil exposures, the NOAEL for sensitive species (sugar beet, dicot) is 0.0000068 lbs a.i./acre and the NOAEL for tolerant species (wheat, monocot) is 0.001125 lbs a,i./acre.

As would be expected for an herbicide, aquatic plants are much more sensitive than aquatic animals to chlorsulfuron and aquatic macrophytes are much more sensitive to chlorsulfuron than

aquatic algae. Toxicity values for sensitive and tolerant species of aquatic macrophytes are based on different species of *Lemna* (duckweed)—i.e., a NOAEC of 0.00024 mg a.i./L in *L. gibba* and an EC_{10} of 0.05 mg a.i./L in *L. paucicostata*. For algae, the NOAEC for sensitive species is 0.0094 mg a.i./L and the NOAEC for tolerant species is 9.3 mg a.i./L.

Fish and aquatic invertebrates are substantially less sensitive to chlorsulfuron than either algae or aquatic macrophytes, and no substantial differences between the sensitivities between fish and aquatic invertebrates are apparent. For both acute and longer-term exposures in sensitive species, a NOAEL of 32 mg a.i./L is used for fish and a NOAEL of 20 mg a.i./L is used for aquatic invertebrates. For acute exposures in tolerant species, a NOAEL of 300 mg a.i./L is used for fish and 200 mg a.i./L is used for aquatic invertebrates. The available data do not support longer-term toxicity values for presumably tolerant species of fish and aquatic invertebrates. This limitation has no substantial impact on the risk assessment because risks to sensitive species are far below the level of concern as discussed further in the risk characterization.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals

In characterizing risk to mammalian wildlife, Forest Service risk assessments generally use the NOAELs which serve as the basis for the acute and chronic RfDs from the human health risk assessment. A more elaborate approach is used if sufficient data are available to characterize variable sensitivities among subgroups of mammals.

As discussed in Section 4.1.2.1, acute toxicity data are available in rats and guinea pigs. Based on an acute LD_{50} value 1363 mg a.i./kg bw in guinea pigs (Hall and Dashiell 1980, MRID 00031408) and several definitive LD_{50} values in rats in the range of about 3000 to nearly 8000 mg a.i./kg bw (Appendix 1, Table A1-1), guinea pigs may be somewhat more sensitive than rats in terms of acute lethality. As summarized in Table 15 and discussed in Section 3.3, the surrogate acute RfD is based on a NOAEL of 75 mg a.i./kg/day from a developmental study in rabbits that involved daily gavage dosing for a period of 13 days (Alvarez 1991b, MRID 41983101). No developmental studies are available in guinea pigs. In terms of the ecological risk assessment, endpoints associated with developmental effects are critical in that these effects can influence population dynamics. Consequently, the acute NOAEL for rabbits of 75 mg a.i./kg bw is used to characterize risks associated with short-term exposures to chlorsulfuron. As discussed further in Section 4.4.2.1 (risk characterization for mammals), none of the short-term exposures lead to HQs that exceed the level of concern. Thus, an elaboration of dose-severity is unnecessary.

As summarized in Table 15 and discussed in Section 3.3, the chronic RfD is based on a NOAEL of 5 mg a.i./kg bw/day from 2-year feeding study in rats (Wood et al. 1981a , MRID 00086003). As discussed in Section 4.1.2.1, subchronic and chronic studies are available in dogs, mice, and rats. Of these three species, rats are the most sensitive. Unlike the case for acute exposures, some upper bound estimates of longer-term exposures exceed the NOAEL. For these exposures, risk characterization is elaborated using the LOAEL of 25 mg a.i./kg bw/day based on decreased body weight and body weight gain from the study by Wood et al. (1981a , MRID 00086003). The selection of this NOAEL is consistent with the most recent EPA ecological assessment (U.S. EPA/OPP/EFED 2012a, p. 19 citing the NOAEL concentration of 500 mg a.i./kg food).

4.3.2.2. Birds

U.S. EPA ecological risk assessments use indefinite LC_{50} values >5000 mg a.i./kg food for risk characterization of acute exposures and a chronic dietary NOAEL of 174 mg a.i./kg food for risk characterization of longer-term exposures (U.S. EPA/OPP/EFED 2004a, p. 15; U.S. EPA/OPP/EFED 2012a, p.18).

The Forest Service prefers to use NOAELs rather than LD_{50} or LC_{50} values for risk characterization of acute exposures (SERA 2014a, Section 4.3.2). As summarized in Appendix 2, Table A2-2, the acute dietary study by Fink et al. (1981, MRID 00090009) identifies an acute dietary NOAEL of 1000 mg a.i./kg diet with a corresponding LOAEL of 1780 mg a.i./kg diet based on a slight decrease in body weight. Based on measured food consumption reported in this study, the dietary NOAEL of 1000 mg a.i./kg diet corresponds to a dose of about 300 mg a.i./kg bw, and this dose is used to characterize acute risks to birds in the current Forest Service risk assessment.

The chronic dietary NOAEC of 174 mg a.i./kg food is from the reproduction study in bobwhite quail conducted by Beavers et al. (1992a, MRID 42634001). As summarized in Appendix 2, Table A2-3, the NOAEL corresponds to a dose of 24.5 mg a.i./kg bw/day based on measured food consumption. The corresponding dietary LOAEC is 961 mg a.i./kg diet and corresponds to a dose of about 135 mg a.i./kg bw/day. The LOAEL is based on decreased body weight. As discussed in Section 4.1.2.2, quail appear to be somewhat more sensitive than mallards, the only other species on which longer-term studies were conducted. Consequently and consistent with the EPA approach, the NOAEL of 24.5 mg a.i./kg bw/day is used to characterize risks to birds associated with longer-term exposures.

4.3.2.3. Reptiles and Amphibians (Terrestrial Phase)

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

4.3.2.4. Terrestrial Invertebrates

If sufficient data are available, Forest Service risk assessments develop dose-response assessments for terrestrial invertebrates, typically earthworms, that involve contact with and oral exposure to contaminated soil (SERA 2014a, Section 4.1.2.4).

As discussed in Section 4.1.2.4 of the current risk assessment, however, the only toxicity value appropriate for dose-response assessment is the indefinite contact LD_{50} value of >215 mg a.i./kg bw for the honeybee (U.S. EPA/OPP/ EFED 2012a, MRID 42129902). Based on the available information, it is not clear if this dose is a NOAEL or simply a dose associated with less than 50% mortality. While this lack of information adds some uncertainty to the risk assessment, the resulting HQs are low, as discussed further in Section 4.4.2.4 (risk characterization for terrestrial invertebrates).

As discussed in Section 4.1.2.4 and summarized in Appendix 3, Table A3-1, studies are available on effects in insects exposed to plants treated with chlorsulfuron. These studies are also discussed in the risk characterization for terrestrial invertebrates (Section 4.4.2.4).

4.3.2.5. Terrestrial Plants (Macrophytes)

As with most herbicides, there are adequate data for developing toxicity values for both sensitive and tolerant plant species involving soil exposures (i.e., herbicide runoff to an untreated field) and foliar exposures (direct spray, wind erosion, or drift). The available studies are discussed in Section 4.1.2.5 and summarized in Appendix 4. Studies on seedling emergence are used to assess risks associated with exposures to soil residues of chlorsulfuron. Studies on vegetative vigor are used to assess risks associated with the deposition of chlorsulfuron onto plants.

As discussed in Section 4.1.2.5 and illustrated in Figures 4 and 5, dicots are somewhat more sensitive than monocots; however, the variability within each group (i.e., monocots and dicots) exceeds the differences between the two groups. This discussion of relative sensitivity in Section 4.1.2.5 focuses on EC_{25} values rather than NOAELs. Definitive toxicity values are more appropriate than NOAELs for comparisons of sensitivity, because the former are estimated from dose-response data and the latter are dependent on the doses used in the particular bioassay. As noted previously, the Forest Service prefers to use NOAECs for dose-response assessments; thus, the focus in this section is on NOAECs rather than EC_{25} values.

In seedling emergence assays, the greater sensitivity of dicots relative to monocots is similar to the pattern with EC_{25} values. The lowest NOAEC is 0.0000068 lb a.i./acre, the NOAEC for sugar beets (a dicot) from the study by McKelvey and Kuratle (1992, MRID 42587201). While this study is cited and discussed in the U.S. EPA/OPP/EFED (2004a) ecological risk assessment in support of the reregistration of chlorsulfuron, this study is not cited in the more recent U.S. EPA/OPP/EFED (2012a) assessment for the registration review of chlorsulfuron. The lowest seedling emergence NOAEC cited in U.S. EPA/OPP/EFED (2012a, p. 22) is 0.000045 lb a.i./acre—i.e., the NOAEC for onions from MRID 46361801. In the absence of information indicating that McKelvey and Kuratle (1992, MRID 42587201) was judged deficient in a more recent review, the lower NOAEC of 0.0000068 lb a.i./acre is used to characterize risks associated with soil exposures in sensitive species of terrestrial plants. In terms of tolerant species, the highest NOAEC from standard toxicity studies typically used by EPA is the NOAEC of 0.000163 lb a.i./acre for sorghum, a monocot (McKelvey and Kuratle 1992, MRID 42587201). Note that this NOAEC is for plant height. The NOAEC for emergence is >0.0219 lb a.i./acre. The lower NOAEC is selected because it is appropriate to use the most sensitive endpoint to characterize potential risks for both sensitive and tolerant species.

The greater sensitivity of dicots relative to monocots is also apparent in NOAECs for vegetative vigor. The lowest NOAEC is 0.0000008 lb a.i./acre—i.e., the NOAEC for rape (a dicot) from MRID 46326801 as summarized by U.S. EPA/OPP/ EFED (2012a, p. 22). The most tolerant species is wheat based on an NOAEC for plant height of 0.001125 lb a.i./acre (McKelvey and Kuratle 1992, MRID 42587201). As illustrated in Figure 5 and discussed in Section 4.1.2.5.2, wheat as well as other members of the Triticeae tribe appear to be the group of terrestrial plants most tolerant to chlorsulfuron.

4.3.2.6. Terrestrial Microorganisms

The effects of chlorsulfuron on soil microorganisms are not discussed in the more recent ecological assessments (U.S. EPA/OPP/EFED 2004a, 2012a), generally because the EPA does not require such studies for the registration of herbicides. Accordingly, Forest Service risk assessments typically do not develop formal dose-response assessments for terrestrial

microorganisms in herbicide risk assessments. Nonetheless, potential risks to terrestrial microorganisms exposed to chlorsulfuron are discussed qualitatively in the risk characterization (Section 4.4.2.6).

4.3.3. Aquatic Organisms

4.3.3.1. Fish

In the most recent EPA ecological assessment on chlorsulfuron (U.S. EPA/OPP/EFED 2012a, p. 19), the most sensitive endpoints used to characterize risks to fish are the indefinite LC_{50} of >300 mg a.i./L in bluegill sunfish for acute exposure (Smith 1979a, MRID 00035258) and the NOAEC of 32 mg a.i./L in the early life-stage study in rainbow trout for longer term exposures (Pierson 1991, MRID 41976405). The EPA does not usually derive separate risk estimates for potentially tolerant species of fish. Implicit in the identification of these values by EPA is the notion that they should apply to the most sensitive species of fish.

U.S. EPA/OPP/EFED (2012a, p. 56) cites but does not discuss the open literature study by Grande et al. (1994) which reports an 96-hour LC_{50} of 40 mg a.i./L with a corresponding NOAEC of 30 mg a.i./L in an acute bioassay in Brown trout (*Salmo trutta*) using a 75% a.i. Glean formulation of chlorsulfuron. As discussed in Section 4.1.3.1, the relationship of the Glean formulation used in this Norwegian study to formulations currently in use in the United States is unclear. Nonetheless, the study by Grande et al. (1994) raises concern for the toxicity of chlorsulfuron and chlorsulfuron formulations to possibly sensitive species of fish. As also discussed in Section 4.1.3.1, the SDS for Telar XP notes an indefinite LC_{50} for chlorsulfuron of >122 mg a.i./L, but it is not clear that this indefinite LC_{50} is equivalent to an NOAEC. Because the Salmonidae may be a sensitive family of fish, the NOAEC of 32 mg a.i./L from the early life-stage study by Smith (1979a, MRID 00035258) is used to characterize risks to sensitive species of fish for both acute and longer-term exposures. While this approach may be viewed as perhaps overly conservative, it has no substantial impact on the risk characterization. As discussed in Section 4.4.3.1 (risk characterization for fish), all of the HQs for fish, both acute and longer-term, are substantially below the level of concern (HQ=1).

As summarized in Appendix 5, Table A5-1, the indefinite LC_{50} of >300 mg a.i./L in bluegill sunfish (Smith 1979a, MRID 00035258) may be viewed as a crude NOAEC—i.e., no mortality or reports of gross signs of toxicity. Consequently, 300 mg a.i./L is used as an NOAEC for potentially tolerant species of fish. As discussed in Section 4.1.3.1, the supposed chronic NOAEC of 980 mg a.i./L may be a reporting error in U.S. EPA/OPP/EFED (2012a). Consequently, this value is not used and a longer-term toxicity value for potentially tolerant species of fish. As noted above, the absence of a longer-term toxicity value for tolerant species of fish has no impact on the qualitative risk characterization, because all of the chronic HQs for sensitive species of fish are far below the level of concern.

4.3.3.2. Amphibians

The lack of toxicity data on aquatic phase amphibians precludes the development of a dose-response assessment for this group of organisms. The U.S. EPA uses fish as surrogates for aquatic phase amphibians, and this approach is discussed further in the risk characterization (Section 4.4.2.3).

4.3.3.3. Aquatic Invertebrates

In the most recent EPA ecological assessment for chlorsulfuron (U.S. EPA/OPP/EFED 2012a, p. 19), the most sensitive endpoints used to characterize risks to aquatic invertebrates are the indefinite LC_{50} of >370 mg a.i./L in *Daphnia magna* for acute exposure (Goodman 1979, MRID 00035262) and the NOAEC of 20 mg a.i./L in *Daphnia magna* in the reproduction study for longer-term exposures (Ward and Boeri 1989, MRID 41976404). As with fish, the EPA does not typically derive separate risk estimates for potentially tolerant species of aquatic invertebrates, and values given by EPA implicitly apply to sensitive species.

As noted previously, the Forest Service prefers to use NOAELs rather than LD_{50} or LC_{50} values for risk characterization of acute exposures. In the absence of an NOAEC for acute exposures, LC_{50} values are typically multiplied by a factor of 0.05 as an approximation of the EPA's variable level of concern conventions—i.e., the level of concern for listed species of 0.05 of the LC_{50} (SERA 2014a, Section 4.3.2). As summarized in Appendix 6, Table A6-1, Goodman (1979, MRID 00035262) report a definitive LC_{50} of 370.9 mg a.i./L. An approximate NOAEL based on this concentration would be about 20 mg a.i./L [370.9 mg a.i./L x 0.05 ≈ 18.545 mg a.i./L]. This concentration is equivalent to the chronic NOAEC in *Daphnia magna* from the reproduction study by Ward and Boeri (1989, MRID 41976404). Consequently and consistent with the approach taken by EPA, 20 mg a.i./L is used as the chronic NOAEC for characterizing risks to sensitive species of aquatic invertebrates.

Based on the available acute toxicity studies, the most tolerant species is the Eastern oyster with an EC_{50} of 385 mg a.i./L for the inhibition of shell growth (Ward and Boeri 1991c, MRID 41976403). This study does not explicitly discuss an NOAEC, and the EPA risk assessments (i.e., U.S. EPA/OPP/EFED 2004a, 2012a) do not define an NOAEC for this study. Based on a review of this study in the preparation of the previous Forest Service risk assessment (SERA 2004a), an NOAEC of 200 mg a.i./L was identified. This NOAEC is maintained in the current risk assessment and used for characterizing acute risks for tolerant species of aquatic invertebrates.

As with fish (Section 4.3.3.1), the available data on aquatic invertebrates is not sufficient to propose a chronic toxicity value for tolerant species of aquatic invertebrates. Also as with fish and as discussed in Section 4.4.3.4 (risk characterization for aquatic invertebrates), this data gap has no impact on the risk characterization because all of the longer-term HQs for sensitive species of aquatic invertebrates are substantially below the level of concern (HQ=1).

4.3.3.4. Aquatic Plants

4.3.3.4.1. Algae

The most recent EPA ecological assessment (U.S. EPA/OPP/EFED 2012a, p. 20) identifies *Pseudokirchneriella subcapitata*, a species of green algae, as the most sensitive non-vascular aquatic plants based on the EC_{50} of 0.05 mg a.i./L and NOAEC of 0.0094 mg a.i./L from the study by Blasberg et al. (1991, MRID 42186801). For vascular plants, the EPA identifies *Lemna gibba* as the most sensitive species based on the EC_{50} of 0.00035 mg a.i./L and NOAEC of 0.00024 mg a.i./L.

As noted in Section 4.1.3.4, NOAEC of 0.0094 mg a.i./L identified by EPA is supported by the mesocosm study conducted by Kallqvist et al. (1994), which notes only transient changes in phytoplankton communities at a concentration of 0.010 mg a.i./L. As summarized in Appendix 7, Table A7-2, and illustrated in Figure 6, Nystrom et al. (1999) reports an EC_{50} of about 0.016 mg a.i./L for growth inhibition for *Synechococcus leopoliensis*, suggesting that some member of the Cyanophyceae family may be more sensitive than *Pseudokirchneriella subcapitata*, a member of the Chlorophyceae family. This concern is addressed qualitatively in the risk characterization for algae (Section 4.4.3.4.1). In the absence of reported NOAECs in the study by Nystrom et al. (1999), the current risk assessment defers to EPA, and the NOAEC of 0.0094 mg a.i./L is used to characterize risks associated with sensitive species of algae.

As also illustrated in Figure 6 and summarized in Appendix 7, Table A7-2, the study by Nystrom et al. (1999) indicates that some species of algae may be highly tolerant to chlorsulfuron exposures with EC_{50} values of up to about 275 mg a.i./L in freshwater species. The best documented NOAEC for an apparently tolerant species of algae comes from the study by Sabater and Carrasco (1997) which notes an EC_{50} of 54 mg a.i./L and a corresponding NOAEC of 9.3 mg a.i./L in *Chlorella saccharophila*, a member of the Chlorellaceae family. The NOAEC of 9.3 mg a.i./L is used for characterizing risks associated with tolerant species of algae.

4.3.3.4.2. Macrophytes

Relative to algae, the dose-response assessment for aquatic macrophytes is straightforward. Based on the EC_{50} of 0.00035 mg a.i./L and corresponding NOAEC of 0.00024 mg a.i./L in *Lemna gibba* from the study by Boeri et al. (2002, MRID 45832901). The most recent EPA ecological assessment cites *Lemna gibba* as the most sensitive species of aquatic macrophyte (U.S. EPA/OPP/EFED 2012a, p. 20). As summarized in Appendix 7, Table A7-4, and illustrated in Figure 7, this is the most sensitive species of the five species on which data are available. Consequently, the current risk assessment adopts the NOAEC of 0.00024 mg a.i./L for characterizing risks to sensitive species of aquatic macrophytes.

Unlike algae, the variability in sensitivities for aquatic macrophytes is modest (Section 4.1.3.4.2). As also summarized in Appendix 7, Table A7-4, and illustrated in Figure 7, the most tolerant species is *Lemna paucicostata*, based on an EC_{50} of 0.018 mg a.i./L (Michel et al. 2004). Michel et al. (2004) do not specify the NOAEC. Based on the dose-response model used by Michel et al. (2004) and the model slope given in the publication, the EC_{10} can be estimated as about 0.05 mg a.i./L [0.018 mg a.i./L x $(10/100\text{-}10)^{1/3.74} \approx 0.05404$ mg a.i./L]. Based on EPA's use of a 10% response as a common endpoint in benchmark dose modelling (U.S. EPA 2012, Section 1.3.2, p. 9), the EC_{10} of 0.05 mg a.i./L is used as a surrogate NOAEC for characterizing risks in tolerant species of aquatic macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

Chlorsulfuron is an effective and potent herbicide likely to cause adverse effects on some nontarget terrestrial and aquatic plant species, unless measures are taken to limit exposure. For terrestrial plants, the dominant factor in the risk characterization is the potency of chlorsulfuron, relative to the application rate. The typical application rate considered in this risk assessment, 0.0625 lb a.i./acre, is above the NOAEC in vegetative vigor (direct spray) assays by a factor greater than 78,000 for sensitive species and 56 for tolerant species. If chlorsulfuron is applied directly to either sensitive or tolerant species, adverse effects in the exposed plants are virtually certain. The HQs associated with drift are also substantial, particularly for sensitive species. At a distance of 900 feet downwind, the HQs for sensitive species are 24 to 969 for fine droplet applications and 24 to 250 for coarse droplet applications, depending on the application method. The HQs associated with soil exposures are also substantial but less than those associated with direct deposition. For runoff, the HQs are 11 (0.000007 to 460) for sensitive species and 0.5 (0.0000003 to 19) for tolerant species. For the use of contaminated irrigation water, the HQs are 2212 (0.02 to 23,364) for sensitive species and 1.6 (0.00001 to 17) for tolerant species. The wide range of HQs reflects the wide range of conditions used in the GLEAMS-Driver modeling to estimate runoff and chlorsulfuron concentrations in surface water. The HQs associated with wind erosion of contaminated soil are 5 (1.1 to 11) for sensitive species and 0.004 (0.0.0008 to 0.008) for tolerant species. The product labels for the formulations designated by the Forest Service specifically note potential hazards to terrestrial vegetation associated with the use of contaminated water for irrigation and with the transport by wind of contaminated soil.

For aquatic plants, risks to sensitive species of macrophytes are greater than risks to sensitive species of algae. For sensitive species of aquatic macrophytes, the acute HQ is 33 with a range of 0.001 to 172 and the longer-term HQ is 17 with a range of 0.0004 to 99. For acute exposures in algae, the acute HQ is 0.8 with a range of 0.00003 to 4 for sensitive species but below the level of concern for tolerant species. For tolerant species of both macrophytes and algae, all longer-term HQs are below the level of concern.

Just as there is little doubt that chlorsulfuron may adversely affect some plant species, there is no clear basis for suggesting that effects on terrestrial or aquatic animals are likely or would be substantial. Adverse effects in mammals, birds, terrestrial insects, and microorganisms are not likely at the typical application rate of 0.0625 lb a.i./acre. One study suggests that latent/sublethal chlorsulfuron toxicity to one plant species could result in adverse reproductive effects in one species of beetle that consumes the leaves of the affected plant. This appears to be a highly specific plant-insect interaction that is not confirmed in publications by other groups of researchers.

The risk characterization for aquatic animals is relatively simple and unambiguous. Chlorsulfuron appears to have a very low potential to cause any direct adverse effects in aquatic animals. All of the upper bounds of the HQs for aquatic animals are extremely low, ranging from 0.0001 (acute exposures in tolerant fish) to 0.002 (acute exposures to sensitive aquatic invertebrates).

While the risk characterization for chlorsulfuron focuses on the potential for direct toxic effects, there is also a potential for indirect effects in virtually all groups of nontarget organisms. Alterations in vegetation following the application of any effective herbicide, including chlorsulfuron, could alter vegetation in ways that may be beneficial to some species and detrimental to others. The magnitudes of these indirect effects are likely to vary over time. If algae are adversely affected by chlorsulfuron, cumulative impacts on aquatic invertebrates and fish could be detrimental due to a decrease in available food and habitat modification. In the event of an accidental spill, oxygen depletion due to decaying vegetation could be detrimental to many aquatic animals.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

The quantitative risk characterization for mammals is summarized in Worksheets G02a of the EXCEL workbook that accompanies this risk assessment (Attachment 1). As is common for pesticides applied to vegetation, the highest exposures, hence the highest HQs, are associated with the consumption of contaminated vegetation.

None of the acute exposure scenarios, including both accidental and non-accidental exposures, exceed the level of concern (HQ=1). The highest HQ is 0.6, the upper bound of the HQ for a small (20 g) mammals consuming contaminated short grass.

For longer-term exposures, none of the central estimates of the HQs exceed the level of concern. At the upper bounds of the HQs, three longer-term exposure scenarios slightly exceed the level of concern. These upper bound HQs involve a small mammal—i.e., the consumption of contaminated grasses with an upper bound HQ of 4, the consumption of contaminated broadleaf vegetation with an upper bound HQ of 2, and the consumption of contaminated tall grass with an upper bound HQ of 1.7. These HQs are similar to RQs derived by the EPA for chronic exposures in a small (15 g) mammal—i.e., an RQ of 2.54 for the consumption of contaminated short grass, an RQ of 1.42 for the consumption of broadleaf vegetation, and an RQ of 1.16 for the consumption of tall grass (U.S. EPA/OPP/EFED 2013a, p. 97). It should be noted that chronic RQs are derived by EPA as the ratio of the exposure to the chronic NOAELs—i.e., essentially identical to HQs used in the current Forest Service risk assessment. The modest differences between the HQs derived in this Forest Service risk assessment and the RQs derived by EPA reflect minor differences in how the exposures and toxicity values were calculated.

As summarized in Table 15 and discussed in Section 3.3.5 (dose-severity relationships), the chronic NOAEL of 5 mg a.i./kg bw/day has a corresponding LOAEL of 25 mg a.i./kg bw/day, based on decreased body weight and body weight gain. This LOAEL corresponds to an HQ of 5 [LOAEL ÷ NOAEL]. The upper bound HQs discussed above are in the range of 1.7 to 4. Consequently, it is not clear that the exposures estimated for an application rate of 0.0625 lb a.i./acre would lead to observable signs of toxicity in small mammals. The potential for other sublethal effects that might be associated with a modest decrease in body cannot be elaborated.

The acute and longer-term non-accidental HQs for mammals are linearly related to the application rate. Taking the highest upper bound acute HQ of 0.6 based on the application rate of 0.0625 lb a.i./acre, the HQ would reach the level of concern (HQ=1) at an application rate of

about 0.1 lb a.i./acre [0.0625 lb a.i./acre ÷ 0.6 ≈ 0.1042 lb a.i./acre]. The chronic HQs would similarly increase with increases in the application rate. If higher application rates are used in Forest Service programs, the qualitative risk characterization could lead to a clearer basis for anticipating acute effects in small mammals and potential longer-term effects in both small and large mammals.

4.4.2.2. Birds

The quantitative risk characterization for birds is summarized in Worksheets G02b of the EXCEL workbook that accompanies this risk assessment (Attachment 1). As with mammals and for the same reason, the highest exposures, hence the highest HQs, are associated with the consumption of contaminated vegetation.

Also as with mammals, none of the acute exposure scenarios evaluated for birds, including both accidental and non-accidental exposures, exceed the level of concern (HQ=1). The highest HQ is 0.4, the upper bound of the HQ for a small (10 g) bird consuming contaminated short grass.

For longer-term exposures, none of the central estimates of the HQs exceed the level of concern. At the upper bounds of the HQs, only one longer-term exposure scenario slightly exceeds the level of concern—i.e., the upper bound HQ of 1.8 for a small bird consuming contaminated short grasses. As discussed in Section 4.3.2.2 (dose-response assessment for birds), the longer-term HQs are based on an estimated NOAEL of 24.5 mg a.i./kg bw/day with a corresponding LOAEL of 135 mg a.i./kg bw/day, based on decreased body weight. This LOAEL corresponds to an HQ of about 5 [135 mg a.i./kg bw/day ÷ 24.5 mg a.i./kg bw/day ≈ 5.51]. Based on this relationship, it does not seem reasonable to assert that frank adverse effects would be evident in birds following an application of chlorsulfuron at a rate of 0.0625 lb a.i./acre. In the absence of field studies or additional information on the sublethal effects of chlorsulfuron in birds, a more definitive qualitative risk characterization cannot be proposed.

While the risk characterization for birds is not severe, it is worth noting that the recent ecological assessment from EPA notes no exceedances in the NOAEL for either acute or chronic exposures in birds (U.S. EPA/OPP/EFED 2013a, p. 97). While the EPA assessment and the current Forest Service risk assessment use the same toxicity study, the HQs in the current risk assessment are slightly higher than EPA's RQs because of differences in methodology. The EPA assessment is based on dietary concentrations in both the toxicity study and the exposure assessment. The HQs in Forest Service risk assessments are based on doses in units of mg a.i./kg bw/day and estimated intakes in units of mg a.i./kg bw/day based on caloric requirements (Section 4.2.2.3).

Also as with mammals, the acute and longer-term non-accidental HQs for birds are linearly related to the application rate. Taking the highest upper bound acute HQ of 0.4 based on the application rate of 0.0625 lb a.i./acre, the HQ would reach the level of concern (HQ=1) at an application rate of about 0.16 lb a.i./acre [0.0625 lb a.i./acre ÷ 0.4 = 0.15625 lb a.i./acre]. The chronic HQs would similarly increase with increases in the application rate. If higher application rates are used in Forest Service programs, the qualitative risk characterization could lead to a clearer basis for concern with potential acute and chronic effects in small birds. The highest HQ for a large (4 kg) bird is 0.2—i.e., the consumption of short grass by a large bird. To reach a level of concern for this exposure scenario, the application rate would need to be above 0.3 lb a.i./acre [0.0625 lb a.i./acre ÷ 0.2 = 0.3125 lb a.i./acre]. As noted in Section 2, the maximum

labeled application rate for any formulation of chlorsulfuron is 0.25 lb a.i./acre. The potential effects for birds of intermediate (i.e., greater than 10 g but less than 4 kg) sizes would need to be addressed in species-specific exposure assessments.

4.4.2.3. Reptiles and Amphibians (Terrestrial Phase)

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

4.4.2.4. Terrestrial Invertebrates

As discussed in Section 4.3.2.4, the only standard toxicity study in terrestrial invertebrates is a single indefinite contact LD_{50} value of >215 mg a.i./kg bw for the honeybee. It is not clear if this toxicity value is a functional NOAEL or a dose associated with partial mortality. As summarized in Worksheet G09 of Attachment 1, however, the direct spray HQ is 0.02, which is below the level of concern by a factor of about 50. If the LD_{50} were definite, the estimated NOAEC would be lower by a factor of 10 and the upper bound HQ would be 0.2, below the level of concern by a factor of 5. Based on these relationships, there is no basis for asserting that chlorsulfuron applied at a rate of 0.0625 lb a.i./acre would pose an acute risk to honeybees in contact exposures. Risks associated with oral exposures, including exposures associated with foraging, cannot be characterized due to the lack of oral toxicity data.

While definitive oral toxicity values are not available on honeybees or other terrestrial insects, available studies on chlorsulfuron address the impact on insects of contact with treated plants (Section 4.1.2.4). As summarized in Appendix 3, Table A3-1, decreased survival was observed in egg masses of *Gastrophysa ploygoni* (Coleoptera: Chrysomelidae) placed on wild buckwheat treated with chlorsulfuron at application rates of about 0.0012 to 0.0024 lb a.i./acre, and increased development time was noted at application rates as low as 0.0000285 lb a.i./acre. The mechanism for this effect is unclear (Kjaer and Elmegaard 1996). Confirming studies from other investigators were not identified in the open literature. Nonetheless, the paper by Kjaer and Elmegaard (1996) raises concern for possible indirect adverse effects on some species of insects following applications of chlorsulfuron.

4.4.2.5. Terrestrial Plants

4.4.2.5.1. Direct Spray and Spray Drift

The HQs for sensitive and tolerant species of terrestrial plants are summarized in Worksheet G05a (fine droplet sizes) and Worksheet G05b (coarse droplet sizes) of Attachment 1, the EXCEL workbook that accompanies this risk assessment. These worksheets are customized to reflect four sets of values for drift: aerial application, ground high-boom broadcast application, ground low-boom broadcast application, and backpack application.

As detailed in Section 4.2.4.2, all estimates of drift are based on AgDRIFT (Teske et al. 2002). As detailed in Section 4.3.2.5 and summarized in Table 18, all HQs are based on NOAECs from studies on vegetative vigor (foliar applications)—i.e., an NOAEC of 0.0000008 lb a.i./acre for a sensitive species of dicot (rape) and a NOAEL of 0.001125 lb a.i./acre for a tolerant species of monocot (wheat). As illustrated in Figure 4 (bottom graph), there is substantial overlap in the sensitivity of dicots and monocots in assays of vegetative vigor; however, the most sensitive species are all dicots. As also illustrated in Figure 4, the sensitivities of tolerant species are similar in both dicots and monocots. Based on this pattern, the HQs for tolerant species would probably apply equally to tolerant species of both monocots and dicots.

Chlorsulfuron is a potent herbicide. If chlorsulfuron is applied directly to either sensitive or tolerant species, adverse effects are virtually certain. The HQ is over 78,000 for sensitive species and 56 for tolerant species. In either case, plant mortality seems plausible. The upper bound HQ for sensitive species is similar to the maximum RQ of 68,488 derived in U.S. EPA/OPP/EFED (2004a, Table 13, p. 24) based on the EC_{05}.

The HQs associated with drift are also substantial, particularly for sensitive species. At a distance of 900 feet downwind, the HQs for sensitive species are 24 to 969 for fine droplet applications and 24 to 250 for coarse droplet applications, depending on the application method. For tolerant species, the HQs are more nuanced. For fine droplet applications, the HQs exceed the level of concern at 500 feet downwind for aerial application (HQ=1.1), 100 feet downwind for high boom ground applications (HQ=1.4), and 25 feet for low boom ground applications. The use of coarse droplets results in much lower HQs for tolerant species. Risks at 25 feet downwind exceed the level of concern (HQ=1) only for aerial applications. For aerial applications, risks remain above the level of concern at 100 feet downwind (HQ=2).

As noted in Section 4.2.4.2 (exposure assessment for off-site drift), the exposure assessments used in the current risk assessment should be viewed as generic estimates. Given the high toxicity of chlorsulfuron to terrestrial vegetation and the resulting high HQs for terrestrial plants, application-specific drift estimates are particularly important for assessing the potential impact of chlorsulfuron on nontarget vegetation in any specific application of chlorsulfuron.

4.4.2.5.2. Soil Exposures by Runoff

Risks to nontarget vegetation associated with runoff and sediment losses to a field adjacent to the treated site are estimated in Worksheet G04 of Attachment 1. For soil exposures, the toxicity values are based on seedling emergence assays. As summarized in Table 18 and discussed in Section 4.3.2.5, HQs are calculated using an NOAEC of 0.0000068 lb a.i./acre for a sensitive species of dicot (sugar beet) and an NOAEC of 0.000163 lb a.i./acre for a tolerant species of monocot (wheat). As illustrated in Figure 3 (upper graph), dicots are somewhat more sensitive than monocots, particularly in terms of the most sensitive monocots and dicots for which data are available. Thus, the risk characterization for sensitive species would most clearly apply to sensitive species of dicots. As with assays for vegetative vigor (Section 4.4.2.5.1) and as illustrated in Figure 4 (upper graph), the sensitivities of tolerant species are similar in both dicots and monocots. Based on this pattern, the HQs for tolerant species would probably apply equally to tolerant species of both monocots and dicots.

For sensitive species of plants (i.e., primarily sensitive dicots), the central estimate of the HQ is 11 with a range of 0.000007 to 460. The HQ for tolerant species (i.e., tolerant dicots or monocots) is 0.5 with a range of 0.0000003 to 19. The wide range of HQs reflects the wide range of conditions used in the GLEAMS-Driver modeling (Section 3.2.3.4.3). Since the HQs for both tolerant and sensitive species overlap the level of concern (HQ=1), the risk characterizations for sensitive and tolerant species are qualitatively similar. In areas that favor runoff (e.g., clay soils and high rates of precipitation), both sensitive and tolerant species could be impacted. Consequently, if runoff is a concern in a specific application of chlorsulfuron, site-specific modeling using GLEAMS-Driver or some other runoff model would be warranted.

As with most exposure scenarios, the HQs are linearly related to application rate. If higher application rates are used, risks to sensitive and tolerant species of terrestrial plants would increase in direct proportion to the higher application rate.

4.4.2.5.3. Contaminated Irrigation Water

The HQs for nontarget plants irrigated with chlorsulfuron contaminated surface water are summarized in Worksheet G06a of the attachments to this risk assessment. As with runoff (Section 4.4.2.5.2), the HQs for both tolerant and sensitive species bracket the level of concern (HQ=1)—i.e., HQs = 1.6 (0.00001 to 17) for tolerant species and HQs = 2212 (0.02 to 23,364) for sensitive species. The differences in the magnitude of the HQs, however, clearly indicate that concerns for sensitive species are much greater than concerns for tolerant species.

The key variables in this exposure scenario are the expected concentrations in ambient water (Section 3.2.3.4.6.1) and the amount of irrigation water applied, which is assumed to be 1 inch as a central estimate with a range of 0.25 inch to 2 inches. As discussed in Section 3.2.3.4.6.1, the variability in estimated surface water concentrations is substantial—i.e., a factor of over 150,000—and this variability dominates the magnitude of the HQs. Consequently, the upper bound risks will be most commonly associated with site conditions, including high rates of rainfall and soils conducive to runoff and/or percolation losses.

The product labels for the representative formulations considered in the current risk assessment (Table 3) explicitly note the potential hazards associated with the contamination of surface water used for irrigation. The ecological risk assessment conducted in support of the Reregistration Eligibility Decision for chlorsulfuron also considers this pathway and derives RQs of 91 to 341 for sensitive species of terrestrial vegetation (U.S. EPA/OPP/EFED 2004a, Table 14, p.25). The RQs derived by EPA differ from those given in the current Forest Service risk assessment because the RQs are based on EC_{25} values rather than NOAECs. In addition, as summarized in Table 12 of the current risk assessment, the surface water modeling used by EPA estimated concentrations of chlorsulfuron in water that span a much narrower range of concentrations than those used in the current Forest Service risk assessment. Risks associated with the contamination of irrigation water are also discussed but not quantified in U.S. EPA/OPP/EFED (2012a, p. 31).

As with the assessment of risks associated with runoff (Section 4.4.2.5.2), site-specific exposure assessments would be justified in applications where the potential contamination of irrigation water is a concern.

4.4.2.5.4. Wind Erosion

Risks to nontarget vegetation associated with wind erosion of contaminated soils are summarized in Worksheet G06b of Attachment 1. Based on the assumptions typically used in Forest Service risk assessments (Section 4.2.4.5), risks associated with this exposure scenario are far below the level of concern for tolerant species [HQs = 0.004 (0.0.0008 to 0.008)] but above the level of concern for sensitive species [HQs = 5 (1.1 to 11)].

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

> *Treated soil particles may move off-site to non-target crop sites through wind or water. ... Do not disturb treated soils to minimize the potential for Alligare Chlorsulfuron 75 movement by soil erosion from wind or water.*
>
> Specimen Label for Alligare Chlorsulfuron 75

Similar language is in the product label for Telar XP:

> *A careful evaluation of the potential for off-site movement from the intended application site, including movement of treated soil by wind or water erosion, must be made prior to using TELAR® XP. This evaluation is particularly critical where desirable vegetation or crops are grown on neighboring land for which the use of TELAR® XP is not labeled.*
>
> Specimen Label for DuPont TELAR XP

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

4.4.2.6. Terrestrial Microorganisms

As discussed in Section 4.3.2.6, Forest Service risk assessments do not typically propose a formal dose-response assessment for terrestrial microorganisms; thus, HQs are not typically derived. Nonetheless, as summarized in Appendix 8, Table A8-2, the maximum concentration of chlorsulfuron estimated in the upper 12 inches of soil is 0.42 mg a.i./kg soil for an application rate of 1 lb a.i./acre. For the application rate of 0.0625 lb a.i./acre considered in the current risk assessment, the peak concentration in soil would be about 0.026 mg a.i./kg soil [0.42 mg a.i./kg soil x 0.625 = 0.02625]. This concentration is below the only definitive toxicity value for chlorsulfuron in microorganisms—i.e., 60 mg a.i./L in a culture media—by a factor of over 2000 [60 mg a.i./L ÷ 0.026 mg a.i./kg soil ≈ 2307]. This is only a crude approximation because differences in the densities of soil and the culture media are not considered. As noted in Section 4.1.2.5, the recent study by Wang et al. (2010) notes that there was no effect on soil microorganisms at soil concentrations of 50 mg a.i./kg soil. The only study reporting detectable effects in soil microorganisms is the study by Junnila et al. (1994) which notes only a transient (i.e., 1 day) decrease in soil nitrification following applications of chlorsulfuron at rates of

0.0035 and 0.01 lb a.i./acre. None of these studies suggest that applications of chlorsulfuron will have a significant impact on soil microorganisms.

4.4.3. Aquatic Organisms

The risk characterization for aquatic organisms is summarized in Worksheet G03 of Attachment 1. As would be expected for an herbicide, aquatic plants are the aquatic organisms at highest risk, and effects on aquatic plants may lead to indirect effects on fish and invertebrates due to food reduction, habitat modification, and the potential for oxygen depletion in the event of an accidental spill.

4.4.3.1. Fish

The risk characterization for fish is relatively simple and benign. None of the HQs for anticipated levels of exposure approaches the level of concern (HQ=1) for acute accidental exposures (maximum HQ of 0.06), acute non-accidental exposures (maximum HQ of 0.001), or longer-term exposures (maximum HQ of 0.0007). This risk characterization for fish is qualitatively identical to that given in the EPA ecological risk assessment in support of the registration review of chlorsulfuron (U.S. EPA/OPP/EFED 2004a, Table 8, p. 15). These HQs are below the level of concern by factors of about 16 for accidental exposures, 1000 for acute non-accidental exposures, and 1400 for longer-term exposures.

Other than to note that extreme accidental scenarios could be imagined that might lead to HQs in excess of the level of concern, these HQs for direct effects require no elaboration.

As discussed in Section 4.4.3.4, chlorsulfuron applications may adversely affect sensitive species of algae (acute exposures only) and aquatic macrophytes (acute and longer-term exposures). Direct effects on aquatic plants could lead to indirect effects on fish, as noted in Section 4.4.1.

4.4.3.2. Amphibians

As discussed in Section 4.3.3.2, no dose-response assessment can be developed for aquatic phase amphibians. The EPA uses data on fish as a surrogate for aquatic phase amphibians (U.S. EPA/OPP/EFED 2012a, p. 35).

4.4.3.4. Aquatic Invertebrates

The risk characterization for aquatic invertebrates is essentially identical to that for fish (Section 4.4.3.1). None of the HQs for anticipated levels of exposure approaches the level of concern (HQ=1) for acute accidental exposures (maximum HQ of 0.09), acute non-accidental exposures (maximum HQ of 0.002), or longer-term exposures (maximum HQ of 0.001). These HQs are below the level of concern by factors of about 11 for accidental exposures, 500 for acute non-accidental exposures, and 1000 for longer-term exposures. The HQs developed in the current risk assessment are consistent with RQs derived by U.S. EPA/OPP/EFED 2004a, Table 8, p. 15), all of which are specified as <0.01.

As with fish, extreme accidental scenarios could be imagined that lead to HQs in excess of the level of concern. As a more practical concern, however, chlorsulfuron applications may adversely affect sensitive species of algae (acute exposures only) and aquatic macrophytes (acute and longer-term exposures). Direct effects on aquatic plants could lead to indirect effects on aquatic invertebrates, as noted in Section 4.4.1.

4.4.3.4. Aquatic Plants

4.4.3.4.1. Algae

As with other receptors, HQs for algae are developed for both sensitive and tolerant species. While this general classification is a simplification for all groups of organisms, an appreciation of this simplification is particularly important for algae. As illustrated in Figure 6 and discussed in Section 4.1.3.4.1, demonstrated differences in sensitivity among species of algae are extremely broad. Based on EC_{50} values for growth (Appendix 7, Table A7-2), these differences cover a factor of over 17,000 [275.51 mg a.i./L ÷ 0.0161 mg a.i./L ≈ 17,112]. Thus, the sensitivity of different species of algae could be better characterized by a continuum. The selection of toxicity values for sensitive and tolerant species of algae is only an extension of the extreme value approach used in Forest Service risk assessments (Section 3.2.3.1.1). The selection of the most sensitive and tolerant species is a basis for discussing the range of effects that might be observed following applications of chlorsulfuron. Because of the wide range of sensitivities, similar applications of chlorsulfuron at different sites could lead to a wide range of effects depending on the sensitivities of the different populations of algae at the sites. While this circumstance is true for any pesticide application, the potential differences are clearly documented for chlorsulfuron.

With the above qualification, the HQs for sensitive species are a concern for acute accidental exposures, acute non-accidental exposures, and longer-term exposures. For accidental exposures, the HQ is 30 with a range of 0.2 to 201. For acute non-accidental exposures, the HQ for sensitive species of algae is 0.8 with a range of 0.00005 to 5. For longer-term exposures, the HQ for sensitive species of algae is 0.4 with a range of 0.00001 to 3. As with other cases of exceedances in the level of concern (HQ=1) for surface water (e.g., Section 4.4.2.5.2 for the impact of runoff on terrestrial plants), the wide range of HQs for sensitive species of algae reflect the wide range of sites and climate conditions in the GLEAMS-Driver modeling (Section 3.2.3.4.3). Consequently, if potential impacts on algae are concerns in a specific application of chlorsulfuron, site-specific modeling using GLEAMS-Driver or some comparable exposure model would be warranted. The duration of effects would depend on site-specific conditions. It should be noted that the half-live for chlorsulfuron in water used in the GLEAMS-Driver modeling—i.e., 160 days, as summarized in Table 11—is a metabolic half-life. Local conditions conducive to dispersal (i.e., high rates of rain and outflow from the contaminated waterbody) could lead to much shorter field half-lives. Again, the processes of dispersal could be estimated using GLEAMS-Driver or other environmental fate models such as PRZM/EXAMS.

4.4.3.4.2. Macrophytes

As illustrated in Figure 7 and discussed in Section 4.1.3.4.2, macrophytes are much more sensitive than algae to chlorsulfuron. Based on the available NOAECs, the differences in sensitivity are a factor of somewhat over 200 [0.05 mg a.i./L ÷ 0.00024 mg a.i./L ≈ 208.33], as summarized in Table 18 and discussed in Section 4.3.3.4.

For sensitive species of aquatic macrophytes, the central estimate of the non-accidental acute HQ is 33 with a range of 0.001 to 172 and the corresponding longer-term HQ is 17 with a range of 0.0004 to 99. The central estimates of the acute HQs are similar to the NOAEL-based RQs derived by EPA—i.e., 18 to 40 (U.S. EPA/OPP/EFED 2004a, Table 10, p. 18). This similarity is to be expected in that both the current and the EPA analyses use the same endpoints—i.e., an

NOAEC of 0.00024 mg a.i./L—and the central estimates of expected concentrations of chlorsulfuron in water are similar in the current assessment and the EPA assessments (as summarized in Table 12 and discussed in Section 3.2.3.4.4). For tolerant species of aquatic macrophytes, the central estimate of the acute non-accidental HQ is 0.2 with a range of 0.000005 to 0.8 and the longer term HQ is 0.08 with a range of 0.000002 to 0.5.

Qualitatively, these HQs lead to different risk characterizations. For tolerant species of macrophytes, there is little concern that expected concentrations of chlorsulfuron in surface water would lead to detectable adverse effects. While the upper bound HQ of 0.8 for acute exposures in tolerant species approaches the level of concern, the wide range of sites and conditions used in in the GLEAMS-Driver modeling (Section 3.2.3.4.3) is likely to encompass most conditions under which chlorsulfuron would be applied by the Forest Service.

For sensitive species, the risk characterization is variable, with the central estimates and lower bounds bracketing the level of concern (HQ=1). If potential impacts on aquatic macrophytes are concerns in a specific application of chlorsulfuron, site-specific modeling could be warranted, particularly in areas with moderate to heavy rainfall.

The HQs for sensitive species of aquatic macrophytes following an accidental spill are 1183 (8 to 7885). These HQs require little elaboration. In the event of an accidental spill similar to the scenarios developed in the current risk assessment, the concentrations of chlorsulfuron would be in the range of about 0.002 to 2 mg a.i./L. These concentrations are in excess of not only the NOAEL but also the EC_{50} for sensitive species—i.e., 0.00035 mg a.i/L for *Lemna gibba* (Appendix 7, Table 7-4). For sensitive species of aquatic macrophytes, these levels of exposure would lead to grossly visible signs of damage and possibly wide-spread mortality in aquatic vegetation. In waterbodies with dense populations of sensitive aquatic macrophytes, decaying vegetation could result in decreases of oxygen concentrations in the water which could adversely affect many aquatic organisms.

For tolerant species of aquatic macrophytes, the HQ for an accidental spill is 6 with a range of 0.04 to 38. At the lower bounds of exposure, no adverse effects are likely. At the central estimate and upper bound of exposures, adverse effects could be evident. As noted above, the upper bound concentration for the accidental spills developed in the current risk assessment is about 2 mg a.i./L. This concentration is above the EC_{50} for tolerant species of aquatic macrophytes (i.e., 0.0018 mg a.i./L) by a factor of about 1000. As with sensitive species, these upper bound exposures could result in substantial mortality in tolerant species of aquatic macrophytes with the potential for oxygen depletion in the water.

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.

ClrRev	Cleared reviews available at https://iaspub.epa.gov/apex/pesticides.
E-Docket01	U.S. EPA E-Docket EPA-HQ-OPP-2004-0219 for Registration Review at http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2004-0219.
E-Docket02	U.S. EPA E-Docket EPA-HQ-OPP-2012-0878 for Registration Review at http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2012-0878/
E-Docket03	Chlorsulfuron; Community Right-to-Know Toxic Chemical Release Reporting. https://www.regulations.gov/docket?D=EPA-HQ-TRI-2013-0393.
MRID2004	CBI studies from previous Forest Service risk assessment.
RA2004	Open literature references from previous Forest Service risk assessment.
Set00	Papers from preliminary scoping.
Set01	Papers from ECOTOX and initial TOXLINE screen.
Set02	Update literature search in August, 2016.
Set03	Focused searches.
Set04	Search following peer review.
Std	Standard references used in most Forest Service risk assessments.

{Abdel-Hamid 1996} Abdel-Hamid MI. 1996. Development and application of a simple procedure for toxicity testing using immobilized algae. Water Sci Technol. 33 (6):129-138. [RA2004]

{Adamczewski et al. 2009} Adamczewski K; Kierzek R; Matysiak K. 2009. Influence of Long-Term Used Herbicides on Resistance Development in *Apera spica*-Venti L. to Sulfonylureas. Communications in Agricultural and Applied Biological Sciences. 74(2):491-6. [Set01]

{Ahtiainen et al. 2003} Ahtiainen JH; Vanhala P; Myllym,,ki A. 2003. Effects of Different Plant Protection Programs on Soil Microbes. Ecotoxicology and Environmental Safety. 54(1):56-64. [Set01]

{Alden and Frith 1991} Alden CL; Frith CH. 1991. The Urinary System. Chapter 15 in :Handbook of Toxicologic Pathology. WM Haschek and CG Rousseaux, editors. Academic Press, New York, NY. pp. 316-381. [RA2004]

{Al-Khatib et al. 1992} Al-Khatib K; Parker R; Fuerst EP. 1992a. Foliar absorption and translocation of herbicides from aqueous solution and treated soil. Weed Sci. 40 (2):281-287. [RA2004]

{Al-Khatib et al. 1992b} Al-Khatib K; Parker R; Fuerst EP. 1992b. Sweet cherry (Prunus avium) response to simulated drift from selected herbicides. Weed Technol. 6 (4):975-979. [RA2004]

{Allen and Fryrear 1977} Allen RR; Fryrear DW. 1977. Limited tillage saves soil, water, and energy. ASAE Annual Meeting, NC State Univ., Raleigh, NC. June 26-29, 1977. 14 pp. [RA2004]

{Allen and Fryrear 1997} Allen RR; Fryrear DW. 1977. Limited tillage saves soil, water, and energy. ASAE Annual Meeting, NC State Univ., Raleigh, NC. June 26-29, 1977. 14 pp. [Std]

{Alligare LLC 2010} Alligare LLC. 2010. Material Safety Data Sheet for Alligare Chlorsulfuron 75. Dated: May 25, 2010. [Set00]

{Alvarez 1991a} Alvarez L. 1991a. Teratogenicity Study of DPX-W4189-165 (Chlorsulfuron) in Rats. Lab Project Number: 8964-001: 734-90. Unpublished study prepared by E.I. du Pont de Nemours and Co. 167 p. MRID 41976406. [MRID2004]

{Alvarez 1991b} Alvarez L. 1991b. Teratogenicity Study of DPX-W4189-165 (Chlorsulfuron) in Rabbits. Lab Project Number: 8965-001: 306-90. Unpublished study prepared by E.I. du Pont de Nemours and Co., Haskell Lab. 195 p. MRID 41983101. [MRID2004]

{Alvarez-Benedi et al. 1998} Alvarez-Benedi J; Carton A; Fernandez JC. 1998. Sorption of tribenuron-methyl, chlorsulfuron, and imazamethabenz-methyl by soils. J Agric Food Chem. 46 (7):2840-2844. [RA2004]

{Anderson 1985a} Anderson RL. 1985a. Environmental effects on metsulfuron and chlorsulfuron bioactivity in soil. J Environ Qual. 14 (4):517-521. [RA2004]

{Anderson 1985b} Anderson LWJ. 1985. Use of Bioassays for Allelochemicals in Aquatic Plants. ACS Symposium Series. 268:351-370. [ECOTOX- 94332]

{Anderson and Barrett 1985} Anderson RL; Barrett MR. 1985. Residual phytotoxicity of chlorsulfuron in 2 soils. J Environ Qual. 14 (1):111-114. [RA2004]

{Anderson et al. 2010} Anderson DM; Carolan VA; Crosland S; Sharples KR; Clench MR. 2010. Examination of the Translocation of Sulfonylurea Herbicides in Sunflower Plants by Matrix-Assisted Laser Desorption/ionisation Mass Spectrometry Imaging. Rapid Communications in Mass Spectrometry. 24(22):3309-19. [Set01]

{Archer et al. 2013} Archer M; Oderda G; Rickards K; Turpin S. 2013. Sulfonylurea Agents & Combination Products, Drug Class Review, 68:20.20 Sulfonylureas. Final Report. University of Utah College of Pharmacy. Salt Lake City, Utah. Available at: http://www.health.utah.gov/pharmacy/ptcommittee/files/Criteria%20Review%20Documents/08.13/08.13%20Sulfonyluria%20Drug%20Class%20Review.pdf. [Set02]

{Armstrong 1988} Armstrong J. 1988. Product Identity, Description of Formulation Process, Formation of Impurities, and Certification of Limits for: End use Product Du Pont Avatar Herbicide. Laboratory Pro ject ID: FPC-88-5-ID. Unpublished compilation prepared by E. I. du Pont de Nemours. MRID 40622706. [MRID2004]

{Ashworth et al. 2014} Ashworth MB; Walsh MJ; Flower KC; Powles SB. 2014. Identification of the First Glyphosate-Resistant Wild Radish (*Raphanus raphanistrum* L.) Populations. Pest Management Science. 70(9):1432-6. [Set01]

{Atkinson 1991} Atkinson J. 1991. A Chronic (1 Year) Oral Toxicity Study in the Dog with DPX-W4189 (Chlorsulfuron) via the Diet. Lab Project Number: 89/3501: 163/91. Unpublished study prepared by Bio/ dynamics, Inc. 716 p. MRID 41862601. [MRID2004]

{Awkerman et al. 2008} Awkerman JA; Raimondo S; Barron MG. 2008. Development of species sensitivity distributions for wildlife using interspecies toxicity correlation models. Environmental Science and Technology. 42(9):3447-52. [Std]

{Beavers et al. 1992a} Beavers J; Foster J; Lynn S; et al. 1992a. H-18,053 (Chlorsulfuron): A One-generation Reproduction Study with the Northern Bobwhite (Colinus virginianus). Lab Project Number: 112-266: 564-92. Unpublished study prepared by Wildlife International Ltd. 185 p. MRID 42634001. [MRID2004]

{Beavers et al. 1992b} Beavers J; Foster J; Lynn S; et al. 1992b. H-18,053 (Chlorsulfuron): A One-Generation Reproduction Study with the Mallard (Anas platyrhynchos). Lab Project Number: 112-267: 565-92. Unpublished study prepared by Wildlife International Ltd. 185 p. MRID 42634002. [MRID2004]

{Beck et al. 1990} Beck KG; ;Wilson RG; Henson MA. 1990. The effects of selected herbicides on musk thistle (*Carduus nutans*) viable achene production. Weed Technol. 4 (3):482-486. [RA2004]

{Belai and Oros 1996} Belai I; Oros G. 1996. Responses of different fungal and plant species to acetolactate synthase inhibitors and their derivatives. J Environ Sci Health B. 31 (3):615-620. [RA2004]

{Berger and Wolfe 1996} Berger BM; Wolfe NL. 1996. Hydrolysis and biodegradation of sulfonylurea herbicides in aqueous buffers and anaerobic water-sediment systems: Assessing fate pathways using molecular descriptors. Environ Toxicol Chem. 15 (9):1500-1507. [RA2004]

{Bergstrom and Stenstrom 1998} Bergstrom L; Stenstrom J. 1998. Environmental fate of chemicals in soil. Ambio. 27 (1):16-23 . [RA2004]

{Bestman et al. 1990} Bestman HD; Devine MD; Born WHV. 1990. Herbicide chlorsulfuron decreases assimilate transport out of treated leaves of field pennycress (Thlaspi arvense L.) seedlings. Plant Physiol. 93 (4):1441-1448. [RA2004]

{Bhandary et al. 1997} Bhandary RM; Whitwell T; Briggs J. 1997. Growth of containerized landscape plants is influenced by herbicide residues in irrigation water. Weed Technol. 11 (4):793-797. [RA2004]

{Bhatti et al. 1995} Bhatti MA; Al-Khatib K; Felsot AS; Parker R; Kadir S. 1995. Effects of simulated chlorsulfuron drift on fruit yield and quality of sweet cherries (Prunus avium L.). Environ Toxicol Chem. 14 (3):537-544. [RA2004]

{Bhatti et al. 1996} Bhatti MA; Al-Khatib K; Parker R. 1996. Wine grape (Vitis vinifera) response to repeated exposure of selected sulfonylurea herbicides and 2,4-D. Weed Technol. 10 (4):951-956. [RA2004]

{Blacklow and Pheloung 1991} Blacklow WM; Pheloung PC. 1991. Sulfonylurea herbicides applied to acidic sandy soils: A bioassay for residues and factors affecting recoveries. Aust J Agric Res. 42 (7):1205-1216 . [RA2004]

{Blackshaw et al. 1990b} Blackshaw RE; Derksen DA; Muendel H-H. 1990b. Herbicides for weed control in safflower (Carthamus tinctorius). Can J Plant Sci. 70 (1):237-246. [RA2004]

{Blair and Martin 1988} Blair AM; Martin TD. 1988. A review of the activity fate and mode of action of sulfonylurea herbicides. Pestic Sci. 22 (3):195-220. [RA2004]

{Blasberg et al. 1991} Blasberg J; Hicks S; Stratton J. 1991. Acute Toxicity of Chlorsulfuron to Selenastrum capricornutum Printz: Final Report. Lab Project Number: AMR-2081-91: 39427. Unpublished study prepared by ABC Laboratories, Inc. 33 p. MRID 42186801. [MRID2004]

{Bodden and Rhodes 1994} Bodden R; Rhodes B. 1994. Metabolism of Chlorsulfuron in Laying Hens-Part A: Dosing, Sample Collection, and Material Balance; Part B: Sample Analysis and Metabolite Identification. Lab Project Number: HWI/6324/108: AMR/2193/91. Unpublished study prepared by Hazleton Wisconsin, In MRID 43143501. [MRID2004]

{Bodmer et al. 2008} Bodmer M; Meier C; Krahenbuhl S; Jick SS; Meier CR. 2008. Metformin, Sulfonylureas, or Other Antidiabetes Drugs and the Risk of Lactic Acidosis or Hypoglycemia. Dabetes Care. 31(11): 2086-2091. [Set03]

{Boeri et al. 2001a} Boeri RL; Wyskiel DC; Ward TJ. 2001a. Chlorsulfuron(DPX-W4189)Technical: Influence on Growth and Growth Rate of the Alga, *Navicula pelliculosa.* Unpublished study performed by T.R Wilbury Laboratories, Inc., Marblehead, MA, Laboratory Study No. 2045-DU, and sponsored by E.I. du Pont de Nemours and Company, Study Number 4467. Experimental start date November 15, 2000 and experimental termination date November 20, 2000. The final report issued January 3, 2003. (As summarized in EPA Data Evaluation Record). Available at: https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/118601/118601.htm. [E-Docket03]

{Boeri et al. 2001b} Boeri RL; Wyskiel DC; Ward TJ. 2001b. Chlorsulfuron (DPX-W4189) Technical: Influence on Growth and Growth Rate of the Alga, *Skeletonema costatum.* Unpublished study performed by T.R Wilbury Laboratories, Inc., Marblehead, MA, Laboratory Study No. 2043-DU, and sponsored by E.L du Pont de Nemours and Company, Study Number 4465. Experimental start date November 29, 2000 and experimental termination date December 4, 2000. The final report issued January 3, 2003. (As summarized in EPA Data Evaluation Record). Available at: https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/118601/118601.htm. [E-Docket03]

{Boeri et al. 2001c} Boeri RL; Wyskiel DC; Ward TJ. 2001c. Chlorsulfuron(DPX- W4189) Technical: Influence on Growth and Growth Rate of the Alga, *Anabaena flos-aquae.* Unpublished study performed by T.R Wilbury Laboratories, Inc., Marblehead, MA, Laboratory Study No. 2044-DU, and sponsored by E.I. du Pont de Nemours and Company, Study Number 4466. Experimental start date November 10, 2000 and experimental termination date November 15, 2000. The final report issued January 3, 2003. (As summarized in EPA Data Evaluation Record). Available at: https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/118601/118601.htm. [E-Docket03]

{Boeri et al. 2002} Boeri RL; Wyskiel DC; Ward TJ. 2002. Chlorsulfuron (DPX-W4189) Technical: Influence on Growth Rate of the Duckweed, *Lemna gibba.* Unpublished study performed by T.R Wilbury Laboratories, Inc., Marblehead, MA, Laboratory Study No. 2042-DU, and sponsored by E.I. du Pont de Nemours and Company, Study Number 4468. Experimental start date October 24, 2000 and experimental termination date May 22, 2002. The final report issued January 3, 2003. (As summarized in EPA Data Evaluation Record). Available at: https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/118601/118601.htm. [E-Docket03]

{Boschin et al. 2003} Boschin G; D'agostina A; Arnoldi A; Marotta E; Zanardini E; Negri M; Valle A; Sorlini C. 2003. Biodegradation of Chlorsulfuron and Metsulfuron-Methyl by *Aspergillus niger* in Laboratory Conditions. Journal of Environmental Science and Health. Part. B, Pesticides, Food Contaminants, and Agricultural Wastes. 38(6):737-46. [Set01]

{Brennan 1999a} Brennan D. 1999a. Technical Grade Chlorsulfuron (DPX-W4189) Analysis and Certification of Product Ingredients. Lab Project Number: AMR 4727-97: S788.849: S7850.160.01.ES. Unpublished study prepared by E.I. du Pont de Nemours and Company. 150p. {OPPTS 830.1550, 830.1700, 830.1750, 830.1800} MRID 449640. [MRID2004]

{Brennan 1999b} Brennan D. 1999b. Technical Grade Chlorsulfuron (DPX-W4189) Manufacturing Description and Formation of Impurities. Lab Project Number: AMR 4869-98. Unpublished study prepared by E.I. du Pont de Nemours and Company. 71 p. {OPPTS 830.1550, 830.1620, 830.1670} MRID 44964002. [MRID2004]

{Brill 1998} Brill F. 1998. Magnitude and Decline of Residues of Chlorsulfuron in Grasses (Including Wheat) Following Application at Maximum Label Rates. Lab Project Number: AMR 3814-96: 43890. Unpublished study prepared by E.I. du Pont de Nemours and Company and ABC Laboratories. 459 p. {OPPTS 860.1500} MRID 44705401. [MRID2004]

{Brown 1990} Brown HM. 1990. Mode of action crop selectivity and soil relations of the sulfonylurea herbicides. Pestic Sci. 29 (3):263-282. [RA2004]

{Buser. 1990} Buser HR. 1990. Atrazine and other s-triazine herbicides in lakes and in rain in Switzerland. Environ. Sci. Technol. 24(7): 1049-1058. [Std]

{Busi et al. 2011} Busi R; Vila-Aiub MM; Powles SB. 2011. Genetic Control of a Cytochrome P450 Metabolism-Based Herbicide Resistance Mechanism in *Lolium rigidum*. Heredity (Edinb). 106(5):817-24. [Set01]}

{Carrasco and Sabater 1997} CarrascoJM; Sabater C. 1997. Toxicity of Atrazine and Chlorsulfuron to Algae. Toxicology and Environmental Chemistry. 59 (1-4):89-99. [ECOTOX-6712]

{CDPR 2012} CDPR (California Department of Pesticide Regulation). 2012. Summary of Toxicology Data, Chlorsulfuron. Original report dated July 1987, last updated April 16, 2012. Available at: http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/2143.pdf. [Set00]

{CDPR 2015} CDPR (California Department of Pesticide Regulation). 2015. Summary of Pesticide Use Report Data 2013, Indexed by Chemical. Report dated May 2015. Available at: www.cdpr.ca.gov/docs/pur/pur13rep/13sum.htm. [Std]

{Chaleff and Mauvais 1984} Chaleff RS; Mauvais CJ. 1984. Acetolactate synthase is the site of action of 2 sulfonylurea herbicides in higher plants. Science. 224 (4656):1443-1445. [RA2004]

{Chamberlain et al. 1996} Chamberlain K; Evans AA; Bromilow RH. 1996. 1-Octanol/water partition coefficient (Kow) and pKa for ionisable pesticides measured by a pH-metric method. Pestic Sci. 47 (3):265-271. [RA2004]

{ChemIDplus 2015} ChemIDplus. 2015. United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/rn/64902-72-3. [Std]

{Chen 1980} Chen HHC. 1980. Benzenesulfonamide, 2-Chloro-N-<<(4-methoxy-6 methyl-1,3,5-triazin-2-YL) Amino> Carbonyl>--(INW-4189): Lethal Concentration Toxicity Study--ChR-CD Rats. Pathology Report No. 9-80. (Unpublished study received Sep 1, 1981 under 352-EX109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245879-Q) MRID 00083963. [MRID2004]

{Christopher et al. 1992} Christopher JT; Powles SB; Holtum AM. 1992. Resistance to Acetolactate Synthase-Inhibiting Herbicides in Annual Ryegrass (*Lolium rigidum*) Involves at Least Two Mechanisms. Plant Physiology. 100: 1909-1913. [Set04]

{Chrzanowski 1980a} Chrzanowski RL. 1980a. Degradation of 14-C DPX-W4189 in Anaerobic Aquatic Environments. Document No. AMR-38-81. (Unpublished study received Nov 13, 1981 under 352-404; prepared in coopera tion with Univ. of Delaware, College of Agriculture, submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL: 070470-K) MRID 00086815 . [MRID2004]

{Chrzanowski and Priester 1991} Chrzanowski R; Priester T. 1991. Degradation of carbon 14 DPX-W4189 in Anaerobic Aquatic Environments. Lab Project Number: AMR 38-91. Unpublished study prepared by E.I. du Pont de Nemours and Co. 45 p. MRID 42156704. [MRID2004]

{Cirujeda and Taberner 2010} Cirujeda A; Taberner A. 2010. Chemical Control of Herbicide-Resistant *Lolium rigidum* Gaud. in North-Eastern Spain. Pest Management Science. 66(12):1380-8. [Set01]

{Clydesdale 1997} Clydesdale, FM. 1997. Food Additives: Toxicology, Regulation, and Properties. CRC Press, Boca Raton, Florida. CD-ROM Database.[Std]

{Cotterman and Saari 1992} Cotterman J C; Saari LL. 1992, Rapid metabolic inactivation is the basis for cross-resistance to chlorsulfuron in diclofop-methylresistant rigid ryegrass (Lolium rigidum) biotype SR4/84. Pesticide Biochemistry and Physiology. 43, 182−192. [Set04]

{Coyner et 2001} Coyner A; Gupta G; Jones T} {Coyner et al. 2001} Coyner A; Gupta G; Jones T. 2001. Effect of chlorsulfuron on growth of submerged aquatic macrophyte Potamogeton pectinatus (sago pondweed). Environ Pollut. 111 (3):453-455. [RA2004]

{Cox 1993} Cox C. 1993. Sulfometuron methyl (Oust). J. Pest. Reform. 13 (4): 30-35. [RA2004]

{Darmency 2013} Darmency H. 2013. Pleiotropic Effects of Herbicide-Resistance Genes on Crop Yield: A Review. Pest Management Science. 69(8):897-904. [Set01]

{Dashiell and Ashley 1980a} Dashiell OL; Ashley P. 1980a. Acute Skin Absorption LD50 Test on Rabbits (EPA Pesticide Registration Guidelines). Haskell Laboratory Report No. 505-80. (Unpublished study received Sep 1, 1981 under 352-EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245879-N) MRID 00083960. [MRID2004]

{Dashiell and Ashley 1980b} Dashiell OL; Ashley P. 1980b. Acute Skin Absorption LD50 Test on Rabbits. Haskell Laboratory Report No. 505-80. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-K) MRID 00086826. [MRID2004]

{Dashiell and Hinckle 1981} Dashiell OL; Hinckle L. 1981. Oral LD50 Test in Rats--EPA Proposed Guidelines. Haskell Laboratory Report No. 74-81. (Unpublished study received Sep 1, 1981 under 352-EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDl:245879-L) MRID 00083958. [MRID2004]

{Dashiell and Silber 1980a} Dashiell OL; Silber LS. 1980a. Eye Irritation in Rabbits--EPA Pesticide Registration. Haskell Laboratory Report No. 1034-80. (Unpublished study received Sep 1, 1981 under 352-EX-109; sub mitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 245879-M) MRID 00083959. [MRID2004]

{Dashiell and Silber 1980b} Dashiell OL; Silber LS. 1980b. Skin Irritation Test on Rabbits for EPA Pesticide Registration. Haskell Laboratory Report No. 355-80. (Unpublished study received Sep 1, 1981 under 352 EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245879-O) MRID 00083961. [MRID2004]

{Dashiell and Silber 1981} Dashiell OL; Silber LS. 1981. Primary Skin Irritation and Sensitization Test on Guinea Pigs. Haskell Laboratory Report No. 1073-80. Rev. (Unpublished study received Sep 1, 1981 un der 352-EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245879-P) MRID 00083962. [MRID2004]

{Davison et al. 1987} Davison JC; Krall JM; Johnson WS. 1987. Response of selected range grass species to chlorsulfuron. Appl Agric Res. 2 (5):337-341. [RA2004]

{Delaware Cooperative 1999} Delaware Cooperative Extension. 1999. Agronomy Facts Series: AF-03. Available at: http://bluehen.ags.udel.edu/deces/af/af-03.htm. [RA2004]

{Delgado-Moreno and Pena 2007} Delgado-Moreno L; Pena A. 2007. Organic Amendments from Olive Cake as a Strategy to Modify the Degradation of Sulfonylurea Herbicides in Soil. Journal of Agricultural and Food Chemistry. 55(15):6213-8. [Set01]

{Dickerman 1981} Dickerman JD. 1981. A familial hemolytic anemia associated with sulfa administration. Hosp. Pract .(Off Ed). 16(9): 41, 44, 47. [RA2004]

{Dietrich and McAleer 1989a} Dietrich R; McAleer N. 1989a. Photodegradation of Phenyl(U) carbon 14 Chlorsulfuron and Triazine-2-carbon 14 Chlorsulfuron in Water Conducted in Sunlight. Lab Report No. AMR-1455-89. Unpublished study prepared by E.I. du Pont de Nemours & Co., Inc., Agricultural Products Dept. 45 p. MRID 41408101. [MRID2004]

{Dietrich and McAleer 1989b} Dietrich R; McAleer N. 1989b. Hydrolysis of Phenyl(U)-carbon 14 Chlorsulfuron and Triazine-2-carbon 14 Chlorsulfuron. Lab Report No. AMR-1455-89.161-1. Unpublished study prepared by E.I. du Pont de Nemours & Co., Inc., Agricultural Products Dept. 61 p. MRID 41408102 . [MRID2004]

{Dietrich and McAleer 1989c} Dietrich R; McAleer N. 1989c. Hydrolysis of Phenyl(U)-carbon 14 Chlorsulfuron and Triazine-2- carbon 14 Chlorsulfuron. Lab Project Number: AMR-1455-89.161-1. Unpublished study prepared by E.I. du Pont de Nemours & Co., Inc. 61 p. MRID 42156701. [MRID2004]

{Dietrich and McAleer 1989d} Dietrich R; McAleer N. 1989d. Photodegradation of Phenyl(U)- carbon 14 Chlorsulfuron and Triazine-2- carbon 14 Chlorsulfuron in Water Conducted in Sunlight. Lab Project Number: AMR-1455-89. Unpublished study prepared by E.I. du Pont de Nemours & Co., Inc. 44 p. MRID 42156702. [MRID2004]

{Dietrich and Taylor 1990} Dietrich R Taylor G. 1990. Field Soil Dissipation of {Phenyl (U)- Carbon 14 }Chlorsulfuron and {Triazine-2- Carbon 14 }Chlorsulfuron in Madera, California:. Lab Project Number: AMR-1417-89: EF-89-03. Unpublished study prepared by E. I. du Pont de Nemours and Co. MRID 41714401. [MRID2004]

{Djanegara 1991a} Djanegara T. 1991a. Field Soil Dissipation Studies of Chlorsulfuron. Lab Project Number: AMR 2205-91. Unpublished study prepared by E. I. du Pont de Nemours & Co. 229 p. MRID 42214202. [MRID2004]

{Djanegara 1991b} Djanegara T. 1991b. Accumulation Studies of Chlorsulfuron in Rotational Crops. Lab Project Number: AMR 2242-91. Unpublished study prepared by E. I. du Pont de Nemours & Co. 157 p. MRID 42214203. [MRID2004]

{Du Pont de Nemours 1977b} Du Pont de Nemours. 1977b. DPX-4189: Index of Toxicity Reports--Summary of Data. (Unpublished study received Jun 16, 1980 under 352-EX-105; CDL:099459-D) MRID 00032101. [MRID2004]

{Du Pont de Nemours 1979a} Du Pont de Nemours. 1979a. Residue Study on Wheat . (Unpublished study received Jun 16, 1980 under 352-105; CDL: 099462-N). (Unpublished study received Jun 16, 1980 under 352-105; CDL: 099462-N) MRID 00035268. [MRID2004]

{Du Pont de Nemours 1980f} Du Pont de Nemours. 1980f. Results of Tests on the Amount of Residue Remaining on Treated Crops: DPX-4189. (Unpublished study received Jun 16, 1980 under 352-105; CDL: 099462-M) MRID 00035267. [MRID2004]

{Du Pont de Nemours 1977a} Du Pont de Nemours. 1977a. DPX-4189: Technical Data Sheet. (Unpublished study received Jun 16, 1980 under 352-EX 105; CDL:099459-E). (Unpublished study received Jun 16, 1980 under 352-EX 105; CDL:099459-E) MRID 00031432. [MRID2004]

{DuPont Crop Protection 2015} DuPont Crop Protection. 2015. Safety Data Sheet on DuPont Telar XP Herbicide. Version 2.0. Revision Date: 06/18/2015. Ref. 130000029428. [Set00]

{Duggleby et al. 2000} Duggleby RG; Kartikasari AER; Wunsch RM.; et al. 2000. Expression in Escherichia coli of a Putative Human Acetohydroxyacid Synthase. Journal of Biochemistry and Molecular Biology. 33(3): 195-201. [Set03]

{Durkin et al. 1995} Durkin PR; Rubin L; Withey J; Meylan W. 1995. Methods of assessing dermal absorption with emphasis on uptake from contaminated vegetation. Toxicol. Indust. Health. 11(1): 63-79. [RA2004]

{Ecobichon 1998} Ecobichon DJ. 1998. Occupational Hazards of Pesticide Exposure – Sampling, Monitoring, Measuring. Taylor & Francis, Philadelphia, PA. 251 pp. [Std]

{ECOTOX 2016} ECOTOX (2016) ECOTOX Release 4.0. The ECOTOX (ECOTOXicology) Database. Available at: http://cfpub.epa.gov/ecotox/. [Std]

{Edwards 1979a} Edwards DF. 1979a. Acute Skin Absorption Test on Rabbits--LD50: Report No. 415-79. Rev. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-F) MRID 00031411. [MRID2004]

{Edwards 1979b} Edwards DF. 1979b. Acute Skin Absorption Test on Rabbits--LD50. Haskell Laboratory Report No. 415-79. (Unpublished study re ceived Sep 1, 1981 under 352-EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245879-I) MRID 00083956. [MRID2004]

{EFSA 2008} EFSA (European Food Safety Authority). 2008. Conclusion regarding the peer review of the pesticide risk assessment of the active substance chlorsulfuron. EFSA Scientific Report 2008; 201, 1-107. Document dated November 26, 2008. Available at: http://www.efsa.europa.eu/en/efsajournal/pub/201r. [Set00]

{Egaas et al. 1994} Egaas E; Skaare JU; Svendsen NO; Sandvik M. 1994. Pesticide Induced Biochemical Changes in Terrestrial Insects, Benthos and Fish as Markers of Contamination of Soils and Waters. Norwegian Journal of Agricultural Science. 3:89-116. [ECOTOX- 16009]

{ENSR 2005} ENSR (INSR International). 2005. Chlorsulfuron, Ecological Risk Assessment: Final Report. Prepared for Bureau of Land Management under Contract No. NAD010156. ENSR Document Number 09090-020-650. Available at: http://digitalcommons.usu.edu/govdocs/74/. [Set00]

{European Commission 2010} European Commission. 2010. Review report for the active substance Chlorsulfuron Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 26 February 2009 in view of the inclusion of Chlorsulfuron in Annex I of Directive 91/414/EEC. Document dated September 28, 2010. [Set00]

{Fahl et al. 1995} Fahl GM; Kreft L; Altenburger R; Faust M; Boedeker W; Grimme LH. 1995. pH-Dependent sorption, bioconcentration and algal toxicity of sulfonylurea herbicides. Aquat Toxicol. 31 (2):175-187. [RA2004/ECOTOX-14937]

{Fairchild et al. 1997} Fairchild JF; Ruessler DS; Haverland PS; Carlson AR. 1997. Comparative sensitivity of Selenastrum capricornutum and Lemna minor to sixteen herbicides. Arch Environ Contam Toxicol. 32 (4):353-457. [RA2004/ECOTOX-18093]

{Fan et al. 2005} Fan ZJ; Ai YW; Qian CF; Li ZM. 2005. Herbicide Activity of Monosulfuron and its Mode of Action. Journal of Environmental Sciences (China). 17(3):399-403. [Set01]

{Fantke and Juraske 2014} Fantke P; Juraske R. 2013. Variability of pesticide dissipation halflives in plants. Environmental Science and Technology. 47: 3548-3562. [Set04]

{Fantke et al. 2014} Fantke P; Gillespie BW; Juraske R; Jolliet O. 2014. Estimating Half-Lives for Pesticide Dissipation from Plants. Environmental Science and Technology. 48: 8588−8602. [Set04]

{FAO/WHO 2003} FAO/WHO (Food and Agriculture Organization/ World Health Organization). 2003. FAO Specifications and Evaluations for Agricultural Pesticides, Chlorsulfuron, 1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea. Available at: http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/chlors04.pdf. [Set00]

{Felix et al. 1988} Felix HR; Chollet R; Harr J. 1998. Use of the Cell Wall-Less Alga *Dunaliella bioculata* in Herbicide Screening Tests. Annals of Applied Biology. 113(1): 55–60. [ECOTOX-13100]

{Felsot et al. 1996}Felsot AS; Bhatti MA; Mink GI; Reisenauer G. 1996. Biomonitoring with Sentinel Plants to Assess Exposure of Nontarget Crops to Atmospheric Deposition of Herbicides. Environmental Toxicology and Chemisty. 15(4): 452-459. [Set00]

{Fenoll et al. 2012} Fenoll J; Hell¡n P; Flores P; Mart¡nez CM; Navarro S. 2012. Photocatalytic Degradation of Five Sulfonylurea Herbicides in Aqueous Semiconductor Suspensions under Natural Sunlight. Chemosphere. 87(8):954-61. [Set01]

{Ferenz 1980a} Ferenz RL. 1980a. LC50-inhalation Test for Pesticide Registra tion--Albino Rats. Haskell Laboratory Report No. 129-80. (Unpublished study received Sep 1, 1981 under 352-EX-109; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 245879-K) MRID 00083957. [MRID2004]

{Ferenz 1980b} Ferenz RL. 1980b. LC50--inhalation Test for Pesticide Registration--Albino Rats. Haskell Laboratory Report No. 129-80. (Unpublished study received Nov 13, 1981 under 352-404; sub mitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-H) MRID 00086825. [MRID2004]

{Fink et al. 1981} Fink R; Beavers JB; Joiner G; et al. 1981. Eight-day Dietary LC 50--Bobwhite Quail. H-12,700-02: Project No. 112-126; HLO-806-81. Final rept. (Unpublished study received Dec 28, 1981 under 352-404; prepared by Wildlife International, Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070534-B) MRID 00090009. [MRID2004]

{Fletcher et al. 1994} Fletcher JS; Nellessen JE; Pfleeger TG. 1994. Literature review and evaluation of the EPA food-chain (Kenega) nomogram, an instrument for estimating pesticide residues on plants. Environ. Toxicol. Chem. 13(9):1383-1391. [Std]

{Fletcher et al. 1996} Fletcher JS; Pfleeger TG; Ratsch HC; Hayes R. 1996. Potential impact of low levels of chlorsulfuron and other herbicides on growth and yield of nontarget plants. Environ Toxicol Chem. 15 (7):1189-1196. [RA2004]

{Flores-Cespedes et al. 2009} Flores-Cespedes F; Daza-Fernandez I; Villafranca-Sanchez M; Fernandez-Perez M. 2009. Use of Ethylcellulose to Control Chlorsulfuron Leaching in a Calcareous Soil. Journal of Agricultural and Food Chemistry. 57(7):2856-61. [Set01]

{Foldenyi et al. 2013} Foldenyi R; Toth Z; Samu G; Ersek C. 2013. Study of Sorption of Two Sulfonylurea Type of Herbicides and Their Additives on Soils and Soil Components. Journal of Environmental Science and Health. Part. B, Pesticides, Food Contaminants, and Agricultural Wastes. 48(9):758-66. [Set01]

{Galloway and Lebowitz 1981a} Galloway SM; Lebowitz H. 1981a. Mutagenicity Evaluation of 12,700 in an in vitro Cytogenetic Assay Measuring Chromosome Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells. Amendment: LBI Project No. 20990; HLO-323-81. (Unpublished study received Nov 13, 1981 under 352-404; prepared by Litton Bionetics, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-Q) MRID 00086830. [MRID2004]

{Galloway and Lebowitz 1981b} Galloway SM; Lebowitz H. 1981b. Mutagenicity Evaluation of 12,700 in an~in vitro~Cytogenetic Assay Measuring Chromosome Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells. Amendment: Genetics Assay No. 5540; HLO-323-81. (Unpublished study received Sep 1, 1981 under 352-403; prepared by Litton Bionetics, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-E) MRID 00088755. [MRID2004]

{Gaston et al. 2003} Gaston S; Ribas-Carbo M; Busquets S; Berry JA; Zabalza A; Royuela M. 2003. Changes in Mitochondrial Electron Partitioning in Response to Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis in Soybean. Plant Physiol. 133(3):1351-9. [Set01]

{Gilliom et al. 2007} Gilliom RJ; Barbash JE; Crawford CG; et al. 2007. Pesticides in the Nation's Streams and Ground Water, 1992–2001. USGS National Water-Quality Assessment Program Circular 1291. Revised February 15, 2007. Available at: http://pubs.usgs.gov/circ/2005/1291/. [Std]

{Goldstein et al. 1974} Goldstein A; Aronow L; Kaman SM. 1974. Principles of Drug Action: The Basis of Pharmacology. 2nd ed. John Wiley and Sons, New York, NY. 854 p.[Std]

{Goodman 1976} Goodman NC. 1976. Primary Skin Irritation and Sensitization Tests on Guinea Pigs. Report No. 794-76. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-L) MRID 00031417. [MRID2004]

{Goodman 1979} Goodman NC. 1979. 48-Hour LC50 to Daphnia magna. Haskell Lab oratory Report No. 152-79. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-H) MRID 00035262. [MRID2004]

{Grande et al. 1994} Grande M; Andersen S; Berge D. 1994. Effects of pesticides on fish: experimental and field studies. Norwegian Journal of Agricultural Sciences Suppl. 13: 195-209. [Set02/RA2004/ ECOTOX 62367]

{Gressel 2009} Gressel J. 2009. Crops with Target-Site Herbicide Resistance for *Orobanche* and *Striga* Control. Pest Management Science. 65(5):560-5. [Set01]

{Grossmann et al. 1992} Grossmann,K; Berghaus R; Retzlaff G. 1992. Heterotrophic Plant Cell Suspension Cultures for Monitoring Biological Activity in Agrochemical Research. Comparison with Screens Using Algae, Germinating Seeds and Whole Plants. Pesticide Science. 35(3): 283-289. [ECOTOX- 78497]

{Gutierrez et al. 2008} Gutierrez C; Campos-Herrera R; Jimenez J. 2008. Comparative Study of the Effect of Selected Agrochemical Products on *Steinernema feltiae* (Rhabditida: Steinernematidae). Biocontrol Science and Technology. 18(1): 101-108 [ECOTOX-109598]

{Hall and Dashiell 1980} Hall JA; Dashiell OL. 1980. Oral LD50 Test in Guinea Pigs. Report No. 308-80. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-C) MRID 00031408. [MRID2004]

{Hamouzov et al. 2014} Hamouzov K; Koscaronnarov P; Salava J; Soukup J; Hamouz P. 2014. Mechanisms of Resistance to Acetolactate Synthase-Inhibiting Herbicides in Populations of *Apera spica*-Venti from the Czech Republic. Pest Management Science. 70(4):541-8. [Set01]

{Han 19??a} Han JCY. 19??a. Aerobic Soil Metabolism of 14C-Phenyl Labeled DPX-4189. AMR-08-80 C. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wil mington, Del.; CDL:099462-T) MRID 00035273. [MRID2004]

{Han 19??b} Han JCY. 19??b. Hydrolysis of 14-C Labeled DPX-W4189. Document No. AMR-39-81. (Unpublished study received Sep 1, 1981 under 352-403; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-G) MRID 00083946. [MRID2004]

{Han 19??c} Han JCY. 19??c. Residue Studies with 14-C DPX-4189 in Blue gill Sunfish. Document No. AMR-32-81. (Unpublished study received Sep 1, 1981 under 352-403; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-L) MRID 00083951. [MRID2004]

{Han 1960a} Han JCY. 1960a. Hydrolysis and Photolysis Studies with 14C DPX-4189. AMR-08-80A. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wil mington, Del.; CDL:099462-Q) MRID 00035270. [MRID2004]

{Han 1960b} Han JCY. 1960b. Photolysis of 14-C Phenyl Labeled DPX-W4189 on Soil. Document No. AMR-42-81. (Unpublished study received Sep 1, 1981 under 352-403; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-H) MRID 00083947. [MRID2004]

{Han 1981a} Han JCY. 1981a. 14C-DPX-W4189 Soil Disappearance Studies in the Field. Document No. AMR-54-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-M) MRID 00086817. [MRID2004]

{Han 1981b} Han JCY. 1981b. Crop Rotation Study with 14-C DPX-W4189 in the Field. Document No. AMR-46-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-N) MRID 00086818. [MRID2004]

{Han 1981c} Han JCY. 1981c. Residue Studies with Glean (TM) Weed Killer in Channel Catfish. Document No. AMR-45-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-Q) MRID 00086820. [MRID2004]

{Han 1981d} Han JCY. 1981d. 14 C-DPX-W4189 Metabolism in Greenhouse and Field Grown Wheat. Document No. AMR-47-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-T) MRID 00086833. [MRID2004]

{Han 1981e} Han JCY. 1981e. 14-C DPX-W4189 Metabolism in Barley. Document No. AMR-55-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-U) MRID 00086834. [MRID2004]

{Han 1981f} Han JCY. 1981f. Metabolism of 14-C DPX-4189 in the Lactating Nanny Goat. Document No. AMR-29-81. (Unpublished study re ceived Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-X) MRID 00086836. [MRID2004]

{Han 1981g} Han JCY. 1981g. The Fate of the Major Wheat Metabolite of 14 C-DPX-W4189 in the Lactating Goat. Document No. AMR-52-81. (Unpublished study received Nov 13, 1981 under 352-404; submit ted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 070471-Y) MRID 00086837. [MRID2004]

{Han et al. 2012} Han H; Yu Q; Purba E; Li M; Walsh M; Friesen S; Powles SB. 2012. A Novel Amino Acid Substitution Ala-122-Tyr in ALS Confers High-Level and Broad Resistance Across ALS-Inhibiting Herbicides. Pest Management Science. 68(8):1164-70. [Set00]

{Han et al. 2013} Han H; Yu Q; Cawthray GR; Powles SB. 2013. Enhanced Herbicide Metabolism Induced by 2,4-D in Herbicide Susceptible *Lolium rigidum* Provides Protection Against Diclofop-Methyl. Pest Management Science. 69(9):996-1000. [Set00]

{Hawkins et al. 1989} Hawkins D; Elsom L; Girkin R; et al. 1989. The Absorption and Disposition of [carbon 14]-DPX-E9636 in the Rat. Lab Project Number: HRC/DPT 1900/891138: AMR-1197-88. Unpublished study prepared by Huntingdon Research Centre Ltd. 76 p. MRID 42540701. [MRID2004]

{Hawkins et al. 1990a} Hawkins D; Kirkpatrick D; Dean G. 1990a. The Photodegradation of Carbon 14 Chlorsulfuron on a Silty Clay Loam Soil. Lab Project Number: HRC/DPT 205/90571: AMR-1563-89. Unpublished study prepared by Huntingdon Research Centre Ltd. 58 p. MRID 41721001. [MRID2004]

{Hawkins et al. 1990b} Hawkins D; Kirkpatrick D; Dean G; et al. 1990b. The Photodegradation of carbon 14 Chlorsulfuron on a Silty Clay Loam Soil. Lab Project Number: HRC/DPT 205/90571: AMR-1563-89. Unpublished study prepared by Huntingdon Research Centre Ltd. 58 p. MRID 42156703. [MRID2004]

{Henry 1977} Henry JE. 1977. Ten-Dose Oral Subacute Test. Report No. 97-77. (Unpublished study received Jun 16, 1980 under 352-EX-105; sub mitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 099460-D) MRID 00031409. [MRID2004]

{Henry and Dashiell 1980} Henry JE; Dashiell OL. 1980. Skin Irritation Test on Rabbits for EPA Pesticide Registration. Report No. 264-80. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-K) MRID 00031416. [MRID2004]

{Herrmann et al. 1985} Herrmann M; Kotzias D; Korte F. 1985. Photochemical behavior of Chlorsulfuron in water and in adsorbed phase. Chemosphere. 14 (1):3-8. [RA2004]

{Hessen et al. 1994} Hessen DO; Kallqvist T; Abdel-Hamid MI; Berge D. 1994. Effects of pesticides on different zooplankton taxa in mesocosm experiments. Norwegian J Agric Sci Suppl. 0 (13):153-161 . [RA2004/ECOTOX-16005]

{Hinckle 1979a} Hinckle L. 1979a. Intraperitoneal LD50 Test. Report No. 403-79. (Unpublished study received Jun 16, 1980 under 352-EX-105; sub mitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 099460-E) MRID 00031410. [MRID2004]

{Hinckle and Dashiell 1980} Hinckle L; Dashiell OL. 1980. Oral LD_{50} Test in Rats--EPA Proposed Guidelines. Report No. 300-80. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-B). MRID 00031407. [MRID2004]

{Hinkle 1979b} Hinkle S. 1979b. Final Report--Avian Dietary Toxicity (LC50) Study in Bobwhite Quail. Project No. 201-523. (Unpublished study received Jun 16, 1980 under 352-105; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-K) MRID 00035265. [MRID2004]

{Hinkle and Bristol 1980a} Hinkle S; Bristol KL. 1980a. Final Report--Acute Oral LD50 Study in Mallard Ducks. Project No. 201-525. (Unpublished study received Jun 16, 1980 under 352-105; prepared by Hazelton Labo ratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-J) MRID 00035264. [MRID2004]

{Hinkle and Twigg 1980} Hinkle S; Twigg CJ. 1980. Final Report--Acute Oral LD50 Study in Bobwhite Quail. Project No. 201-538. (Unpublished study re ceived Jun 16, 1980 under 352-105; prepared by Hazleton Labora tories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-I) MRID 00035263. [MRID2004]

{Hinkle and Wentz 1979} Hinkle S; Wentz KL. 1979. Final Report--Avian Dietary Toxicity (LC50) in Mallard Ducks. Project No. 201-524. (Unpublished study received Jun 16, 1980 under 352-105; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-L) MRID 00035266. [MRID2004]

{Hoberman 1980} Hoberman AM. 1980. Teratology Study in Rabbits. Project No. 201536; HLO-534-80. Rev. final rept. (Unpublished study received Sep 1, 1981 under 352-403; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wil mington, Del.; CDL:245878-F) MRID 00083945. [MRID2004]

{Hoberman and Fieser 1980a} Hoberman AM; Fieser SE. 1980a. Dominant Lethal Evaluation in Rats. Project No. 201-539; HLO-789-80. Final rept. (Unpub lished study received Sep 1, 1981 under 352-403; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-D) MRID 00083944. [MRID2004]

{Hoberman and Fieser 1980b} Hoberman AM; Fieser S. 1980b. Dominant Lethal Evaluation in Rats. Project No. 201-539; HLO-789-80. Final rept. (Unpub lished study received Nov 13, 1981 under 352-404; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-P) MRID 00086829. [MRID2004]

{Hoberman et al. 1980} Hoberman AM; Wolfe GW; Durloo RS. 1980. Teratology Study in Rabbits. Project No. 201-536; HLO-534-80. Rev. final rept. (Unpublished study received Nov 13, 1981 under 352-404; pre pared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL: 070471-N) MRID 0008682. [MRID2004]

{Hoerger and Kenaga. 1972} Hoerger F; Kenaga EE. 1972. Pesticide residues on plants: Correlation of representative data as a basis for estimation of their magnitude in the environment. In: Environmental Quality and Safety, Volume I: Global Aspects of Toxicology and Technology as Applied to the Environment. F. Coulston and F. Kerte (eds.). Academic Press, New York, NY. pp. 9-28.[Std]

{HSDB 2006} HSDB (Hazardous Substances Database). Chlorsulfuron. Available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. Last revision date: 12/20/2006. [Set00]

{Hu et al. 2011} Hu T; He S; Yang G; Zeng H; Wang G; Chen Z; Huang X. 2011. Isolation and Characterization of a Rice Glutathione S-Transferase Gene Promoter Regulated by Herbicides and Hormones. Plant Cell Reports. 30(4):539-49. [Set01]

{Humphrey and Dykes 2008} Humphrey JAC; Dykes ES. 2008. Thermal energy conduction in a honey bee comb due to cell-heating bees. J Theoretical Biology. 250 (1): 194-208. [Std]

{Hunt 1981} Hunt OR. 1981. Metabolism of 14-C DPX-W4189 by Rats. Document No. AMR-5381. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-R) MRID 00086831. [MRID2004]

{Hutton 1992} Hutton D. 1992. Chronic Toxicity of DPX-W4189-94 to *Daphnia magna*. Supplement #1: Lab Project Number: 87-89. Unpublished study prepared by E.I. du Pont de Nemours and Co. 8 p. MRID 42309701. [MRID2004]

{Iivanainen and Heinonen-Tanski 1991} Iivanainen E; Heinonen-Tanski H. 1991. Degradation and leaching of chlorsulfuron in three different soils. Acta Agric Scand. 41 (1):85-92. [RA2004]

{IPCS/WHO 2010} International Programme on Chemical Safety/World Health Organization. 2010. The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2009. WHO, Geneva, Switzerland. Available at: http://www.who.int/ipcs/publications/pesticides_hazard_2009.pdf. [Std]

{Issaragrisil et al. 1997} Issaragrisil S; Kaufman DW; Anderson T; Chansung K; Thamprasit T; Sirijirachai J; Piankijagum A; Porapakkham Y; Vannasaeng S; Leaverton PE; Shapiro S; Young NS. 1997. Low drug attributability of aplastic anemia in Thailand. The Aplastic Anemia Study Group. Blood. 89(11): 4034-4039. [RA2004]

{James et al. 1999} James TK; Holland PT; Rahman A; Lu YR. 1999. Degradation of the sulfonylurea herbicides chlorsulfuron and triasulfuron in a high-organic-matter volcanic soil. Weed Res. 39 (2):137-147 [RA2004]

{Jander et al. 2003} Jander G; Baerson SR; Hudak JA; Gonzalez KA; Gruys KJ; Last RL. 2003. Ethylmethanesulfonate Saturation Mutagenesis in *Arabidopsis* to Determine Frequency of Herbicide Resistance. Plant Physiol. 131(1):139-46. [Set01]

{Jettner et al. 1999} Jettner RJ; Walker SR; Churchett JD; Blamey FPC; Adkins SW; Bell K. 1999. Plant sensitivity to atrazine and chlorsulfuron residues in a soil-free system. Weed Res. 39 (4):287-295. [RA2004]

{Joshi et al. 1985} Joshi MM; Brown HM; Romesser JA. 1985. Degradation of chlorsulfuron by soil microorganisms. Weed Sci. 33 (6):888-893. [RA2004]

{Joutel et al. 1996} Joutel A; Ducros A; Alamowitch S; Cruaudb C; Domengaa V; Maréchala E; Vahedic K; Chabriatc H; Bousserc MG; Tournier-Lasservea E. 1996. A human homolog of bacterial acetolactate synthase genes maps within the CADASIL critical region. Genomics. 38(2):192-198. (Cited in U.S. EPA/OPP 2015a) [Set03]

{Juhler et al. 2008} Juhler RK; Henriksen TH; Ernstsen V; Vinther FP; Rosenberg P. 2008. Impact of Basic Soil Parameters on Pesticide Disappearance Investigated by Multivariate Partial Least Square Regression and Statistics. Journal of Environmental Quality. 37(5):1719-32. [Set01]

{Julis 1980} Julis AJ. 1980. The Effect of DPX-4189 on Microorganisms and Microbial Populations of Soils. AMR-13-80. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-X) MRID 00035277. [MRID2004]

{Junnila et al. 1994} Junnila S; Heinonen-Tanski H; Ervio L-R; Laitinen P. 1994. Phytotoxic persistence and microbiological effects of chlorsulfuron and metsulfuron in Finnish soils. Weed Res. 34 (6):413-423. [RA2004]

{Juraske et al. 2008} Juraske R; Anton A; Castells F. 2008. Estimating half-lives of pesticides in/on vegetation for use in multimedia fate and exposure models. Chemosphere. 70(10): 1748-1755. [Set04]

{Kallqvist and Romstad 1994} Kallqvist T; Romstad R. 1994. Effects of agricultural pesticides on planktonic algae and cyanobacteria examples of interspecies sensitivity variations. Norwegian J Agric Sci Suppl. 0 (13):117-131. [RA2004/ECOTOX-16010]

{Kallqvist et al. 1994} Kallqvist T; Abdel-Hamid MI; Berge D. 1994. Effects of agricultural pesticides on freshwater plankton communities in enclosures. Norwegian J Agric Sci Suppl. 0 (13):133-152. [RA2004/ECOTOX-16006]

{Kaloumenos et al. 2011} Kaloumenos NS; Adamouli VN; Dordas CA; Eleftherohorinos IG. 2011. Corn Poppy (*Papaver rhoeas*) Cross-Resistance to ALS-Inhibiting Herbicides. Pest Management Science. 67(5):574-85. [Set01]

{Kalra and Gupta 2015} Kalra S; Gupta Y. 2015. Sulfonylureas. Journal of the Pakistan Medical Association. 65(1); 101-104. [Set03]

{Kalra et al. 2015} Kalra S; Aamir AH; Raza A; et al. 2015. Place of sulfonylureas in the management of type 2 diabetes mellitus in South Asia: A consensus statement. Indian Journal of Endocrinology and Metabolism. Indian Journal of Endocrinology and Metabolism. 19(5): 577-596. [Set03]

{Kashian and Dodson 2002} Kashian DR; Dodson SI. 2002. Effects of Common-Use Pesticides on Developmental and Reproductive Processes in *Daphnia*. Toxicology and Environmental Health. 18(5): 225-235. [ECOTOX-93397]

{Kaushik et al. 2006} Kaushik S; Inderjit; Streibig JC; Cedergreen N. 2006. Activities of Mixtures of Soil-Applied Herbicides with Different Molecular Targets. Pest Management Science. 62(11):1092-7. [Set01]

{Kegley et al. 2014} Kegley SE; Hill BR; Orme S; Choi AH. XXXXXXXX: PAN Pesticide Database, Pesticide Action Network, North America (Oakland, CA, 2014), http://www.pesticideinfo.org . © 2000-2014 Pesticide Action Network, North America. All rights reserved. [Set00]

{Kjaer and Elmegaard 1996} Kjaer C; Elmegaard N. 1996. Effect of herbicide treatment on host plant quality for a leaf-eating beetle. Pestic Sci. 47 (4):319-325. [RA2004]

{Kjaer and Heimbach 2001} Kjaer C; Heimbach U. 2001. Relationships between sulfonylurea herbicide treatment of host plants and the performance of herbivorous insects. Pest Manag Sci. 57 (12):1161-1166. [RA2004]

{Klemens and Orescan 1995} Klemens A; Orescan D. 1995. Residues of Chlorsulfuron in Weat Grain and Its Processed Fractions Following Application of Glean Herbicide. Supplement No. 1: Lab Project Number: AMR/2221/92: GLE/2221/92: 92/P1510. Unpublished study prepared by DuPont Experimental Station. MRID 43507501. [MIRD2004]

{Klemens and Tomic 1993} Klemens A; Tomic D. 1993. Residues of Chlorsulfuron in Wheat Grain and its Processed Fractions Following Application of Glean Herbicide. Lab Project Number: AMR 2221-92: GLE-2221-92: 92-P1510. Unpublished study prepared by E.I. du Pont de Nemours and Co.; Engineering Biosciences. MRID 42900601. [MIRD2004]

{Klemens et al. 1995} Klemens A; Oranzi D; Croes R et al. 1995. Magnitude of Residues of Chlorsulfuron in Wheat Following Application of Glean FC Herbicide at Maximum Label Rates. Lab Project Number: AMR/2570/93. Unpublished study prepared by E.I. du Pont de Nemours and Co. 239 p. MRID 43767301. [MIRD2004]

{Kolkman et al. 2004} Kolkman JM; Slabaugh MB; Bruniard JM; Berry S; Bushman BS; Olungu C; Maes N; Abratti G; Zambelli A; Miller JF; Leon A; Knapp SJ. 2004. Acetohydroxyacid Synthase Mutations Conferring Resistance to Imidazolinone or Sulfonylurea Herbicides in Sunflower. Theoretical and Applied Genetics. 109(6):1147-59. [Set01]

{Kotoula-Syka et al. 1993a} Kotoula-Syka E; Eleftherohorinos IG; Gagianas AA; Sficas AG. 1993a. Persistence of preemergence applications of chlorsulfuron, metsulfuron, triasulfuron, and tribenuron in three soils in Greece. Weed Sci. 41 (2):246-250. [RA2004]

{Krahn and Waterer 1980a} Krahn DF; Waterer JC. 1980a. Chinese Hamster Ovary Cell Assay for Mutagenicity. Haskell Laboratory Report No. 475-80. Rev. (Unpublished study received Sep 1, 1981 under 352-403; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 245878-C) MRID 00083943. [MRID2004]

{Krahn and Waterer 1980b} Krahn DF; Waterer JC. 1980b. Chinese Hamster Ovary Cell Assay for Mutagenicity. Haskell Laboratory Report No. 475-80. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-O) MRID 00086828. [MRID2004]

{Kuk and Bugos 2007} Kuk YI; Bugos NR. 2007. Cross-Resistance Profile of Mesosulfuron-Methyl-Resistant Italian Ryegrass in the Southern United States. Pest Management Science. 63(4):349-57. [Set01]

{Larney et al. 1999} Larney FJ; Cessna AJ; Bullock MS. 1999. Herbicide transport on wind-eroded sediment. Journal of Environmental Quality. 28(5): 1412-1421. [Std]

{Lee 1992} Lee P. 1992. Metabolic Fate of Chlorsulfuron in Wheat and Barley. Lab Project Number: AMR 2263-91. Unpublished study prepared by E. I. du Pont de Nemours and Co. 65 p. MRID 42248701. [MRID2004]

{Lu et al. 2007} Lu YQ; Baker J; Preston C. 2007. The Spread of Resistance to Acetolactate Synthase Inhibiting Herbicides in a Wind Borne, Self-Pollinated Weed Species, *Lactuca serriola* L. Theoretical and Applied Genetics. 115(4):443-50. [Set01]

{Ma et al. 2002} Ma J; Xu L; Wang S. 2002. A Quick, Simple, and Accurate Method of Screening Herbicide Activity Using Green Algae Cell Suspension Cultures. Weed Science. 50(5): 555-559. [Std-Compendia/ECOTOX-158793]

{Mallory-Smith and Retzinger 2003} Mallory-Smith CA; Retzinger J. 2003. Revised Classification of Herbicides by Site of Action for Weed Resistance Management Strategies. Weed Technology. 17: 605-619. [Std]

{Marrs et al. 1989} Marrs RH; Williams CT; Frost AJ; Plant RA. 1989. Assessment of the effects of herbicide spray drift on a range of plant species of conservation interest. Environ Pollut. 59 (1):71-86 . [RA2004]

{McCourt et al. 2005} McCourt JA; Pang SS; Guddat LW; Duggleby RG. 2005. Elucidating the Specificity of Binding of Sulfonylurea Herbicides to Acetohydroxyacid Synthase. Biochemistry. 44(7):2330-8. [Set01]

{McKelvey and Kuratle 1991} McKelvey R; Kuratle H. 1991. Influence of Chlorsulfuron on Seed Germination, Seedling Emergence and Vegetative Vigor of Several Terrestrial Plants. Lab Project Number: AMR 2070-91. Unpublished study prepared by E.I. du Pont de Nemours and Co. 235 p. MRID 42201001 . [MRID2004]

{McKelvey and Kuratle 1992} McKelvey R; Kuratle H. 1992. Influence of Chlorsulfuron on Seed Germination, Seedling Emergence, and Vegetative Vigor of Several Terrestrial Plants. Revision No. 1. Lab Project Number: AMR 2070-91. Unpublished study prepared by E.I. du Pont de Nemours and Co. 235 p. MRID 42587201. [MRID2004]

{Melander et al. 1989} Melander A; Bitzen P-O; Faber O; Groop L. 1989. Sulphonylurea antidiabetic drups: An update of their clinical pharmacology and rational therapeutic use. Drugs. 37: 58-72. [RA2004]

{Mersie and Foy 1986} Mersie W; Foy CL. 1986. Adsorption desorption and mobility of chlorsulfuron in soils. J Agric Food Chem. 34 (1):89-92. [RA2004]

{Michel et al. 2004} Michel A; Johnson RD: Duke SO; Scheffler BE. 2004. Dose-Response Relationships Between Herbicides with Different Modes of Action and Growth of *Lemna paucicostata*: An Improved Ecotoxicological Method. Environmental Toxicology and Chemistry. 23(4): 1074-1079. [ECOTOX-72796]

{Moore and Elliott 1989} Moore JH; Elliott JF. 1989. Wine grapevine tolerance to chlorsulfuron and metsulfuron methyl herbicides. Plant Prot Q. 4 (3):100-103. [RA2004]

{Moyer 1995} Moyer JR. 1995. Sulfonylurea herbicide effects on following crops. Weed Technol. 9 (2):373-379. [RA2004]

{Moyer et al. 1989} Moyer JR; Bergen P; Kozub GC. 1989. Chlorsulfuron persistence and response of legumes in an alkaline soil. J Environ Sci Health B. 24 (1):37-56. [RA2004]

{Moyer et al. 1990a} Moyer JR; Esau R; Kozub GC. 1990a. Chlorsulfuron persistence and response of nine rotational crops in alkaline soils of southern Alberta (Canada). Weed Technol. 4 (3):543-548. [RA2004]

{Moyer et al. 1990b} Moyer JR; Hironaka R; Kozub GC; Bergen P. 1990b. Effect of herbicide treatments on dandelion, alfalfa and sainfoin yields and quality. Can J Plant Sci. 70 (4):1105-1114. [RA2004]

{Mylchreest 2005} Mylchreest, E. (2005) Chlorsulfuron (DPX-W4189) Technical: Multigeneration Reproduction Study in Rats. DuPont Haskell Laboratory for Health and Environmental; Sciences. Project No. DUPONT.13495, 14601, 904. September 11, 2003 – June 4, 2004. MRID 46493201. Unpublished. (As summarized in EPA Data Evaluation Record). Available at: https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/118601/118601.htm. [E-Docket03]

{Nagy 1987} Nagy KA. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecol. Monogr. 57: 111-128. [Std]

{Nagy 2005} Nagy KA. 2005. Field metabolic rate and body size. Journal of Experimental Biology. 208: 1621-1625. [Std]

{NAS 2013} NAS (National Academy of Sciences). 2013. Assessing Risks to Endangered and Threatened Species from Pesticides. Committee on Ecological Risk Assessment under FIFRA and ESA, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies, National Research Council. International Standard Book Number-13: 978-0-309-28583-4. 194 pp. [Std]

{Nystrom et al. 1999} Nystrom B; Bjornsater B; Blanck H. 1999. Effects of sulfonylurea herbicides on non-target aquatic micro-organisms: Growth inhibition of micro-algae and short-term inhibition of adenine and thymidine incorporation in periphyton communities. Aquatic Toxicology. 47 (1):9-22. [Set02/RA2004]

{Obrigawitch et al. 1998} Obrigawitch TT; Cook G; Wetherington J. 1998. Assessment of effects on non-target plants from sulfonylurea herbicides using field approaches. Pestic Sci. 52 (3):199-217. [RA2004]

{Olofsdotter et al. 1994} Olofsdotter M; Olesen A; Andersen SB; Streibig JC. 1994. A comparison of herbicide bioassays in cell cultures and whole plants. Weed Res. 34 (6):387-394. [RA2004]

{Orcaray et al. 2010} Orcaray L; Igal M; Marino D; Zabalza A; Royuela M. 2010. The Possible Role of Quinate in the Mode of Action of Glyphosate and Acetolactate Synthase Inhibitors. Pest Management Science. 66(3):262-9. [Set01]

{Orcaray et al. 2011} Orcaray L; Igal M; Zabalza A; Royuela M. 2011. Role of Exogenously Supplied Ferulic and p-Coumaric Acids in Mimicking the Mode of Action of Acetolactate Synthase Inhibiting Herbicides. Journal of Agricultural and Food Chemistry. 59(18):10162-8. [Set01]

{Padilla et al. 2012} PadillaS; Corum D; Padnos B; et al. 2012. Zebrafish Developmental Screening of the ToxCast Phase I Chemical Library. Reproductive Toxicology. 33(2): 174-187. [ECOTOX-161191]

{Patric 1976} Patric JH. 1976. Soil Erosion in the Eastern Forest. Journal of Forestry. 74(10): 671-677. [Std]

{Pauli et al. 2000} Pauli BD; Perrault JA; Money SL. 2000. RATL: A Database of Reptile and Amphibian Toxicology Literature. National Wildlife Research Centre 2000, Canadian Wildlife Service, Environmental Conservation Branch, Technical Report Series Number 357. Available at: http://publications.gc.ca/Collection/CW69-5-357E.pdf. [Std]

{Peterson et al. 1994} Peterson HG; Boutin C; Martin PA; Freemark KE; Ruecker NJ; Moody MJ. 1994. Aquatic phyto-toxicity of 23 pesticides applied at expected environmental concentrations. Aquat Toxicol. 28 (3-4):275-292. [RA2004/ECOTOX-13800]

{Petit et al. 1997} Petit F; le Goff P; Cravedi J-P; Valotaire Y; Pakdel F. 1997. Two complementary bioassays for screening the estrogenic potency of xenobiotics: Recombinant yeast for trout estrogen receptor and trout hepatocyte cultures. J Mol Endocrinol. 19 (3):321-335. [RA2004]

{Pierson 1991} Pierson K. 1991. Flow-Through 77 Day Toxicity of DPX-W4189-170 to Embryo and Larval Rainbow Trout, Oncorhynchus mykiss. Lab Project Number: 494-91: MR-4581-866. Unpublished study prepared by E.I. du Pont de Nemours and Co. 471 p. MRID 41976405 . [MRID2004]

{Plowchalk 1994} Plowchalk D. 1994. Metabolism of (carbon 14)-Chlorsulfuron in the Lactating Goat. Lab Project Number: 9517-001: 258-94. Unpublished study prepared by Du Pont. MRID 43388401 . [MRID2004]

{Posthuma et al. 2002} Posthuma L; Suter GW; Trass TP. 2002. Species Sensitivity Distributions. Lewis Publishers, Boca Raton, Florida, 587 pp. Available at: http://www.crcnetbase.com/isbn/9781420032314 . [Std]

{Priester 1991a} Priester T. 1991a. Aerobic Soil Metabolism of Chlorsulfuron. Lab Project Number: AMR 2213-91. Unpublished study prepared by E.I. du Pont de Nemours and Co. 305 p. MRID 42214201. [MRID2004]

{Priester 1991b} Priester T. 1991b. Fish Accumulation Potential for Chlorsulfuron. Lab Project Number: AMR 2238-91. Unpublished study prepared by E. I. du Pont de Nemours & Co. 61 p. MRID 42214204 [MRID2004]

{Quaranta et al. 2009} Quaranta A; Bellantuono V; Cassano G: Lippe C. 2009. Why Amphibians Are More Sensitive than Mammals to Xenobiotics. PLoS ONE. 4: (11): 1-4. [Std]

{Rapisarda 1965} Rapisarda C. 1965. Microbial Degradation of 14C-Phenyl Labeled DPX-4189 in Soil. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wil mington, Del.; CDL:099462-V) MRID 00035275. [MRID2004]

{Rapisarda 1981a} Rapisarda C. 1981a. Microbial Degradation of 14-C DPX-4189 in Soil. Document No. AMR-43-81. (Unpublished study received Sep 1, 1981 under 352-403; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:245878-K) MRID 00083950. [MRID2004]

{Rapisarda 1981b} Rapisarda C. 1981b. Microbial Degradation of 14-C DPX-4189 in Soil. Document No. AMR-43-81. (Unpublished study received Nov 13, 1981 under 352-404; prepared in cooperation with Univ. of Delaware, College of Agricultural Sciences, submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-J) MRID 00086814. [MRID2004]

{Rapisarda 1981c} Rapisarda C. 1981c. Rotational Crop Studies with ^14 C-Pehnyl Labeled DPX-W4189 in the Greenhouse. Document No. AMR-49-81. (Unpublished study received Nov 13, 1981 under 352-404; prepared in cooperation with Univ. of Delaware, College of Agricultural Sciences, submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-O). [MRID2004]

{Rapisarda et al. 1978} Rapisarda C; Shrivastava SP; Butler LD. 1978. Physical Properties of DPX-4189: Octanol/Water Partition Ratio, Solubilities, and Soil Absorption Data. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-R) MRID 00035271. [MRID2004]

{Ravelli et al. 1997} Ravelli A; Pantani O; Calamai L; Fusi P. 1997. Rates of chlorsulfuron degradation in three Brazilian oxisols. Weed Res. 37 (1):51-59. [RA2004]

{Reichle et al. 1973} Reichle DE, Goldstein RA; Van Hook RI; Dodson DJ. 1973. Analysis of Insect Consumption in a Forest Canopy. Ecology. 54: 1076-1084. [Std]

{Reid 2006} Reid FA. 2006. A Field Guide to Mammals of North America North of Mexico. Fourth Edition. The Peterson Field Guide Series. Houghton Mifflin Company, Boston MA. 570 pp. [Std]

{Rhodes 1994} Rhodes B. 1994. Terrestrial Field Soil Dissipation of (carbon 14)-Chlorsulfuron. Lab Project Number: AMR 2266-91. Unpublished Study Prepared by DuPont Agricultural products and University of Idaho. 99 p. MRID 43421401. [MRID2004]

{Rhodes 1995} Rhodes B. 1995. Metabolism of Chlorsulfuron in Laying Hens: Supplement No. 1: Part B: Sample Analysis and Metabolite Identification. Lab Project Number: AMR 2193-91. Unpublished study prepared by DuPont Agricultural Products. 36 p. MRID 43600801. [MRID2004]

{Ribo 1988} Ribo JM. 1988. The octanol-water partition coefficient of the herbicide chlorsulfuron as a function of pH. Chemosphere. 17 (4):709-716. [RA2004]

{Rogers et al. 1978} Rogers AS; Culik R; Matarese CM; et al. 1978. Teratological Study of 2-Chloro-N- (4-methoxy-6-methyl-1,3,5-triazin-2-yl) aminocarbonyl benzenesulfonamide (INW-4189) in Rats. Report No. 583-78. (Unpublished study received Jun 16, 1980 under 352EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099461-E) MRID 00031424. [RA2004]

{Roux et al. 2005} Roux F; Camilleri C; B,rard A; Reboud X. 2005. Multigenerational Versus Single Generation Studies to Estimate Herbicide Resistance Fitness Cost in *Arabidopsis thaliana*. Evolution. 59(10):2264-9. [Set01]

{Rovesti and Deseo 1990} Rovesti L; Deseo KV. 1990. Compatibility of chemical pesticides with the entomopathogenic nematodes: Steinernema carpocapsae Weiser and Steinernema feltiae Filipjev (Nematoda: Steinernematidae). Nematologica. 36 (2):237-245. [RA2004]

{Russell 1977} Russell JF Jr. 1977. Mutagenic Activity of Benzenesulfonamide, 2-Chloro-N- (4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl - in the Salmonella/Microsome Assay. Report No. 121-77. (Unpublished study received Jun 16, 1980 under 352-EX-105; submit ted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 099461-F) MRID 00031425. [MRID2004]

{Ryberg et al. 2011} Ryberg KR; Vecchia AV; Martin JD; Gilliom RJ. 2011. Trends in Pesticide Concentrations in Urban Streams in the United States, 1992–2008. USGS National Water-Quality Assessment Program. Available at: https://pubs.usgs.gov/sir/2010/5139/. [Std]

{Saari et al. 1990} Saari LL; Cotterman JC; Primiani MM. 1990. Mechanism of sulfonylurea herbicide resistance in the broadleaf wee, *Kochia scoparia*. Plant Physiology. 93: 55-61. [Set04]

{Sabater and Carrasco 1997} Sabater C; Carrasco JM. 1997. Effects of chlorsulfuron on growth of three freshwater species of phytoplankton. Bull Environ Contam Toxicol. 58 (5):807-813. [RA2004/ECOTOX-17988]

{Sala et al. 2008} Sala CA; Bulos M; Echarte M; Whitt SR; Ascenzi R. 2008. Molecular and Biochemical Characterization of An Induced Mutation Conferring Imidazolinone Resistance in Sunflower. Theoretical and Applied Genetics. 118(1):105-12. [Set01]

{Sarmah et al. 1998} Sarmah AK; Kookana RS; Alston AM. 1998. Fate and behaviour of triasulfuron, metsulfuron-methyl, and chlorsulfuron in the Australian soil environment: A review. Aust J Agric Res. 49 (5):775-790. [RA2004]

{Sarmah et al. 1999} Sarmah AK; Kookana RS; Alston AM. 1999. Degradation of chlorsulfuron and triasulfuron in alkaline soils under laboratory conditions. Weed Res. 39 (2):83-94. [RA2004]

{Sarmah et al. 2000} Sarmah AK; Kookana RS; Duffy MJ; Alston AM; Harch BD. 2000. Hydrolysis of triasulfuron, metsulfuron-methyl and chlorsulfuron in alkaline soil and aqueous solutions. Pest Management Science. 56: 463-471. [Set02/RA2004]

{Schmuckler 1992} Schmuckler M. 1992. Determination of the Water Solubility of Chlorsulfuron. W4189 (Revision): Lab Project Number: W4189.B. Unpublished study prepared by E.I. du Pont de Nemours and Co. 27 p. MRID 42454104. [MRID2004]

{Schmuckler and Moore 1992} Schmuckler M; Moore L. 1992. Physical and Chemical Characteristics of Chlorsulfuron. Lab Project Number: AMR 2370-92. Unpublished study prepared by E. I. du Pont de Nemours and Co. 25 p. MRID 42454102. [MRID2004]

{Schneider et al. 1980} Schneider PW Jr; Smith LW; Barnes JR; et al. 1980. Six Month Feeding Study in Dogs with 2-Chloro-N- (4-methoxy-6-meth yl-1,3,5-triazin-2-yl)aminocarbonyl benzenesulfonamide (INW 4189). Report No. 108-80. Final rept. (Unpublished study including pathology report no. 53-79, received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099461-A) MRID 00031420. [MRID2004]

{Scott 1996} Scott JG. 1996. Inhibitors of CYP6D1 in house fly microsomes. Insect Biochem Mol Biol. 26 (7):645-649. [RA2004]

{SERA 2004a} SERA (Syracuse Environmental Research Associates, Inc.). 2004a. Chlorsulfuron, Human Health and Ecological Risk Assessment – Final Report. SERA TR 04-43-18-01c. Report dated November 21, 2004. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2004b} SERA (Syracuse Environmental Research Associates, Inc.). 2004b. Metsulfuron methyl, Human Health and Ecological Risk Assessment – Final Report. SERA TR 04-43-17-01c. Report dated December 9, 2004. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2004c} SERA (Syracuse Environmental Research Associates, Inc.). 2004c. Sulfometuron methyl, Human Health and Ecological Risk Assessment – Final Report. SERA TR 03-43-17-02c. Report dated December 14, 2004. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2007a} SERA (Syracuse Environmental Research Associates, Inc.). 2007a. Gleams-Driver User Guide (Version 1.8). SERA TR 07-52-05-08a. Report dated December 31, 2007. [Std]

{SERA 2007b} SERA (Syracuse Environmental Research Associates, Inc.). 2007b. Aminopyralid Human Health and Ecological Risk Assessment – FINAL REPORT. SERA TR-052-04-04a. Report dated June 28, 2007. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2009} SERA (Syracuse Environmental Research Associates, Inc.). 2009. Technical Comparison of EPA, BLM and Forest Service Pesticide Risk Assessments, Final Report. SERA TR-052-19-02. Report dated July 29, 2009. Available at: http://www.fs.fed.us/foresthealth/pesticide/pdfs/SERA_TR-052-19-02_Risk_Comparison.pdf. [Std]

{SERA 2010} SERA (Syracuse Environmental Research Associates, Inc.). 2010. Glyphosate, Human Health and Ecological Risk Assessment, Final Report. SERA TR-052-22-03a. Document dated November 29, 2010. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2011b} SERA (Syracuse Environmental Research Associates, Inc.). 2011b. Memorandum on Release of Gleams-Driver 1.9.3. Memo dated November 6, 2011. Available at: www.sera-inc.com. [Std]

{SERA 2014a} SERA (Syracuse Environmental Research Associates, Inc.). 2014a. Preparation of Environmental Documentation and Risk Assessments, SERA MD-2014-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. [Std]

{SERA 2014b} SERA (Syracuse Environmental Research Associates, Inc.). 2014b. Reassessment of Worker Exposure Rates – FINAL REPORT. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2014c} SERA (Syracuse Environmental Research Associates, Inc.). 2014c. Scoping/Screening Level Risk Assessment on Clethodim: Final Report. SERA TR-056-08-02b. Document dated October 30, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std]

{SERA 2016a} SERA (Syracuse Environmental Research Associates, Inc.). 2016a. WorksheetMaker Version 6.01, User Guide. SERA MD-2016-WSM-01b. Document dated July 29, 2016. Syracuse Environmental Research Associates, Inc. [Std]

{Shrivastava 1979} Shrivastava SP. 1979. Metabolism of 14C-DPX-4189 in Rats. Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL: 099461-G. MRID 00031426. [MRID2004]

{Silber 1980} Silber LS. 1980. Eye Irritation in Rabbits--EPA Pesticide Registration. Report No. 130-80. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-J) MRID 00031415. [MRID2004]

{Silber and Dashiell 1980} Silber LS; Dashiell OL. 1980. Acute Skin Absorption LD_{50} Test on Rabbits (EPA Pesticide Registration Guidelines). Report No. 211-80. (Unpublished study received Jun 16, 1980 under 352EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-G) MRID 00031412. [MRID2004]

{Slates and Moore 1981} Slates RV; Moore DW II. 1981. Fate of DPX-W4189 Ingested by Dairy Cattle. Document No. AMR-48-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070471-Z) MRID 00086838. [MRID2004]

{Slavov et al. 2005} Slavov S; Valkov V; Batchvarova R; Atanassova S; Alexandrova M; Atanassov A. 2005. Chlorsulfuron Resistant Transgenic Tobacco as a Tool for Broomrape Control. Transgenic Research. 14(3):273-8. [Set01]

{Smith 1979a} Smith EJ. 1979a. 96-Hour LC50 to Bluegill Sunfish. Haskell Laboratory Report No. 385-79. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-D) MRID 00035258. [MRID2004]

{Smith 1979b} Smith EJ. 1979b. 96-Hour LC50 to Bluegill Sunfish. Haskell Laboratory Report No. 386-79. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-E) MRID 00035259. [MRID2004]

{Smith 1979c} Smith EJ. 1979c. 96-Hour LC50 to Fathead Minnows. Haskell Laboratory Report No. 384-79. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-F) MRID 00035260. [MRID2004]

{Smith 1979d} Smith EJ. 1979d. 96-Hour LC50 to Channel Catfish. Haskell Laboratory Report No. 856-79. (Unpublished study received Jun 16, 1980 under 352-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099462-G) MRID 00035261. [MRID2004]

{Smith 1986} Smith AE. 1986. Persistence of the herbicides carbon-14 chlorsulfuron and carbon-14 metsulfuron-methyl in prairie soils under laboratory conditions. Bull Environ Contam Toxicol. 37 (5):698-704. [RA2004]

{Smith et al. 1980} Smith LW; Kaplan AM; Gibson JR; et al. 1980. Ninety-Day Range-Finding Feeding Study with 2-Chloro-N- (4-methoxy-6-meth yl-1,3,5-triazin-2-yl)aminocarbonyl benzenesulfonamide (INW 4189) in Mice. Report No. 69-80. (Unpublished study including pathology report no. 55-78, received Jun 16, 1980 under 352-EX 105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099461-B) MRID 00031421. [MRID2004]

{Sohlstrom et al. 1998} Sohlstrom A; Katsman A; Kind KL; Grant PA; Owens PC; Robinson JS; Owens JA. 1998. Effects of acute and chronic food restriction on the insulin-like growth factor axis in the guinea pig. Journal of Endocrinology. 157: 107–114. [Std]

{Song et al. 2013} Song J; Gu J; Zhai Y; Wu W; Wang H; Ruan Z; Shi Y; Yan Y. 2013. Biodegradation of nicosulfuron by a *Talaromyces flavus* LZM1. Bioresource Technology. 140:243-8. [Set01]

{Sorensen et al. 1998} Sorensen PB; Mogensen BB; Gyldenkaerne S; Rasmussen AG. 1998. Pesticide leaching assessment method for ranking both single substances and scenarios of multiple substance use. Chemosphere. 36 (10):2251-2276. [RA2004]

{Stork 1995} Stork PR. 1995. Field leaching and degradation of soil applied herbicides in a gradationally textured alkaline soil: Chlorsulfuron and triasulfuron. Aust J Agric Res. 46 (7):1445-1458 . [RA2004]

{Strek 1998a} Strek HJ. 1998a. Fate of chlorsulfuron in the environment. 1. Laboratory evaluations. Pestic Sci. 53 (1):29-51. [RA2004]

{Strek 1998b} Strek HJ. 1998b. Fate of chlorsulfuron in the environment. 2. Field evaluations. Pestic Sci. 53 (1):52-70. [RA2004]

{Strek and Spaan 1997} Strek G; Spaan WP. 1997. Wind erosion control with crop residues in the Sahel. Soil Sci. Soc. Am. J. 61(3): 911-917. [Std]

{Strek and Stein 1997} Strek G; Stein A. 1997. Mapping wind-blown mass transport by modeling variability in space and time. Soil Sci. Soc. Am. J. 61(1): 232-239. [Std]

{Stry 2001} Stry J. 2001. Magnitude of Residues of Chlorsulfuron in Pasture Grasses Following Application of Chlorsulfuron Herbicide at Maximum Label Rates. Lab Project Number: 46352: 4046: DUPONT-4046. Unpublished study prepared by E.I. du Pont de Nemours and Company. 107 p. MRID 45630001. [MRID2004]

{Technology Sciences Group 2014} Technology Sciences Group. 2014. Request for Reconsideration to Delist. Letter to California EPA dated February 25, 2014. [Set00]

{Teske et al. 2002} Teske ME; Bird SL; Esterly DM; Ray SL; Perry SG. 2002. A User's Guide for AgDRIFT 2.0.05: A Tiered Approach for the Assessment of Spray Drift. Continuum Dynamics, Inc. Public Use Version. C.D.I. Report No. 01-02. Report dated January 2002.

{Thongsinthusak et al. 1999} Thongsinthusak T; Ross JH; Dong MH. 1999. Significance of Dermal Dose Levels in Dermal Absorption Studies of Pesticides. California Environmental Protection Agency, HS – 1801 December 15, 1999. Available at: http://www.cdpr.ca.gov/docs/whs/pdf/hs1801.pdf. [Std]

{Tomlin 2003} Tomlin C. 2003. E-Pesticide Manual, Version 3.1. BCPC Publications. Available at: http://www.bcpcbookshop.co.uk. [RA2004]

{Trivits 1979} Trivits RL. 1979. Oral LD50 Test in Fasted Male and Female Rats. Report No. 399-79. (Unpublished study received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-A) MRID 00031406. [MRID2004]

{Tucker and Hirsch 1972} Tucker HS; Hirsch JI. 1972. Sulfonamide-Sulfonylurea Interaction. New England Journal of Medicine. 286: 110-111. [Set03]

{Turgut et al. 2003} Turgut C; Grezichen A; Fomin A. 2003. Toxicity of Sulfonylurea Herbicides to Dicotyledonous Macrophyte *Myriophyllum aquaticum* in a 14 Day Bioassay. Fresenius Environmental Bulletin. 12(6): 619-622. [ECOTOX-81879]

{U.S. EPA 2002} U.S. EPA (United States Environmental Protection Agency). 2002. Chlorsulfuron; Pesticide Tolerance. Federal Register. 67(157): 52866-52873. Available at: https://www.federalregister.gov/. [RA2004]

{U.S. EPA 2012} U.S. EPA (U.S. Environmental Protection Agency). 2012. Benchmark Dose Technical Guidance, EPA/100/R-12/01. Document dated June 2012. Risk Assessment Forum Available from: https://www.epa.gov/sites/production/files/2015-01/documents/benchmark_dose_guidance.pdf [Std]

{U.S. EPA 2016} U.S. EPA (U.S. Environmental Protection Agency). 2016. U.S. Environmental Protection Agency Endocrine Disruptor Screening Program, Tier 1 Assessments. Available at: https://www.epa.gov/ingredients-used-pesticide-products/endocrine-disruptor-screening-program-tier-1-assessments. [Std]

{U.S. EPA/NCEA 1987} U.S. EPA (U.S. Environmental Protection Agency/National Center for Environmental Assessment). 1987. Integrated Risk Information System (IRIS) entry for chlorsulfuron (Archived). Available at: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0027_summary.pdf. [Std]

{U.S. EPA/NCEA 1997} U.S. EPA (U.S. Environmental Protection Agency/National Center for Environmental Assessment). 1997. Exposure Factors Handbook. National Center for Environmental Assessment, U.S. EPA, Washington, DC. Available at: https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NCEA&direntryid=12464 [Std]

{U.S. EPA/OCSPP 2015} U.S. EPA/OCSPP (U.S. Environmental Protection Agency/ Office of Chemical Safety and Pollution Prevention). 2015. OCSPP Harmonized Test Guidelines – Master List. Last Updated November, 2015. Available at: https://www.epa.gov/sites/production/files/2015-11/documents/ocspp-testguidelines_masterlist-2015-11-19.pdf. [Std]

{U.S. EPA/OPP 2005a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2005a. Reregistration Eligibility Decision for Chlorsulfuron. Document dated May 20, 2005. Available at: https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_PC-118601_20-May-05.pdf. [E-Docket01]

{U.S. EPA/OPP 2005b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2005b. R.E.D. FACTS: Chlorsulfuron. http://archive.epa.gov/pesticides/reregistration/web/pdf/chlorsulfuron_factsheet.pdf. [E-Docket01]

{U.S. EPA/OPP 2007a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2007a. Chlorsulfuron: Waiver Requests: 21-Day Dermal Toxicity Study (DB Barcode 0313364) and Subchronic Inhalation Toxicity Study (DB Barcode D31336.5). Document dated June 14, 2007. [ClrRev]

{U.S. EPA/OPP 2008} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2008. FQPA Index Reservoir Screening Tool, Version 1.1.1. March 26, 2008. [Std]

{U.S. EPA/OPP 2012a U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2012a. BEAD Chemical Profile for Registration Review: Chlorsulfuron (118601). Document dated June 25, 2012. [E-Docket02]

{U.S. EPA/OPP 2012b U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2012b. Chlorsulfuron (118601) Screening Level Usage Analysis (SLUA). Document dated May 3, 2012. [E-Docket02]

{U.S. EPA/OPP 2013a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2013a. Chlorsulfuron Final Work Plan, Registration Review, Case Number 0631. Document dated May 21, 2013. [E-Docket02]

{U.S. EPA/OPP 2013b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2013b. Chlorsulfuron; Community Right-to-Know Toxic Chemical Release Reporting. Federal Register. 78 (236): 73787-73793. [E-Docket03]

{U.S. EPA/OPP 2015a} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2015a. Sulfonylureas: Screening Analysis of Toxicological Profiles to Consider Whether a Candidate Common Mechanism Group Can Be Established. Document dated September 9, 2015. [E-Docket02]

{U.S. EPA/OPP 2015b} U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 2015b. Label Review Manual. Updated 2015. Available at: http://www2.epa.gov/sites/production/files/2015-08/documents/lrm-chap1-18-aug-2015.pdf. [Std]

{U.S. EPA/OPP/EFED 2001} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2001. Ecological Risk Assessor Orientation Package, Draft Version August 2001, Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. [Std]

{U.S. EPA/OPP/EFED 2002a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2002a. Drinking Water Assessment to Support TRED for Chlorsulfuron. Document dated June 25, 2002. Appendix 8 in U.S. EPA/OPP/EFED 2004a. [E-Docket01]

{U.S. EPA/OPP/EFED 2004a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2004a. Ecological Risk Assessment in Support of the Reregistration Eligibility Decision for Chlorsulfuron. Document dated September 10, 2004. [E-Docket01]

{U.S. EPA/OPP/EFED 2004b} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2004b. Revised assessment of risk to non-target plants associated with chlorsulfuron spray drift. Document dated July 27, 2004. [E-Docket01]

{U.S. EPA/OPP/EFED 2012a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2012a. Registration Review - Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Chlorsulfuron (PC Code 118601; DP Barcode D403354). Document dated Nov. 15, 2012. [E-Docket02]

{U.S. EPA/OPP/EFED 2015a} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2015a. Preliminary Ecological Risk Assessment for Registration Review of 22 Sulfonylurea Herbicides. Document dated August 26, 2015. [E-Docket02]

{U.S. EPA/OPP/EFED 2015b} U.S. EPA/OPP/EFED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Environmental Fate and Effects Division). 2015b. Drinking Water Exposure Assessment for the Registration Review of 22 Sulfonylurea Herbicides. Document dated August 12, 2015. [E-Docket02]

{U.S. EPA/OPP/HED 2002a} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2002a. Chlorsulfuron: Occupational and Residential Exposure and Risk Assessment/Characterization for Reregistration Eligibility Decision Document and the Proposed use on Pasture and Rangeland Grasses. Document dated July 1, 2002. [E-Docket01]

{U.S. EPA/OPP/HED 2002b} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2002a. Toxicology Chapter for Chlorsulfuron. Document dated July 17, 2002. [ClrRev]

{U.S. EPA/OPP/HED 2012a} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2012a. Chlorsulfuron: Registration Review Scoping Document for Human Health Assessments. Document dated December 6, 2012. [E-Docket02]

{U.S. EPA/OPP/HED 2012b} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2012b. Chlorsulfuron: Review of Human Incidents. Document dated July 31, 2012. [E-Docket02]

{U.S. EPA/OPP/HED 2013a} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2013a. Sulfonylureas: Summary of Hazard and Science Policy Council (HASPOC) Meeting on July 18,2013: Recommendations on Data Requirement for Immunotoxicity Studies for Sulfonylurea Pesticides. Document dated August 6, 2013. [E-Docket02]

{U.S. EPA/OPP/HED 2015a} U.S. EPA/OPP/HED (U.S. Environmental Protection Agency/Office of Pesticide Programs/Health Effects Division). 2015a. Chlorsulfuron. Draft Human Health Risk Assessment in Support of Registration Review. Document dated Sepember 4, 2015. [E-Docket02]

{U.S. EPA/OPPTS 1998a} U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxic Substances). 1998a. Health Effects Test Guidelines, OPPTS 870.7485, Metabolism and Pharmacokinetics. EPA 712–C–98–244. Document dated August 1998. Available at: http://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines. [Std]

{U.S. EPA/OPPTS 1998b} U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxic Substances). 1998b. Health Effects Test Guidelines, OPPTS 870.1300, Acute Inhalation Toxicity. EPA 712–C–98–193. Document dated August 1998. Available at: https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines. [Std]

{U.S. EPA/OPPTS 1998c} U.S. EPA/OPPT (U.S. Environmental Protection Agency/Office of Pollution Prevention and Toxic Substances). 1998c. Health Effects Test Guidelines, OPPTS 870.3465, 90-Day Inhalation Toxicity. EPA 712–C–98–204. Document dated August 1998. Available at: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0156-0014. [Std]

{U.S. EPA/OPPTS 2000} U.S. EPA/OPPTS (U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances). 2000. Health Effects Test Guidelines, OPPTS 870.3550, Reproduction/Developmental Toxicity Screening Test. EPA712–C–00–367. July 2000. Available at: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0156-0015. [Std]

{U.S. EPA/ORD 1992} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 1992. Dermal Exposure Assessment: Principles and Applications. EPA/600/8-91/011B. Interim Report. Exposure Assessment Group, Office of Health and Environmental Assessment, Washington, DC. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12188. [Std]

{U.S. EPA/ORD 1993} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 1993. Wildlife Exposure Factors Handbook. Volumes 1 and 2. EPA/600/R-93/187a,b. Pagination not continuous. NTIS PB94-174778 and PB94-174779. [Std]

{U.S. EPA/ORD 2007} U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 2007. Dermal Exposure Assessment: A Summary of EPA Approaches. EPA/600/R-07/040F. Report dated September 2007. Available at http://www.epa.gov/ncea. [Std]

{USDA 2014} USDA (U.S. Department of Agriculture. 2014. Pesticide Data Program, Annual Summary, Calendar Year 2013. Available at: http://www.ams.usda.gov/sites/default/files/media/2013%20PDP%20Anuual%20Summary.pdf. [Set00]

{USDA/NRCS 1999} USDA/NRCS (United States Department of Agriculture/Natural Resources Conservation Service). 1999. Grassland Birds. Available at: http://www.nrcs.usda.gov/Internet/FSE_DOCUMENTS/nrcs143_009930.pdf. [Std]

{USGS 2015} USGS (U.S. Geological Survey). 2015. Preliminary Pesticide Use Maps for 2012. [Std]

{van Hemmen. 1992} van Hemmen JJ. 1992. Agricultural pesticide exposure data bases for risk assessment. Rev. Environ. Contam. Toxicol. 126: 1-85.[Std]

{Varanasi et al. 2015} Varanasi VK; Godar AS; Currie RS; Dille AJ; Thompson CR; Stahlman PW; Jugulam M. 2015. Field-evolved resistance to four modes of action of herbicides in a single kochia (*Kochia scoparia* L. Schrad.) population. Pest Management Science. 71(9):1207-12. [Set02]

{Vicari et al. 1994} Vicari A; Catizone P; Zimdahl RL. 1994. Persistence and mobility of chlorsulfuron and metsulfuron under different soil and climatic conditions. Weed Res. 34 (3):147-155. [RA2004]

{Vincent 1990} Vincent D. 1990. Assessment of IN W4189-165 in the In Vitro Unscheduled DNA Synthesis Assay in Primary Rat Hepatocytes. Lab Project Number: HLR 573-90: 4581-783. Unpublished study prepared by E.I. du Pont de Nemours and Co. 15 p. MRID 42545601. [MRID2004]

{Waldbauer 1968} Waldbauer GP. 1968. The consumption and utilization of food by insects. Advan Insect Physiol. 5: 229-288. [Std]

{Walker and Brown 1983} Walker A; Brown PA. 1983. Measurement and prediction of chlorsulfuron persistence in soil. Bull Environ Contam Toxicol. 30 (3):365-372. [RA2004]

{Wang et al. 2010} Wang YS; Chen WC; Lin LC; Yen JH. 2010. Dissipation of Herbicides Chlorsulfuron and Imazosulfuron in the Soil and the Effects on the Soil Bacterial Community. Journal of Environmental Science and Health. Part. B, Pesticides, Food Contaminants, and Agricultural Wastes. 45(5):449-55. [Set01]

{Ward and Boeri 1989} Ward T; Boeri R. 1989. Chronic Toxicity of DPX-W4189-94 to Daphnia magna. Lab Project Number: 4581-655: 87-89. Unpublished study prepared by E.I. du Pont de Nemours and Co. 27 p. MRID 41976404. [MRID2004]

{Ward and Boeri 1991a} Ward T; Boeri R. 1991a. Static Acute Toxicity of DPX-W4189-165 (Chlorsulfuron) to the Sheepshead Minnow, Cyprindon variegatus. Lab Project Number: MR-4581-866: 516-91: 9130-DU. Unpublished study prepared by EnviroSystems Division. 31 p. MRID 41976401. [MRID2004]

{Ward and Boeri 1991b} Ward T; Boeri R. 1991b. Static Acute Toxicity of DPX-W4189-165 (Chlorsulfuron) to the Mysid, Mysidopsis bahia. Lab Project Number: MR-4581-866: 523-91: 9131-DU. Unpublished study prepared by EnviroSystems Division. 31 p. MRID 41976402. [MRID2004]

{Ward and Boeri 1991c} Ward T; Boeri R. 1991c. Static Acute Toxicity of DPX-W4189-165 (Chlorsulfuron) to Bivalve Mollusc Embryos and Larvae. Lab Project Number: MR-4581-866: 524-91: 9132-DU. Unpublished study prepared by EnviroSystems Division. 31 p. MRID 41976403. [MRID2004]

{Ward and Boeri 1991d} Ward T; Boeri R. 1991d. Static Acute Toxicity of DPX-W4189-165 (Chlorsulfuron) to Bivalve Mollusc Embryos and Larvae. Lab Project Number: 524-91: MR-4581-866. Unpublished study prepared by EnviroSystems Division, Resource Analysts, Inc. 31 p. MRID 42328601. [MRID2004]

{Wei et al. 1998} Wei L; Yu H; Sun Y; Fen J; Wang L. 1998. The effects of three sulfonylurea herbicides and their degradation products on the green algae *Chlorella pyrenoidosa*. Chemosphere. 37 (4):747-751. [RA2004]

{Wei et al. 1999} Wei L; Yu H; Cao J; Sun Y; Fen J; Wang L. 1999. Determination and prediction of partition coefficient and toxicity for sulfonylurea herbicides and their degradation products. Chemosphere. 38 (7):1713-1719. [RA2004]

{Weinberg et al. 2006} Weinberg T; Stephenson GR; Mclean MD; Hall JC. 2006. MCPA (4-Chloro-2-Ethylphenoxyacetate) Resistance in Hemp-Nettle (*Galeopsis tetrahit* L.). Journal of Agricultural and Food Chemistry. 54(24):9126-34. [Set01]

{Wen-Sheng et al. 2006} Wen-Sheng X; Xiang-Jing W; Tian-Rui R; Su-Qin C. 2006. Purification of Recombinant Wheat Cytochrome P450 Monooxygenase Expressed in Yeast and its Properties. Protein Expression and Purification. 45(1):54-9. [Set01]

{Werck-Reichhart et al. 2000} Werck-Reichhart; Hehn A; Didierjean L. 2000. Cytochromes P450 for engineering herbicide tolerance. Trends in Plant Science. 5(9): 116-123. [Set04]

{WHO 2006} WHO (World Health Organization). 2006. Environmental Health Criteria 235, Dermal Absorption. Available at: http://www.who.int/ipcs/publications/ehc/ehc235.pdf. [Std]

{Willis and McDowell. 1987} Willis, GH; McDowell, LL. 1987. Pesticide persistence on foliage. Reviews of Environmental Contamination and Toxicology. 100: 23-73. [Std]

{Wimmer et al. 1993} Wimmw MJ; Smith RK; Wallinga DI; Toney SR; Faber DC; Miracle JE; Carnes JT; Rutherford AB. 1993. Persistence of Diflubenzuron on Appalachian Forest Leaves after Aerial Application of Dimilin. J Agric Food Chem. 41: 2184-2190. [Std]

{Winegardner 1996} Winegardner DL. 1996. An Introduction to Soils for Environmental Professionals. CRC Press, Boca Raton, Florida. 270 pp.[Std]

{Winston 1987} Winston ML. 1987. The Biology of the Honey Bee. Harvard University Press, Cambridge, MA. ISBN 0-674-07409-2 280 pp. [Std]

{Wood 1980} Wood CK. 1980. Summary of Progress on a Three-Generation Six Litter Reproduction Study in Rats with 2-Chloro-N- (4-methoxy-6methyl-1,3,5-triazin-2-yl)aminocarbonyl benzenesulfonamide (INW4189). (Unpublished study received Jun 16, 1980 under 352-EX 105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099461-D) MRID 00031423. [MRID2004]

{Wood et al. 1980a} Wood CK; Schneider PW Jr; Smith LW; et al. 1980a. Long Term Feeding Study with 2-Chloro-N- (4-methoxy-6-methyl-1,3,5 triazin-2-yl)aminocarbonyl benzenesulfonamide (INW-4189) in Rats. Report No. 283-80. Interim rept. (Unpublished study in cluding pathology report no. 12-80, received Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-N) MRID 00031419. [MRID2004]

{Wood et al. 1980b} Wood CK; Schneider PW Jr; Smith LW; et al. 1980b. Long Term Feeding Study with 2-Chloro-N-¢(4-methoxy-6-methyl-1,3,5 triazin-2-yl)aminocarbonyl|benzenesulfonamide (INW-4189) in Mice: Report No. 203-80. Interim rept. (Unpublished study re ceived Jun 16, 1980 under 352-EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099461-C) MRID 00031422. [MRID2004]

{Wood et al. 1980c} Wood CK; Schneider PW Jr; Smith LW; et al. 1980c. Ninety-Day Feeding Study with 2-Chloro-N- (4-methoxy-6-methyl-1,3,5triazin-2-yl)aminocarbonyl benzenesulfonamide (INW-4189) in Rats. Report No. 80-80. Final rept. (Unpublished study including pathology report no. 24-79, received Jun 16, 1980 under 352EX-105; submitted by E.I. du Pont de Nemours & Co., Wilmington, Del.; CDL:099460-M) MRID 00031418. [MRID2004]

{Wood et al. 1981a} Wood CK; Wollenberg EJ; Hall CL; et al. 1981a. Long-term Feeding Study with 2-Chloro-N-(4-methoxy-6-methyl-1,3,5 triazin-2-yl) Aminocarbonyl benzenesulfonamide (INW-4189) in Rats. Haskell Laboratory Report No. 557-81. Final rept. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. Du pont de Nemours & Co., Inc., Wilmington, Del.; CDL: 070472-A; 070473; 070474; 070475; 070476) MRID 00086003. [MRID2004]

{Wood et al. 1981b} Wood CK; Wollenberg EJ; Turner DT; et al. 1981b. Long term Feeding Study with INW-4189 in Mice. Haskell Laboratory Report No. 836-81. Final rept. (Unpublished study received Dec 28, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070535-A; 070536; 070537; 070538; 070539; 070540) MRID 00090030. [MRID2004]

{Xiang et al. 2005} Xiang WS; Wang XJ; Ren TR; Ju XL. 2005. Expression of a Wheat Cytochrome P450 Monooxygenase in Yeast and its Inhibition by Glyphosate. Pest Management Science. 61(4):402-6. [Set01]

{Ye et al. 2004} Ye QF; Wu JM; Sun JH. 2004. Bioavailability of Bound Residue Derived from ^{14}C-Labeled Chlorsulfuron in Soil and its Mechanism of Phytotoxicity. Journal of Environmental Sciences (China). 16(2):262-7. [Set01]

{Zabalza et al. 2004} Zabalza A; Orcaray L; Gaston S; Royuela M. 2004. Carbohydrate Accumulation in Leaves of Plants Treated with the Herbicide Chlorsulfuron or Imazethapyr Is Due to a Decrease in Sink Strength. Journal of Agricultural and Food Chemistry. 52(25):7601-6. [Set01]

{Zendzian 2010} Zendzian RP. 2010. Dermal Absorption of Pesticides in the Rat. American Industrial Hygiene Association Journal. 61(4): 473-483. [Set03]

{Zheng et al. 2008} Zheng W; Yates SR; Papiernik SK. 2008. Transformation Kinetics and Mechanism of the Sulfonylurea Herbicides Pyrazosulfuron Ethyl and Halosulfuron Methyl in Aqueous Solutions. Journal of Agricultural and Food Chemistry. 56: 56, 7367–7372. [Set03]

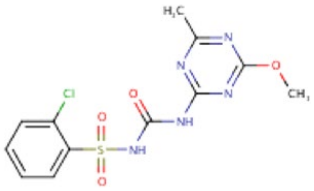
{Zohar et al. 2003} Zohar Y; Einav M; Chipman DM; Barak Z. 2003. Acetohydroxyacid Synthase from *Mycobacterium avium* and its Inhibition by Sulfonylureas and Imidazolinones. Biochim Biophys Acta. 1649(1):97-105. [Set01]

Table 1: Summary of Open Literature Most Relevant to Risk Assessment

Topic	Citations[1]
Terrestrial Species	
Birds	No new studies identified.
Invertebrates, Terrestrial	No new studies identified.
Plants, Terrestrial *General* [2]	Anderson et al. 2010; Fan et al. 2005; Gaston et al. 2003; Kaushik et al. 2006; McCourt et al. 2005; Orcaray et al. 2010; Orcaray et al. 2011; Slavov et al. 2005; Wen-Sheng et al. 2006; Xiang et al. 2005; Ye et al. 2004; Zabalza et al. 2004;
Nontarget plants	
Resistance in plants	Adamczewski et al. 2009; Ashworth et al. 2014; Busi et al. 2011; Cirujeda and Taberner 2010; Darmency 2013; Gressel 2009; Hamouzov et al. 2014; Han et al. 2012; Han et al. 2013; Hu et al. 2011; Jander et al. 2003; Kaloumenos et al. 2011; Kolkman et al. 2004; Kuk and Bugos 2007; Lu et al. 2007; Roux et al. 2005; Sala et al. 2008; Weinberg et al. 2006;
Terrestrial Microorganisms	Ahtiainen et al. 2003; Wang et al. 2010; Zohar et al. 2003; Zohar et al. 2003
Aquatic Species	
Fish	Padilla et al. 2012
Invertebrates, Aquatic.	Kashian and Dodson 2002
Plants, Aquatic	Michel et al. 2004; Turgut et al. 2003
Environmental Fate	
Environmental Fate and Properties	Delgado-Moreno and Pena 2007; Foldenyi et al. 2013; Fenoll et al. 2012; Flores-Cespedes et al. 2009; Juhler et al. 2008; Song et al. 2013; Ye et al. 2004
Reviews	
EPA	U.S. EPA/OPP 2005a (RED), 2013b, 2015a; U.S. EPA/OPP/EFED 2002a, 2004a, 2004b, 2012a, 2015a,b; U.S. EPA/OPP/HED 2002a, 2002b, 2012a,b, 2013a, 2015a
Other	CDPR 2012; EFSA 2008; ENSR 2005; European Commission 2010; FAO/WHO 2003; HSDB 2006

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

Table 2: Chemical and Physical Properties

Item	Value	Reference[1]
	Identifiers	
Common name:	Chlorsulfuron	Tomlin 2004
CAS Name	2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl] benzenesulfonamide	Tomlin 2004
IUPAC Name	1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea	Tomlin 2004
CAS No.	64902-72-3	ChemIDplus 2015; Tomlin 2004
Chemical Group	Sulfonylurea	Tomlin 2004; U.S. EPA/OPP 2005a
Development Codes	DPX 4189 (DuPont); W4189;	Tomlin 2004
PC Code/ OPP Chemical Code	118601	U.S. EPA/OPP 2005a; U.S. EPA/OPP/EFED 2012a
Molecular formula	$C_{12}H_{12}ClN_5O_4S$	ChemIDplus 2015; Tomlin 2004
Mechanistic group	acetolactate synthase (ALS) inhibitor	Tomlin 2004; U.S. EPA/OPP/EFED 2015a
Resistance Categories	HRAC B; WSSA 2;	Tomlin 2004; Mallory-Smith and Retzinger 2003
Smiles Code	`Cc1nc(nc(n1)OC)NC(=O)NS(=O)(=O)c2ccccc2Cl`	ChemIDplus 2015
	`C1=CC=CC(=C1[S](NC(NC2=NC(=NC(=N2)C)OC)=O)(=O)=O)Cl`	EPA/OPP/EFED 2015a
Structure		ChemIDplus 2015
	Chemical Properties(1)	
Aqueous photolysis	EPA assessment: Stable Study author assessment: Stable at pH 9 and 7. DT_{50} of 23 days at pH 5.	Dietrich and McAleer 1989d, MRID 42156702, U.S. EPA/OPP/EFED 2012a Acceptable study
	198 days	Strek 1998a
Hydrolysis	**pH at 25°C** / **DT_{50} (days)** 5 / 23.1-22.4 7 / Stable 9 / Stable	MRID: 42156701, U.S. EPA/OPP/EFED 2012a Acceptable study
	pH at 25°C / **DT_{50} (days)** 5 / 24 7 / >365 9 / >365	Strek 1998a
K_{ow}	≈0.102 [logP = -0.99 (pH 7)]	Tomlin 2004; Fenoll et al. 2012
	pH / **K_{ow}** 5 / 2.13 7 / 0.1 9 / 0.04 `Working Note: Kow of 0.1 used in the current Forest Service risk assessment.`	U.S. EPA/OPP/EFED 2004a, p. 8
	1.11	U.S. EPA/OPP 2005a, p. 3
	1.4 [logP = 0.17 (pH 7.1)], UV method 0.2[logP = -0.67 (pH 7.1)], HPLC method	Ribo 1988

Item	Value	Reference[1]
	<table><tr><th>pH</th><th>K_{ow}</th></tr><tr><td>5</td><td>2.07</td></tr><tr><td>7</td><td>0.11</td></tr><tr><td>7</td><td>0.0947</td></tr><tr><td>9</td><td>0.0387</td></tr></table> Note: Two values for pH 7 are apparent replicate measurements	MRID: 42454107, U.S. EPA/OPP/EFED 2012a
Molecular weight (g/mole)	357.7768	ChemIDplus 2015
	357.8 Working Note: This MW is used in current risk assessment.	Tomlin 2004; U.S. EPA/OPP/EFED 204a
	357.7709	U.S. EPA/OPP 2005a
	357.77	U.S. EPA/OPP/EFED 2012a
Melting point	170-173 °C (purity 98%)	Tomlin 2004
	174-178° C	U.S. EPA/OPP 2005a
Soil Photolysis, DT_{50}	138 days, clay loam, triazine label 183 days, clay loam, phenyl label 25±5°C, pH 8.0	MRID 41721001, U.S. EPA/OPP/EFED 2012a
pK_a	3.4	U.S. EPA/OPP/EFED 2012a; Schmuckler and Moore 1992/ MRID 42454102
	3.63	Ch
Vapor pressure	$3x10^{-6}$ mPa (25 °C)	Tomlin 2004
	4.6 x 10^{-6} mmHg at 25° C	U.S. EPA/OPP 2005a
	2.3×10^{-11} torr at 25°C	MRID: 42454105, U.S. EPA/OPP/EFED 2012a
Water solubility	27.9 g/L (pH 7)	Bergstrom and Stenstrom 1998
	<table><tr><th>pH</th><th>Value (mg/L)</th></tr><tr><td>5</td><td>590</td></tr><tr><td>7</td><td>31,800</td></tr></table> 25°C	Tomlin 2004
	125 ppm at 25° C	U.S. EPA/OPP 2005a
	<table><tr><th>pH</th><th>Value (mg/L)</th></tr><tr><td>5</td><td>587±18.7</td></tr><tr><td>7</td><td>3,180,000</td></tr></table> 25°C The value for pH 7 appears to be an error/typo.	MRID 42454104, U.S. EPA/OPP/EFED 2012a
	<table><tr><th>pH</th><th>Value (mg/L)</th></tr><tr><td>5</td><td>587</td></tr><tr><td>7</td><td>31,800</td></tr></table> 25°C Working Note: The value at pH 7 is used quantitatively in the current risk assessment.	USDA/ARS 1998; Schmuckler 1992a, MRID 42454104, U.S. EPA/OPP/EFED 2002a, Table 2
	100-120 mg/L at 22 °C	Rapisarda et al. 1978, MRID 00035271
	7,000 mg/L	Knisel and Davis 2000

Item	Value	Reference[1]
	Environmental Properties	
Aquatic, aerobic metabolism	No data	U.S. EPA/OPP/EFED 2012a
Aquatic, anaerobic metabolism	DT_{50}s: 47 to 445 days (5 assays: 47, 66, 86, 170, 445 days) Studies do not fulfill guidelines. Shorter half-lives reported in original study (109-263 days)	Chrzanowski and Priester 1991, MRID 42156704, U.S. EPA/OPP/EFED 2012a, p. 13, *Supplemental not for use in modeling*.
Aquatic sediments	DT_{50}s: 20 to 22 weeks (140-154 days)	Chrzanowski 1980a, MRID 00086815, EPA/OPP/EFED 2012a, p. 13, *Supplemental not for use in modeling*.
	DT_{50}: > 365 days	Strek 1998a
Bioconcentration in fish (BCF)	Not likely to bioconcentrate based on K_{ow}.	MRID: 42454107, U.S. EPA/OPP/EFED 2012a
	Bluegill sunfish, <1 in edible tissue	Han 19??c, MRID 00083951; Priester 1991b (DER)
	Channel catfish: BCF 1.5 in edible muscle and BCF<12 in viscera and liver. Working Note: For edible portions of fish, a BCF of 1 is used in the current risk assessment for acute exposures and a factor of 1.5 is used for longer-term exposures. For whole fish, a BCF of 1 is used for acute exposures and a BCF of 12 is used for longer-term exposures. See Section 3.2.3.5.	Han 1981c, MRID 00086820; Priester 1991b (DER)
Foliar washoff fraction	0.75	Knisel and Davis 2000
Foliar half-life	30 days	Knisel and Davis 2000
	20 (4-75) days [Method of Juraske et al. (2008)]	Section 3.2.3.4.3.
	0.3 (0.07 to 1.27) days [Method of Fanke et al. (2014]	Section 3.2.3.4.3.
	≈0.04 to 0.5 days (ryegrass seedlings)	Cotterman and Saari (1992); Section 3.2.3.4.3.
K_{oc}	36 (14-60)	USDA/ARS 1998
	40	Knisel and Davis 2000
	17-20 (silt loam) 13 (sandy loam)	Strek 1998a
K_d K_{oc}	**Soil** / **K_d** / **K_{oc}** Loam / 0.28 / 35 Sandy loam / 0.09 / 8 Silt loam / 0.38 / 20 Silt loam / 0.91 / 21 Average Kd = 0.415.	MRID: 42156705, U.S. EPA/OPP/EFED 2012a
Soil half-life, aerobic metabolism	17.3 days (parent, first-order, silt loam, 25°C, pH 6.4) 22.4 days (parent and unextractable, first-order, silt loam, 25°C, pH 6.4). 299 days (total residues, first-order, silt loam, 25°C, pH 6.4).	MRID 00035275, U.S. EPA/OPP/EFED 2012a
	32 (13-88)	USDA/ARS 1998
	168 days (clay)	Smith 1986
	37 days (loam)	Anderson and Barrett 1985
	47 days (sand)	Sarmah et al. 1999
	22-38 days	James et al. 1999
	61.65 to 97.18 days	Delgado-Moreno and Pena 2007
Soil hydrolysis	53 days (sterile sandy clay)	Sarmah et al. 2000

Item	Value	Reference[1]
Soil field dissipation half-life	28-56 days	Alvarez-Benedi et al. 1998
	24-72 days	Djanegara 1991a, MRID 42214201
	13-14 days	James et al. 1999
	56 (10-185) days	USDA/ARS 1998
	40 days	Walker and Brown 1983
	6.8 to 28.4 days	Wang et al. 2010
Water Half-life	203 days [k=0.0034 day^{-1}]	USDA/ARS 1998
	198 days (dark) 80 days (exposed to light)	Strek 1998b
	69 days at pH 7.1	Sarmah et al. 2000

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

See Section 2.2 for initial discussion.

Table 3: Designated and Representative Formulations

Formulation Name/ EPA Registration Number/ Manufacturer/ Date of most recent EPA label	Form % a.i. (w/w), density Maximum Application Rate	Other ingredients/ Recommended Adjuvants	Application Methods (application volumes)[2]
Chlorsulfuron 75/ 81927-43/Alligare, LLC / May 5, 2015	Dry flowable, 75%, 0.58-0.70 g/mL 3 ounces formulation/acre [≈0.14 lb a.i./acre]	Not specified on label or MSDS. Use *high quality spray adjuvant (but not LI-700 or other acidifying adjuvants) for postemergence weed control*. No specific details on amounts.	Ground broadcast (20-40 GPA) Aerial broadcast (100-300 GPA). Spot applications (100-300 GPA)
Telar XP/ 432-1561/ Bayer Environmental Science [1] / July 16, 2015	Dry flowable, 75%, density not specified on SDS. 2.6 oz formulation/acre [0.12 lb a.i./acre] Lower rates for Conservation Reserve Program	5-10% modified lignin sulfonate salt (NOS on SDS) 15-20% other ingredients not specified on SDS Label recommends the use of a *suitable surfactant*. No additional details.	Ground broadcast (10-40 GPA) Aerial broadcast (at least 3 GPA) Spot applications (about 13 to 130 GPA)

[1] Telar XP was transferred from DuPont to Bayer on April 27, 2015
[2] GPA=Gallons per acre.

Source: EPA Pesticide Product Label System (http://iaspub.epa.gov/apex/pesticides/f?p=PPLS:1).
See Section 2.2 for initial discussion.

Table 4: Regional Summary of Chlorsulfuron Use by the Forest Service from 2000 to 2004

Use Parameter	Region 1	Region 2[3]	Region 4	Region 5	All
Number of Applications[1]	7	21	22	1	
Total Pounds	155.19	79.76	56.929	0.0619	291.9377
Total Acres	1771.05	1189.73	2561.0765	1.5	5523.3565
Average lbs/acre[2]	0.088	0.067	0.022	0.041	0.053
Minimum lbs/acre	0.046	0.014	0.0024	N/A	0.0024
Maximum lbs/acre	0.094	0.238	0.273	N/A	0.273

[1] All applications listed as "noxious weed control" except for the 1 application in Region 5 which is listed as "housekeeping/facilities".

[2] Weighted average for all applications – i.e., total pounds/total acres.

[3] Three applications from Region 2 for 2004 are censored – i.e., 0.9 lbs to zero acres in Forest 14, 59.49 lb to 1.5 acres in Forest 15, and 1.8 lb to 1.75 acres in Forest 12. The zero acre entry is an obvious data entry error. The latter two entries yield atypically high application rates – i.e., 39.66 lbs a.i./acre (an obvious error) and 1.029 lbs a.i./acre (an atypically high rate and probably an error).

Source: http://www.fs.fed.us/foresthealth/pesticide/reports.shtml.

See Section 2.5 for discussion.

Table 5: Summary of LD_{50} values for chlorsulfuron and chlorsulfuron formulations

Agent (purity or % a.i.)	LD_{50} as material tested (mg/kg)	LD_{50} as active ingredient (mg a.i./kg)	Reference
Chlorsulfuron (95% pure)	5545 (males) 6293 (females)	5268 (males) 5978 (females)	Trivits 1979, MRID 00031406
Chlorsulfuron formulation (80% a.i.)	7699 (males) 8891 (females)	6159 (males) 7113 (females)	Hinckle and Dashiell 1980, MRID 00031407
Chlorsulfuron formulation, dry flowable formulation (75% a.i.)	3053 (males) 2341 (females)	2290 (males) 1756 (females)	Dashiell and Hinckle 1981 MRID 00083958
Chlorsulfuron 75, dry flowable formulation (75% a.i.)	>5000 (NOS)		Alligare LLC 2010, MSDS for Chlorsulfuron 75
Telar XP, dry flowable formulation (75% a.i.)	>2000 (NOS)		DuPont Crop Protection 2015, SDS for Telar XP

See Section 3.1.4 for initial discussion.

Table 6: Directed Foliar Applications - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	Glyphosate	Section 3.2.2.1.3.	2
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.00041	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.0003	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.00006	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.002	SERA 2014b, Table 14	7
Subject Chemical	Chlorsulfuron		8
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.00018	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	0.4390243902		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.0001317073	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.0000263415	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.0008780488	SERA 2014b, Eq. 22	14

See Section 3.2.1 for discussion.

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

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

Note: These values are rounded to one significant place in the workbooks.

Table 7: Ground Broadcast Applications - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.2.1.3.	2
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.00066	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.0001	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.000002	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.005	SERA 2014b, Table 14	7
Subject Chemical	Chlorsulfuron		8
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.00018	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	0.2727272727		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.0000272727	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.0000005455	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.0013636364	SERA 2014b, Eq. 22	14

See Section 3.2.1 for discussion.

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

- Determine the first-order dermal absorption rate coefficient for the chemical under review. See SERA 2014a, Section 3.1.3.2.2.
- Select the reference chemical. See SERA 2014b, Section 4.1.6.1.
- Fill in the information on the reference chemical in the upper section of the above table.
- Fill in the first-order dermal absorption rate coefficient for the chemical under review in the Value column of Row 9 in the above table.

Update the estimated values for ratio of the k_a values and the occupational exposure rates for the chemical under review – i.e., the green shaded cells in the above table. The simplest way to update these fields is to select each of the 4 green shaded cells (one at a time and in order), press the right mouse button, and select 'Update field'.

Note: These values are rounded to one significant place in the workbooks.

Table 8: Aerial Applications - Derivation of Worker Exposure Rates

Item	Value	Reference/Note	Row
Reference Chemical	2,4-D	Section 3.2.2.1.3.	2
First-order dermal absorption rate coefficient for reference chemical (hour^{-1}) [ka_{Ref}]	0.00066	SERA 2014b	3
Occupational Exposure Rates for Reference Chemical			4
Central Estimate	0.00002	SERA 2014b, Table 14	5
Lower 95% Prediction Bound	0.0000005	SERA 2014b, Table 14	6
Upper 95% Prediction Bound	0.0008	SERA 2014b, Table 14	7
Subject Chemical	Chlorsulfuron		8
First-order dermal absorption rate coefficient for subject chemical (hour^{-1}) [ka_P]	0.00018	Section 3.1.3.2.2	9
$ka_P \div ka_{Ref}$	0.2727272727		10
Occupational Exposure Rates for Subject Chemical (Imidacloprid)			11
Central Estimate	0.0000054545	SERA 2014b, Eq. 22	12
Lower 95% Prediction Bound	0.0000001364	SERA 2014b, Eq. 22	13
Upper 95% Prediction Bound	0.0002181818	SERA 2014b, Eq. 22	14

See Section 3.2.1 for discussion.

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

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

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

Table 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 Section 3.2.3.4.3 for initial discussion.

Table 10: Input Parameters for Fields and Waterbodies Used in Gleams-Driver Modeling

Field Characteristics	Description	Pond Characteristics	Description
Type of site and surface (FOREST)	Field (0)	Surface area	1 acre
Treated and total field areas	10 acres	Drainage area:	10 acres
Field width	660 feet	Initial Depth	2 meters
Slope	0.1 (loam and clay) 0.05 (sand)	Minimum Depth	1 meter
Depth of root zone	36 inches	Maximum Depth	3 meters
Cover factor	0.15	Relative Sediment Depth	0.02
Type of clay	Mixed		
Surface cover	No surface depressions		

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

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

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

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

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

See Section 3.2.3.4.3 for initial discussion.

Table 11: Chemical parameters used in Gleams-Driver modeling

Parameter	Values	Note/Reference
Halftimes (days)		
Aquatic Sediment	7300	Note 1
Foliar	20 (4 – 75)	Section 3.2.3.4.3.
Soil	80 (17.3-299)	Note 2
Water	160	Note 3
Soil $K_{o/c}$, mL/g	21 (8-40)	Note 4
Sediment K_d, mL/g	0.415 (0.09-0.91)	Note 5
Water Solubility, mg/L	31,800	U.S. EPA/OPP/EFED 2002a, Table 2
Foliar wash-off fraction	0.75	Knisel and Davis 2000
Fraction applied to foliage	0.5	Standard assumption
Depth of Soil Incorporation	1 cm	Standard assumption
Irrigation after application	none	
Initial Application Date	June 15	Note 6

Notes

Number	Text
1	Assumed to be stable with a half-life of 10 years. Strek (1998a) reports an anaerobic half-life of >365 days. Shorter half-lives reported in Chrzanowski and Priester (1991) and Chrzanowski (1980a) but these are not classified as appropriate for modelling. See Table 1.
2	Central estimate taken from U.S. EPA/OPP/EFED 2002a, Table 2. Degradation in soil is highly dependent on microbial activity (Priester 1991a) and may vary substantially within a given type of soil. Lower and upper bounds taken from MRID 00035275. See Table 1 for details.
3	Taken as 2x the central estimate of aerobic soil half-life per U.S. EPA/OPP/EFED 2002a.
4	Central estimate taken from U.S. EPA/OPP/EFED 2002a, Table 2. Upper bound from Bergstrom and Strenstrom (1998) and value recommended by Knisel and Davis (2000). Lower bound from MRID: 42156705. See Table 1 for details.
5	Average value and range from MRID: 42156705. See Table 1 for details.
6	Based on product labels, applications are typically made in spring or early summer. This is not a sensitive parameter.

See Section 3.2.3.4.3 for initial discussion.

Table 12: Summary of Modeled Concentrations in Surface Water

Scenario/Source	Peak Concentrations (ppb or µg/L per lb/acre)	Long-Term Average Concentrations (ppb or µg/L per lb/acre)
Direct Spray and Spray Drift		
Pond, Direct Spray (Section 3.2.3.4.2) [1]	112	N/A
Pond, drift at 25 feet (Section 3.2.3.4.2) [1]	25 (Aerial) 12 (High Ground boom) 3.9 (Low Ground boom) 0.93 (Backpack)	N/A
Stream, Direct Spray (Section 3.2.3.4.2) [2]	91	N/A
Stream, drift at 25 feet (Section 3.2.3.4.2) [2]	20 (Aerial) 9.5 (High Ground boom) 3.2 (Low Ground boom) 0.76 (Backpack)	N/A
GLEAMS-Driver Modelling (Appendix 8)		
Pond, Section 3.2.3.4.4, Appendix 8, Tables 7 and 8	**Soil** / **Conc.** Clay: 67.3 (0.12 - 320) Loam: 97.4 (0.004 - 410)) Sand: 210 (1.43 - 660) Average of all soils: 124.9	**Soil** / **Conc.** Clay: 32.8 (0.05 - 158) Loam: 49 (0.0016 - 237) Sand: 109 (0.6 - 380) Average of all soils: 63.6
Stream, Section 3.2.3.4.4, Appendix 8, Tables 5 and 6	**Soil** / **Conc.** Clay: 15.7 (0.3 - 55) Loam: 24.6 (0.009 - 93) Sand: 60.8 (1.94 - 167)	**Soil** / **Conc.** Clay: 1.54 (0.0011 - 7.5) Loam: 1.97 (0.00005 - 8.9) Sand: 3.02 (0.016 - 9.9)
EPA Tier 1 Models (Appendix 9)		
FIRST (Index Reservoir Model)	99.3 (90.3-102.9)	34.9 (30.6-36-9)
PRZM-GW (Ground water)	5.2 (0.29-127)	N/A
EPA FIRST Model for Drinking Water Assessment[3]		
Bulb Vegetables	71.03	24.94
EPA PRZM/EXAMS modeling[4]		
Wheat	274	
Turf	152	

[1] See Attachment 1, Worksheet B04c. Values normalized by dividing by the application rate of 0.0625 lb a.i./acre and converting from mg/L to µg/L.

[2] See Attachment 1, Worksheet B04d. Values normalized by dividing by the application rate of 0.0625 lb a.i./acre and converting from mg/L to µg/L.

[3] Data from U.S. EPA/OPP/EFED (2002), p. 77. Maximum acute modelled concentrations for turf applications of 46.811 µg/L for 2 applications at an application rate of 0.333 lb a.i./acre. WCR = 46.811 µg/L ÷ (0.333 x 2) ≈ 71.03 µg/L per lb a.i./acre. Average annual concentration of 16.446 µg/L for 2 applications at an application rate of 0.333 lb a.i./acre. WCR ≈ 16.446 µg/L ÷ (0.333 x 2) ≈ 24.94 µg/L per lb a.i./acre.

[4] Data from U.S. EPA/OPP/EFED (2004a), p. 18. Wheat: maximum acute modelled concentrations 6.3 µg/L an application rate of 0.023 lb a.i./acre. WCR = 6.3 µg/L ÷ 0.023 lb a.i./acre ≈ 273.91 µg/L per lb a.i./acre. Turf: maximum acute modelled concentrations 9.5 µg/L an application rate of 0.0625 lb a.i./acre. WCR = 9.5 µg/L ÷ 0.0625 lb a.i./acre = 152 µg/L per lb a.i./acre.

See Sections 3.2.3.4.3 and 3.2.3.4.4 for initial discussion.

/

Table 13: Concentrations in surface water used in this risk assessment

	Peak WCR[1]	Longer-term WCR[1]
Central	0.125	0.0636
Lower	0.000004	0.0000016
Upper	0.66	0.38

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

See Section 3.2.3.4.6 for discussion

Table 14: Estimated residues in food items per lb a.i. applied

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

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

[a] U.S. EPA/EFED 2001, p. 44 as adopted from Fletcher et al. (1997).
[b] Central values × (Central Value ÷ Upper Value).

Table 15: Summary of toxicity values used in human health risk assessment

Acute – single exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2015a, Table 4.3.1, p. 8
Study	Alvarez 1991b, MRID 41983101
NOAEL Dose	75 mg/kg bw/day
LOAEL Dose	200 mg/kg bw/day
LOAEL Endpoint(s)	Decreased body weight and body weight gain.
Species, sex	Rabbit
Uncertainty Factor/MOE	100
Equivalent RfD	0.75

Note: The EPA risk assessments use these values for short-term (1-30 days) dermal and inhalation exposures in risk assessment for workers (U.S. EPA/OPP/HED 2015a, Table 4.3.2, p. 8).

Chronic – lifetime exposure

Element	Derivation of RfD
EPA Document	U.S. EPA/OPP/HED 2015a, Table 4.3.1, p. 8
Study	Wood et al. 1981a , MRID 00086003
NOAEL Dose	5 mg/kg bw/day
LOAEL Dose	25 mg/kg bw/day
LOAEL Endpoint(s)	Decreased body weight and body weight gain.
Species, sex	Rats, males
Uncertainty Factor/MOE	100
Equivalent RfD	0.05 mg/kg bw/day

See Section 3.3 for discussion.

Table 16: Terrestrial Nontarget Animals Used in Ecological Risk Assessment

MAMMALS [1]

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

BIRDS [2]

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

INVERTEBRATES [3]

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

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

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

Table 17: Diets: Metabolizable Energy of Various Food Commodities

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

[1] Metabolizable energy. Unless otherwise specified, the values are taken from U.S. EPA/ORD (1993), Table 3-1, p. 3-5 as adopted from Nagy 1987.

[2] From U.S. EPA/ORD (1993), Table 4-2, p. 4-14 unless otherwise specified.

[3] Based on a gross caloric value of 2.2 kcal/g bw (U.S. EPA/ORD 1993, Table 4-2). An assimilation factor for mammals eating fruit not identified. Use estimate for birds (see below).

[4] Based on a gross caloric value of 2.2 kcal/g bw (U.S. EPA/ORD 1993, Table 4-2) and an assimilation factor for the consumption of fruit by birds of 51% [2.2 kcal/g bw x 0.51 ≈ 1.1 kcal/g bw]

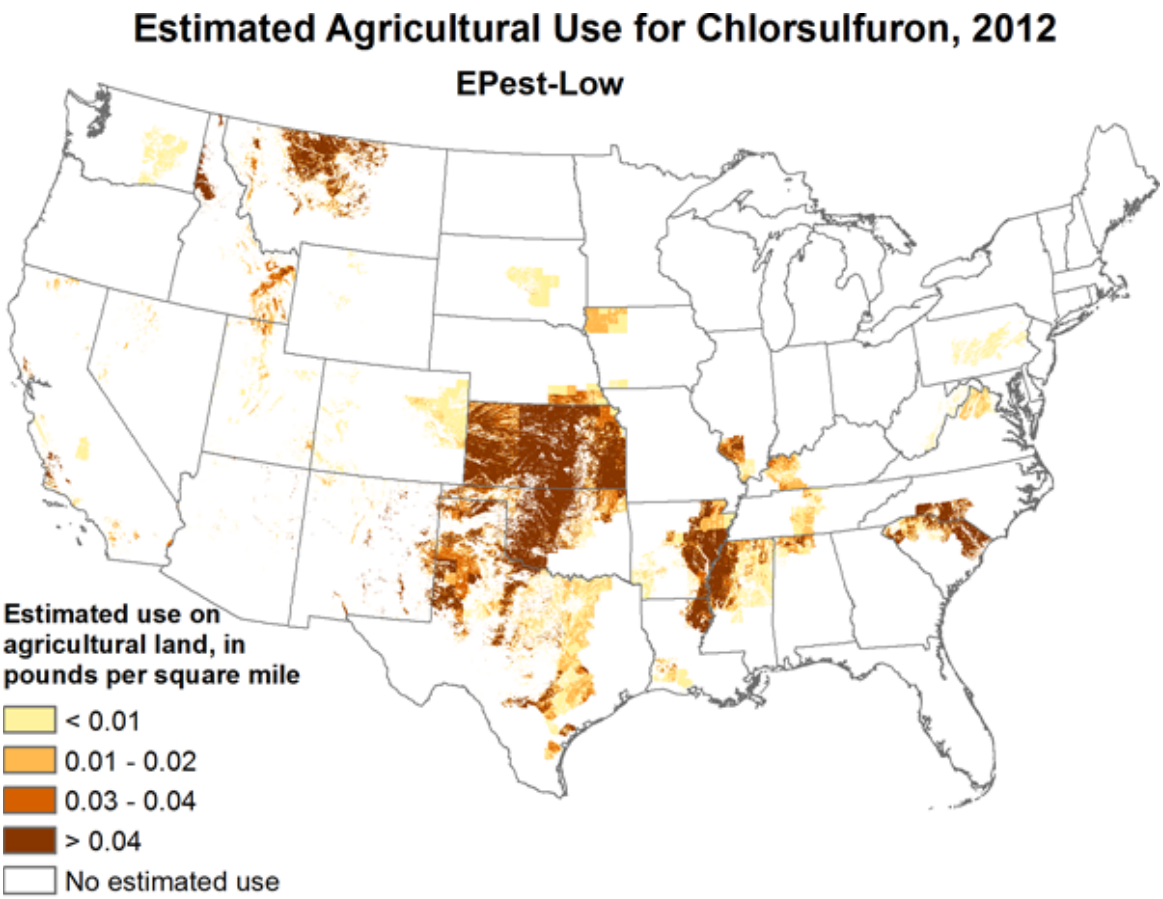
[5] Based on a gross caloric value of 4.2 kcal/g bw for dicot leaves (U.S. EPA/ORD 1993, Table 4-2). For birds, the value is corrected by an assimilation factor for the consumption leaves by birds of 47% [4.2 kcal/g bw x 0.47 = 1.974 kcal/g bw]

See Sections 4.2.2.3 for discussion.

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

Group/Duration	Organism	Endpoint	Toxicity Value (a.i.)	Reference
Terrestrial Animals				
Acute				
Mammals (including canids)		NOAEL, rabbit	75 mg/kg bw	Section 4.3.2.1.
Birds		NOAEL, Quail	300 mg/kg bw	Section 4.3.2.2
Honey Bee (contact)		Indefinite LD_{50}	216 mg/kg bw	Section 4.3.2.4.2
Longer-term				
Mammals		NOAEL, rat	5 mg/kg bw/day	Section 4.3.2.1
Bird		NOAEL, quail	24.5 mg/kg bw/day	Section 4.3.2.2.
Terrestrial Plants				
Soil	Sensitive	Sugar beet (dicot), NOAEL	0.0000068 lb/acre	Section 4.3.2.5.2
	Tolerant	Sorghum (monocot), NOAEL	0.000163 lb/acre	
Foliar	Sensitive	Rape (dicot), NOAEL	0.0000008 lb/acre	Section 4.3.2.5.2
	Tolerant	Wheat (monocot), NOAEL	0.001125 lb/acre	
Aquatic Animals				
Acute				
Fish	Sensitive	Use chronic value	32 mg/L	Section 4.3.3.1
	Tolerant	NOAEC (mortality), bluegill	300 mg/L	
Invertebrates	Sensitive	Use chronic value	20 mg/L	Section 4.3.3.3
	Tolerant	NOAEC, oyster	200 mg/L	
Longer-term				
Fish	Sensitive	NOAEC (egg-fry), trout	32 mg/L	Section 4.3.3.1
	Tolerant	Not identified	N/A	
Invertebrates	Sensitive	NOAEC, *Daphnia magna*	20 mg/L	Section 4.3.3.3
	Tolerant	Not identified	N/A	
Aquatic Plants				
Algae	Sensitive	*P. subcapitata*, NOAEC	0.0094 mg/L	Section 4.3.3.4
	Tolerant	*Chlorella* sp., NOAEC	9.3 mg/L	Section 4.3.3.4
Macrophytes	Sensitive	*Lemna gibba*, NOAEC	0.00024 mg/L	Section 4.3.3.4
	Tolerant	*Lemna paucicostata*, EC_{10}	0.05 mg/L	Section 4.3.3.4

See Section 4.2.1 for initial discussion.



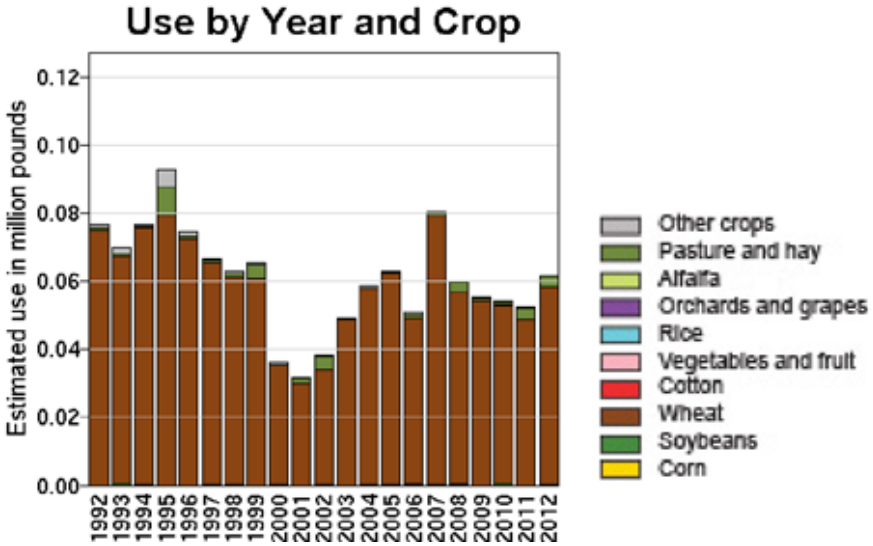


Figure 1: Lower Bound Estimated Agricultural Use of Chlorsulfuron for 2012

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

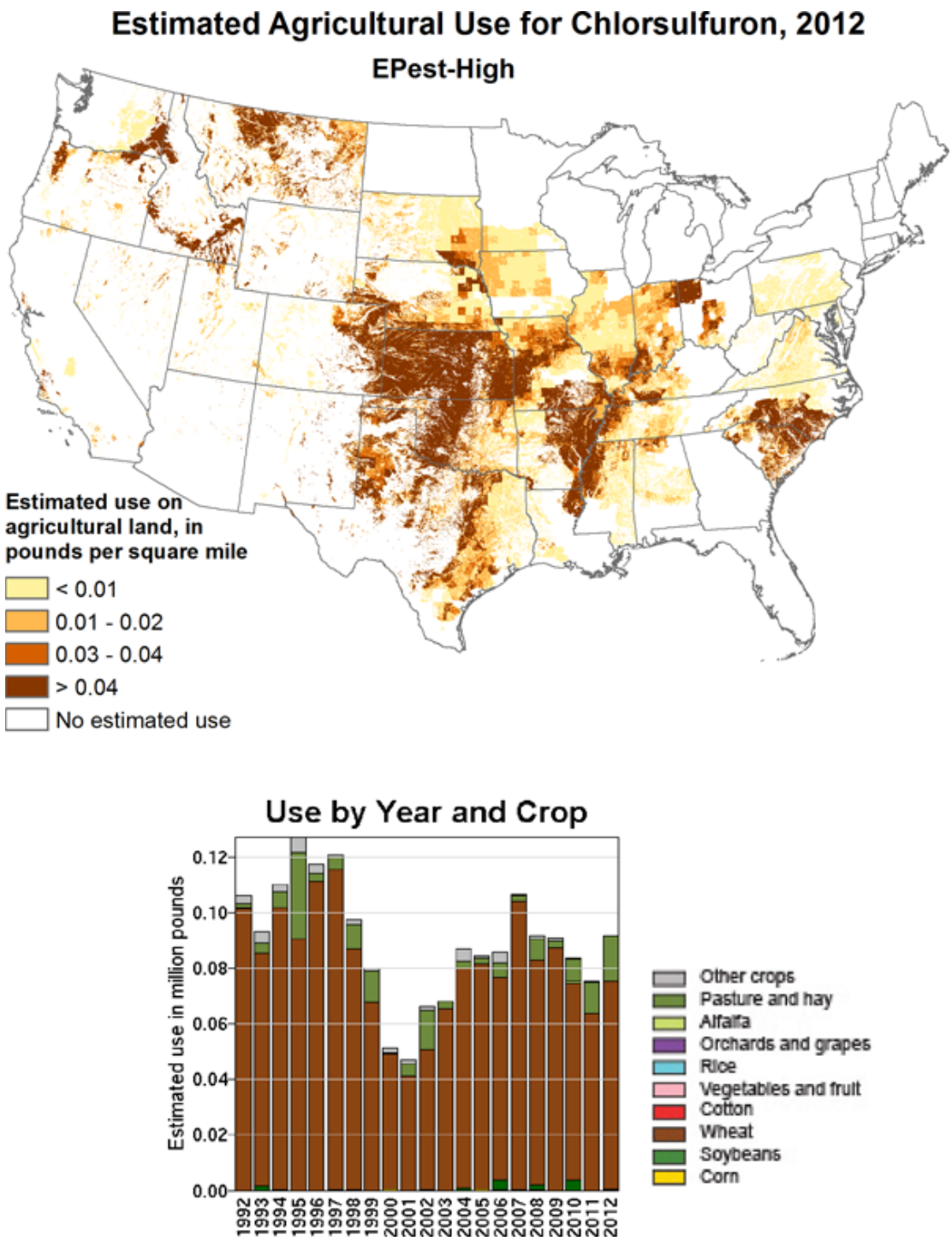


Figure 2: Upper Bound Estimated Agricultural Use of Chlorsulfuron for 2012

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

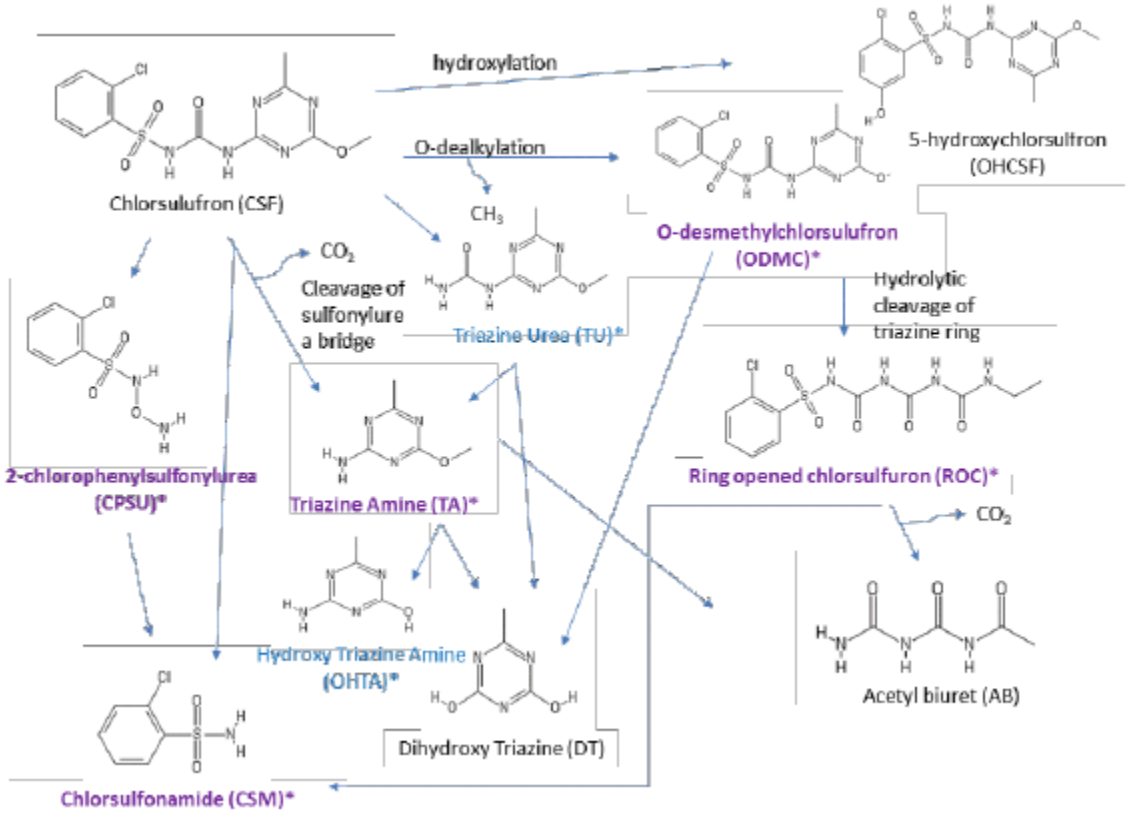


Figure 3: Environmental Metabolites of Chlorsulfuron

Note from EPA: Purple and bold values were present at greater than 10% of applied radioactivity in laboratory studies and the asterisk indicates the compound was observed in a lysimeter study. Residues that were not major but were observed in lysimeter studies are blue.

Source: U.S. EPA/OPP/EFED 2012a, Figure 1, p. 15.
See Section 3.1.15.1 for discussion.

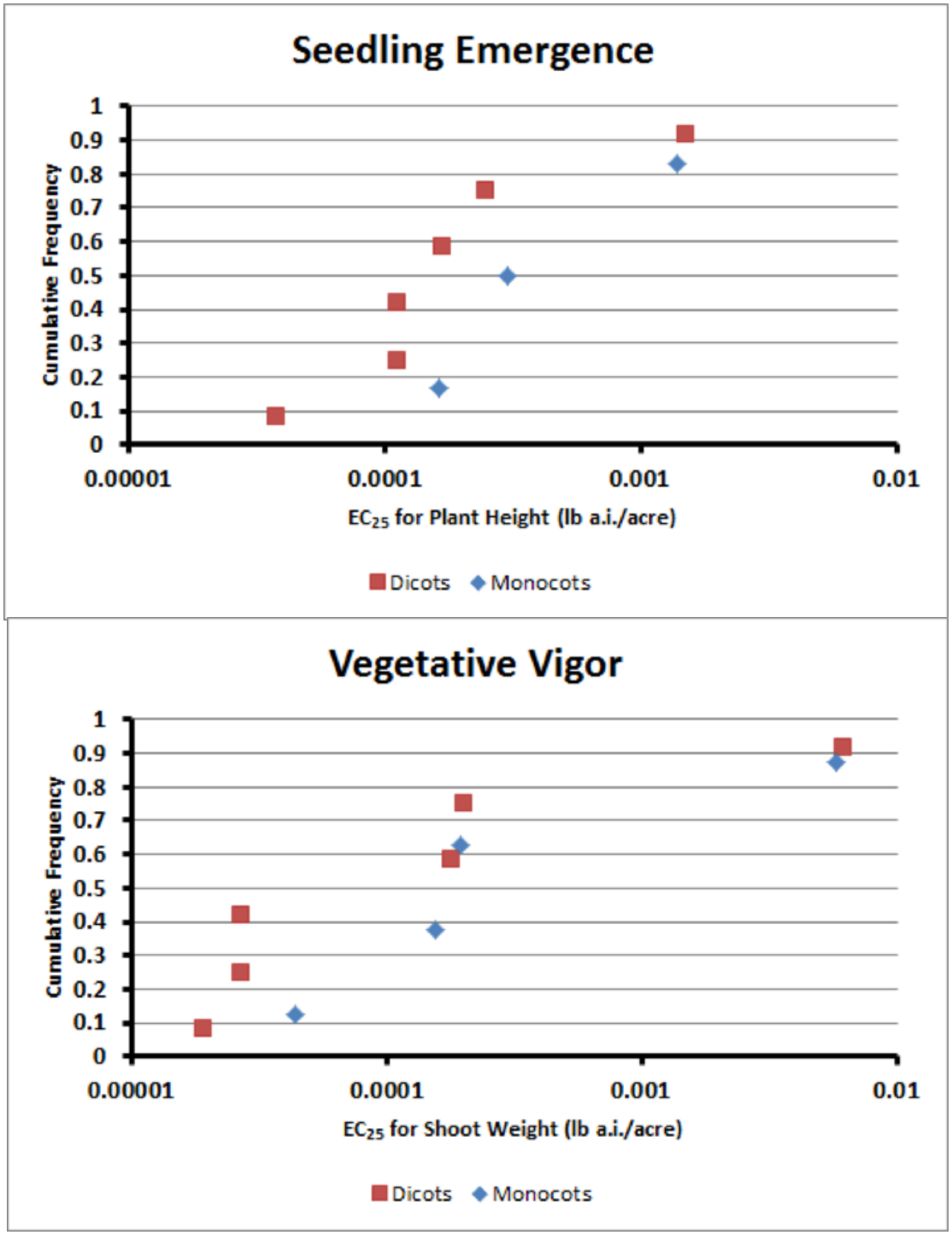


Figure 4: Relative Sensitivities of Monocots and Dicots

See Appendix 4, Tables A4-1 and A4-2 for data.
See Section 4.1.2.5.2 for initial discussion.

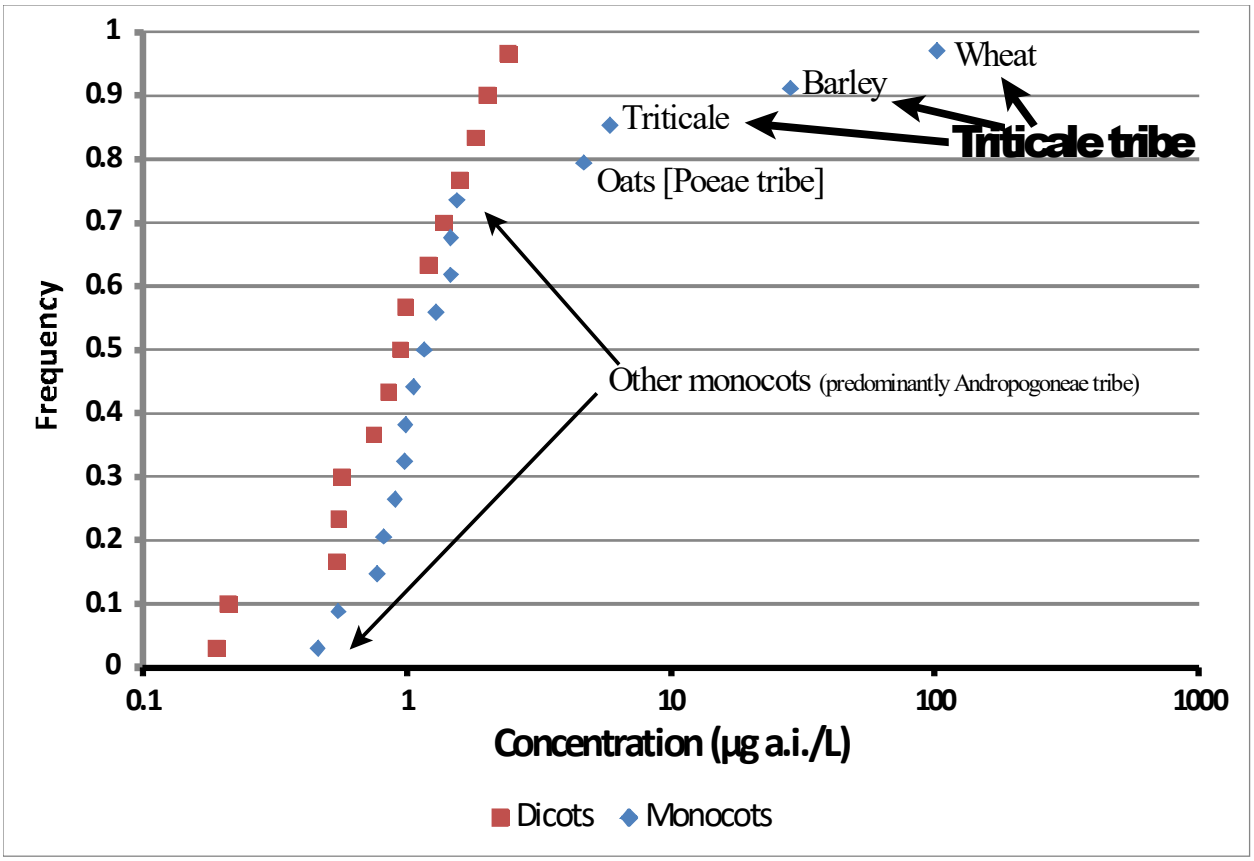


Figure 5: Summary of EC_{50} values in phytotoxicity assays by Jettner et al. (1999)

See Appendix 4, Table A4-4 for data.
See Section 4.1.2.5.2 for initial discussion.

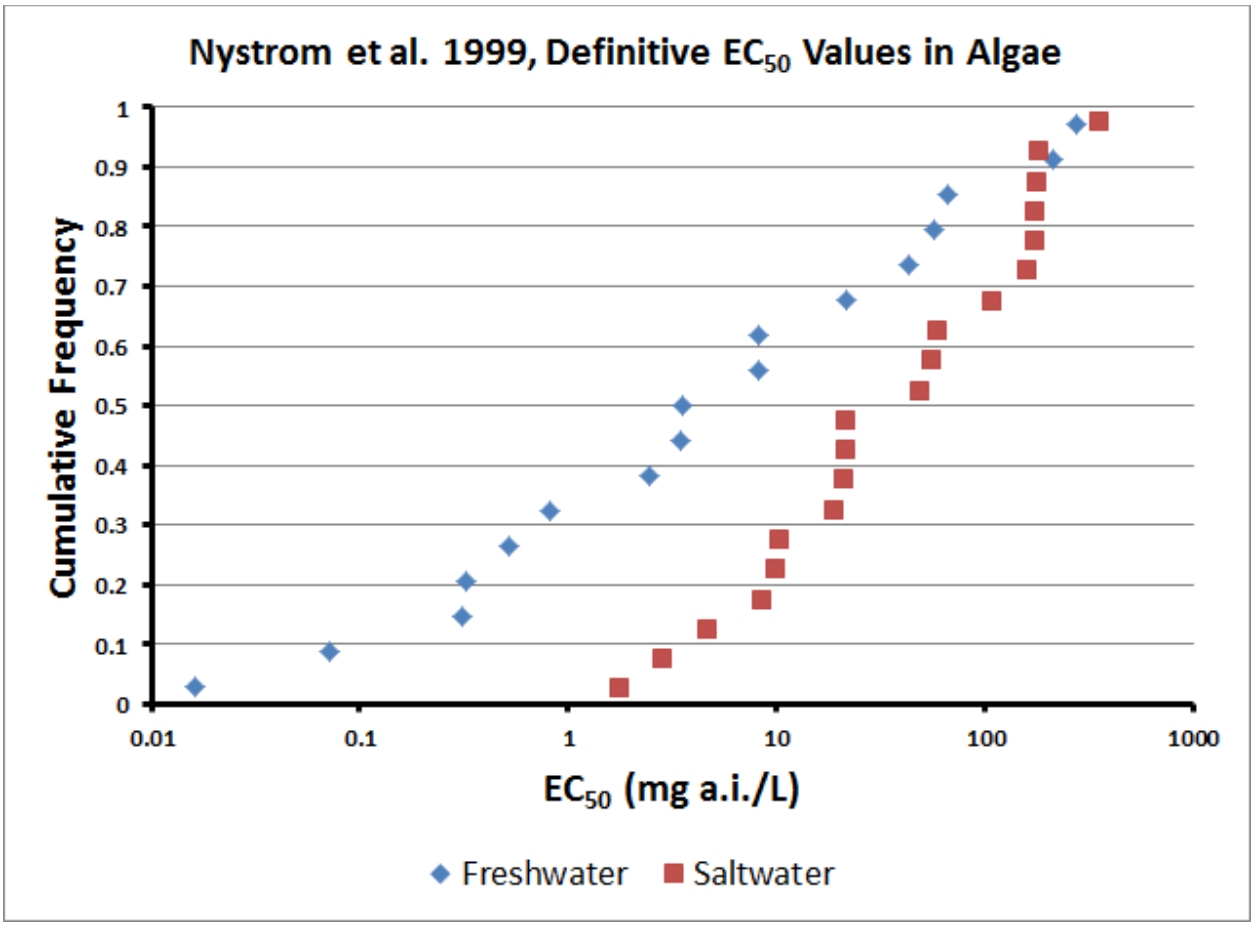


Figure 6: Definitive EC_{50} values for algae

Source: Nystrom et al. 1999, Table 3, p. 16.
See Section 4.1.3.4.1 for initial discussion.

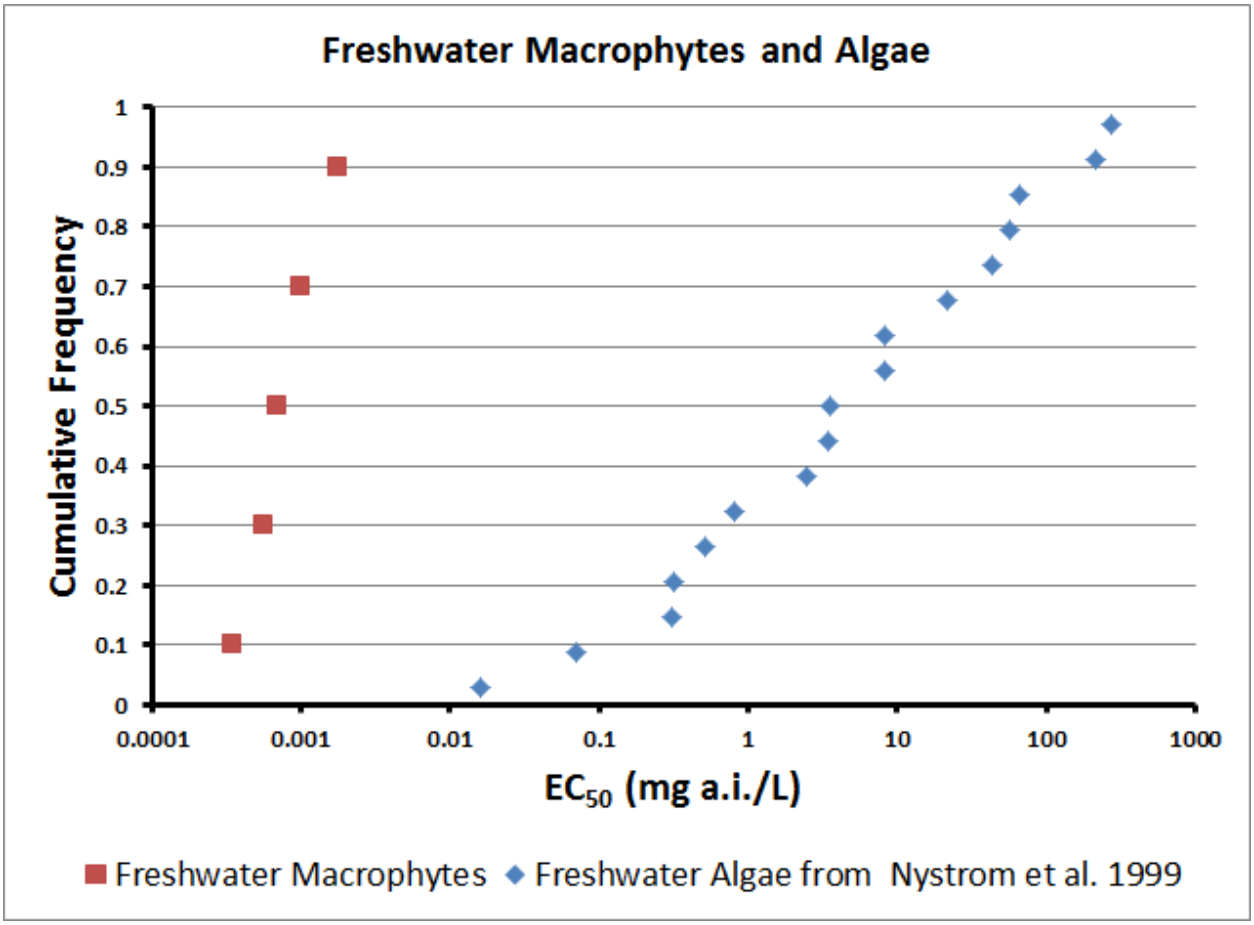


Figure 7: Comparison of Toxicity to Freshwater Macrophytes and Freshwater Algae

Source: Appendix 7, Table A7-4.
See Section 4.1.3.4.2 for initial discussion.

Appendix 1: Toxicity to mammals.

Table A1-1: Acute Oral and Intraperitoneal LD_{50} Values 145
Table A1-2: Subchronic and Chronic Toxicity Studies 148
Table A1-3: Reproductive and Developmental Studies..... 156
Table A1-4: Skin Irritation and Sensitization Studies 161
Table A1-5: Eye Irritation Studies 163
Table A1-6: Dermal Toxicity..... 164
Table A1-7: Inhalation Toxicity 166
Table A1-8: Mutagenicity Assays 167

Table A1-1: Acute Oral and Intraperitoneal LD_{50} Values

Species	Compound	Response	Reference
Gavage			
Rats, ChR-CD strain, young adult males (4 groups of 10) fasted 20 hours prior to dosing.	Single gavage dose of 4000, 5000, 6000, or 7000 mg/kg bw. TGAI, benzene-sulfonmide (DPX-4189, INW-4189-19, Haskell #12,361)(~95% a.i.) suspended in corn oil. 14-day observation period.	LD_{50}: 5545 mg/kg bw (males) (95% CI: 4723-6648 mg/kg bw) LD_{50}: 6293 mg/kg bw (females) (95% CI: 4113-9524 mg/kg bw) Effects at all dose levels: humped posture and stained faces and perineal areas Common effects not observed at all dose levels: half-shut eyes, lethargy, chromodacryorrhea, salivation and diarrhea Frequently observed signs of toxicity: prostration, hematuria, weakness, piloerection, lacrimation, and stained undersides of feet and bodies. Mortality: 1-4 days after dosing with moderate weight losses for 1-4 days and sporadic weight losses through day 14 in survivors. Gross pathological changes observed at 4000-7000 mg/kg bw in thymus, liver, lungs, brain, heart, spleen, kidney, eye, pancreas, testis, GI tract, skin, and stomach	Trivits 1979 MRID 00031406 Also cited in FAO/ WHO (2003), Tomlin (2004), and HSDB 2005. Cited, with rounding of toxicity values in U.S. EPA/OPP/HED 2015a and U.S. EPA/OPP/EFED 2004a. Toxicity Category: IV
Rats, ChR-CD strain, young adult males (4 groups of 10) and females(5 groups of 10), fasted approximately 24 hours prior to dosing.	Single gavage dose of 5000, 6000, 7000, or 9000 mg/kg bw. Formulation: benzene-sulfonamide (DPX-4189, Haskell #13,402) (80% a.i.) suspended in corn oil.	LD_{50} =7699 mg/kg bw (males) (95% CI =6996-8891 mg/kg bw) LD_{50} =7634mg/kg bw (females) (95% CI =6806-9198 mg/kg bw) Most frequently observed clinical signs included stained and wet perineal area, stained face, weakness, and slight to moderate weight loss.	Hinckle and Dashiell 1980 MRID 00031407

Species	Compound	Response	Reference
	14 day observation period.	Mortality occurred within 1-4 days of dosing. Gross pathology indicated changes to lungs, thymus, spleen, kidneys, stomach, liver, testes, brain, and eyes.	
Rats, Crl:CD strain, fasted young adult males and female, 10/dose group	Single gavage dose of 3000, 3200, 3500, or 4000 mg/kg. Formulation: benzene-sulfonamide (INW-4189-83) (Haskell #13,808) (DPX-4189, **75% dry flowable**) (75% a.i., 25% inerts) in corn oil suspension.	Males: LD_{50} =3053 mg/kg bw (95% CI =1123-3342 mg/kg bw) LD_{50} =2341mg/kg bw) (95% CI =1969-2623 mg/kg bw) Gross pathological changes in lungs at all dose levels; changes seen in thymus, brain, stomach, GI tract, liver, and eyes at most dose levels; organ changes in salivary lymph nodes, spleen, adrenals, and kidneys; clinical signs observed at most doses levels included diarrhea, stained and wet perineal area, stained face, eyes half-closed, weakness, lethargy, and weight loss; all deaths occurred within 3 days after dosing.	Dashiell and Hinckle 1981 MRID 00083958
Rats	N.S.	LD_{50} > 5,000 mg/kg bw	Alligare LLC 2010, MSDS for Chlorsulfuron 75
Rats	N.S.	LD_{50} > 2000 mg/kg bw	DuPont Crop Protection 2015, SDS for Telar XP
Guinea pigs, young adult males (3 groups of 10)	Single gavage doses of 1000, 1500, or 2000 mg/kg bw benzenesulfon-amide (INW-4189-57) (91.9% by analysis) suspended in corn oil. Observation: 14 days.	LD_{50} =1363 mg/kg bw Commonly observed clinical signs of toxicity included stained faces and perineal area, half-shut eyes, and weight loss. Mortality occurred with 9 days after dosing. Gross pathological changes were observed in the lungs.	Hall and Dashiell 1980 MRID 00031408
I.P.			
Rats, young adult males (4 groups of 10) observed for 14 days (average body weights ranged from 256- 269 g).	Single IP doses of 1200, 1400, 1600, or 2500 mg/kg benzenesulfon-amide (INW-4189-19) (approximately 100%) suspended in corn oil	LD_{50}: 1450 mg/kg bw (95% CI =1352-1575 mg/kg bw) Commonly observed clinical signs of toxicity included half-closed eyes, stained face and perineal areas, diarrhea, weakness, lethargy, and weight loss.	Hinckle 1979 MRID 00031410

Appendix 1: Toxicity to mammals *(continued)*

Species	Compound	Response	Reference
		Complete mortality (10 of 10 rats) at 2500 mg/kg. Gross pathology revealed the compound throughout organ surfaces, adhesions in the liver and diaphragm, slight enlargement of the lymph nodes, and hyperinflation of the lungs.	

See Section 3.1.4 for general discussion.

Table A1-2: Subchronic and Chronic Toxicity Studies

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Subchronic			
Mice, weanling, males and females, 10/sex/dose group	Dietary concentrations of 0, 500, 2500, 5000, or 7500 ppm sulfonamide (INW-4189-19). Duration: 3 months U.S. EPA/OPP/HED 2015a, p. 20: Equivalent doses: **M**: 0, 150, 783, 1557, or 2130 mg/kg/day **F**: 0, 220, 1214, 2134, or 3176 mg/kg/day	No mortality; no adverse effects on weight gain, food consumption, or food efficiency Males at 5000 or 7500 ppm had lower erythrocyte counts and higher mean corpuscular volumes and mean corpuscular hemoglobin values, compared with male controls Females at 5000 or 7500 ppm had fewer neutrophilic granulocytes and more lymphocytes, compared with female controls No adverse effects observed in any mice at 500 or 2500 ppm INW-4189. NOEL = 2500 ppm Histological NOEL = 7500 ppm (Du Pont de Nemours 1977b) U.S. EPA/OPP/HED 2015a, p. 20: NOAEL: 1557 mg/kg bw/day LOAEL: 2130 mg/kg bw/day, based on incidence of retinal dysplasia and adrenal capsular cell proliferation	Smith et al. 1980 MRID 00031421 (full study) Du Pont de Nemours 1977b MRID 00032101 (study summary)

Appendix 1: Toxicity to mammals *(continued)*

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Mice, weanling, males and females, 80/sex/dose group	Dietary concentrations of 0, 500, 2500, or 5000 ppm benzenesulfon-amide (INW-4189-22, Haskell #12,700) Duration: 52 weeks	Mortality rate (4-15%) suggestive of compound-related effect was statistically significant ($p \leq 0.05$) in males and females at 5000 ppm, compared with controls. Specific mortality rates were: controls: males (4/80); females (3/80), 500 ppm: males (8/80); females (6/80), 2500 ppm: males (11/80); females (9/80) 5000 ppm: males (12/80); females (11/80). Decreases in mean body weights and mean total body weight gains were observed in both sexes at 5000 ppm and in females at 500 and 100 ppm; mean daily food consumption but not food efficiency was decreased in all treated female mice, compared with controls. No further observations were made regarding treatment-related effects on nutritional, behavioral, clinical, biochemical, hematological, gross pathological, or histopathological parameters. Histological NOEL = 5000 ppm (Du Pont de Nemours 1977b)	Wood et al. 1980c MRID 00031422 Du Pont de Nemours 1977b MRID 00032101
Rats, 10 young adult males; positive control group of 10 young adult males	Gavage doses of 2200 mg/kg/day benzene-sulfonamide (INW-4189-4) 30% suspension in corn oil 5 times/week for 2 weeks Duration: 14 days	Mortality: 2/10 (deaths occurred after 5th and 9th doses). No treatment related gross or histopathological effects were observed.	Henry 1977 MRID 00031409

Appendix 1: Toxicity to mammals *(continued)*

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Rats, weanling, males and females, 10/sex/dose group	In the diet at concentrations of 0, 100, 500, or 2500 ppm INW-4189 (≈95% pure) Duration: 90 days U.S. EPA/OPP/HED 2015a, p. 20: Equivalent doses: **M**: 0, 6.5, 33.7, or 161.1 mg/kg/day **F**: 0, 8.1,40.4, or 216.6 mg/kg/day	No mortality; changes in plasma creatinine, hematocrits, and erythrocyte counts, which exhibited only slight correlations to the amount of INW-4189 added to the diet could not be clearly related to the dietary presence of the test compound; a decrease in urine pH among male rats exposed to concentrations of 500 or 2500 ppm INW-4189 in the diet was considered of unclear biological significance in the absence of treatment-related histopathological effects in the kidney; no other dietary , biochemical, hematological, clinical, or behavioral changes were attributed to the dietary presence of the test material; no gross pathological or histopathological abnormalities or lesions were observed that could be attributed to the dietary presence of INW-4189. Histological NOEL = 2500 ppm (Du Pont de Nemours 1977b) U.S. EPA/OPP/HED 2015a, p. 20: NOAEL: 161.1 mg/kg bw/day Dosing inadequate; well below the limit dose (Unacceptable/Guideline)	Wood et al. 1980a MRID 00031418 (full study) Du Pont de Nemours 1977b MRID 00032101 (study summary)

Appendix 1: Toxicity to mammals *(continued)*

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Rats, weanling, males and females, 80/sex/dose group	Dietary concentrations of 0, 100, 500, or 2500 ppm INW-4189-22 (≈95% pure). Duration: 52 weeks	Significant ($p \leq 0.05$) and consistent decreases in weight gain, mean body weights, and food consumption in male rats in 2500 ppm dose group, compared with controls; slight but not statistically significant decrease in mean body weights of males in 500 ppm dose group during weeks 1-51, compared with controls; decreased mean total body weight gain by the end of the study in male rats in 500 ppm dose group; no adverse effects on mean body weights or weight gain in males in the 100 ppm dose group or in females at any dose level; male rats in the 500 and 2500 ppm dose groups had decreased erythrocyte counts and mean corpuscular hemoglobin concentrations as well as increased hematocrits, mean cell volumes and mean cell hemoglobin concentrations; female rats in all dose groups had an increased incidence of stained and discolored fur; no further treatment-related nutritional, clinical, biochemical, urinary, gross pathological or histopathological changes were observed. Histological NOEL = 2500 ppm (Du Pont de Nemours 1977b)	Wood et al. 1980b MRID 00031419 (full study) Du Pont de Nemours 1977b MRID 00032101 (study summary)

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Dogs, young adult purebred beagles, males and females, 4/sex/dose group	Dietary concentrations of 0, 100, 500, or 2500 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) (~95% a.i.) for 26 weeks. Duration: 26 weeks <u>U.S. EPA/OPP/HED 2015a, p. 20:</u> Equivalent doses of 0, 3.7, 18.5, or 82.3 mg/kg bw/day (M/F).	No mortality; significant increase in relative numbers of lymphocytes and eosinophils in males at 500 and 2500 ppm, compared with controls; lower than average serum glutamic-pyruvic transaminase activity in control females that caused apparent increase in that enzyme activity in females at 2500 ppm; decreased albumin concentrations throughout the study in all treated males, compared with controls, which was neither dose related nor attributed to dietary presence of test material; no treatment-related pathological changes; changes in relative organ weights not attributed to dietary presence of test material included decreases in the relative weights of the pituitary in males at 2500 ppm and decreased relative thyroid/parathyroid weights in males in all treatment groups. Histological NOEL = 2500 ppm (Du Pont de Nemours 1977b) <u>U.S. EPA/OPP/HED 2015a, p. 20</u>: NOAEL: 82.3 mg/kg bw/day LOAEL: >82.3 mg/kg bw/day	Schneider et al. 1992 MRID 00031420 (full study) Du Pont de Nemours 1977b MRID 00032101 (summary)

Appendix 1: Toxicity to mammals *(continued)*

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Chronic			
Mice, CD, males and females, 80/sex/dose group	Dietary concentrations of 0, 100, 500, or 5000 ppm benzenesulfonamide [INW-4189-22; Haskell #12,700-01 (95% pure) Duration: 2 years. U.S. EPA/OPP/HED 2015a, p. 20: Equivalent doses of 0, 15, 108, or 750 mg/kg bw/day (M/F) by a standard conversion factor.	Statistically significant decreases in mean body weights and weight gains were observed in male and female mice at 5000 ppm; other body weight effects, particularly in females at 100 and 500 ppm may have been due to the lower daily food consumption observed in these treatment groups. No treatment-related behavioral, clinical, hematological, gross pathological or histological changes were observed; survival and the incidence and time to first observation of palpable tissue masses and the incidence of tumors among treated mice were not significant, compared with controls; no treatment related oncogenicity was observed in the study. NOEL = 500 ppm U.S. EPA/OPP/HED 2015a, p. 20: NOAEL: 108 mg/kg bw/day LOAEL: 750 mg/kg bw/day, based on decreased body weights and body weight gains.	Wood et al. 1981b MRID 00090030

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Rats, CD, males and females, 80/sex dose group	Dietary concentrations of 0, 100, 500, or 2500 ppm technical grade benzenesulfon-amide (INW-4189) Duration: 2 years. U.S. EPA/OPP/HED 2015a, p. 20: Equivalent doses of 0, 5, 25, or 125 mg/kg bw/day.	Treatment related adverse effects included decreases in mean body weights and weight gains among male rats in the 2500 ppm group and to a lesser extent and particularly during year 2 of the study among male rats in the 500 ppm group. The body weight effects observed at 2500 ppm among males were accompanied by decreased efficiency in the use of food for body weight gain. Dose related hematological effects including decreased erythrocyte counts; increased hematocrits, mean corpuscular volumes and corpuscular hemoglobin value; and slightly decreased mean corpuscular hemoglobin concentrations were observed only during the first year in males at 500 and 2500 ppm. The investigators indicate that although the findings suggest the presence of reticulocytosis, the reticulocyte counts were not measured during this period. Consequently, the investigators conclude that in the absence of clarifying data, the biological significance of these hematological effects is unclear. Except as noted above, no behavioral, nutritional, clinical, hematological, gross, or histopathological abnormalities were observed. Survival and the incidence of palpable tissue masses among treated rats were comparable to those of control group rats. Study authors: NOAEL = 100 ppm (5 mg/kg bw/day) U.S. EPA/OPP/HED 2015a, p. 20: NOAEL: 5 mg/kg bw/day LOAEL: 25 mg/kg bw/day based on decreased body weights and body weight gains in males.	Wood et al. 1981a MRID 00086003 **Note: This is the basis for the chronic RfD for members of the general population. U.S. EPA/OPP/HED 2015a, p. 8.**

Appendix 1: Toxicity to mammals *(continued)*

Organism	Agent/Exposure	Response	MRID, Study Date, Classification
Dogs, beagles, 6 ½ months old, males (mean wgt = 9.3 kg) and females (mean wgt = 8.2 kg), 5/sex/dose group	Dietary concentrations of 100, 2000 or 7500 ppm chlorsulfuron (DPX-W4189) (~97.5% a.i.) (beige powder) for 1 year. U.S. EPA/OPP/HED 2015a, p. 20: Equivalent doses: **M**: 0, 3.5, 65.6, or 21.5 mg/kg/day **F**: 0, 3.5, 60.6, or 254.5 mg/kg/day	Hematological changes and slight body weight changes in females at 7500 ppm; NOEL = 2000 ppm. No treatment-related mortality; greatest treatment-related effect on body weight observed in females at 7500 ppm; treatment-related decreases in erythrocyte count, hemoglobin and hematocrit were observed in high-dose (7500 ppm) females at months 3, 6, and 9, most of which were statistically significant from controls. U.S. EPA/OPP/HED 2015a, p. 20: NOAEL: 60.6 mg/kg bw/day LOAEL: 215 mg/kg bw/day based on decreased body gain, erythrocyte counts, and hemoglobin levels	Atkinson 1991 MRID 41862601

See Section 3.1.5 for discussion.

Table A1-3: Reproductive and Developmental Studies

Species	Exposure	Response	MRID(s), (Year), Classification
Developmental			
Rabbits, New Zealand white, nulliparous females, wgt = 2491.3-3671.8 g, mean wgt = 3055.1 g ± 23.35 g, 20/dose group	Daily dose levels of 0, 25, 75, 200, 400, and 1000 mg/kg bw/day as chlorsulfuron (DPX-W4189-165) (98.2% purity) by gavage on days 7-19 of gestation. U.S. PA/OPP/HED 2015a, p. 21: 0, 25, 75, 200, or 400 mg/kg/day (original study), 400 or 1000 mg/kg/day (supplemental study).	Evidence of maternal toxicity at 1000 mg/kg/day included a significant incidence of mortality and abortions, a significant increase in the incidence of females with clinical signs, significant decreases in mean maternal body weight, and significantly reduced mean maternal weight gains for days 7-29. At 400 mg/kg/day, the only evidence of maternal toxicity was a significant decrease in mean maternal adjusted body weight gains on days 7-29; this finding was accompanied by a significant trend. No other maternal toxic effects were seen at any dose level. Increase in fetal malformations and decreases in fetal body weights. U.S. EPA/OPP/HED 2015a, p. 8. Maternal NOAEL: 75 mg/kg/day Maternal LOAEL: 200 mg/kg/day based on decreases in body weights and body weight gains. Fetal NOAEL: 200 mg/kg bw/day Fetal LOAEL: 400 mg/kg bw/day based on increases in visceral malformations and decreases in fetal body weights.	Alvarez 1991b MRID 41983101 Supplemental **Note: This is the basis for the short-term incidental oral d/r assessment for members of the general population as well as the short- and intermediate term occupational assessment. U.S. EPA/OPP/HED 2015a, p. 8.** **Also summarized in EFSA 2008 and FAO/WHO 2003.**

Rats, females, nulliparous 64 days old, wgt = 245.1-38.0 g, mean wgt =291.9 g ± 1.12 g, 25/dose group	Doses: 0, 55, 165, 500 or 1500 mg/kg chlorsulfuron (DPX-W4189-165) (98.2% pure) by gavage on days 7-16 of gestation.	Significant maternal toxicity at daily dose levels ≥500 mg/kg; fetal toxicity observed only at 1500 mg/kg, which was a maternally toxic dose level. At 1500 mg/kg dose level, maternal toxicity was expressed as mortality (spontaneous deaths in one female on day 12 and in another on day 18 of gestation); significant weight loss and reduced body weight gain especially on days 9-11 of gestation; significant decreases in food consumption throughout the dosing period; and a significant increase in the number of females with clinical findings (20/25) was significantly increased. Fetal toxicity was manifested as a significant decrease in fetal weight; there were no significant increases in fetal malformations or variations. At 500 mg/kg dose level, effects on body weight, feed consumption, and the incidence of clinical effects (12/25) were similar but less severe than those observed at the high-dose level. At 165 or 55 mg/kg dose levels, there was no indication of adverse effects on maternal bodyweights, feed consumption, or clinical findings, and there were no effects on mean nidations or live fetuses/litter, in utero survival, or mean corpora lutea counts. Maternal: NOAEL = 165 mg/kg/day Fetal NOAEL = 500 mg/kg/day <u>U.S. EPA/OPP/HED 2015a, p. 20-21</u>: NOAEL: 165 mg/kg bw/day LOAEL: 500 mg/kg bw/day, based on clinical signs (vaginal discharge with associated alopecia). At HDT, there were two deaths (GD 12 and 18), and additional clinical signs (swollen limbs and faces) Developmental NOAEL: 500 mg/kg//day Developmental LOAEL: 1500 mg/kg/day, based on decreased fetal body weight.	Alvarez 1991a MRID 41976406 Acceptable/Guideline Also summarized in EFSA 2008 and FAO/WHO 2003.
Rabbits, New Zealand white	Chlorsulfuron in corn oil (controls) or 10, 25,	Two rabbits, one at 25 mg/kg bw and one at 75 mg/kg died on gestation	Hoberman 1980 MRID 00083945

Species	Exposure	Response	MRID(s), (Year), Classification
females, body weights of 3.4-5.4 kg, 16 rabbits in control group and low-dose group, 17 rabbits in mid- and high-dose groups	or 75 mg/kg bw (Haskell #12,700) administered by gavage on days 6-19 of gestation.	days 18 and 12, respectively, and one rabbit at 75 mg/kg was sacrificed in extremis on day 28; dose-related decrease observed in mean weight change and decreased food consumption in all treatment groups throughout the dosing period, but changes were not significant; no treatment-related effects observed on uterine and ovarian weights, pregnancy rates, implantation efficiency, mean fetal lengths and weights, or percent of males/litter; an increased incidence of resorptions and a decreased incidence in fetal viability were observed in all treatment group, compared with controls, but both effects were statistically significant only in the high-dose group (75 mg/kg bw); no significant differences with respect to skeletal anomalies, compared with controls. NOEL for teratogenicity = 75 mg/kg bw NOEL for embryotoxicity = 25 mg/kg bw	Hoberman et al. 1980 MRID 00086827 [These appear to be different submissions of the same study.] Working Note: These studies are not reviewed in U.S. EPA/OPP/HED 2002b, 2012a, 2015a
Rats, Charles River, 2- to 3-days pregnant	Dietary concentrations of 0,100, 500, or 2500 ppm benzenesulfonamide (INW-4189-13) on days 6 through 15 of gestation.	No embryotoxic or teratogenic effects observed; no effects on food consumption or weight gain, compared with controls; no clinical signs of toxicity, behavioral changes, or pathological changes in observed organs and tissues; no adverse effects on the numbers of implantation sites, resorptions, or live fetuses; and no adverse effects on embryonal development.	Rogers et al. 1978 MRID 00031424 Working Note: Not cited or reviewed in U.S. EPA/OPP/HED 2002b, 2012a, 2015a

Species	Exposure	Response	MRID(s), (Year), Classification
Reproduction			
Rats, Crl:CD® (SD)IGS BR, 30/sex/dose	Dietary concentrations of chlorsulfuron (97.6%; Batch#DPX-W4189-723) throughout 10-week premating period and through gestation/lactation (up to 107 days). Nominal concentrations: 0, 100, 500, 2500, or 7500 ppm Equivalent to doses of: 0, 6, 30,151, or 456 mg/kg/day (males)/ 0, 7, 39, 188, or 591 mg/kg/day (females)	No treatment-related effects on survival, clinical signs, organ weights or gross/microscopic findings in adult rats of either sex or generation. High Dose: Slight reductions observed in body weight (males 94% of control)/body-weight gain (P1 males 88%/F1 males 94% of control), mainly in males, accompanied by decreases in food efficiency (82%-91% of controls) in both generations during the premating periods. **Parental systemic NOAEL**: 2500 ppm (151/188 mg/kg/day, M/F) **Parental systemic LOAEL**: 7500 ppm (456/591 mg/kg/day, M/F) based on decreased body weight, weight gain and food consumption. No effects observed on litter size, live birth index, number born dead, viability and lactation indices, clinical observations, or sex ratio. No treatment-related effects on organ weights (brain, spleen, thymus) or gross microscopic observations in either generation. No treatment-related effects observed on ovarian follicle counts in F_1 females, sperm and estrous cycle parameters in P_1 and F_1 adults, mating, pre-coital interval, fertility, gestation length, number of implantation sites, or implantation efficiency in either the P_1 or F_1 generation. **Reproductive NOAEL**: 7500 ppm (456/498 mg/kg/day) (HDT) **Offspring NOAEL**: 7500 ppm (456/498 mg/kg/day) (HDT)	Mylchreest 2005 (as summarized in Data Evaluation Record) U.S. EPA/OPP/HED 2015a MRID 46493201 (Acceptable/ Guideline)

Species	Exposure	Response	MRID(s), (Year), Classification
Rats, CD®, 20 males and 20 females taken from each treatment level in the 2-year feeding study	3-Generation reproduction study in which the F_0 generation rats taken from the 2-year feeding study summarized in Table A1-2. Dietary Concentrations: 0, 100, 500, or 2500 ppm chlorsulfuron (98.2% pure) for 98 days. U.S. PA/OPP/HED 2015a, p. 21: (0, 100, 500, or 2500 ppm) 0, 5, 25, or 125 mg/kg/day	The only treatment-related adverse effect was a slightly decreased fertility index in the 2500 ppm rats. There were no adverse effects on the mean number of pups per litter or on gestation, lactation, viability indices, litter survival, or mean weanling body weight and weight gains. No treatment-related gross or histopathological changes were observed in weanling rats from the F3B litters. U.S. EPA/OPP/HED 2015a, p. 21: Parental NOEL: 2500 ppm (125 mg/kg/day) Parental LOEL: >2500 ppm (125 mg/kg/day), no effects observed. Reproductive NOEL: 100 ppm (5 mg/kg/day) Reproductive LOEL: 500 ppm (25 mg/kg/day), based on decreased female fertility. Offspring NOEL 2500 ppm (125 mg/kg/day) Offspring LOEL >2500 ppm, no effects observed.	Wood et al. 1981a MRID 00086003 U.S. EPA/OPP/HED 2015a, p. 21 (Unacceptable/ Non-guideline)
Rats, males and females, 20/sex/dose group	Three-generation, six-litter feeding study using in diet concentrations of 0, 100, 500, or 2500 ppm benzene- sulfonamide (INW-4189).	No adverse effects on the reproductive or lactation performance of rats in the 100 or 500 ppm dose groups; Slight alterations in the reproductive and lactation performance observed in the F_{1B} generation rats in the 2500 ppm dose group during the production of F_{2A} litter did not appear to be clearly compound-related. NOEL: 500 ppm, based on decreased fertility indices.	Wood 1980 MRID 00031423 Working Note: This appears to an early submission of Wood et al. 1981a.

Table A1-4: Skin Irritation and Sensitization Studies

Species	Exposure	Response	Reference
Skin Irritation			
NOS	Primary skin irritation (NOS)	Slightly irritating to skin Toxicity Category IV	U.S. EPA/OPP/HED 2015a MRID 46449006
Rabbits, albino, 6 males	0.5 g solid benzene-sulfonamide (INW-4189-51, Haskell #13,402) (**80% a.i.**) slightly moistened with physiological saline applied to 2 intact and 2 abraded skin areas of hair-free trunk and lateral areas. Treated areas covered with double-thickness gauze squares and rubber sheeting secured with adhesive tap for 24 hours. After exposure, treated sites were wiped to remove remaining test material.	Test compound found not to be a primary skin irritant. Draize score ranged from 0.0 to 2.63.	Henry and Dashiell 1980 MRID 00031416
Guinea pigs, albino, 10 males, average weight of 763 g	Primary irritation test involved application via lightly rubbing of 1 drop (~0.05 mL) each of 30% and 3% suspension (w/v) of benzene-sulfonamide (INW-4189-3, Haskell #10,539) in propylene glycol on shaved intact shoulder skin.	No irritation observed.	Goodman 1976 MRID 00031417
Rabbits, 6 albino males	0.5 g benzenesulfonamide (INW-4189, Haskell #13,520, DPX-4189, **75% dry flowable**) as received was applied as an aqueous paste to 2 intact and 2 abraded skin areas of each rabbit. Treated areas were covered with gauze pads, layer of plastic wrap, stretch gauze bandage and elastic adhesive for 24 hours. Treated sites wiped to remove any remaining test material and observed at 72 hours, and 6 and 7 days after treatment.	Not a primary skin irritant. The test material produced no to mild skin irritation on intact and abraded skin of 6 rabbits.	Dashiell and Silber 1980b MRID 00083961
Guinea pigs, Duncan-Hartley males, 3/dose group.	Dermal application 6, 15, 30, or 60% (w/v)benzene sulfonamide (INW-4189-83 DPX-4189,**75% dry flowable**; Haskell #13,808) (75% a.i.) in dimethyl phthalate (DMP). Ranging finding study.	Negative results for skin irritation at 60% in DMP.	Dashiell and Silber 1981 MRID 00083962

Appendix 1: Toxicity to mammals *(continued)*

Species	Exposure	Response	Reference
Skin Sensitization			
NOS	Dermal sensitization (NOS)	Not a skin sensitizer	U.S. EPA/OPP/HED 2015a MRID 46449007
Guinea pigs, albino, 10 males (treatment group) 10 males (control group received similar applications at time of challenge), average weight of 796 g.	Test of sensitization potential involved a series of 4 sacral intradermal injections (1/week for 3 weeks). Injections consisted of 0.1 mL of a 1% solution (w/v) of test material in dimethyl phthalate. After 2-week rest period, guinea pigs were challenged for sensitization by applying and lightly rubbing in 1 drop (~0.05 mL) each of 30% and 3% suspension (w/v) of benzene-sulfonamide (INW-4189-3) in propylene glycol on shaved intact shoulder skin.	No sensitization response was observed.	Goodman 1976 MRID 00031417
Guinea pigs, Duncan-Hartley males, 3/dose group	Sensitization Test involved a series of 4 sacral intradermal injections of 0.1 mL benzene-sulfonamide (INW4189-83; DPX-4189,75% dry flowable; Haskell #13,808) (75% a.i.) of 1.0% suspension in DMP1 each week beginning after treatment for primary irritation. After 13-day rest period, challenge phase began with application via lightly rubbing 0.05 mL of 6 or 60% suspension of test material in DMP on shaved intact shoulder skin. Control (10 unexposed guinea pigs) of the same age received identical topical applications.	Slight irritation observed at 60% in both test and control guinea pigs at challenge. No sensitization response observed at 60% concentration during challenge. Sensitization response ratio - 0/10.	Dashiell and Silber 1981 MRID 00083962

Table A1-5: Eye Irritation Studies

Species	Exposure	Response	Reference
NOS	Primary eye irritation (NOS)	Not an eye irritant Toxicity Category IV	U.S. EPA/OPP/HED 2015a MRID 46449005
Rabbits, albino, 9 males	0.1 mL (~ 30 mg) of an 80% formulation of chlorsulfuron (DPX-4189, 75% dry flowable) (Haskell #13,402) administered to right eye (left eye served as untreated control). In 3/9 rabbits the right eye was washed w/tap water after 20 seconds; treated eyes of other 6 rabbits were not washed. Eyes examined on days 1, 2, 3, 4, 7, 14 and 19 after treatment.	Unwashed eyes: transient local to moderate areas of slight corneal clouding and mild to no conjunctival irritation. Washed eyes: transient small to local areas of slight corneal clouding and mild to no conjunctival irritation. No iritic involvement observed in washed or unwashed eyes. All eyes were normal 3-4 days after treatment.	Silber 1980 MRID 00031415
Rabbits, 9 New Zealand white males	0.1 mL (73 mg of formulation) benzenesulfonamide (DPX-4189, **75% dry flowable**) (Haskell # 13,808) (75% a.i.) administered to right eye (left eye served as untreated control). After 20 seconds, the right eye of 3/9 was washed for 1 minute w/tap water; treated eyes of other 6 rabbits were not washed. Eyes examined days 1, 2, 3, 4, 7, 14, and 18 until all ocular signs subsided.	Transient slight corneal clouding and mild conjunctivitis was observed in washed and unwashed eyes; transient slight iritic injection was observed in unwashed eyes and persistent iritic swelling in one washed eye; all unwashed eyes were normal 3 days after treatment; 2/3 washed eyes were normal at 4 days.	Dashiell and Silber 1980a MRID 00083959

Table A1-6: Dermal Toxicity

Species	Exposure	Response	Reference
Acute			
Rabbits, albino, 5 adult males for 2000 mg/kg dose and 10 adult males and 10 adult females for 3400 mg/kg dose; observed for 14-day recovery period and sacrificed.	Single dose of 2000 or 3400 mg/kg as received benzene-sulfonamide (INW-4189-19, Haskell #12,361) (composition ~100%) (moistened with physiological saline) applied to abraded skin on back of each rabbit. Treated areas covered with gauze pads, layer of plastic wrap, stretch gauze bandage and elastic adhesive for 24 hours. Treated sites washed with water and dried after exposure. Necropsy performed on two rabbits from each dose group	LD_{50}: >3400 mg/kg (males and females) Mortality in one rabbit on day 5 after treatment did not appear to be compound related. The rabbit that died had slight skin irritation which persisted through 2 days. All survivors had initial weight loss. No clinical signs of toxicity other than diarrhea in one male. No clinical signs of toxicity observed in females throughout duration of study. U.S. EPA/OPP/HED 2015a, p. 20: LD_{50}: 3400 mg/kg U.S. EPA/OPP 2007a, p. 2 LD_{50}: >3400 mg/kg bw	Edwards 1979a MRID 00031411 Edwards 1979b MRID 00083956 Edwards 1979c MRID 00086824 [These appear to be different submissions of the same study.] Edwards 1979b cited in U.S. EPA/OPP/HED 2015a Toxicity Category: III
Rabbits, albino, 5 adult males and 5 adult females observed for 14-day recovery period and sacrificed.	Single dose of 2000 mg/kg benzene-sulfonamide (DPX-4189; INW-4189-51, Haskell #13,402) (a.i. = 80%) (physiological saline added to form a paste) applied to abraded skin of shaved back. Treated areas covered with gauze pads, layer of plastic wrap, stretch gauze bandage and elastic adhesive for 24 hours. Treated sites wiped dry after exposure.	LD_{50}: >2000 mg/kg (males and females) Observations included slight to moderate erythema with slight swelling; mortality in 1/5 males rabbits within 3 days of treatment; and sporadic weight loss in rabbits during test period.	Silber and Dashiell 1980 MRID 00031412

Appendix 1: Toxicity to mammals *(continued)*

Species	Exposure	Response	Reference
Rabbits, New Zealand white, adults, 5 males and 5 females observed for 14-day period and sacrificed.	Single dose of 2000 mg/kg as received benzene-sulfonamide (INW-4189-611, Haskell #13,520, 75% **dry flowable**) (a.i. = 75%) (moistened with physiological saline) applied to abraded skin of shaved back. Treated areas were covered with gauze pads, layer of plastic wrap, stretch gauze bandage and elastic adhesive for 24 hours. Treated sites wiped dry after exposure.	LD_{50} >2000 mg/kg (males and females) No mortality; sporadic weight loss (males and females); mild to slight kin irritation observed 1-4 days (males) and 1-5 days (females) after treatment with no overt clinical signs of toxicity.	Dashiell and Ashley 1980a MRID 00083960 Dashiell and Ashley 1980b MRID 00086826 [These appear to be different submissions of the same study.]

Table A1-7: Inhalation Toxicity

Species	Exposure	Response	Reference
Rats, young adult, 10 males (weight 257-294 g) and 10 females (weight 210-259 g)	4-hour exposure (males: head only) (females: nose only) to TWA concentration of 5.9 mg/L benzenesulfonamide (INW-4189) (Haskell # 12,700) dust (composition: about 95%), followed by 14-day recovery and then sacrifice (3 animals of each sex were subjected to complete gross necropsy). Test material was considered to be 100% pure a.i. Working Note: Chen 1980 reports a concentration of 5 mg/L	No systemic pathological findings believed to be compound induced. All animals had inflammation/irritation of the nasal passages. Specific tissue changes included mild focal squamous metaplasia of nasal turbinate mucosa and unilateral focal atrophy of nasal gland acini with cystic dilation of ducts in 2/6 rats subject to necropsy. U.S. EPA/OPP/HED 2015a, p. 20: LC_{50} = 5.9 mg/L	Chen 1980 MRID 00083963 Ferenz 1980a MRID 00083957 Ferenz 1980b MRID 00086825 [Appear to be different submissions of same studies] EPA Toxicity Category: IV

Table A1-8: Mutagenicity Assays

Organism/ Assay System	Exposure	Response	Reference
S. typhimurium/E.coli (Gene mutation)	10-5000 µg/plate, +/- S9 (NOS)	Negative, (+/-) S9 mix	U.S. EPA/OPP/HED 2015a MRID 47179902 (Acceptable/ Guideline)
Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100 in the presence or absence of a liver microsomal system (S-9)	up to 30 µg/petri plate U.S. EPA/OPP/HED 2015a, p. 21: 6-30 µg/plate, +/- S9	No significant increase in mutation frequencies. U.S. EPA/OPP/HED 2015a, p. 21: Negative, (+/-) S9 mix	Russell 1977 MRID 00031425 (Unacceptable/ upgradable)
Mouse bone marrow micronucleus	0, 500, 1000, or 2000 mg/kg, gavage	Negative	U.S. EPA/OPP/HED 2015a MRID 47179903 (Acceptable/ Guideline)
Chinese hamster ovary (CHO) cells in the presence or absence of a liver microsomal system (S-9)	20-60 µL benzenesulfonamide (INW-4189-22, Haskell #12,700), (about 95% purity) U.S. EPA/OPP/HED 2015a, p. 21: 0.028-2.8 mM, +/- S9	No dose-related cytotoxicity either with or without S-9 activation	Krahn and Waterer 1980a MRID 00083943 (Unacceptable/ upgradable) Krahn and Waterer 1980b MRID 00086828 [These appear to be different submissions of the same study.]
Chinese hamster ovary (CHO) cells in the presence or absence of a liver microsomal system (S-9)	≤5 mg/mL benzene-sulfonamide (Haskell #12,700) with or with metabolic activation	No aberrations in CHO cells with or without metabolic activation	Galloway and Lebowitz 1981a MRID 00086830 Galloway and Lebowitz 1981b MRID 00086830 [These appear to be different submissions of the same study.]
in vitro cytogenetics assay; chromosome aberration [CHO-WBI cells]	16.7-5000 µg/mL, +/- S9	Negative	U.S. EPA/OPP/HED 2015a MRID 00088755 (Acceptable)

Appendix 1: Toxicity to mammals *(continued)*

Organism/ Assay System	Exposure	Response	Reference
Dominant lethal mutations assay, Rats, Sprague-Dawley, males, 49-days-old, average weights 192-279 g, 10 controls and 10/dose group	Dietary concentrations of 0 (basal diet), 100, 500, or 5000 ppm Haskell #12,700 (white powder)(purity assumed to 100%for purposes of dose calculations) for 10 weeks	No morality; treatment related effects included decreased weight gain in the mid- to high dose groups, compared with controls; increased mean incidence of resorptions/litter; decreased mean incidence of fetal viability in females mated to high-dose males during week 2 of breeding; no adverse effects on the mean number of implantations, resorptions, dead fetuses, or live fetuses. No dominant lethal mutations observed.	Hoberman and Fieser 1980a MRID 00083944 (Unacceptable) Hoberman and Fieser 1980b MRID 00086829 [These appear to be different submissions of the same study.]
Rat hepatocytes, hepatic primary culture/DNA repair assay	≤2.0 mg/mL Haskell #12,700 dissolved in DMSO U.S. EPA/OPP/HED 2015a, p. 21: 0.0002-2.0 mg/mL Confirmatory: 0.0004-4.0 mg/mL	No genotoxic effects.	Williams et al. 1981 MRID 00090008 (Unacceptable/ upgradable)
Rat hepatocytes, unscheduled DNA synthesis	0-3750 µg/mL IN W4189-165 dissolved in DMSO	No effect on unscheduled DNA synthesis	Vincent 1990 MRID 42545601

Appendix 2: Toxicity to birds

Table A2-1: Acute Oral/Gavage Toxicity to Birds 169
Table A2-2: Acute Dietary Toxicity to Birds 170
Table A2-3: Reproductive and Subchronic Toxicity to Birds 171

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

Species	Exposure	Response	Reference
Bobwhite quail (*Colinus virginianus*) Males (initial body weight 176-234g) and females (initial body weight 179-238 g), 5/sex /dose group	Doses: 312.5 to 5000 mg/kg H-12361(white crystalline powder; In 0.5% methyl-cellulose; controls received 10 mL/kg 0.5% methlycellulose alone	LD_{50} >5000 mg a.i./kg bw (males and females)	Hinkle and Twigg 1980 MRID 00035263 Practically non-toxic
Mallard ducks (*Anas platyrhynchos*), males (initial weight 960-1280 g) and females (initial weight 900-1255 g), 5/sex/dose group	Doses: 312.5 to 5000 mg/kg H-12361 suspended in corn oil; controls received 20 mL/kg corn oil.	LD_{50} >5000 mg a.i./kg bw (males and females)	Hinkle and Bristol 1980 MRID 00035264

Table A2-2: Acute Dietary Toxicity to Birds

Species	Exposure	Response	Reference
Bobwhite quail (*Colinus virginianus*), 10/dose group (NOS)	Dietary Concentrations: 156.25-5000 ppm H-12361. 5 days on test diet followed by 3 days on basal diet.	LC_{50} >5000 ppm Due to mortality which did not appear to be treatment related (i.e., few deaths occurring at the highest dose levels) the LC_{50} is estimated to be >5000 mg/kg	Hinkle 1979b MRID 00035265
Bobwhite quail (*Colinus virginianus*), 14-days old, 10 birds/dose group	Dietary Concentrations: 0, 562, 1000, 1780, 3160, and 5620 ppm Haskell #12,700 5 days on test diet followed by 3 days on basal diet. Average daily food consumption/bird ≈9.1 g. Average body weight ≈ 30.6 g. Food conversion factor: 9.1 g ÷ 30.6 g ≈0.2973 g food/g bw. Body weights were reported as group averages for each treatment group at the beginning of the exposure period (Day 1) and 3 days after the end of exposure (Day 8). To determine an average body weight, the average of Day 1 (22.4 g) and Day 8 (38.8 g) weights was taken.	LC_{50} >5620 ppm No mortality; at 562 ppm, one bird had lesions of nostril picking on days 2-4; all other birds at all concentration levels were normal in appearance and behavior throughout the test period. Body weight gain was slightly depressed at 1780 and 5620 ppm. NOAEL: 1000 mg/kg diet based on reduced body weight at 1780 mg/kg bw. 1000 mg/kg diet x 0.3 kg diet/kg bw ≈ 300 mg/kg bw/day.	Fink et al. 1981 MRID 00090009
Mallard ducks (*Anas platyrhynchos*), ≈2-weeks old, 10/dose group (NOS)	Dietary Concentrations: 156.25-5000 ppm H-12361. 5 days on test diet followed by 3 days on basal diet.	LC_{50} >5000 mg a.i./kg-diet	Hinkle and Wentz 1979 MRID 00032566 Practically non-toxic Working Note: Used by U.S. EPA/OPP/EFED 2004a, Table 7, for risk characterization.

Table A2-3: Reproductive and Subchronic Toxicity to Birds

Species	Exposure	Response	Reference[1]
Bobwhite quail (*Colinus virginianus*), males and females, 25 weeks old, 16/sex/dose group	Dietary Concentrations: 0, 40, 200, or 1000 ppm chlorsulfuron (H-12361). 22 weeks (1-generation reproduction study) The average fractional food consumption of 0.14 was determined by dividing the average food consumption/bird/day (individual animal data provided in Table 2, p. 31 of Beavers et al. 1992a) by an average body weight during the 22-week study (individual animal data provided in Table 1, p. 29 of Beavers et al. 1992a).	No treatment-related mortalities or no overt signs of toxicity at any concentration level throughout the study; no apparent treatment-related effects on body weight at 40 or 200 ppm concentrations or in males at the 1000 ppm, compared with controls; at 1000 ppm test concentration there may have been a slight effect upon the body weight gain of hens during the first 8 weeks of the study; no treatment related effects observed on food consumption or reproductive parameters at any test concentration. U.S. EPA/OPP/EFED 2012a, p. 19: NOAEC = 174 mg a.i./kg-diet LOAEC (reproduction) = 961 mg a.i./kg-diet NOAEL: 174 mg/kg diet x 0.14 kg food/kg bw ≈ 24.5 mg/kg bw/day. LOAEL: 961 mg a.i./kg diet x 0.14 kg food/kg bw ≈135 mg a.i./kg bw/day based on decreased body weight. Working Note: The NOAEC and LOAEC values from EPA appear to be based on monitored rather than nominal concentrations.	Beavers et al. 1992a MRID 42634001 Acceptable Working Note: Used by U.S. EPA/OPP/EFED 2004a, Table 7, for risk characterization.
Mallard ducks, males and females, 16/sex/dose group.	Dietary Concentrations: 0, 40, 200, or 1000 ppm chlorsulfuron (Haskell# 18,053). 20 weeks (1-generation reproduction study)	No treatment related mortalities or overt signs of toxicity, no apparent treatment related effects on body weight, food consumption, or reproductive parameters. NOEC = 1000 ppm U.S. EPA/OPP/EFED 2012a, p. 91: NOAEC ≥961 mg a.i./kg-diet LOAEC >961 mg a.i./kg-diet	Beavers et al. 1992b MRID 42634002 Acceptable

Appendix 3: Toxicity to Terrestrial Invertebrates.

Table A3-1: Insects and Other Arthropds 172
Table A3-2: Species other than arthropods 173

Table A3-1: Insects and Other Arthropods

Species	Exposure	Response	Reference
Oral			
Gastrophysa ploygoni (Coleoptera)	Polygonum convolvuvus (dicot) treated at up 1.6 g a.i./ha (0.0014 lb a.i./acre).	Weight of larvae unchanged for chlorsulfuron sprayed leaves compared to larvae feeding on control leaves. See Table 2 of paper.	Kjaer and Elmegaard 1996
Growth			
Gastrophysa ploygoni (Coleoptera)	*Polygonum convolvuvus* (wild buckwheat, dicot) sprayed at 0.32, 0.67, 1.32, and 2.68 g/ha. [i.e., 0.000032 to 0.0024 lb a.i./acre]. Eggs placed on plants.	Survival from egg hatch to imago was significantly affected by chlorsulfuron applied to the host plant at rates of 1.32 and 2.68 g/ha. Increased mortality was observed mainly in the first two instars. No effect was observed at the 2 lowest rates. Development time was increased at the 2 lowest applications rates (not tested at higher rates).	Kjaer and Elmegaard 1996
Pieris brassicae (Lepidoptera) and *Gastrophysa polygoni* (Coleoptera)	Chlorsulfuron (Glean, a 75% formulation) was applied to plants on 4 consecutive days at a rate ranging from 0.025 to 0.8 g a.i./ha (≈0.000022 to 0.0007 lb a.i./acre). Newly hatched larvae were placed on plants 4 days after spraying. Insects removed after 12 days.	No significant effects on survival and relative growth rate (larval fresh weight or adult dry weight) of P. brassicae or G. Polygoni. However, plants had significantly reduced root growth rate, but not shoot growth rate.	Kjaer and Heimbach 2001
Contact (µg/organism)			
Honeybee (*Apis mellifera*)	TGAI, 48 hours	LC_{50}: >25 µg a.i./bee Working Note: Using a standard body weight of 116 mg for the honeybee, the >LD_{50} corresponds to [25 µg ÷ 0.116 g ≈ 216 µg/g bw or mg/kg bw]	U.S. EPA/OPP/ EFED 2012a, MRID 42129902 Acceptable

Species	Exposure	Response	Reference
Contact (spray)			
Gastrophysa polygoni (Coleoptera: Chrysomelidae), first instar, 3 replicates of 10 per group	Concentrations: 0.0012, 0.012, 0.12 and l.2 mg/cm^2. Duration: 6 days (until pupation). Working note: Rates correspond to about 0.107 to 107 lb a.i./acre.	No significant changes in mortality rate were observed for any exposure level.	Kjaer and Elmegaard 1996

Table A3-2: Species other than arthropods

Species	Exposure	Response	Reference
Soil Exposures			
Steinernema carpocapsae and *Steinernema feltiae* (beneficial nematodes)	Chlorsulfuron (NOS) Concentrations: 312, 625, 1250, 2500, 5000, and 10,000 ppm (mg a.i./L) in aqueous solution. Duration: 72 hours	No effects on reproduction, infectivity to wax moth (*Galleria mellonella*) larvae, viability and movement. No additional details. See Table II of paper.	Rovesti and Desco 1990
Steinernema feltiae (benefical nematode), commercial and natural strains	Glean (NOS): 150 ppm Exposure: 48 hours Working Note: 150 ppm, presumably 150 mg a.i./L is characterized as the 'field concentration'. This is within the range of concentrations considered in this risk assessment – i.e., 750 (25-2500) mg a.i./L.	Little impact on commercial strain (11.8% mortality) but more substantial impact (42% mortality) on natural strain.	Gutierrez et al. 2008

Appendix 4: Toxicity to Terrestrial Plants

Table A4-1: Seedling Emergence, Standard Assays 174
Table A4-2: Vegetative Vigor, Standard Assays 176
Table A4-3: Other Toxicity Studies 178
Table A4-4: Supplemental data from Jettner et al. 1999 181
Table A4-5: Field/Efficacy Studies 182

Table A4-1: Seedling Emergence, Standard Assays

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference [1]</th></tr>
<tr><td>Monocots</td><td></td><td></td><td></td></tr>
<tr><td>See Column 3</td><td>Chlorsulfuron (98.2% pure).
Single application of chlorsulfuron mixed with 0.25%X-77 surfactant.
Range of application rates tested varied depending upon species tested. The lowest application rate used was in onions (0.0000088 lb/acre).
Test solutions applied as a pre-emergence soil surface application.</td><td>Summary from U.S. EPA/OPP/EFED 2004a, p. 26.
<table>
<tr><th>Species</th><th>*End-point</th><th>NOAEL (lb a.i./acre)</th><th>EC_{25} (lb a.i./acre)</th></tr>
<tr><td>Corn</td><td>PH</td><td><0.00035</td><td>0.0003</td></tr>
<tr><td></td><td>Em</td><td>0.000439</td><td>0.05</td></tr>
<tr><td>Onion</td><td>PH</td><td>$3.5x10^{-5}$</td><td>0.000163</td></tr>
<tr><td></td><td>Em</td><td>$3.5x10^{-5}$</td><td>0.000413</td></tr>
<tr><td>Sorghum</td><td>PH</td><td>0.000163</td><td>0.00138</td></tr>
<tr><td></td><td>Em</td><td>>0.0219</td><td>ND</td></tr>
</table>
* PH= Plant height; Em=Emergence; ND = Not determined. Value in bold used by EPA for risk characterization.
Sugar beet [Amaranthaceae] is most sensitive species.</td><td>McKelvey and Kuratle 1992
MRID 42587201
Also summarized in U.S. EPA/OPP/ EFED 2004a.</td></tr>
<tr><td>Onion (Allium cepa), most sensitive monocot</td><td>NOS</td><td>Endpoint: Decreased dry weight
NOAEC: 0.000045 ($4.5x10^{-5}$) lbs a.i./acre
EC_{25}: 0.0003 ($3x10^{-4}$) lbs a.i./acre

Working Note: The NOAEL for onion is slightly lower in the above study by McKelvey and Kuratle 1991. Onion is the most sensitive species.</td><td>MRID 46361801
U.S. EPA/OPP/ EFED 2012a, p. 19
Used by EPA as most sensitive monocot for seedling emergence.</td></tr>
</table>

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference [1]</th></tr>
<tr><td>Dicots</td><td></td><td></td><td></td></tr>
<tr><td>See Column 3</td><td>Chlorsulfuron (98.2% pure).
Single application of chlorsulfuron mixed with 0.25%X-77 surfactant.
Range of application rates tested varied depending upon species tested. The lowest application rate used was in onions (0.0000088 lb/acre).
Test solutions applied as a pre-emergence soil surface application.</td><td>Summary from U.S. EPA/OPP/EFED 2004a, p. 26.
<table>
<tr><th>Species</th><th>*End-point</th><th>NOAEL (lb a.i./acre)</th><th>EC_{25} (lb a.i./acre)</th></tr>
<tr><td>Cucumber</td><td>PH</td><td>$3.5x10^{-5}$</td><td>$2.5x10^{-4}$</td></tr>
<tr><td></td><td>Em</td><td>>0.00439</td><td>ND</td></tr>
<tr><td>Pea</td><td>PH</td><td>$3.5x10^{-5}$</td><td>$1.13x10^{-4}$</td></tr>
<tr><td></td><td>Em</td><td>$1.76x10^{-4}$</td><td>$2.81x10^{-4}$</td></tr>
<tr><td>Rape</td><td>PH</td><td>$3.5x10^{-5}$</td><td>$1.13x10^{-4}$</td></tr>
<tr><td></td><td>Em</td><td>>0.00439</td><td>ND</td></tr>
<tr><td>Soybean</td><td>PH</td><td>$8.75x10^{-4}$</td><td>0.0015</td></tr>
<tr><td></td><td>Em</td><td>>0.00439</td><td>ND</td></tr>
<tr><td>Sugarbeet</td><td>PH</td><td>$6.8x10^{-6}$</td><td>$3.8x10^{-5}$</td></tr>
<tr><td></td><td>Em</td><td>$1.76x10^{-4}$</td><td>$2.81x10^{-4}$</td></tr>
<tr><td>Tomato</td><td>PH</td><td>$3.51x10^{-5}$</td><td>$1.69x10^{-4}$</td></tr>
<tr><td></td><td>Em</td><td>>0.02194</td><td>ND</td></tr>
</table>
* PH= Plant height; Em=Emergence; ND = Not determined. Value in bold used by EPA for risk characterization.
Working Note: Sugar beet [Amaranthaceae] is most sensitive species for seedling emergence. Note that a monocot (onion) is the most sensitive species for vegetative vigor. Overall, seedling emergence is most sensitive endpoint.</td><td>McKelvey and Kuratle 1992
MRID 42587201
Also summarized in U.S. EPA/OPP/ EFED 2004a.

NOTE: This study is cited but not summarized or discussed in U.S. EPA/OPP/ EFED 2012a, p. 22. For seedling emergence, plant height in sugar beet is the lowest NOAEC.</td></tr>
<tr><td>Pea (Pisum sativum), most sensitive dicot</td><td>NOS</td><td>NOAEC: 0.00018 ($1.8x10^{-4}$) lbs a.i /acre
EC_{25}: 0.000022 ($2.2x10^{-5}$) lbs a.i./acre

Working Note: The EC_{50} is lower than the NOAEC. This sometimes happens depending on the slope of the dose-response curve and variability in the responses.
Also note that the NOAEC for plant height for sugar beet from the study by McKelvey and Kuratle 1992, MRID 42587201, is somewhat lower – i.e., 0.0000068 lb a.i./acre.</td><td>MRID 46361801
U.S. EPA/OPP/ EFED 2012a, p. 22.

Working Note: Used by EFED 2012a, p. 19, for most sensitive dicot in seedling emergence.</td></tr>
</table>

Table A4-2: Vegetative Vigor, Standard Assays

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference [1]</th></tr>
<tr><td>Monocots</td><td></td><td></td><td></td></tr>
<tr><td>See Table in column 3</td><td>Chlorsulfuron (98.2% pure).
Single application of chlorsulfuron mixed with 0.25%X-77 surfactant.
Range of application rates tested varied depending upon species tested. The lowest application rate used was in onions (0.0000088 lb/acre).</td><td>Summary from U.S. EPA/OPP/EFED 2004a, p. 27.
<table>
<tr><th>Species</th><th>*End-point</th><th>NOAEL (lb a.i./acre)</th><th>EC_{25} (lb a.i./acre)</th></tr>
<tr><td>Corn</td><td>PH</td><td>0.000225</td><td>0.000625</td></tr>
<tr><td></td><td>SW</td><td>0.000225</td><td>0.0001937</td></tr>
<tr><td>Onion</td><td>PH</td><td>$8.7x10^{-6}$</td><td>0.0000368</td></tr>
<tr><td></td><td>SW</td><td>$8.7x10^{-6}$</td><td>0.0000044</td></tr>
<tr><td>Sorghum</td><td>PH</td><td>0.000225</td><td>0.002625</td></tr>
<tr><td></td><td>SW</td><td><0.000720</td><td>0.0001562</td></tr>
<tr><td>Wheat</td><td>PH</td><td>0.001125</td><td>0.05563</td></tr>
<tr><td></td><td>SW</td><td>0.02813</td><td>0.005813</td></tr>
</table>
* PH= Plant height; SW=Shoot Weight; ND = Not determined. Value in bold used by EPA for risk characterization.
Value in bold used by EPA for risk characterization.
EPA Note: The most sensitive parameter in the vegetative vigor toxicity study was the sugarbeet root weight (EC05 = 0.000000019375 lbs ai/acre). However, the EC05 for onion shoot weight (0.000000045625 lbs ai/acre) was used in the risk assessment for endangered species because this endpoint provided stronger results.</td><td>McKelvey and Kuratle 1992
MRID 42587201
Also summarized in U.S. EPA/OPP/ EFED 2004a.</td></tr>
<tr><td>Onion (Allium cepa), most sensitive monocot</td><td>NOS</td><td>Endpoint: dry weight and shoot height
EC_{25}: 0.000022 ($2.2x10^{-5}$) lbs a.i /acre
EC_{05}: 0.0000026 ($2.2x10^{-6}$) lbs a.i./acre

Working Note: The EC05 from this study is somewhat below the NOAEL from the above study by McKelvey and Kuratle (1992) – i.e., 0.0000087 lb a.i./acre.</td><td>MRID 46326801
U.S. EPA/OPP/ EFED 2012a, p. 22

Used by EFED 2012a, p. 19, as most sensitive monocot for vegetative vigor.</td></tr>
</table>

<table>
<tr><th>Species</th><th>Exposure</th><th>Response</th><th>Reference [1]</th></tr>
<tr><td>Dicots</td><td></td><td></td><td></td></tr>
<tr><td>See Table in column 3</td><td>Chlorsulfuron (98.2% pure).
Single application of chlorsulfuron mixed with 0.25%X-77 surfactant.
Range of application rates tested varied depending upon species tested. The lowest application rate used was in onions (0.0000088 lb/acre).</td><td>Summary from U.S. EPA/OPP/EFED 2004a, p. 27.
<table>
<tr><th>Species</th><th>*End-point</th><th>NOAEL (lb a.i./acre)</th><th>EC_{25} (lb a.i./acre)</th></tr>
<tr><td>Cucumber</td><td>PH</td><td>0.000225</td><td>0.001875</td></tr>
<tr><td></td><td>SW</td><td>0.001125</td><td>0.006125</td></tr>
<tr><td>Pea</td><td>PH</td><td>0.00045</td><td>0.00025</td></tr>
<tr><td></td><td>SW</td><td>0.000045</td><td>0.000181</td></tr>
<tr><td>Rape</td><td>PH</td><td>0.000045</td><td>0.0001</td></tr>
<tr><td></td><td>Em</td><td>$8.7x10^{-6}$</td><td>0.0002</td></tr>
<tr><td>Soybean</td><td>PH</td><td>0.000045</td><td>0.0000443</td></tr>
<tr><td></td><td>SW</td><td>$8.7x10^{-6}$</td><td>0.0000193</td></tr>
<tr><td>Sugarbeet</td><td>PH</td><td>$8.7x10^{-6}$</td><td>0.0002062</td></tr>
<tr><td></td><td>SW</td><td>$8.7x10^{-6}$</td><td>0.0000268</td></tr>
<tr><td>Tomato</td><td>PH</td><td>0.000045</td><td>0.0002062</td></tr>
<tr><td></td><td>SW</td><td>0.000045</td><td>0.0000268</td></tr>
</table>
* PH= Plant height; SW=Shoot Weight; ND = Not determined.</td><td>McKelvey and Kuratle 1992
MRID 42587201
Also summarized in U.S. EPA/OPP/ EFED 2004a.</td></tr>
<tr><td>Rape (Brassica rapa), most sensitive dicot</td><td>NOS</td><td>Endpoint: dry weight and shoot height
EC_{05}: 0.0000008 ($8x10^{-7}$) lbs a.i /acre
EC_{25}: 0.00001 ($1x10^{-5}$) lbs a.i./acre

Working Note: The EC_{05} from this study is substantially below the NOAEC for rape ($4.5x10^{-5}$ lb a.i./acre in MRID 42587201).</td><td>MRID 46326801
U.S. EPA/OPP/ EFED 2012a, p. 22

Used by EFED 2012a, p. 20, for most sensitive dicot in vegetative vigor.

Working Note: This study is cited in the RED for chlorsulfuron (U.S. EPA/OPP 2005a) but is not cited in the EFED risk assessment in support of the RED (i.e., U.S. EPA-OPP-EFED 2004a)</td></tr>
</table>

Table A4-3: Other Toxicity Studies

Species	Exposure	Response	Reference
Monocots			
6 species of grass: crested wheatgrass, Russian wild rye, alkali grass, tall fescue, Bermuda grass, alkali sacaton	Chlorsulfuron (NOS) Greenhouse assay. Pre- and post-emergence with chlorsulfuron at rates of 0.023, 0.047, 0.093, and 0.14 lb/acre.	No effects on germination in any grass for any chlorsulfuron exposure level. Alkali grass and tall fescue were killed or severely damaged at all rates regardless of timing. Crested wheat grass and Russian wild rye tolerant to all pre- and post-emergence applications.	Davison et al. 1987
Dicots			
Canola (rapeseed), smartweed, soybean, sunflower	Greenhous assay Glean formulation (NOS) Chlorsulfuron application rate ranged from 2.3×10^{-5} to 1.8×10^{-4} kg/ha (corresponding to ≈0.000021 to 0.00016 lb/acre).	Most susceptible species were canola and soybean. For canola, application of 9.2×10^{-5}kg/ha (0.000082 lb/acre) reduced total seed weight to 9% of control. For soybean, application of 0.00018 kg/ha (0.00016 lb/acre) reduced total seed weight to 1% of control. Working Note: The above LOAEL for corn is somewhat below the NOAEL of 0.00225 lb a.i./acre from vegetation vigor assay by McKelvey and Kuratle 1992. The LOAEL for soybean is substantially above the EC_{25} of 0.0000193 lb a.i./acre from vegetation vigor study by McKelvey and Kuratle 1992.	Fletcher et al. 1996
Turnip (*Brassica rapa*)	Greenhouse soil assay. Chlorsulfuron (Glean formulation, 75% a.i.) concentrations in soil ranged from 0.005 to 15 µg a.i./kg soil (Table 1 of paper).	Visual symptoms observed within 1-2 days of application. Modest variability in ED_{50} values (wet weight) in different soils – i.e., 0.3 to 0.61 µg a.i./kg soil (Table 3 of paper)	Gunther et al. 1989

Appendix 4: Toxicity to Terrestrial Plants *(continued)*

Species	Exposure	Response	Reference
Rape seed (*Brassica napus*) [Dicot]	Chlorsulfuron, WG Glean 20 DF. Fraction of Recommended Application Rates: 0, 0.025, 0.05, 0.1, 0.2, 0.4, and 0.8 for recommended rate of 4 g a.i./ha. Application Rate: 0, 0.00009, 0.00018, 0.00036, and 0.00071, 0.0014, and 0.0029 lb a.i./acre.	No change in shoot weight. A significant dose-related decrease in root weight at application rates of 0.00036 lb a.i./acre and higher. Apparent NOAEC: 0.00018 lb a.i./acre. See Figure 1D of paper. No quantitative dose-response values given in paper.	Kjaer and Heinback 2001
Daucus carota (carrot), *Stellaria media* (chickweed), *Chemopodium album* (pigweed)	Pot assays, Source and purity of chlorsulfuron not specified.	Fresh and dry weight determined. Low doses stimulated growth in both assays. ED50 (measured as fresh weight) - *Daucus carota*, 0.32 g/acre (95%CI 0.18-0.46) [0.00029 lb/acre]] *Stellaria media*, 0.12 g/ha (95%CI 0.08-0.16) [0.00011 lb/acre] *Chenopodium album*, 1.21 g/ha (95%CI 0.49-1.94) [0.00019 lb/acre]	Olofsdotter et al. 1994
Sunflower, 4 strains	Chlorsulfuron 12.5 g a.i./ha	Substantial variability in strains with no damage in one resistant strain.	Sala et al. 2008
Kochia scoparia (invasive Eurasian dicot), resistant strain	Greenhouse pot assay Glean XP with 0.25% nonionic surfactant: 0, 9, 10, 36 and 72 g a.i./ha	High survival rate (≈87%) in resistant strain. Strain was also resistant to glyphosate and atrazine.	Varanasi et al. 2015
Hemp-nettle (*Galeopsis tetrahit*) (invasive Eurasian dicot)	Glean (NOS) with 0.1% surfactant, foliar	GR_{50} (whole plant) 0.1 g a.i./ha in MCPA resistant strain. 0.14 g a.i./ha in MCPA tolerant strain. Working Note: No apparent cross-resistant with MCPA (auxin herbicide)	Weinberg et al. 2006

Species	Exposure	Response	Reference
Mixed			
22 plant species, monocots and dicots See Table A4-4 below for details	Greenhouse assay using hydroponic exposures. Chlorsulfuron (Glean, 75% a.i. formulation)	EC_{50}: Most sensitive species, *Medicago scutellata* (snail medic, Dicot): 2.1 µg a.i./L. Least sensitive species, Triticale (Monocot): 5.86 µg a.i./L. Paper reports ED_{10}, ED_{30}, and ED_{50} for all species. See Table 1 of paper for details	Jettner et al. 1999 See supplement data in Table A4-4 below. See Figure 6 in the current Forest Service risk assessment for illustration.

Table A4-4: Supplemental data from Jettner et al. 1999

Ordinal Rank	Species, Cultiver [Order]	EC_{50} µg/L	Relative Frequency
	Dicots		
1	Lucerne (alfalfa) [Order Fabales]	0.19	0.029412
2	Snail medic (*Medicago scutellata*) [Order Fabales]	0.21	0.1
3	Sunflower [Order Asterales]	0.54	0.166667
4	Rapistrum rugosum [Order Brassicales]	0.55	0.233333
5	Linseed [Order Malpighiales]	0.57	0.3
6	Navy bean [Order Fabales]	0.75	0.366667
7	Soybean [Order Fabales]	0.85	0.433333
8	Chickpea, Baarwon [Order Fabales]	0.94	0.5
9	Peanut [Order Fabales]	0.99	0.566667
10	Mung bean [Order Fabales]	1.21	0.633333
11	Lablab [Order Fabales]	1.38	0.7
12	Chickpea, Baarwon [Order Fabales]	1.59	0.766667
13	Cotton [Order Malvales]	1.81	0.833333
14	Oilseed rape [Order Brassicales]	2.01	0.9
15	Cowpea [Order Fabales]	2.42	0.966667
	Monocots		
1	Maize, Pacific 276 [Andropogoneae tribe]	0.46	0.029412
2	Maize, Hycorn 74	0.55	0.088235
3	Maize, Hycorm 82	0.77	0.147059
4	Maize, DK 764	0.82	0.205882
5	Maize	0.9	0.264706
6	Maize, Pioneer C79	0.98	0.323529
7	Maize, Pioneer 3245	0.99	0.382353
8	Maize, Pioneer 3394	1.06	0.441176
9	Maize, Pioneer 3270	1.16	0.5
10	Maize GH5010	1.29	0.558824
11	Canary grass	1.47	0.617647
12	*Phalaris paradoxa*	1.47	0.676471
13	Sorghum [Andropogoneae tribe]	1.55	0.735294
14	Oat [Poeae tribe]	4.67	0.794118
15	Triticale [Triticeae tribe]	5.88	0.852941
16	Barley [Triticeae tribe]	28.5	0.911765
17	Wheat [Triticeae tribe]	102	0.970588

See Section 4.1.2.5 for initial discussion.
Data from Table 2 in Jettner et al. 1999.

Table A4-5: Field/Efficacy Studies

Species	Exposure	Response	Reference
Apera spica-venti (monocot), common windgrass	Glean 75 WG, Application rates: 9.4 and 18.8 g/ha (≈0.0084 and 0.017 lb a.i./acre)	Six years of repeated application (2003 to 2008). Decrease in control. 82% to 41% at lower dose and 92% to 50% at higher dose. Resistance transferred to other plants via pollen.	Adamczewski et al. 2009
Sweet cherries (*Prunus avium*)	Chlorsulfuron (NOS) Reported Application rates g a.i./ha: 4.26, 14.2, 42.6, and 142 g/ha Application Rates, lb a.i./acre: 0.0041, 0.013, 0.038, and 0.13 lb a.i./acre	Detectable visual injury even at lowest application rate. Chlorosis, leaf malformation and discolored veins. Slow and impaired regrowth in surviving trees.	Al-Khatib et al. 1992b
Sweet cherries (*Prunus avium*), three different cultivars: Rainier, Chinook, and Bing	Application rates: 0.026 to 2.33 g/ha or 0.000023 to 0.0021 lbs/acre). All treatments included 0.25% v/v nonionic surfactant "X-77".	Dose-dependent increase in symptom severity in all cultivars. Effects observed at all application rates. Chinook was the most susceptible cultivar; Bing was the least sensitive.	Bhatti et al. 1995
Target Species: *Lolium rigidum* (monocot), ryegrass Crop: Wheat or barley [Triticeae tribe]	Glean 75 WG, 750 g/ha, 0.011 kg/ha (≈0.0098 lb/acre)	Slight damage to barley at one location. Generally poor efficacy, presumably due to resistance.	Cirujeda and Taberner 2010
Wine grapes, *Vitis vinifera* (22 varieties)	Glean (75% a.i.): 60 and 180 g/ha (0.054 and 0.16 lb/acre) applied at the pre-bud burst stage. Not clear if rates are in units of a.i. or formulation.	No indication of toxicity based visual damage, pruning weight, fruit yield or number of grape bunches.	Moore and Elliott 1989
Alfalfa (dicot) and redroot pigweed (dicot)	Applications of chlorsulfuron (NOS) at 0.12 to 9.6 g/ha (amount of a.i. not specified) (corresponds to 00.00011 to 0.0086 lb/acre).	GR_{50} (growth inhibition) Alfalfa = 0.35 g/ha (0.00031 lb/acre) [Table 2 of paper]; Redroot pigweed = 1.67g/ha (0.0015 lb/acre) [Figure 4 of paper]. Working Note: Growth chamber assay for alfalfa yielded similar toxicity value of 0.39 g/ha (0.00035 lb/acre).	Moyer 1995

Appendix 4: Toxicity to Terrestrial Plants *(continued)*

Species	Exposure	Response	Reference
Review: includes several species of non-target fruit, grain and fiber and several species of crops grown for forage and pasture	**Review: variable exposures.**	Reports NOECs or LOECs for many species. For foliar application - Lowest NOEL = 0.125 g a.i./ha (0.00011 lb/acre in cherries Highest NOEL = 135 g a.i./ha (0.12 lb/acre)	Obrigawitch et al. 1998
Target Species: *Orobanche ramosa* (broomrape), chlorsulfuron resistant strain. Crop: Tobacco	Glean (75% a.i.), 37.5 and 60 g a.i./ha (≈0.33 and 0.54 lb a.i./acre), 2 applications with 15 day intervals	Completely effective under both greenhouse and field conditions (Table 4 of paper). Two resistant strains identified with resistance factors of 5.3 and 5.6 (Table 3 of paper)	Slavov et al. 2005

Appendix 5: Toxicity to fish.

Table A5-1: Acute Toxicity in Fish 184
Table A5-2: Chronic toxicity in Fish 186

Table A5-1: Acute Toxicity in Fish

Species	Exposure	Response	Reference
Active ingredient			
Bluegill sunfish (*Lepomis macrochirus*)	115-300 mg a.i./L benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF Static, 96-hour exposure. See Note 1 below on use of DMF. Working Note: U.S. EPA/OPP/EFED (2012a, Table 7, p. 19) indicates that the test species was rainbow trout. This is an error. The test species was bluegill sunfish. This is correctly noted in the EFED bibliography on p. 56.	LC_{50} >300 mg a.i./L With the exception of the 255 mg a.i./L concentration, no mortality was observed in any test group. In the 255 mg a.i./L group, 10% mortality was observer. However, no deaths were observed in the 300 mg a.i./L exposure group.	Smith 1979a MRID 00035258 Acceptable Working Note: Used by U.S. EPA/OPP/ EFED 2012a, p. 19 to classify chlorsulfuron as *Practically Nontoxic* to fish.
Bluegill sunfish (*Lepomis macrochirus*)	Chlorsulfuron (NOS)	96h-LC50: >128 mg a.i./L	SDS for Telar XP (Dupont 2015)
Channel catfish (*Ictalurus punctatus*)	1-50 mg a.i./L benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent). Static, 96 hours. See Note 1 below.	No mortality was observed in any test group. LC_{50} >50 mg a.i./L	Smith 1979d MRID 00035261
Fathead minnow (*Pimephales promelas*)	115-300 mg a.i./L benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent). Duration: 96 hours See Note 1 below.	10% mortality observed in the 185 mg a.i./L and 300 mg a.i./L groups. No mortalities observed in the 217 and 255 mg a.i./L groups or at concentrations below 186 mg a.i./L. LC_{50} >300 mg a.i./L	Smith 1979c MRID 00035260
Rainbow trout (*Salmo gairdneri*)	Chlorsulfuron technical (NOS)	96-h LC_{50}: > 122 mg a.i./L	SDS for Telar XP (Dupont 2015)

Appendix 5: Toxicity to fish *(continued)*

Species	Exposure	Response	Reference
Rainbow trout (*Salmo gairdneri*)	95-250 mg a.i./L benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent) Static, 96 hour exposure. See Note 1 below.	LC_{50} >250 mg a.i./L No mortality was observed in any test group.	Smith 1979b MRID 00035259 Consistent with MSDS for Chlorsulfuron 75 (Alligare LLC 2010).
Sheepshead minnow (*Cyprinodon variegatus*), juveniles	Mean measured concentrations of 132-980 mg a.i./L (nominal concentrations of 133-1025 mg a.i./L) chlorsulfuron (DPX-W4189-165) (98.2% pure) Static, 96 hours.	No mortality was observed in any test group. LC_{50}: >980 mg a.i./L	Ward and Boeri 1991a MRID 41976401 Acceptable Consistent with the MSDS for Chlorsulfuron 75 (Alligare LLC 2010) and SDS for Telar XP (Dupont 2015).
Formulations			
Brown trout (*Salmo trutta*)	Glean (75% formulation) at concentrations ranging from 10 to 100 mg a.i./L. Duration: 96 hours	LC_{50} = 40 mg a.i./L NOAEC (mortality): 30 mg a.i./L	Grande et al. 1994 MRID 45202909 Working Note: This is an open literature publication.

Note 1: Test material poorly soluble in water; higher concentrations could not be tested due to possible toxicity associated with dimethylformamide (DMF) as carrier solvent.

Table A5-2: Chronic toxicity in Fish

Species	Exposure	Response	Reference
Rainbow trout (*Oncorhynchus mykiss*), embryos, alevins, and fingerlings	Mean measured concentrations of 18-900 mg a.i./L (nominal concentrations of 15.6-1000 mg a.i./L) chlorsulfuron (DPX-W4189-170) (97.9% pure) under flow-through conditions. Duration: 77 days	Survival of embryos and alevins did not differ from controls. Survival of fingerlings significantly reduced in 900 mg a.i./L dose group (40% mortality). Not deaths were observed at any other exposure level. <u>Study authors assessment</u> NOEC = 32 mg a.i./L LOEC = 66 mg a.i./L, based on length of the trout at test conclusion. length showed the greatest sensitivity to exposure	Pierson 1991 MRID 41976405 U.S. EPA/OPP/EFED 2012a, p. 91 Acceptable
Sheepshead minnow (*Cyprinodon variegatus*)	Chlorsulfuron (NOS)	NOAEC: 980 mg a.i./L LOAEC: no identified.	MRID 41976401 U.S. EPA/OPP/EFED 2012a, p. 91 Acceptable Note: This is cited as a 1991 study but is not included or cited in the U.S. EPA/OPP/EFED 2004a. In addition, the study is not cited in the EFED summary table on p. 19. Lastly, the MRID number is identical to Ward and Boeri (1991a). As summarized in Table A6-1 above, a chronic study had not been identified in the original Forest Service risk assessment (SERA 2004a) which had access to the full study. Because of concerns with the available information on this study, the study is not used in the dose-response assessment for fish.

Appendix 6: Toxicity to aquatic invertebrates

Table A6-1: Acute Toxicity in Aquatic Invertebrates 187
Table A6-2: Chronic toxicity in Aquatic Invertebrates 188

Table A6-1: Acute Toxicity in Aquatic Invertebrates

Species	Exposure	Response	Reference
Daphnia magna	Benzenesulfonamide (DPX-4189, INW-4189-22, Haskell #12,700). 188 to 500 ppm for 48 hours under static unaerated conditions.	LC_{50} = 370.9 (346.4-400.2) ppm 90% mortality in 500 ppm exposure group. U.S. EPA/OPP/EFED 2012a, p. 19: EC_{50} >370 mg a.i./L Practically Non-toxic	Goodman 1979 MRID 00035262 Acceptable Used by U.S. EPA/OPP/EFED 2004a, p. 14 for risk characterization. The MSDS for Chlorsulfuron 75 (Alligare LLC 2010) cites an LC50 of >370 mg a.i./L
Daphnia magna	Chlorsulfuron (purity not specified) concentrations range from 0.01 to 100 mg/L for 48 hours	LC_{50} > 100 mg/L. Estimated mortality of 30% at 100 mg/L concentration. NOEC = 10 mg/L	Hessen et al. 1994
Daphnia magna	Chlorsulfuron (NOS) Exposure: 48 hours	EC50: >112 mg a.i./L	SDS for Telar XP (Dupont 2015)
Daphnia pulex	Chlorsulfuron (purity not specified) concentrations range from 0.01 to 100 mg/L for 48 hours	LC_{50}: 32 to 100 mg/L. No mortality at 32 mg/L, 100% mortality at 100 mg/L concentration. NOAEC = 32 mg/L	Hessen et al. 1994
Mysidopsis bahia (a.k.a. *Americamysis bahia*)	Chlorsulfuron (DPX-W4189-165)(98.2% pure) mean measured concentrations of 12-99 mg/L (nominal concentrations of 13-100 mg/L U.S. EPA/OPP/EFED 2012a, p. 19: Duration: 96 hours	LC_{50} =89 mg/L NOEC = 35 mg/L U.S. EPA/OPP/EFED 2012a, p. 91: LC_{50} >89 mg a.i./L Slightly toxic	Ward and Boeri 1991b MRID 41976402 Acceptable Used by U.S. EPA/OPP/EFED 2004a, p. 14 for risk characterization. Cited in the SDS with SDS for Telar XP (Dupont 2015)

Species	Exposure	Response	Reference
Eastern oyster (*Crassostrea virginica*) embryos and larvae	Chlorsulfuron (DPX-W4189-165)(98.2% pure) mean measured concentrations of 120-905 mg/L (nominal concentrations of 130-1000 mg/L). Static unaerated conditions for 48 hours.	In the 535 and 905 mg/L dose groups, all animals appear abnormal. At the highest dose tested, survival was reduced to approximately 75% of controls. EC_{50} = 385 mg/L (359-414 mg/L) based on shell growth LC_{25} = 905 mg/L NOEC not reported, although 98% of animals appeared normal in the 200 mg/L group. <u>U.S. EPA/OPP/EFED 2012a, p. 91:</u> <u>MRID 42328601</u> EC_{50} = 376 mg a.i./L based on shell growth.	Ward and Boeri 1991c MRID 41976403 Ward and Boeri 1991d MRID 41976403 [These appear to be different submissions of the same study.] The EC_{50} of 385 mg a.i./L is cited on the MSDS for Chlorsulfuron 75 (Alligare LLC 2010) Cites in U.S. EPA/ OPP/EFED 2012a as MRID 42328601

Table A6-2: Chronic Toxicity in Aquatic Invertebrates

Species	Exposure	Response	Reference
Daphnia magna, less than 24-hours old, no solvent control was used.	Chlorsulfuron (DXP-W4189-94) (95.4% pure). Concentrations: 9.3, 20, 36, 79, 140, or 300 mg/L . Duration: 21 days	At concentrations of 20 mg/L and lower, there were no adverse effects on survival, reproduction (total offspring and offspring/reproduction day) or growth (adult length). No mortalities reported, except the 150 ppm group (5% mortality). Reproduction (both total offspring and offspring/reproduction day) was the most sensitive indicator of toxicity. NOEL = 20 mg/L LOAEL: 36 mg/L based on total offspring and number of offspring per day.	Ward and Boeri 1989 MRID 41976404 Supplemental Hutton 1992 MRID 42309701 (correction of incorrect reference to use of a solvent control)

Appendix 7: Toxicity to Aquatic Plants

Table A7-1: Algae 189
Table A7-2: EC_{50} values for algal growth from Nystrom et al. 1999 194
Table A7-3: Macrophytes 195
Table A7-4: Summary of EC_{50} Values for Aquatic Macrophytes 197

Table A7-1: Algae

Species	Exposure	Response	Reference
Anabaena flos-aquae, freshwater algae, 7-day-old cultures, 3 replicates/dose	Chlorsulfuron (97.79% pure) for 120 hours under static conditions Nominal concentrations: 0, 0.25, 0.50, 1.0, 2.0, or 4.1 mg a.i./L Measured concentrations: <LOQ, 0.236, 0.485, 0.961, 1.92, or 3.95 mg a.i./L	EC_{50}= (biomass) 0.61 mg a.i./L NOAEC (biomass and cell density) =0.24 mg a.i./L Boeri et al. 2001c (DER); Cell Density: NOEC: 0.236 mg a.i./L LOEC: 0.485 mg a.i./L EC_{50}: 0.78 mg a.i./L Growth rate: NOEC: 0.485 mg a.i./L EC_{50}: 1.77 Area Under the Growth Curve (Biomass): NOEC: 0.236 mg a.i./L EC_{50}: 0.609	Boeri et al. 2001c (Data Evaluation Record) U.S. EPA/OPP/EFED 2012a MRID 45832903 Acceptable
Chlamydomonas noctigama, green algae Freshwater assay	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 0.6 mg a.i./L	Kalliquist and Romstad 1994
Chlorella fusca, freshwater green algae	Chlorsulfuron (> 99% pure) concentrations ranged from approximately 0.1 µmol/L to 0.3mmol/L for 24 hours.	EC_{50} (Growth inhibition) = 0.56 mg a.i./L or 1.6 µmol/L EC_{50} (Inhibition of cell reproduction) = 0.40 mg a.i./L or 1.1 µmol/L	Fahl et al. 1995
Chlorella pyrenoidosa	Cell suspensions in 50 mg a.i./L	Modest (50 to 69%) inhibition. See Table 3 of paper. Few details provided.	Ma et al. 2002
Chlorella pyrenoidosa, green algae	Chlorsulfuron (>95% pure) and two chlorsulfuron degradation products (structures provided, but compound not named) for 96 hours - concentrations tested were not specified	Report Log EC_{50}: -0.39 EC_{50}: ≈0.41 mg a.i./L Degradation products substantially less toxic (see Table 1 of paper).	Wei et al. 1998

Appendix 7: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Chlorella saccharophila	Chlorsulfuron (95% pure) concentrations ranging from 0.07 to 184.7 ppm (mg a.i./L) for 96 hours	Growth inhibition: NOAEC: 9.3 mg a.i./L EC_{50}: 54.0 (41.5-66.9) mg a.i./L	Sabater and Carrasco 1997
Chlorella vulgaris	Chlorsulfuron (95%), concentrations ranging from 0.07 to 184.7 mg a.i./L Exposure Period: 96 hours	96-h EC_{50}: 74.5 mg a.i./L Working Note: See matched studies with *Scenedesmus acutus* and *Pseudanabaena galeata*	Carrasco and Sabater 1997
Crytomonas purindoifera, flagellate	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 60 mg a.i./L	Kalliquist and Romstad 1994
Cyclotella sp., diatom	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 1.0 mg a.i./L	Kalliquist and Romstad 1994
Microcystis aeruginosa, cyanobacteria, freshwater	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 10 mg a.i./L	Kalliquist and Romstad 1994
Navicula pelliculosa, freshwater algae	Chlorsulfuron (NOS) for 120 hours under static conditions Nominal concentrations: 0 or 130 mg a.i./L Mean-measured concentrations: <0.0621 or 126 mg a.i./L	EC_{50} (cell density, biomass and growth rate) >126 mg a.i./L NOAEC (cell density, biomass and growth rate) = 126 mg a.i./L	Boeri et al. 2001a (Data Evaluation Record) U.S. EPA/OPP/EFED 2012a MRID 45832904 Acceptable
Pseudanabaena galeata	Chlorsulfuron (95%), concentrations ranging from 0.07 to 184.7 mg a.i./L Exposure Period: 96 hours	96-h EC_{50}: 21.1 mg a.i./L Working Note: See matched studies with *Scenedesmus acutus* and *Pseudanabaena galeata*	Carrasco and Sabater 1997
Pseudanabaena galeata	Chlorsulfuron (95% pure) concentrations ranging from 0.07 to 184.7 ppm (mg a.i./L) for 96 hours	Growth inhibition: NOAEC: 3.9 mg a.i./L EC_{50}: 16.3 (13.7-19.0) mg a.i./L	Sabater and Carrasco 1997

Appendix 7: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Scenedesmus acutus	Chlorsulfuron (95%), concentrations ranging from 0.07 to 184.7 mg a.i./L Exposure Period: 96 hours	96-h EC_{50}: 0.19 mg a.i./L Working Note: See matched studies with *Chlorella vulgaris* and *Pseudanabaena galeata*	Carrasco and Sabater 1997
Scenedesmus acutus	Chlorsulfuron (95% pure) concentrations ranging from 0.07 to 184.7 ppm (mg a.i./L) for 96 hours	Growth inhibition: NOAEC: 0.07 mg a.i./L EC_{50}: 0.22 (0.19-0.26) mg a.i./L	Sabater and Carrasco 1997
Pseudokirchneriella subcapitata (a.k.a. *Selenastrum capricornutum*), green algae	Measured test concentrations of 9.4, 17, 33, 58.5, or 103 µg/L chlorsulfuron (DPV-W4189-165) (98.2% pure chlorsulfuron) for 120 hours	EC_{50} = 0.05 mg a.i./L (0.04-0.06 mg a.i./L) No observation of unusual cell shape, color differences, flocculation, adherence of algae to test vessels, aggregation of algal cell, precipitation in test solution, or stimulation. 23-73 % growth inhibition in cultures treated with > 17 µg a.i./L NOAEC = 0.0094 mg a.i./L All endpoints based on cell density. U.S.EPA/OPP/EFED 2012a, p. 20 EC_{50} (cell density) = 0.05 mg a.i./L NOAEC (cell density) = 0.0094 mg a.i./L	Blasberg et al. 1991 MRID 42186801 U.S.EPA/OPP/EFED 2012a, p. 20 Supplemental (*EC_{50} calculated using nominal concentrations and erroneously reported as 0.000055 mg a.i./L in previous EPA risk assessment [Table 9]).* **Used by U.S. EPA/ OPP/EFED 2012a, Table 7, p. 20 as most sensitive species. Several one lower LC50 available in Nystrom et al. 1999. See below.**
Pseudokirchneriella subcapitata (a.k.a. *Selenastrum capricornutum*), green algae	Measured test concentration of Glean (containing 75% chlorsulfuron) of 0.0032, 0.01, 0.032, 0.1, 0.32, 1.0, 3.2, 10, 32, 100, and 329 mg a.i./L for 96 hours. Separate tests conducted using free cells, immobilized cells and bottle assay.	Free algae: EC_{50} = 0.68 mg a.i./L Immobilized cultures: EC_{50} = 0.81mg a.i./L bottle test assay: EC_{50} = 0.7 mg a.i./L Results based on inhibition of algal growth (algal dry weight).	Abdel-Hamid 1996

Appendix 7: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Pseudokirchneriella subcapitata (a.k.a. *Selenastrum capricornutum*), green algae	Exposure for 96 hours, chlorsulfuron concentration range not specified, chlorsulfuron purity not specified	Growth inhibition was determined based on biomass. EC_{50} = 0.123 mg a.i./L (109-161) NOAEC < 0.019 mg a.i./L LOAEC = 0.019 mg a.i./L	Fairchild et al. 1997
Pseudokirchneriella subcapitata (a.k.a. *Selenastrum capricornutum*), green algae	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 0.8 mg a.i./L	Kalliquist and Romstad 1994
Skeletonema costatum, algae, 3 replicates /dose	Chlorsulfuron (97.79% pure) for 120 hours under static conditions Nominal concentrations: 0 or 130 mg a.i./L Measured concentrations: <0.0163 or 126 mg a.i./L	EC_{50} (cell density, biomass and growth rate) >126 mg a.i./L NOAEC (cell density, biomass and growth rate) = 126 mg a.i./L	Boeri et al. 2001b (Data Evaluation Record) U.S. EPA/OPP/EFED 2012a MRID 45832902 Acceptable
Synechococcus leopoliensis, cyanobacteria, marine	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg a.i./L for 72 hours	EC_{50} (growth rate): 0.5 mg a.i./L	Kalliquist and Romstad 1994
17 species of fresh water and 20 species of marine algae SPECIAL NOTE: See Table A8-2 below for details. **Note: This study is not discussed in EPA risk assessments and is not included in ECOTOX.**	Chlorsulfuron (75% formulation), typical concentration range tested was 1 to 1000 µM (a.i.) (0.358to 358 mg a.i./L), although based on reported EC_{50} results, lower doses were tested in some species. Exposure time not specified.	Inhibition of growth assayed as chlorophyll α fluorescence. SPECIAL NOTE: See Table A8-2 below for details. Most sensitive species: *Synechococcus leopoliensis* EC_{50}: 0.0161 mg a.i./L Estimated NOAEC (EC_{50} ÷ 20): 0.0008 mg a.i./L Most tolerant species: *Porphyridium cruentum* EC_{50}: 359 mg a.i./L Estimated NOAEC (EC_{50} ÷ 20): 18 mg a.i./L	Nystrom et al. 1999 **Note: The estimated NOAEC is below the NOAEC of 0.0091 mg a.i./L from Blasberg et al. 1991, MRID 42186801 – i.e., the study used by EPA. The estimated NOAEC is consistent with reported NOAEC of 0.001 mg a.i./L from Kalliquist et al. 1994. See below.**

Species	Exposure	Response	Reference
Other Assays			
4 species of algae, 6 species of cyanobactiera	Single concentration: 0.02 mg a.i./L. Exposure duration: 22 hours	Algae: No inhibition of ^{14}C uptake Cyanobacteria: Statistically significant reduction of 23% in *Microcystis aeruginosa* but no change in 5 other species.	Peterson et al. 1994
Mixed algal species in oligotrophic lake enclosure (i.e., mesocosms) Note: This study is not discussed in EPA risk assessments and is not included in ECOTOX.	chlorsulfuron (purity not specified) Nominal concentrations at start of study: 0, 1, 10, and 100 µg/L. Duration: up to 16 days. No analysis of chlorsulfuron concentrations in water during study. Only one enclosure per exposure level with two enclosures as controls. Each enclosure was 4 m deep and 2.5 m in diameter (≈ 20 m^3).	Transient decreases in biomass development (as measured by chlorophyll-α) observed at 10 and 100 µg/L concentrations. At 100 µg/L, inhibition was evident throughout the 16 day exposure. At 10 µg/L, only a transient decrease at Day 2. No substantial decrease on Days 6-16, See Figure 10 of paper. No substantial decrease in photosynthesis relative to controls. See Figure 14 of paper. At all exposure levels, species diversity was modestly decreased. The differences at 1 and 10 µg/L not substantial. See Figure 18 of paper. Authors note that zooplankton density was very low and did not likely impact the changes in phytoplankton. 0.001 mg a.i./L: No effects on biomass. 0.01 mg a.i./L: Transient decrease in biomass. 0.1 mg a.i./L: Decrease in biomass at all observation periods.	Kalliquist et al. 1994

Table A7-2: EC_{50} values for algal growth from Nystrom et al. 1999

Species	Abbreviation	EC_{50} µM	EC_{50} mg a.i./L	Frequency
Freshwater				
Synechococcus leopoliensis	SYNE LEO	0.045	0.0161	0.0294
Monoraphidium	MONO PUS	0.2	0.0716	0.0882
Bumilleriopsis filiformis	BUMI FIL	0.86	0.3077	0.1471
Monoraphidium contortum	MONO CON	0.9	0.322	0.2059
Phormidium luridum	PHOR LUR	1.45	0.5188	0.2647
Pediastrum sp.	PEDIASTZ	2.3	0.8229	0.3235
Pseudokirchneriella subcapitata	SELE CAP	6.9	2.4688	0.3824
Diatoma elongata	DIAT ELO	9.6	3.4349	0.4412
Scenedesmus obtusiusculus	SCEN OBT	10	3.578	0.5
Raphidonema longiseta	RAPH LON	23	8.2294	0.5588
Chlamydomonas dysosmos	CHLA DYS	23	8.2294	0.6176
Stichococcus chloranthus	STIC CHL	61	21.826	0.6765
Chlorella emersonii	CHLO EME	121	43.294	0.7353
Chlamydomonas reinhardtii	CHLA REI	161	57.606	0.7941
Asterionella formosa	ASTE FOR	187	66.909	0.8529
Cryptomonas pyrenoidifera	CRYP PYR	595	212.89	0.9118
Cyclotella cryptica	CYCL CRY	770	275.51	0.9706
Saltwater				
Platymonas subcordiformis	PLAT SUB	5	1.789	0.025
Tetraselmis sp.	TETRASEZ	8	2.8624	0.075
Nodularia harveyana	NODU HAR	13	4.6514	0.125
Amphidinium carterae	AMPH CAR	24	8.5872	0.175
Prorocentrum minimum	PROR MIN	28	10.018	0.225
Anacystis montana	ANAC MON	29	10.376	0.275
Dunaliella tertiolecta	DUNA TER	53	18.963	0.325
Ditylum brightwellii	DITY BRI	59	21.11	0.375
Pornhyridium aerugineum	PORP AER	60	21.468	0.425
Cryptomonas baltica	CRYP BAL	61	21.826	0.475
Pavlova lutherii	PAVL LUT	136	48.661	0.525
Skeletonema costatum	SKEL COS	156	55.817	0.575
Chlorella ovalis	CHLO OVA	165	59.037	0.625
Emiliana huxleyi	EMIL HUX	307	109.84	0.675
Isochrysis galbana	ISOC GAL	447	159.94	0.725
Thalassiosira pseudonana	THAL PSE	485	173.53	0.775
Rhodomonas lens	RHOD LEN	493	176.4	0.825
Rhodella sp.	RHODEZ	500	178.9	0.875
Phaeodactylum tricornutum	PHAE TRI	507	181.4	0.925
Porphyridium cruentum	PORP CRU	1003	358.87	0.975

See Section 4.1.3.4.1 for initial discussion and Figure 6 for illustration.

Table A7-3: Macrophytes

Species	Exposure	Response	Reference
Lemna minor (duckweed) [Monocot]	Chlorsulfuron (NOS) 96 hour exposure	Growth inhibition was determined based on biomass. EC_{50} = 0.0007 mg a.i./L (0.0005-0.0009) NOEC = 0.0004 mg a.i./L LOEC = 0.0007 mg a.i./L	Fairchild et al. 1997
Lemna minor (duckweed) [Monocot]	Single concentration of 0.02 mg a.i./L. Exposure duration: 7 days	86% inhibition of 7-day growth	Peterson et al. 1994
Lemna gibba (duckweed), 10-days-old, 5 plants/replicate, 3 replicates (3 fronds/plant – 15 total fronds/replicate) [Monocot]	Chlorsulfuron technical (97.79% pure) for 14 days under static conditions Nominal concentrations: 0, 0.050, 0.12, 0.24, 0.48, or 0.96 µg/L Measured concentrations: 0.00531, 0.0573, 0.112, 0.242, 0.5298 or 0.928 µg/L Duration: 14 days	EC_{50} (dry wt) = 0.00035 mg a.i./L NOAEC (frond no. and dry wt) = 0.00024 mg a.i./L LOAEC (frond no. and dry wt) = 0.00048 mg a.i./L	Boeri et al. 2002 (Data Evaluation Record) MRID 45832901 U.S. EPA/OPP/EFED 2012a Supplement (*study conducted as a static test*) Used by U.S. EPA/OPP/EFED 2012a, p. 20 for risk characterization.
Lemna paucicostata (duckweed) [Monocot]	Chlorsulfuron Duration: 7 days	EC_{50}: 0.005 µM (≈0.0018 mg a.i./L) Slope: 3.74 Approximate EC_{10}: 0.05 mg a.i./L [0.018 mg a.i./L x $(10/100\text{-}10)^{1/3.74} \approx 0.05404$ mg a.i./L]	Michel et al. 2004
Hydrilla verticillata [Monocot]	Chlorsulfuron (source and purity not specified). Concentrations: 0, 1, 5, and 10 µg/L Observations at 10, 14, and 24 days. Duration of Exposure: 14 days. Plants transferred to clear water on Day 14.	Concentration related decreases in shoot length at all concentrations over all observation periods. Decreases more substantial at 10 and 14 days relative to 24 days. Increases in the percent of new shoots at all concentrations (not clearly concentration-related). No systematic differences at Days 10, 14, and 24. See Table XI of paper for details. LOAEL: 0.0001 mg a.i./L based on 80% decrease in length of new shoots.	Anderson 1985b Working Note: This paper is cited in ECOTOX (2016) are Reference Number 94332. The paper is not cited in U.S. EPA/OPP/ EFED 2004a or 2012a

Appendix 7: Toxicity to Aquatic Plants *(continued)*

Species	Exposure	Response	Reference
Myriophyllum aquaticum (parrot feather watermilfoil) [Dicot]	Chlorsulfuron (source and purity not specified) Exposure: 14 days	EC_{50} values by endpoint Chlorophyll a: 1.6 x 10^{-9} M (≈0.000572 mg a.i./L) Chlorophyll b and carotenoid 2.8 x 10^{-9} M (≈0.001 mg a.i./L) Plant height: 1.2 x 10^{-8} M (≈0.00043 mg a.i./L) Working Note: Based on Figure 1 of paper, the apparent NOAEC for plant height is about 10^{-6} M or 0.3578 mg a.i./L. This is not consistent with the EC_{50} value given above and in Figure 1 of the paper. There appears to be a labelling error in Figure 1 of the paper.	Turgut et al. 2003
Potamogeton pectinatus (a.k.a. *Stuckenia pectinata*), Sago pondweed [Monocot]	Concentrations: 0.25, 0.5, 1.0 or 2.0 µg/L in an environmental growth chamber Duration: 28 days	At 0.00025 mg a.i./L, reduction in leaf length (76%) and number of leaves (50%), number of stems (50%). At doses >0.0005 mg/L, reduction in length of stems (47%). At doses 0.001 mg/L, significant reductions in wet and dry weights 50% of plants died At dose of 0.002 mg a.i./L 100% death .	Coyner et al. 2001

Table A7-4: Summary of EC_{50} Values for Aquatic Macrophytes

Type	Species	Days	EC_{50} mg/L	Reference	Freq.
Monocot	Lemna gibba	14	0.00035	Boeri et al. 2002, MRID 4583290	0.1
Dicot	Myriophyllum aquaticum	14	0.000572	Turgut et al. 2003	0.3
Monocot	Lemna minor	4	0.0007	Fairchild et al. 1997	0.5
Monocot	Potamogeton pectinatus	28	0.001	Coyner et al. 2001	0.7
Monocot	Lemna paucicostata	7	0.0018	Michel et al. 2004	0.9

See this appendix, Table A8-3 for more detailed summary.
See Section 4.1.3.4.2 for initial discussion.
See Figure 7 for illustration.

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.000112 (0 - 0.00203)	0 (0 - 0.00004)	0 (0 - 0)
Dry and Temperate Location	0.000094 (0 - 0.00108)	0 (0 - 2.86E-05)	0 (0 - 1.23E-08)
Dry and Cold Location	0.000068 (0 - 0.00301)	0 (0 - 2.56E-07)	0 (0 - 0)
Average Rainfall and Warm Location	0.0047 (0.00043 - 0.0234)	0.000057 (2.71E-06 - 0.0007)	0 (0 - 3.05E-07)
Average Rainfall and Temperate Location	0.0038 (0.00066 - 0.0233)	0.000046 (2.25E-06 - 0.00079)	8.40E-10 (0 - 1.48E-07)
Average Rainfall and Cool Location	0.00281 (0.000266 - 0.0124)	2.02E-05 (4.70E-08 - 0.00041)	0 (0 - 1.00E-08)
Wet and Warm Location	0.00275 (0.00049 - 0.016)	1.91E-05 (5.80E-07 - 0.00048)	7.60E-10 (0 - 7.70E-08)
Wet and Temperate Location	0.00177 (0.0004 - 0.0113)	1.43E-05 (6.20E-07 - 0.000303)	0 (0 - 4.70E-08)
Wet and Cool Location	0.0165 (0.0061 - 0.05)	0.0007 (0.000093 - 0.00311)	2.56E-09 (0 - 1.40E-06)
Average of Central Values:	0.0036	9.50E-05	4.60E-10
25th Percentile:	1.12E-04	0	0
Maximum:	0.05	0.00311	1.40E-06
Summary:	0.0036 (1.12E-04 - 0.05)	9.50E-05 (0 - 0.00311)	4.60E-10 (0 - 1.40E-06)

Summary of Values used in workbooks (rounded to 2 significant places).
See Section 4.2.4.3 for discussion

Estimate	Value
Average among soils	0.0012
Lowest non-zero value for sand – i.e., central estimate for wet/warm location.	0.00000000076
Maximum (clay)	0.05

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.244 (0.219 - 0.307)	0.236 (0.202 - 0.281)	0.227 (0.204 - 0.284)
Dry and Temperate Location	0.3 (0.224 - 0.35)	0.275 (0.215 - 0.33)	0.264 (0.21 - 0.33)
Dry and Cold Location	0.4 (0.36 - 0.42)	0.37 (0.312 - 0.39)	0.34 (0.242 - 0.38)
Average Rainfall and Warm Location	0.225 (0.216 - 0.256)	0.206 (0.202 - 0.224)	0.205 (0.201 - 0.208)
Average Rainfall and Temperate Location	0.231 (0.219 - 0.272)	0.208 (0.203 - 0.235)	0.205 (0.202 - 0.208)
Average Rainfall and Cool Location	0.232 (0.221 - 0.267)	0.209 (0.204 - 0.222)	0.206 (0.202 - 0.207)
Wet and Warm Location	0.22 (0.216 - 0.221)	0.205 (0.201 - 0.206)	0.205 (0.201 - 0.206)
Wet and Temperate Location	0.221 (0.216 - 0.222)	0.206 (0.201 - 0.206)	0.205 (0.202 - 0.206)
Wet and Cool Location	0.216 (0.209 - 0.222)	0.201 (0.185 - 0.206)	0.187 (0.145 - 0.206)
Average of Central Values:	0.254	0.235	0.227
25th Percentile:	0.221	0.206	0.205
Maximum:	0.42	0.39	0.38
Summary:	0.254 (0.221 - 0.42)	0.235 (0.206 - 0.39)	0.227 (0.205 - 0.38)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.081 (0.073 - 0.102)	0.079 (0.067 - 0.094)	0.077 (0.068 - 0.096)
Dry and Temperate Location	0.102 (0.075 - 0.12)	0.094 (0.072 - 0.111)	0.093 (0.073 - 0.112)
Dry and Cold Location	0.135 (0.12 - 0.141)	0.126 (0.109 - 0.131)	0.125 (0.107 - 0.132)
Average Rainfall and Warm Location	0.086 (0.073 - 0.102)	0.075 (0.068 - 0.093)	0.07 (0.067 - 0.083)
Average Rainfall and Temperate Location	0.1 (0.077 - 0.118)	0.087 (0.069 - 0.105)	0.071 (0.068 - 0.09)
Average Rainfall and Cool Location	0.106 (0.08 - 0.126)	0.093 (0.073 - 0.11)	0.071 (0.068 - 0.084)
Wet and Warm Location	0.074 (0.073 - 0.082)	0.068 (0.067 - 0.07)	0.068 (0.067 - 0.069)
Wet and Temperate Location	0.075 (0.073 - 0.085)	0.069 (0.068 - 0.075)	0.068 (0.067 - 0.069)
Wet and Cool Location	0.077 (0.073 - 0.092)	0.069 (0.067 - 0.075)	0.068 (0.066 - 0.069)
Average of Central Values:	0.093	0.084	0.079
25th Percentile:	0.077	0.069	0.068
Maximum:	0.141	0.131	0.132
Summary:	0.093 (0.077 - 0.141)	0.084 (0.069 - 0.131)	0.079 (0.068 - 0.132)

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

Site	Clay	Loam	Sand
Dry and Warm Location	24 (8 - 36)	18 (4 - 36)	18 (8 - 36)
Dry and Temperate Location	30 (12 - 36)	24 (8 - 36)	36 (8 - 36)
Dry and Cold Location	36 (30 - 36)	36 (24 - 36)	36 (30 - 36)
Average Rainfall and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average Rainfall and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Warm Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Temperate Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Wet and Cool Location	36 (36 - 36)	36 (36 - 36)	36 (36 - 36)
Average of Central Values:	34	32.7	34
25th Percentile:	36	36	36
Maximum:	36	36	36
Summary:	34 (36 - 36)	32.7 (36 - 36)	34 (36 - 36)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.3 (0 - 5.1)	0 (0 - 0.27)	0 (0 - 3.3)
Dry and Temperate Location	0.29 (0 - 2.25)	0 (0 - 11.8)	0.004 (0 - 57)
Dry and Cold Location	0.29 (0 - 5.9)	0.009 (0 - 1.02)	1.94 (0 - 35)
Average Rainfall and Warm Location	13.4 (4.5 - 39)	20.5 (1.92 - 64)	74 (25.7 - 125)
Average Rainfall and Temperate Location	16 (5.1 - 42)	25.3 (3.2 - 60)	70 (20.7 - 131)
Average Rainfall and Cool Location	21 (7.4 - 44)	35 (7.8 - 71)	85 (37 - 139)
Wet and Warm Location	21.8 (7.6 - 40)	38 (9.6 - 70)	95 (37 - 167)
Wet and Temperate Location	28.2 (10.2 - 42)	44 (20.9 - 75)	94 (38 - 146)
Wet and Cool Location	40 (28.9 - 55)	59 (37 - 93)	127 (97 - 162)
Average of Central Values:	15.7	24.6	60.8
25th Percentile:	0.3	0.009	1.94
Maximum:	55	93	167
Summary:	15.7 (0.3 - 55)	24.6 (0.009 - 93)	60.8 (1.94 - 167)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.0011 (0 - 0.019)	0 (0 - 0.0011)	0 (0 - 0.03)
Dry and Temperate Location	0.0011 (0 - 0.018)	0 (0 - 0.13)	0.000011 (0 - 1)
Dry and Cold Location	0.0009 (0 - 0.018)	0.00005 (0 - 0.015)	0.016 (0 - 0.5)
Average Rainfall and Warm Location	0.3 (0.07 - 1.64)	0.6 (0.05 - 3.01)	2.56 (0.8 - 5.8)
Average Rainfall and Temperate Location	0.7 (0.12 - 2.56)	1.33 (0.14 - 3.7)	3.7 (1.09 - 6.6)
Average Rainfall and Cool Location	1.36 (0.25 - 3.8)	2.21 (0.4 - 4.9)	4.8 (1.99 - 7.4)
Wet and Warm Location	2.72 (0.7 - 4.4)	3.2 (0.8 - 5.3)	4.3 (1.31 - 7)
Wet and Temperate Location	3.5 (1.42 - 5.3)	3.7 (1.76 - 5.7)	4.3 (1.55 - 6.6)
Wet and Cool Location	5.3 (3.14 - 7.5)	6.7 (4 - 8.9)	7.5 (4.6 - 9.9)
Average of Central Values:	1.54	1.97	3.02
25th Percentile:	0.0011	0.00005	0.016
Maximum:	7.5	8.9	9.9
Summary:	1.54 (0.0011 - 7.5)	1.97 (0.00005 - 8.9)	3.02 (0.016 - 9.9)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.12 (0 - 2.37)	0 (0 - 0.11)	0 (0 - 2.64)
Dry and Temperate Location	0.11 (0 - 1.8)	0 (0 - 11.5)	0.0008 (0 - 84)
Dry and Cold Location	0.09 (0 - 3.3)	0.004 (0 - 1.15)	1.43 (0 - 47)
Average Rainfall and Warm Location	37 (10.1 - 169)	84 (5 - 370)	320 (100 - 640)
Average Rainfall and Temperate Location	65 (12.3 - 217)	117 (9.2 - 320)	320 (90 - 630)
Average Rainfall and Cool Location	110 (23.2 - 304)	182 (32 - 400)	420 (158 - 660)
Wet and Warm Location	114 (23.5 - 232)	140 (29.3 - 330)	370 (102 - 600)
Wet and Temperate Location	83 (33 - 208)	85 (39 - 201)	155 (60 - 340)
Wet and Cool Location	196 (98 - 320)	269 (179 - 410)	306 (147 - 500)
Average of Central Values:	67.3	97.4	210
25th Percentile:	0.12	0.004	1.43
Maximum:	320	410	660
Summary:	67.3 (0.12 - 320)	97.4 (0.004 - 410)	210 (1.43 - 660)

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

Site	Clay	Loam	Sand
Dry and Warm Location	0.04 (0 - 1)	0 (0 - 0.07)	0 (0 - 1.19)
Dry and Temperate Location	0.05 (0 - 0.7)	0 (0 - 6.7)	0.0004 (0 - 43)
Dry and Cold Location	0.04 (0 - 1)	0.0016 (0 - 0.4)	0.6 (0 - 15.8)
Average Rainfall and Warm Location	18.1 (4.1 - 95)	39 (1.68 - 213)	179 (56 - 340)
Average Rainfall and Temperate Location	31.6 (5.1 - 135)	60 (3.9 - 212)	223 (56 - 380)
Average Rainfall and Cool Location	53 (9.9 - 157)	103 (16.4 - 237)	258 (112 - 370)
Wet and Warm Location	60 (13.2 - 129)	63 (11.4 - 157)	112 (34 - 218)
Wet and Temperate Location	48 (13.9 - 112)	40 (10.3 - 110)	41 (11.1 - 91)
Wet and Cool Location	84 (46 - 158)	136 (72 - 213)	168 (68 - 264)
Average of Central Values:	32.8	49	109
25th Percentile:	0.05	0.0016	0.6
Maximum:	158	237	380
Summary:	32.8 (0.05 - 158)	49 (0.0016 - 237)	109 (0.6 - 380)

Appendix 9: EPA Surface Water Models

Input[1]	Central	Lower Bound Run	Upper Bound Run
Application rate (lb a.i./acre)	1	1	1
Proportion of Area Treated	1	1	1
K_{oc}	21	40	8
Soil aerobic half-time	80	17.3	299
Wetted in	No	No	No
Drift/Application Efficiency	0%/100% [D]	0%/100% [D]	0%/100% [D]
Incorporation depth (cm)	0	0	0
Water Solubility (mg/L)	31,800	31,800	31,800
Aerobic aquatic half-life (days)[4]	160	160	160
Aquatic photolysis	0	0	0
Proportion of Area Treated	1	1	1
FIRST Output (µg/L)	**Peak**	**Annual Average**	
Single Application			
Central Estimate	99.307	34.877	
Lower Bound	90.306	30.588	
Upper Bound	102.858	36.885	
PRZM-GW Output (µg/L)	**Peak**		
Single Application			
Central Estimate	5.2		
Lower Bound	0.29		
Upper Bound	127		

[1] See inputs for GLEAMS-Driver in Table 11 of risk assessment.

FIRST Output Files

Single Application

CENTRAL ESTIMATE (Central Estimate of Koc)

```
   RUN No.   1 FOR Chlorsulfuron    ON   None          * INPUT VALUES *
   ----------------------------------------------------------------------
    RATE (#/AC)   No.APPS &   SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
     ONE(MULT)    INTERVAL    Koc   (PPM )   (%DRIFT)     AREA    (IN)
   ----------------------------------------------------------------------
  1.000(  1.000)   1   1      21.031800.0   GRANUL( 0.0) 100.0   0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   ----------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   ----------------------------------------------------------------------
     80.00        2           0.00    0.00-    0.00  160.00     160.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
   ----------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION            CONCENTRATION
   ----------------------------------------------------------------------
            99.307                     34.877
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
LOWER BOUND (Upper Bound of Koc)
   RUN No.   2 FOR Chlorsulfuron    ON   None          * INPUT VALUES *
   ----------------------------------------------------------------------
    RATE (#/AC)   No.APPS &   SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
     ONE(MULT)    INTERVAL    Koc   (PPM )   (%DRIFT)     AREA    (IN)
   ----------------------------------------------------------------------
  1.000(  1.000)   1   1      40.031800.0   GRANUL( 0.0) 100.0   0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   ----------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   ----------------------------------------------------------------------
     17.30        2           0.00    0.00-    0.00  160.00     160.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
   ----------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION            CONCENTRATION
   ----------------------------------------------------------------------
            90.306                     30.588
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

UPPER BOUND (Lower Bound of Koc)
   RUN No.   3 FOR Chlorsulfuron    ON   None          * INPUT VALUES *
   ----------------------------------------------------------------------
    RATE (#/AC)   No.APPS &   SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
     ONE(MULT)    INTERVAL    Koc   (PPM )   (%DRIFT)     AREA    (IN)
   ----------------------------------------------------------------------
  1.000(  1.000)   1   1       8.031800.0   GRANUL( 0.0) 100.0   0.0


   FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
   ----------------------------------------------------------------------
   METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
    (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
   ----------------------------------------------------------------------
    299.00        2           0.00    0.00-    0.00  160.00     160.00


   UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.1  MAR 26, 2008
   ----------------------------------------------------------------------
        PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
          CONCENTRATION            CONCENTRATION
   ----------------------------------------------------------------------
           102.858                     36.885

* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```

SciGrow version 2.3 Output files

Single Application

CENTRAL ESTIMATE (Central Estimate of Koc)

```
SciGrow version 2.3
 chemical:Chlorsulfuron
 time is  8/19/2016  13:58:22
 ----------------------------------------------------------------------
  Application      Number of       Total Use    Koc      Soil Aerobic
  rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
 ----------------------------------------------------------------------
      1.000           1.0           1.000      2.10E+01       80.0
 ----------------------------------------------------------------------
 groundwater screening cond (ppb) =   5.20E+00
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```

LOWER BOUND (Upper Bound of Koc)

```
SciGrow version 2.3
 chemical:Chlorsulfuron
 time is  8/19/2016  13:59:42
 ----------------------------------------------------------------------
  Application      Number of       Total Use    Koc      Soil Aerobic
  rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
 ----------------------------------------------------------------------
      1.000           1.0           1.000      4.00E+01       17.3
 ----------------------------------------------------------------------
 groundwater screening cond (ppb) =   2.09E-01
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```

UPPER BOUND (Lower Bound of Koc)

```
SciGrow version 2.3
 chemical:Chlorsulfuron
 time is  8/19/2016  14: 0:57
 ----------------------------------------------------------------------
  Application      Number of       Total Use    Koc      Soil Aerobic
  rate (lb/acre)  applications   (lb/acre/yr)  (ml/g)   metabolism (days)
 ----------------------------------------------------------------------
      1.000           1.0           1.000      8.00E+00      299.0
 ----------------------------------------------------------------------
 groundwater screening cond (ppb) =   1.27E+02
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```