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Chlorsulfuron - Human Health and Ecological Risk Assessment – Final Report

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LIST OF WORKSHEETS

Supplement 1: Chlorsulfuron – WordPerfect Worksheets for Human Health and Ecological Risk Assessments, SERA WPWS 04-43-18-02a, Version 2.04d, dated November 16, 2004.

Supplement 2: Clopyralid -EXCEL Worksheets for Human Health and Ecological Risk Assessments, SERA EXWS 04-43-18-02a, Version 2.04d, dated November 16, 2004.

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
a.e.	acid equivalents
AEL	adverse-effect level
a.i.	active ingredient
ALS	acetolactate synthase
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
g	gram
ha	hectare
HQ	hazard quotient
IARC	International Agency for Research on Cancer
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
m	meter
M	male
MMAD	mass median aerodynamic diameter
MCS	multiple chemical sensitivity

mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MW	molecular weight
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
NTP	National Toxicology Program
OM	organic matter
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SRC	Syracuse Research Corporation
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
WHO	World Health Organization

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

OVERVIEW

Adverse effects on some nontarget plant species, both terrestrial and aquatic, are plausible 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 – i.e., the typical application rate considered in this risk assessment is over 6000 times higher than the no-observed effect concentration (NOEC) in direct spray assays of the most sensitive nontarget species. The highest application rate that may be considered in Forest Service programs is over 25,000 times the NOEC and about a factor of 2 above the NOEC in tolerant species. Given these relationships, damage to nontarget plant species after ground broadcast applications could extend to distances of greater than 900 feet from the application site. This risk characterization applies only to ground broadcast applications. When used in directed foliar applications (i.e., backpack), offsite drift could be reduced substantially but the extent of this reduction cannot be quantified.

Damage to aquatic plants, particularly macrophytes, is likely to be less substantial but still noteworthy. At the typical application rate, peak concentrations of chlorsulfuron in water could result in damage to aquatic macrophytes – i.e., hazard quotients ranging from 1.2 to about 24 based on an EC_{50} for growth inhibition. Thus, if chlorsulfuron is applied in areas where transport to water containing aquatic macrophytes is likely, it would be plausible that detectable damage could be observed. Aquatic algae do not appear to be as sensitive to chlorsulfuron and the hazard quotient is only modestly above the level of concern based on an acute NOEC. Thus, it is not clear if any substantial damage would be likely in aquatic algae.

Just as there is little reason to doubt that adverse effects on some plant species are plausible, there is no clear basis for suggesting that effects on humans or wildlife (terrestrial or aquatic animals) are likely or would be substantial. In workers involved in ground broadcast applications, the level of concern is modestly exceeded at the highest application rate (0.25 lb/acre) and the level of concern is reached at an application rate of 0.14 lb/acre.

PROGRAM DESCRIPTION

Chlorsulfuron is recommended for preemergent and early postemergent control of many annual, biennial, and perennial broadleaf weeds. Three formulations of chlorsulfuron are available in the United States: Telar® DF and Glean®, which are produced by Dupont, and Corsair ™, which is produced by Riverdale. Chlorsulfuron is formulated as a dry flowable granule that is mixed with water and applied as a spray. All three formulations contain 75% (w/w) chlorsulfuron and 25% (w/w) inert ingredients. Telar DF and Corsair are labeled for non-crop, industrial use and Glean is labeled for agricultural use. None of the formulations are specifically registered for forestry use.

Chlorsulfuron is used in Forest Service programs only for the control of noxious weeds. 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, since one formulation of chlorsulfuron (Glean) is registered for aerial applications, 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 rate of 0.056 lbs/acre is used, with a range of 0.0059 to 0.25 lbs/acre. This range is based on lowest and highest labeled application rates recommended on the manufacturer's label. The Forest Service used approximately 33 lbs of chlorsulfuron in 2002, the most recent year for which use statistics are available.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification – In experimental mammals, the acute oral LD_{50} for chlorsulfuron 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, suggest a clear or specific target organ toxicity. Appropriate tests have provided 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. 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. The kinetics of absorption of chlorsulfuron following dermal, oral or inhalation exposure are not documented in the available literature. 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, which then 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.

Exposure Assessment – Exposure assessments are conducted for both workers and members of the general public for the typical application rate of 0.056 lb/acre. The consequences of using the maximum application rate that might be used by the Forest Service, 0.25 lb/acre, are discussed in the risk characterization.

For workers, three types of application methods are generally modeled in Forest Service risk assessments: directed ground, broadcast ground, and aerial. Neither Telar nor Corsair, however, are registered for aerial application and estimates of exposures for workers involved in aerial application are not used in the risk characterization. Central estimates of exposure for ground workers are approximately 0.0007 mg/kg/day for directed ground spray and 0.001 mg/kg/day for broadcast ground spray. Upper range of exposures are approximately 0.0045 mg/kg/day for directed ground spray and 0.0085 mg/kg/day for broadcast ground spray. All of the accidental exposure scenarios for workers involve dermal exposures and all of these accidental exposures lead to estimates of dose that are either in the range of or substantially below the general exposure estimates for workers.

For the general public, the range of acute exposures is from approximately 0.0000002 mg/kg associated with the lower range for dermal exposure from an accidental spray on the lower legs to 0.09 mg/kg associated with the upper range for consumption of contaminated water by a child following an accidental spill of chlorsulfuron into a small pond. High dose estimates are also associated with consumption of contaminated fruit (approximately 0.01 mg/kg) and fish (approximately 0.008 mg/kg for subsistence populations). For chronic or longer term exposures, the modeled exposures are much lower than for acute exposures, ranging from approximately 0.000000001 mg/kg/day associated with the lower range for the normal consumption of fish to approximately 0.004 mg/kg/day associated with the upper range for consumption of contaminated fruit.

Dose-Response Assessment – The Office of Pesticide Programs of the U.S. EPA has derived a chronic RfD of 0.05 mg/kg/day for chlorsulfuron. This RfD is based on a chronic rat NOAEL of 5 mg/kg/day (Wood et al. 1980b) and an uncertainty factor of 100. In the same study, the LOAEL was 25 mg/kg/day and the effect noted was a weight loss and decreased weight gain. No frank signs of toxicity were seen at this or higher dose levels. This NOAEL for chronic toxic effects is below the NOAEL of 25 mg/kg/day for reproductive effects (Wood et al. 1981a). Thus, doses at or below the RfD will be below the level of concern for reproductive effects. For acute/incidental exposures, the U.S. EPA uses an acute NOAEL of 75 mg/kg/day with an uncertainty factor of 300 resulting in an acute RfD of 0.25 mg/kg/day [75 mg/kg/day / 300]. Both of these values are used in the current risk assessment for characterizing risks associated with exposures to chlorsulfuron.

Risk Characterization – For both workers and members of the general public, typical exposures to chlorsulfuron do not lead to estimated doses that exceed a level of concern. For workers, the upper range of hazard quotients is below the level of concern for backpack and aerial applications but somewhat above the level of concern for ground broadcast applications at the highest application rate. For ground broadcast applications, the level of concern is reached at an application rate of 0.14 lb/acre. For members of the general public, the upper limits for hazard quotients are below a level of concern except for the accidental spill of a large amount of

chlorsulfuron into a very small pond. Even this exposure scenario results in only a small excursion above the acute RfD and is not likely to be toxicologically significant, because of the short duration of exposure relative to those considered in the derivation of the RfD.

Mild irritation to the skin and eyes can result from exposure to relatively high levels of 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.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification – The mammalian toxicity of chlorsulfuron is relatively well characterized in experimental mammals; however, there is relatively little information regarding nontarget wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., weight loss and decreased body weight gain). Results of acute toxicity and reproduction studies in birds indicate that birds appear to be no more sensitive than experimental mammals to the toxic effects of chlorsulfuron. There is very little information on the effects of chlorsulfuron in terrestrial invertebrates, as standard toxicity bioassays were not identified in the published literature or the U.S. EPA files. No significant change in mortality rate was observed following exposure of larvae of *Gastrophysa ploygoni*, a species of leaf beetle, by direct spray or in feeding studies using chlorsulfuron treated leaves, although survival from egg hatch to imago was significantly decreased by chlorsulfuron applied to the host plant.

The toxicity of chlorsulfuron to terrestrial plants was studied extensively and is well characterized. Chlorsulfuron inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. This effect is considered quantitatively in the dose-response assessment and is one of the primary effects of concern in this risk assessment. The lowest EC_{50} value reported following direct spray is 0.000023 lbs/acre in cherries. The lowest NOEL reported was in onion (0.0000088 lb/acre).

Terrestrial microorganisms also have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. However, chlorsulfuron appears to be only mildly toxic to terrestrial microorganisms and results a field study suggest that effects are transient.

Acute toxicity studies have been conducted in several species of fish. A single study investigated the effects of chronic exposure of to chlorsulfuron in rainbow trout. Due to limited water solubililty of chlorsulfuron, full dose-response curves could not be generated. However, fish do not appear particularly susceptible to chlorsulfuron toxicity, with LC_{50} values in most species exceeding the limit of solubility for chlorsulfuron (250 to 980 ppm). Based on 96 hour LC_{50} values, the most susceptible species is the brown trout, with an LC_{50} value of 40 mg/L. Chlorsulfuron also appears to be relatively non-toxic to aquatic invertebrates. Standard toxicity bioassays to assess the effects of chlorsulfuron on aquatic invertebrates were conducted in daphnia and mysid shrimp. Similar LC_{50} values are reported for both species. For reproductive effects, an NOEC of 20 mg/L was reported in a 21-day exposure study in *D. magna*.

The available data suggest that chlorsulfuron, like many other herbicides, is much more toxic to aquatic plants than to aquatic animals. The toxicity of chlorsulfuron has been examined in both algae and aquatic macrophytes. Studies on the mechanism of action of chlorsulfuron in aquatic plants were not identified. However, chlorsulfuron is assumed to have the same mechanism of action in aquatic plants as in terrestrial plants. Based on the results of several studies in algae, the species-dependent variation in sensitivity based on EC_{50} values for growth inhibition is very large, ranging from 0.011 mg/L in *Synechococcus leopoliensis* to 359 mg/L in *Porphyridium cruentum*. Results of a mesocosm study suggest chlorsulfuron can cause changes in phytoplankton communities at concentrations as low as 1 μg/L. Only three studies were identified regarding the toxicity of chlorsulfuron to aquatic plants, two studies in duckweed and one study in sago pondweed. Comparison of 96-hour EC_{50} values for sago pondweed (0.25 μg/L) and duckweed (0.7 μg/L) show that pondweed is slightly more sensitive than duckweed.

Exposure Assessment – Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or contact with contaminated vegetation. In acute exposure scenarios, the highest exposures for small terrestrial vertebrates will occur after a direct spray and could reach up to about 1.36 mg/kg under typical exposure conditions. There is a wide range of exposures anticipated from the consumption of contaminated vegetation by terrestrial animals: central estimates range from 0.07 mg/kg for a small mammal to 1.51 mg/kg for a large bird under typical exposure conditions, with upper ranges of about 15 mg/kg for a small mammal and 42 mg/kg for a large bird. The consumption of contaminated water will generally lead to much lower levels of exposure. A similar pattern is seen for chronic exposures. Estimated daily doses for the a small mammal from the consumption of contaminated vegetation at the application site are in the range of about 0.003 mg/kg to 0.01 mg/kg. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, which range from 0.0000008 mg/kg/day to 0.000007 mg/kg/day for a small mammal. Based on general relationships of body size to body volume, larger vertebrates will receive lower doses and smaller animals, such as insects, will recieve much higher doses than small vertebrates under comparable exposure conditions. Because of the apparently low toxicity of chlorsulfuron to animals, the rather substantial variations in the different exposure assessments have little impact on the assessment of risk to terrestrial animals.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion and the use of contaminated irrigation water. Unintended direct spray is expressed simply as the application rate considered in this risk assessment, 0.056 lb a.e./acre and should be regarded as an extreme/accidental form of exposure that is not likely to occur in most Forest Service applications. Estimates for the other routes of exposure are much less. All of these exposure scenarios are dominated by situational variability because the levels of exposure are highly dependent on site-specific conditions. Thus, the exposure estimates are intended to represent conservative but plausible ranges that could occur but these ranges may over-estimate or under-estimate actual exposures in some cases. Spray drift is based on estimates from AGDRIFT. The proportion of the applied amount transported off-site from runoff is based on GLEAMS modeling of clay, loam, and sand. The amount of chlorsulfuron that might be transported off-site from wind erosion is based on estimates of annual soil loss associated with wind erosion and the assumption that the herbicide is incorporated into the top 1

cm of soil. Exposure from the use of contaminated irrigation water is based on the same data used to estimate human exposure from the consumption of contaminated ambient water and involves both monitoring studies as well as GLEAMS modeling.

Exposures to aquatic plants and animals is based on essentially the same information used to assess the exposure to terrestrial species from contaminated water. The peak estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.01 (0.01 to 0.2) mg a.e./L at an application rate of 1 lb a.e./acre. For longer-term exposures, average estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.0006 (0.0009 to 0.0001) mg a.e./L at an application rate of 1 lb a.e./acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application rates considered in this risk assessment.

Dose-Response Assessment – For terrestrial mammals, the dose-response assessment is based on the same data as the human health risk assessment (i.e., an acute NOAEL of 75 mg/kg/day and a chronic NOAEL of 5 mg/kg/day). None of the exposure scenarios, acute or longer term, result in exposure estimates that exceed this NOAEL. Birds appear to be substantially less sensitive to chlorsulfuron than mammals with an acute NOAEL 1686 mg/kg/day of from a 5-day feeding study and a longer-term NOAEL from a reproduction study of 140 mg/kg/day. Toxicity data on terrestrial invertebrates are not extensive. Based on direct spray studies, no mortality would be expected at application rates of up to 107 lb/acre. Indirect effects to herbivorous insects associated with sublethal effects on treated vegetation have been noted at very low application rates – i.e., about 0.001 lb/acre to 0.002 lb/acre. Soil microorganisms do not appear to be sensitive to chlorsulfuron with an NOEC of 10 ppm (or 10 μg/g soil).

The toxicity of chlorsulfuron to terrestrial plants can be characterized relatively well. A very broad range of sensitivities for various types of plants is apparent, with grasses appearing far more tolerant than most other species. For assessing the potential consequences of exposure to nontarget plants via runoff, an NOEC for seedling emergence of 0.000035 lb/acre is used for sensitive species and the corresponding value for tolerant species is 0.022 lb/acre. For assessing the impact of drift, an NOEC for vegetative vigor of 0.0000088 lb/acre is used for sensitive species and the corresponding value for tolerant species is 0.14 lb/acre.

The data on toxicity to fish and aquatic invertebrates are limited. For acute exposures, the NOEC of 30 mg/L in brown trout is used for the most sensitive species and the NOEC of 300 mg/L in rainbow trout is used for the most tolerant species. Toxicity values for chronic toxicity may be based on the available egg-and-fry/early life stage studies; only one study of chronic exposure in fish, a 77-day exposure of rainbow trout with an NOEC of 32 mg/L. This value is used directly as a longer term NOEC in tolerant species because the rainbow trout appears to be a relatively tolerant species in acute toxicity assays. Using the relative potency for acute exposures of 10 (brown trout relative to rainbow trout), NOEC for sensitive species is estimated at 3.2 mg/L. The lowest NOEC value for acute exposure in an aquatic invertebrate is 10 mg/L in *Daphnia magna* and the highest NOEC is 35 mg/L in *Mysidopsis bahia* , a mysid shrimp. Although mysid shrimp are saltwater species, the assumption is made that some freshwater species may be as tolerant as the most tolerant saltwater species. For long-term exposure of aquatic invertebrates, only one study was identified in the available literature – a 21-day

exposure study in *Daphnia magna* reporting an NOEC for mortality of 20 mg/L. Since *Daphnia magna* were identified as the most sensitive species in acute exposure studies, they will also be considered as the most sensitive species for chronic exposure. In the absence of data in a more tolerant species, the relative potency comparing *Daphnia magna* to *Mysidopsis bahia* is used to estimate a chronic exposure NOEC for *Mysidopsis bahia*, the most tolerant species in acute exposure studies. Based on a relative potency factor of 3.5 and a chronic NOEC of 20 mg/L in *Daphnia magna*, the NOEC in *Mysidopsis bahia* is estimated to be 70 mg/L.

Aquatic plants, particularly macrophytes, appear to be much more sensitive to chlorsulfuron than aquatic animals. An NOEC of 0.00047 mg/L in *Lemna minor* is used for quantifying effects in aquatic macrophytes. This value is comparable to other studies in aquatic macrophytes. Thus, there is no basis for differentiating sensitive and tolerant species of aquatic macrophytes. There is, however, a wide range of toxicity values for aquatic algae. The most sensitive algal species appears to be *Selenastrum capricornutum*, with a 96-hour EC_{50} of 0.05 mg/L and a corresponding NOEC of 0.01 mg/L. The most tolerant species of freshwater algae appears to be *Cyclotella crypitica*, with an EC_{50} value of 276 mg/L.

Risk Characterization – Chlorsulfuron is an effective and potent herbicide and adverse effects on some nontarget plant species, both terrestrial and aquatic, are plausible 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, 0.056 lb/acre, is over 6000 times higher than the NOEC determined in vegetative vigor (direct spray) assay of the most sensitive nontarget species – i.e, 0.0000088 lb/acre in onions and sugar beets – and only a factor of 2.5 below the NOEC for the most tolerant species in the same assay – i.e., 0.14 lb/acre in wheat, wild rye, and some other grasses. The highest application rate that may be considered in Forest Service programs – i.e., 0.25 lb/acre – is over 25,000 times the NOEC in sensitive species and about a factor of 2 above the NOEC in tolerant species. Given these relationships, damage to nontarget plant species after ground broadcast applications could extend to distances of greater than 900 feet from the application site. This risk characterization applies only to ground broadcast applications. When used in directed foliar applications (i.e., backpack), offsite drift could be reduced substantially but the extent of this reduction cannot be quantified.

The NOEC values for soil exposures (assayed in the seedling emergence test) are 0.000035 lb/acre for sensitive species and 0.022 lb/acre for tolerant species, values that are substantially higher than those in the vegetative vigor assay. Nonetheless, the offsite movement of chlorosulfuron via runoff could be substantial under conditions that favor runoff – i.e., clay soils – and hazard quotients in the range of 75 to nearly 1000 are estimated for sensitive species over a wide range of rainfall rates – i.e., 15 inches to 250 inches per year. In very arid regions in which runoff might not be substantial, wind erosion could result in damage to nontarget plant species. The plausibility of observing such damage would, however, be highly dependent on local conditions. This risk characterization would be applicable to either broadcast ground or directed foliar applications.

Damage to aquatic plants, particularly macrophytes, is less substantial but still noteworthy. At the typical application rate, peak concentrations of chlorsulfuron in water could result in damage

to aquatic macrophytes – i.e., hazard quotients ranging from 1.2 to about 24 based on an EC_{50} for growth inhibition. Thus, if chlorsulfuron is applied in areas where transport to water containing aquatic macrophytes is likely, it would be plausible that detectable damage could be observed.

Aquatic algae do not appear to be as sensitive to chlorsulfuron and the hazard quotient is only modestly above the level of concern based on an acute NOEC. Thus, it is not clear if any substantial damage would be likely in aquatic algae. At the upper range of the application rate covered in this risk assessment, the hazard quotient would exceed the level of concern by a factor of about 3. Again, it is not certain that this would result in any substantial adverse effect.

Just as there is little reason to doubt that adverse effects on some plant species are plausible, 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 using typical or worst-case exposure assumptions at the typical application rate of 0.056 lb a.e./acre or the maximum application rate of 0.25 lb a.e./acre. One study has suggested 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 and this effect has not been noted in subsequent studies by the same group of investigators using other plant-insect pairs. As with the human health risk assessment, this characterization of risk must be qualified. Chlorsulfuron has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging nontarget species. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects are anticipated in terrestrial animals.

Similarly, the risk characterization for aquatic animals is relatively simple and unambiguous. Chlorsulfuron appears to have a very low potential to cause any adverse effects in aquatic animals. All of the hazard quotients for aquatic animals are extremely low, ranging from 0.00000008 (longer term exposures in tolerant invertebrates) to 0.001 (acute exposures to sensitive aquatic invertebrates). At the maximum application rate of 0.25 lbs/acre, the risk characterization is unchanged: the highest hazard quotient 0.001 would be increased to 0.005, below the level of concern by a factor of 200.

1. INTRODUCTION

The USDA Forest Service uses chlorsulfuron in its vegetation management programs. This document provides risk assessments for human-health effects and ecological effects to support an assessment of the environmental consequences of these uses.

Although this is a technical support document and addresses some specialized technical areas, 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 2001).

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. No published reviews regarding human health or ecological effects of chlorsulfuron have been encountered. Moreover, almost all of the mammalian toxicology studies and most of the ecotoxicology studies are unpublished reports submitted to the U.S. EPA as part of the registration process for chlorsulfuron.

Because of the lack of a detailed, recent review concerning chlorsulfuron and the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA FIFRA/CBI files was conducted. Full text copies of relevant studies were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies were reviewed, discussed in Sections 3 and 4 as necessary, and synopses of the most relevant studies are provided in the appendices to this document. While this document discusses the studies required to support the risk assessments, it makes no attempt to summarize all of the information. The Forest Service will update this and other similar risk assessments on a periodic basis and welcomes input from the general public on the selection of studies included in the risk assessment. 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.

For the most part, the risk assessment methods used in this document are similar to those used in risk assessments previously conducted for the Forest Service as well as risk assessments conducted by other government agencies. Details regarding the specific methods used to prepare the human health risk assessment are provided in SERA (2001).

This document has four chapters, including the introduction, program description, risk assessment for human health effects, and risk assessment for ecological effects or effects on wildlife species. Each of the two risk assessment chapters has four major sections, including an identification of the hazards associated with chlorsulfuron and its commercial formulation, an assessment of potential exposure to the product, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These are the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

Variability and *uncertainty* may be dominant factors in any risk assessment, and these factors should be expressed. Within the context of a risk assessment, the terms *variability* and *uncertainty* signify different conditions. *Variability* reflects the knowledge of how things may change. Variability may take several forms. For this risk assessment, three types of variability are distinguished: *statistical*, *situational*, and *arbitrary*. *Statistical variability* reflects, at least, apparently random patterns in data. For example, various types of estimates used in this risk assessment involve relationships of certain physical properties to certain biological properties. In such cases, best or maximum likelihood estimates can be calculated as well as upper and lower confidence intervals that reflect the statistical variability in the relationships. *Situational variability* describes variations depending on known circumstances. For example, the application rate or the applied concentration of a herbicide will vary according to local conditions and goals. As discussed in the following section, the limits on this variability are known and there is some information to indicate what the variations are. In other words, *situational variability* is not random. *Arbitrary variability*, as the name implies, represents an attempt to describe changes that cannot be characterized statistically or by a given set of conditions that cannot be well defined. This type of variability dominates some spill scenarios involving either a spill of a chemical on to the surface of the skin or a spill of a chemical into water. In either case, exposure depends on the amount of chemical spilled and the area of skin or volume of water that is contaminated.

Variability reflects a knowledge or at least an explicit assumption about how things may change, while *uncertainty* reflects a lack of knowledge. For example, the focus of the human health dose-response assessment is an estimation of an "acceptable" or "no adverse effect" dose that will not be associated with adverse human health effects. For chlorsulfuron and for most other chemicals, however, this estimation regarding human health must be based on data from experimental animal studies, which cover only a limited number of effects. Generally, judgment is the basis for the methods used to make the assessment. Although the judgments may reflect a consensus (i.e., be used by many groups in a reasonably consistent manner), the resulting estimations of risk cannot be proven analytically. In other words, the estimates regarding risk involve uncertainty.

In considering different forms of variability, almost no risk estimate presented in this document is given as a single number. Usually, risk is expressed as a central estimate and a range, which is sometimes very large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations. Some of the calculations are relatively simple are included in the body of the document. Some sets of the calculations, however, are cumbersome. For those calculations, worksheets are included with this risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. Documentation for these worksheets (SERA 2003) is available at www.sera-inc.com. As detailed in this documentation, two versions of the worksheets are available: one in a word processing format (Supplement 1) and one in a spreadsheet format (Supplement 2). The worksheets that are in the spreadsheet format are used only as a check of the worksheets that are in the word processing format. Both sets of worksheets are provided with the hard-text copy of this risk assessment as well as with the electronic version of the risk assessment.

2. PROGRAM DESCRIPTION

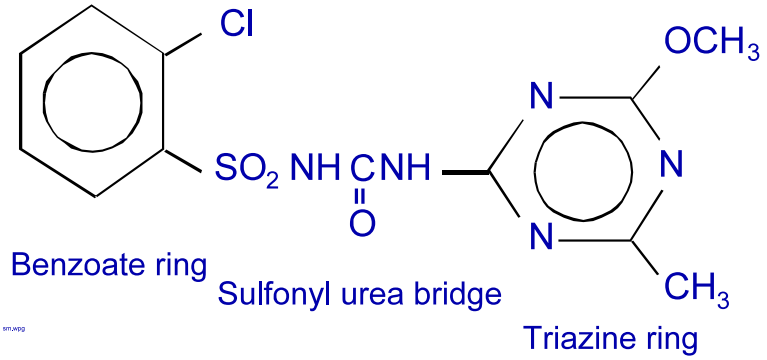
2.1. OVERVIEW

Chlorsulfuron is recommended for preemergent and early postemergent control of many annual, biennial, and perennial broadleaf weeds. Three formulations of chlorsulfuron are available in the United States: Telar® DF and Glean®, which are produced by Dupont, and Corsair ™, which is produced by Riverdale. Chlorsulfuron is formulated as a dry flowable granule that is mixed with water and applied as a spray. All three formulations contain 75% (w/w) chlorsulfuron and 25% (w/w) inert ingredients. Telar DF and Corsair are labeled for non-crop, industrial use and Glean is labeled for agricultural use. None of the formulations are specifically registered for forestry use.

Chlorsulfuron is used in Forest Service programs only for the control of noxious weeds. 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, since one formulation of chlorsulfuron (Glean) is registered for aerial applications, 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 rate of 0.056 lbs/acre is used, with a range of 0.0059 to 0.25 lbs/acre. This range is based on lowest and highest labeled application rates recommended on the manufacturer's label. The Forest Service used approximately 33 lbs of chlorsulfuron in 2002, the most recent year for which use statistics are available.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Chlorsulfuron is the common mane for 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]benzenesulfonamide. It is essentially a chlorobenzene ring linked to a methyl ($-CH_3$) and methoxy ($-0CH_3$) substituted triazine ring by a sulfonyl urea bridge:



Selected chemical and physical properties of chlorsulfuron are summarized in Table 2-1. Additional information is presented in worksheet B03.

Three formulations of chlorsulfuron are available in the United States: Telar® DF and Glean®, both of which are produced by Dupont, and Corsair ™, which is produced by Riverdale.

Chlorosulfuron is formulated as a dry flowable granule that is mixed with water and applied as a spray. All three formulations contain 75% (w/w) chlorsulfuron and 25% (w/w) inert ingredients. The identity of all inerts for each formulation has been disclosed to the U.S. EPA as part of the registration process and this information has been reviewed in the preparation of this risk assessment (Section 3.1.15). This information is classified as CBI (confidential business information) under Section 7(d) and Section (10) of FIFRA. Except as noted below, this information cannot be specifically disclosed in this risk assessment. Since the inerts are not identified on the product labels or the material safety data sheets, the lack of disclosure indicates that none of the inerts are classified as hazardous (C&P Press 2003). Nonetheless, as discussed by Levine (1996), the testing requirements for inerts are less rigorous than the testing requirements for active ingredients (i.e., chlorsulfuron).

All formulations are labeled for the control of many annual, biennial, and perennial broadleaf weeds. None of the formulations are specifically registered for forestry use. Telar DF and Corsair are labeled specifically for noncrop, industrial site use and Glean is labeled for agricultural use (C&P Press 2003). For Telar DF, there is a label specifically for use in California (DuPont 1998a). For all formulations, it is recommended that a non-ionic surfactant always be added as an adjuvant for postemergence applications.

2.3. APPLICATION METHODS

The most common methods of ground application for Telar DF and Corsair involve backpack (selective foliar) and boom spray (broadcast foliar) operations. In selective foliar applications, the herbicide sprayer or container is carried by backpack and the herbicide is applied to selected target vegetation. Application crews may treat up to shoulder high brush, which means that chemical contact with the arms, hands, or face is plausible. To reduce the likelihood of significant exposure, application crews are directed not to walk through treated vegetation. Usually, a worker treats approximately 0.5 acres/hour with a plausible range of 0.25-1.0 acre/hour (USDA 1989a,b,c).

Boom spray is used primarily in rights-of-way management. Spray equipment mounted on tractors or trucks is used to apply the herbicide on either side of the roadway. Usually, about 8 acres are treated in a 45-minute period (approximately 11 acres/hour). Some special truck mounted spray systems may be used to treat up to 12 acres in a 35-minute period with approximately 300 gallons of herbicide mixture (approximately 21 acres/hour and 510 gallons/hour) (USDA 1989a, p. 2-9 to 2-10).

Glean is the only formulation of chlorsulfuron registered for aerial applications (DuPont 1998c). Although this is not an application method that the Forest Service will typically employ for chlorosulfuron, this method is covered by this risk assessment in the event that the Forest Service may need to consider aerial applications. The product label does not specify the type of aircraft that should be used to aerial applications. Glean is applied under pressure through specially designed spray nozzles and booms. The nozzles are designed to minimize turbulence and maintain a large droplet size, both of which contribute to a reduction in spray drift. In aerial applications, approximately 40–100 acres may be treated per hour (USDA 1989a,b,c).

2.4. MIXING AND APPLICATION RATES

The specific application rates used in a ground application vary according to local conditions and the nature of the target vegetation. Recommended application rates (www.greenbook.net), expressed as ounces per acre, are different for the three formulations. All formulations contain 75% chlorsulfuron by weight. For Telar DF an application rate of ⅛ to 3 ounces formulation per acre, corresponding to 0.0.0938 to 2.25 ounces a.i. or 0.0089 to 0.141 pounds a.i. per acre, is recommended. For Corsair an application rate of 1 to 5 ⅓ ounces formulation per acre, corresponding to 0.76 to 4.0 ounces a.i. or 0.0469 to 0.25 pounds a.i. per acre is recommended. For Glean, an application rate of 1/6 to ½ ounces formulation per acre, corresponding to 0.125 to 0.375 ounces a.i. or 0.0078 to 0.0234 pounds a.i. per acre , is recommended.

The use of chlorsulfuron in Forest Service Programs for fiscal year 2001, the most recent year for which data are available, is summarized in Table 2-2. Chlorsulfuron is used currently in Forest Service Programs only for noxious weed control. Based on the total amount used and number of acres treated, the average application rate for chlorsulfuron is approximately 0.056 lbs/acre, with a range of 0.008 to 0.1 pounds per acre.

For this risk assessment, the typical application rate for chlorsulfuron will be taken as 0.056 lbs/acre, which is the average application rate for all applications conducted by the Forest Service in 2001. The range of application rates will be taken as 0.0059 lbs/acre to 0.25 lbs/acre, which is based on the lower and upper limits of the labeled rates, to reflect plausible ranges that the Forest Service may use. The worksheets that accompany this risk assessment are based on the typical application rate of 0.056 lbs/acre rather than the full range of application rates. The consequences of varying application rates within the range of 0.0059 to 0.25 lb/acre is considered in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

For non-crop, industrial use, mixing volumes of 10 to 300 gallons of water per acre are recommended, depending upon the application method and the specific formulation. For Telar DF, recommended mixing volumes of 10 to 40 gallons per acre are recommended for broadcast and invert spray applications, and 100 to 300 gallons per acre for handgun applications. For Corsair, mixing volumes 2 to 3 gallons per 1000 square feet, corresponding to approximately 87 to 130 gallons per acre, are recommended for backpack applications and a minimum of 20 gallons per acre is recommended to boom-type sprayers. Neither Talar DF or Corsair are labeled for aerial applications. For agricultural use, recommended mixing volumes for Glean are 3 to 20 gallons per acre ground applications and 1 to 5 gallons per acre for aerial applications. For this risk assessment, the extent to which these formulations are diluted prior to application primarily influences dermal and direct spray scenarios, both of which are dependent on the 'field dilution' (i.e., the concentration of chlorsulfuron in the applied spray). The higher the concentration of chlorsulfuron , the greater the risk. For this risk assessment, the lowest dilution will be taken at 10 gallons/acre, the minimum recommended for ground broadcast applications. The highest dilution (i.e., that which results in the lowest risk) will be based on 300 gallons of water per acre, the highest application volume recommended for ground broadcast.

It should be noted that the selection of application rates and dilution volumes in this risk assessment is intended to simply reflect typical or central estimates as well as plausible lower and upper ranges. In the assessment of specific program activities, the Forest Service will use

program specific application rates in the worksheets that are included with this report to assess any potential risks for a proposed application.

2.5. USE STATISTICS

The USDA Forest Service (USDA/FS 2002) tracks and reports use by geographical areas referred to as "*Regions*". As illustrated in Figure 2-1, the Forest Service classification divides the U.S. into nine regions designated from Region 1 (Northern) to Region 10 (Alaska). [Note: There is no *Region 7* in the Forest Service system.] Chlorsulfuron is only used in three regions, Region 1 (Northern), Region 2 (Rocky Mountain) and Region 4 (Intermountain). As illustrated in Figure 2-1 and detailed further in Table 2-2, the heaviest use of chlorsulfuron occurs in Region 1 (83.9% of total use by pounds applied or 67.1% of total use by acres treated). Smaller quantities are used in Region 2, and only a very small amount is used in Region 4.

Data on the amount of chlorsulfuron used in agriculture have not been encountered in the open literature. Only one formulation of chlorsulfuron, Glean, is currently registered for agricultural applications. Because Glean is produced by only a single manufacturer, this information may be classified as proprietary. Thus, at this time, it is not possible to estimate reliably the amount of chlorsulfuron that the Forest Service uses relative to other groups that may also use this product.

3. HUMAN HEALTH RISK ASSESSMENT

3.1 HAZARD IDENTIFICATION

3.1.1 Overview. In experimental mammals, the acute oral LD_{50} for chlorsulfuron 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, suggest a clear or specific target organ toxicity. Appropriate tests have provided 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. 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. The kinetics of absorption of chlorsulfuron following dermal, oral or inhalation exposure are not documented in the available literature. 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, which then 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

Although the mechanism of phytotoxic action of sulfonylurea herbicides including chlorsulfuron is characterized in some detail (Section 4.1.2.5), the mechanism of toxic action in mammals or other animal species is not well characterized.

As noted in the recent review on a closely related herbicide, sulfometuron methyl (Cox 1993), and described in detail by Melander et al. (1989), several of the sulfonylureas are biologically

active in humans and are used or were considered for use in the treatment of non-insulin-dependent diabetes mellitus (NIDDM or type 2 diabetes). A variety of sulfonylureas reduce blood glucose, stimulating the release of insulin from pancreatic B cells, and some sulfonylureas may reduce the hepatic extraction of insulin. Secondarily, some sulfonylureas may affect levels of blood cholesterol and serum triglycerides.

Hematological changes were observed in some of the toxicity studies of chlorsulfuron in mammals. Exposure to some sulfonamides have been associated with the development of hemolytic anemia in humans (Issaragrisil et al. 1997). This finding is supported by an earlier, more qualitative association of sulfonamide with anemia in humans (Dickerman 1981). However, no mechanism of action for this effect has been identified.

3.1.3 Kinetics and Metabolism

Limited information is available on the toxicokinetics of chlorsulfuron. The kinetics of absorption of chlorsulfuron following dermal, oral or inhalation exposure are not documented in the available literature. The lack of experimental data regarding the dermal absorption of chlorsulfuron adds substantial uncertainties to this risk assessment. Nonetheless, the available laboratory data in rabbits and guinea pigs, albeit relatively sparse, do not suggest that chlorsulfuron is likely to be absorbed through the skin in amounts that may cause systemic toxic effects (Appendix 1, Dermal Administration Studies). Uncertainties in the rates of dermal absorption, although they are substantial, can be estimated quantitatively and are incorporated in the human health exposure assessment (Section 3.2).

Dermal exposure scenarios involving immersion or prolonged contact with chemical solutions use Fick's first law and require an estimate of the permeability coefficient, K_p, expressed in cm/hour. Using the method recommended by U.S. EPA (1992), the estimated dermal permeability coefficient for chlorsulfuron is 0.0000005 cm/hour with a 95% confidence interval of 0.0000001-0.000002 cm/hour. These estimates are used in all exposure assessments that are based on Fick's first law. The calculations for these estimates are presented in worksheet B05.

For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the skin's surface, dermal absorption rates (proportion of the deposited dose per unit time) rather than dermal permeability rates are used in the exposure assessment. The estimated first-order dermal absorption coefficient is 0.000087 $hour^{-1}$ with 95% confidence intervals of 0.000012-0.00063 $hour^{-1}$. The calculations for these estimates are presented in Worksheet B04.

The distribution of chlorsulfuron has been studied in rats (Hawkins et al. 1989, Hunt 1981), goats (Han 1981f, Plowchalk 1994, Lee 1992b), dairy cows (Slates and Moore 1981), and hens (Bodden and Rhodes 1994, Rhodes 1995). Chlorsulfuron does not appear to concentrate or be retained in tissues following either single or multiple dose administration. Studies in rats show that chlorsulfuron reaches its highest tissue concentration in blood (Hawkins 1981). In goats and dairy cows, chlorsulfuron was distributed to kidney, liver and muscle but not to fat (Han 1981f, Lee 1992b, Plowchalk 1994, Slates and Moore 1981). In hens, only negligible amounts of chlorsulfuron or its metabolites were found in edible tissues and eggs (Bodden and Rhodes 1994, Rhodes 1995).

In rats, chlorsulfuron appears to follow two main metabolic pathways, either contraction of the sulfonylurea linkage with subsequent oxidation and hydroxylation reactions (the major pathway) or cleavage of the sulfonylurea bridge (Hawkins et al. 1989). The major metabolite identified in the urine of rats is 2-chlorobenzenesulfonamide (a hydrolysis product), although other minor metabolites have also identified in urine (Hunt 1981, Shrivastava 1979). Conjugation products, mainly N-glucuronides, have also been identified in the urine of goats (Han 1981f, Lee 1992b, Plowchalk 1994).

The elimination of chlorsulfuron has been 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 Rhodes199 , 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 a similar excretion and metabolism patterns as chlorsulfuron administered directly to goats (Han 1981g).

3.1.4 Acute Oral Toxicity

Other than standard bioassays for acute toxicity that were conducted as part of the registration process, there is little information regarding the acute toxicity of chlorsulfuron. As summarized in Appendix 1, several acute oral studies involving acute oral in rats and one study in guinea pigs are available. Comparison of the LD_{50} values in rats for chlorsulfuron and formulations containing 80% and 75% chlorsulfuron are provided in Table 3-2. The acute LD_{50} of chlorsulfuron (95% a.i.) was 5545 mg/kg (95% CI 4723-6648 mg/kg; equivalent to 5268 mg a.i./kg) in male rats and 6293 mg/kg in female rats (95% CI 4413-9524 mg/kg; equivalent to 5978 mg a.i./kg) (Tirvits 1979). LD_{50} values for the formulation containing 80% chlorsulfuron were higher than for chlorsulfuron (male rats: 7699 mg/kg, 95% CI 6996-8891 mg/kg, equivalent to 6159 mg a.i./kg; female rats: 7634 mg/kg, 95% CI 6806-9198 mg/kg, equivalent to 7113 mg a.i./kg). The LD_{50} values for the 75% chlorsulfuron formulation (male rats: 3053 mg/kg, 95% CI 1123-3342 mg/kg, equivalent to 2290 mg a.i./kg; female rats: 2341 mg/kg, 95% CI 1969-2623 mg/kg, equivalent to 1756 mg a.i./kg) were over 50% lower than those obtained for chlorsulfuron (95% a.i.). The reason for the difference between LD_{50} values for chlorsulfuron and the 75% chlorsulfuron formulation is unclear. One possible explanation could be differences in sensitivity of rat strains; acute toxicity tests for chlorsulfuron were conducted using the ChR-CD strain and tests for the 75% formulation were conducted using the Crl:CD strain. Unfortunately, acute toxicity data for chlorsulfuron and chlorsulfuron formulations were only available from single studies and results have not been confirmed in additional laboratory tests. Without additional data, it is not possible to determine if the LD_{50} value for the 75% formulation is truly lower than pure chlorsulfuron. However, since the LD_{50} value for the 80% formulation is higher than that for pure chlorsulfuron, it is most likely that the difference

observed between chlorsulfuron and the 75% formulation is due to variations in experimental conditions.

The lowest LD_{50} value for chlorsulfuron (91.9% a.i.) reported in any acute oral toxicity is 1363 mg/kg (equivalent to 1253 mg a.i./kg, 95% confidence limits not defined) in guinea pigs (Hall and Dashiell 1980). After the administration of 2200 mg/kg/day chlorsulfuron (95% a.i.) for 10 days to a group of 10 rats, two rats died but no treatment related gross or histopathological effects were observed (Henry 1977). It should be noted that the 20% mortality rate is not statistically significant using the Fisher Exact Test – i.e., $p = 0.236842$.

Qualitative assessments of toxicity were also made in all acute toxicity studies. Clinical signs of toxicity reported include weight loss, diarrhea, weakness, wet and stained peritoneal area, lethargy, and humped posture. Adverse effects were observed at the lowest dose tested (1000 mg/kg of 95% a.i.; equivalent to 950 mg a.i./kg) (Hinckle and Dashiell 1981) and were similar for chlorsulfuron and the chlorsulfuron formulations. Non-specific, gross pathological changes in several organs were also observed and were similar for chlorsulfuron and chlorsulfuron formulations.

3.1.5. Subchronic and Chronic Systemic Toxic Effects

Systemic toxicity encompasses virtually any effects that a chemical has after the chemical has been absorbed. Certain types of effects, however, are of particular concern and involve a specific subset of tests. Such special effects are considered in following subsections and include effects on the nervous system (Section 3.1.6), immune system (Section 3.1.7), endocrine function (3.1.8), development or reproduction (Section 3.1.9), and carcinogenicity or mutagenicity (Section 3.1.10). This section encompasses the remaining signs of general and non-specific toxicity.

The subchronic or chronic toxicity of chlorsulfuron to humans or mammals is not documented in the published literature, and all of the available toxicological data comes from unpublished studies that were conducted to support the registration of chlorsulfuron as a herbicide. As summarized in Appendix 2, there are two chronic exposure studies in rats (Wood et al. 1980b, Wood et al. 1981a), two chronic exposure studies in dogs (Atkinson 1991, Schneider et al. 1992), and three chronic exposure studies in mice (Smith et al. 1980, Wood et al. 1980c, 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. No studies investigating the effects of subchronic or chronic exposure by non-oral routes were identified.

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 52-week feeding study in male and female rats (80 rats/sex/dose) in which chlorsulfuron (~95% pure) was administered at dietary concentrations that resulted in daily doses of 5, 25, and 125 mg/kg/day (Wood et al. 1980b). 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. No effect on body weight or weight gain was observed for female rats in any treatment group. Thus, the NOEL for weight loss and decreased weight gain in this study was 5 mg/kg/day. Weight loss and decreased weight gain have also been observed following subchronic exposure to rabbits (Hoberman 1980) and chronic exposure to mice (Wood et al. 1980c, Wood et al.1981b). While observations of weight loss and decreased weight gain suggest that chlorsulfuron could be associated with an underlying change in metabolism, studies specifically investigating the effects of chlorsulfuron on metabolism have not been conducted. Weight loss and decreased weight gain do not suggest a clear or specific target organ toxicity.

In addition to weight loss and decreased weight gain, dose related hematologic effects have been observed following subchronic exposure to mice (Smith et al. 1980), and dogs (Schneider et al. 1992) and chronic exposure to rats (Wood et al. 1980b) and dogs (Atkinson 1991). 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 were reported in a chronic exposure study in mice (Smith et al. 1980). Results of these studies, which are discussed in more detail in Section 3.1.7 (Effects on Immune System), may indicate that chlorsulfuron is immunotoxic. Chronic exposure of male rats to 25 and 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 histopathologic changes were observed in organs of rats exposed 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

As discussed in Durkin and Diamond (2002), a *neurotoxicant* is chemical that disrupts the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of *neurotoxicant* is critical because it distinguishes agents that act directly on the nervous system *(direct neurotoxicants*) from those agents that might produce neurologic effects that are secondary to other forms of toxicity (*indirect neurotoxicants*). Virtually any chemical will cause signs of neurotoxicity in severely poisoned animals and thus can be classified as an indirect neurotoxicant. This is the case for chlorsulfuron in that exposure to acute high doses of chlorsulfuron produces lethargy and weakness (Appendix 1 B i.e., Trivits 1979; Hinckle and Dashiell 1981; Hinckle 1979). These reports, however, do not implicate chlorsulfuron as a direct neurotoxicant.

3.1.7 Effects on Immune System

There is very little direct information on which to assess the immunotoxic potential of chlorsulfuron. Dermal studies in rabbits show that chlorsulfuron does not produce sensitization (Section 3.1.11). Results of long-term exposure studies in dogs and mice show that chlorsulfuron may produce changes to immune system function. In female dogs exposed to 25 or 125 mg/kg/day chlorsulfuron (95% a.i.) for 26 weeks, increases in lymphocytes and eosinophils were observed (Schneider et al .1992). Effects were not seen at the 5 mg/kg/day

dose or in male dogs at any dose. In mice exposed to 25, 125, 250, or 375 mg/kg/day chlorsulfuron (100% a.i.) for 3 months, neutrophilic granulocytes were decreased and lymphocyte counts were increased in female mice in the 250 and 375 mg/kg/day exposure groups (Smith et al. 1980). Effects were not observed in female mice at lower doses or in male mice at any dose. While results of these studies suggest that exposure to chlorsulfuron may produce changes in immune system parameters, the observations in these studies do not provide conclusive evidence supporting the immunotoxic potential of chlorsulfuron.

3.1.8 Effects on Endocrine System

As noted in Section 3.1.1., a variety of sulfonylureas reduce blood glucose by stimulating the release of insulin from pancreatic B cells, and some sulfonylureas reduce the hepatic extraction of insulin. No studies investigating the effects of chlorsulfuron on insulin release or metabolism were identified. As noted in Appendix 1 and Appendix 2, both weight loss and weight gain are observed in animals treated with chlorsulfuron, implying a change in metabolic status. However, there is no evidence to suggest that changes in weight are due to effects of chlorsulfuron on the endocrine system. Decreased pituitary and thyroid weights were observed in male dogs exposed to chlorsulfuron (~95% a.i.) for 26 weeks (Schneider et al. 1992). However, these changes were not considered to be treatment related. With the exception of a slight decrease in the fertility index in rats exposed to125 mg/kg/day chlorsulfuron (a.i.) in a three-generation reproductive study (Wood et al. 1981a), there is no evidence that chlorsulfuron produces adverse effects on the reproductive endocrine system. Thus, no evidence for chlorsulfuron producing direct effects on the endocrine system was found.

3.1.9 Reproductive and Teratogenic Effects

Studies investigating the reproductive effects of chlorsulfuron in humans or mammals are not documented in the published literature, and all of the available toxicological data comes from unpublished studies that were conducted to support the registration of chlorsulfuron as a herbicide. As summarized in Appendix 2, studies assessing the reproductive and teratogenic effects of chlorsulfuron have been conducted in rabbits (Alvarez 1991b, Hoberman 1980) and rats (Alvarez 1991b, Rodgers et al. 1978, Wood 1980, Wood et al. 1981a,).

Chlorsulfuron is not teratogenic, but is embryo toxic at high exposure levels. An increase in the number of fetal resorptions and a decrease in fetal viability, indicating embryo toxicity, were observed in rabbits exposed to75 mg/kg/day (100% a.i.) on gestational days 9-19 (Hoberman 1980). Similar effects were also observed in the 10 and 25 mg/kg/day exposure groups, although changes did not reach statistical significance. Teratogenic effects were not observed in any dose group. No teratogenic effects were observed in rats exposed to chlorsulfuron (~98%) doses ranging from 55 to 1500 mg/kg administered on days 7-16 of gestation (Alvarez 1991a). The only effect observed was depressed fetal weights in the 1500 mg/kg/day exposure group. Exposure of rats for three-generations to chlorsulfuron (95% and 92 % a.i.) at doses of 5, 25, and 125 mg/kg/day did not result in significant treatment-related effects (Wood 1980). The only adverse effect on reproductive function reported was a slightly decreased fertility index rats exposed to 125 mg/kg/day. The NOEL for reproductive effects in rats is 25 mg/kg/day. Other than weight loss, no significant maternal toxicity was reported in these studies. Thus, chlorsulfuron does not appear to have significant adverse effects on reproductive function.

3.1.10 Carcinogenicity and Mutagenicity

Chlorsulfuron has been tested for mutagenicity in a number of different test systems and has been assayed for carcinogenic activity in rats and mice. Study results are summarized in Appendices 2 and 3. No evidence of carcinogenic activity was found in any of the chronic toxicity studies conducted on chlorsulfuron. Exposure of rats to chlorsulfuron (a.i.) at dose up to 125 mg/kg/day for 2 years did not increase the incidence of tumors compared to controls (Wood et al. 1981a). Negative results were also obtained from carcinogenicity studies in mice exposed to chlorsulfuron (a.i.) or 2 years at doses up to 250 mg/kg/day (Wood et al. 1980c). Results of *in vitro* mutagenicity studies in several *Salmonella typhimurium* strains and in Chinese hamster ovary cells show that chlorsulfuron is not mutagenic, either with or without metabolic activation (Russell 1977, Galloway and Lebowitz 1981a). Negative results were also obtained from genotoxicity studies in primary rat hepatocyte cultures (Williams et al 1981, Vincent 1990). In addition, *in vivo* studies in rats show that chlorsulfuron at exposure levels up to 250 mg/kg/day for 10 weeks does not produce dominant lethal mutations (Hoberman and Fieser 1980a).

3.1.11 Irritation and Sensitization (Effects on Skin and Eyes)

Chlorsulfuron is classified as moderate eye irritant (Category III) but as non-irritant to the skin (Category IV). Chlorsulfuron was tested for irritant effects on the skin of rabbits and guinea pigs and the eyes of rabbits. As summarized in Appendix 1, the results of several acute dermal studies show that formulations containing up to 80% chlorsulfuron produced only mild skin irritation. Dermal application of 0.5g of a 75% formulation of chlorsulfuron to intact and abraded skin produced mild erythema that resolved within 4-6 days (Dashiell and Silber 1980b, Henry and Dashiell 1980). Based on Draize scores, chlorsulfuron was not found to be a primary irritant in rabbits. Dermal application of a approximately 0.05 mL of solutions containing up to 60% of a 75% chlorsulfuron formulation did not produce skin irritation or a sensitization response in guinea pigs (Goodman 1976, Dashiell and Silber 1981).

Application of formulations containing 75% and 80% chlorsulfuron to the eyes of rabbits produced mild irritant effects to the cornea and conjunctiva (Appendix 1). Transient, mild corneal clouding and mild to no conjunctival swelling and discharged were observed rabbits following single application of 0.1 mL of a 75% formulation (Silber 1980). No signs of iritic irritation were observed. Transient, slight corneal clouding, conjunctivitis, and iritic swelling were observed following single application of 0.1 mL of a 80% formulation (Dashiell and Silber 1980a). Eyes returned to normal within 4 days. Accordingly, the MSDS for both Glean and Telar warn that exposure to these formulations may cause eye irritation (C&P Press 2003).

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.

Studies on the systemic toxicity of chlorsulfuron following dermal exposure have been conducted in rabbits (summarized in Appendix 1). Dermal exposure to doses up to 3400 mg/kg

(chlorsulfuron ,100% a.i.) were not associated with any signs of significant systemic toxicity in rabbits based on standard acute/single application bioassays with 14-day observation periods (Edwards 1979a,b). Only 1 death, which was not considered to be treatment related, was reported (Edwards 1979b). Thus, the LD_{50} for dermal exposure of chlorsulfuron in rabbits is >3400 mg/kg (Edwards 1979b). The only signs of systemic toxicity reported in these studies were sporadic weight and diarrhea. Similar results were obtained in dermal exposure studies of formulations containing 75% or 80% chlorsulfuron at doses up to 3400 mg formulation/kg (Dashiell and Ashley 1980a, Silber and Dashiell 1980). In general, dermal LD_{50} values are higher than oral LD_{50} values (e.g., Gaines 1969). Acute oral exposure studies for chlorsulfuron in rabbits were not identified in the literature. However, since the reported acute oral LD_{50} values of chlorsulfuron in rats are all 2341 mg/kg or greater and in guinea pigs is 1363 mg/kg (see Appendix 1), the lack of toxic effects at dermal doses of up to 3400 mg/kg is not unexpected (Edwards 1979a, Edwards 1979b).

3.1.13 Inhalation Exposure

Four inhalation toxicity studies on chlorsulfuron are listed in Appendix 1 (Chen 1980, Fereuz 1980a,b, Fereuz and Chen 1980). Based upon close examination of these study reports, it appears these four reports are all the same study. Therefore, only one study provides information on the toxicity of chlorsulfuron by inhalation exposure. Acute inhalation of chlorsulfuron at a concentration of 5.9 mg/L in dust for four-hours to 10 male and 10 female rats did not results in any systemic adverse effects considered to be treatment related (Chen 1980). Necropsy performed 14 days after exposure on 3 male and 3 female rats did not reveal any treatment-related tissue changes to lungs, liver, kidneys, testes, epididymis, ovary, or uterine horns. While no systemic effects were noted, microscopic changes to the nasal mucosa, including focal atrophy of the nasal gland acini and mild focal squamous metaplasia, were noted in 2/6 rats subjected to necropsy. These histological findings were consistent with chronic rhinitis or with post-injury repair processes.

3.1.14 Inerts and Adjuvants

The formulation of chlorsulfuron used by the Forest Service contains materials other than chlorsulfuron that are included as adjuvants to improve either efficacy or ease of handling and storage. The identity of these materials is confidential. The inerts were disclosed to the U.S. EPA (Armstrong 1988a; Brennan 1999a,b) and were reviewed in the preparation of this risk assessment. All that can be disclosed explicitly is that none of the additives are classified by the U.S. EPA as toxic.

As noted in Section 2.2, the manufacturers recommend that chlorsulfuron formulations be mixed with a non-ionic surfactant. There is no published literature or information in the FIFRA files that would permit an assessment of toxicological effects of chlorsulfuron mixed with surfactant.

3.1.15 Impurities and Metabolites

Virtually no chemical synthesis yields a totally pure product. Technical grade chlorsulfuron, as with other technical grade products, undoubtedly contains some impurities. To some extent, concern for impurities in technical grade chlorsulfuron is reduced by the fact that the existing toxicity studies on chlorsulfuron were conducted with the technical grade product. Thus, if

toxic impurities are present in the technical grade product, they are likely to be encompassed by the available toxicity studies on the technical grade product.

No studies investigating the toxicity of the chlorsulfuron metabolites produced by mammals were identified in the published literature or unpublished studies. The toxicity of the metabolites of chlorsulfuron is likely to be encompassed by the available mammalian toxicity studies. As discussed in Section 3.1.3 (Kinetics and Metabolism), metabolites of chlorsulfuron are rapidly excreted and do not appear to concentrate in any tissue.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. Exposure assessments are conducted for both workers and members of the general public for the typical application rate of 0.056 lb/acre. The consequences of using the maximum application rate that might be used by the Forest Service, 0.25 lb/acre, are discussed in the risk characterization.

For workers, three types of application methods are generally modeled in Forest Service risk assessments: directed ground, broadcast ground, and aerial. Neither Telar nor Corsair, however, are registered for aerial application and estimates of exposures for workers involved in aerial application are not used in the risk characterization. Central estimates of exposure for ground workers are approximately 0.0007 mg/kg/day for directed ground spray and 0.001 mg/kg/day for broadcast ground spray. Upper range of exposures are approximately 0.0045 mg/kg/day for directed ground spray and 0.0085 mg/kg/day for broadcast ground spray. All of the accidental exposure scenarios for workers involve dermal exposures and all of these accidental exposures lead to estimates of dose that are either in the range of or substantially below the general exposure estimates for workers.

For the general public, the range of acute exposures is from approximately 0.0000002 mg/kg associated with the lower range for dermal exposure from an accidental spray on the lower legs to 0.09 mg/kg associated with the upper range for consumption of contaminated water by a child following an accidental spill of chlorsulfuron into a small pond. High dose estimates are also associated with consumption of contaminated fruit (approximately 0.01 mg/kg) and fish (approximately 0.008 mg/kg for subsistence populations). For chronic or longer term exposures, the modeled exposures are much lower than for acute exposures, ranging from approximately 0.000000001 mg/kg/day associated with the lower range for the normal consumption of fish to approximately 0.004 mg/kg/day associated with the upper range for consumption of contaminated fruit.

3.2.2. Workers.

The Forest Service uses a standard set of exposure assessments in all risk assessment documents. While these exposure assessments vary depending on the characteristics of the specific chemical as well as the relevant data on the specific chemical, the organization and assumptions used in the exposure assessments are standard and consistent. All of the exposure assessments for workers as well as members of the general public are detailed in the worksheets on chlorsulfuron that accompany this risk assessment (Supplement 1). Documentation for these worksheets (SERA 2003) is available at www.sera-inc.com. This section on workers and the following section on the general public provides are plain verbal description of the worksheets and discuss chlorsulfuron specific data that are used in the worksheets.

A summary of the exposure assessments for workers is presented in Worksheet E02 of the worksheets for chlorsulfuron that accompany this risk assessment. Two types of exposure assessments are considered: general and accidental/incidental. The term *general* exposure assessment is used to designate those exposures that involve estimates of absorbed dose based on the handling of a specified amount of a chemical during specific types of applications. The accidental/incidental exposure scenarios involve specific types of events that could occur during any type of application. The exposure assessments developed in this section as well as other

similar assessments for the general public (Section 3.2.3) are based on the typical application rate of 0.056 lbs a.i./acre (Section 2). The consequences of using different application rates in the range considered by the Forest Service are discussed further in the risk characterization (Section 3.4).

3.2.2.1. General Exposures – As described in SERA (2001), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. Based on analyses of several different pesticides using a variety of application methods, default exposure rates are estimated for three different types of applications: directed foliar (backpack), boom spray (hydraulic ground spray), and aerial.

The specific assumptions used for each application method are detailed in worksheets C01a (directed foliar), C01b (broadcast foliar), and C01c (aerial). It should be noted that neither Telar nor Corsair are registered for aerial application. Thus, Worksheet C01c is included in the worksheets for consistency with other Forest Service risk assessments but the resulting exposure assessments are not used in the risk characterization (Section 3.4). In the worksheets, the central estimate of the amount handled per day is calculated as the product of the central estimates of the acres treated per day and the application rate. The typical application rate is taken directly from the program description (see Section 2.4).

No worker exposure studies with chlorsulfuron were found in the literature. As described in SERA (2001), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. These exposure rates are based on worker exposure studies on nine different pesticides with molecular weights ranging from 221 to 416 and log K_{ow} values at pH 7 ranging from -0.75 to 6.50. The estimated exposure rates are based on estimated absorbed doses in workers as well as the amounts of the chemical handled by the workers. As summarized in Table 2-1 of this risk assessment, the molecular weight of chlorsulfuron is 357.8 and the log K_{ow} at pH 7 is approximately -1.0. Because the K_{ow} for chlorsulfuron is slightly below the range of K_{ow} values used in formulating the regression model, confidence in these assessments are diminished. This uncertainty is compounded by the uncertainties inherent in the available data on worker exposure. As described in SERA (2001), the ranges of estimated occupational exposure rates vary substantially among individuals and groups, (i.e., by a factor of 50 for backpack applicators and a factor of 100 for mechanical ground sprayers). It seems that much of the variability can be attributed to the hygienic measures taken by individual workers (i.e., how careful the workers are to avoid unnecessary exposure); however, pharmacokinetic differences among individuals (i.e., how individuals absorb and excrete the compound) also may be important.

An estimate of the number of acres treated per hour is needed to apply these worker exposure rates. These values are taken from previous USDA risk assessments (USDA 1989a,b,c). The number of hours worked per day is expressed as a range, the lower end of which is based on an 8-hour work day with 1 hour at each end of the work day spent in activities that do not involve herbicide exposure. The upper end of the range, 8 hours per day, is based on an extended (10-hour) work day, allowing for 1 hour at each end of the work day to be spent in activities that do not involve herbicide exposure.

It is recognized that the use of 6 hours as the lower range of time spent per day applying herbicides is not a true lower limit. It is conceivable and perhaps common for workers to spend much less time in the actual application of a herbicide if they are engaged in other activities. Thus, using 6 hours may overestimate exposure. In the absence of any published or otherwise documented work practice statistics to support the use of a lower limit, this approach is used as a protective assumption.

The range of acres treated per hour and hours worked per day is used to calculate a range for the number of acres treated per day. For this calculation as well as others in this section involving the multiplication of ranges, the lower end of the resulting range is the product of the lower end of one range and the lower end of the other range. Similarly, the upper end of the resulting range is the product of the upper end of one range and the upper end of the other range. This approach is taken to encompass as broadly as possible the range of potential exposures.

The central estimate of the acres treated per day is taken as the arithmetic average of the range. Because of the relatively narrow limits of the ranges for backpack and boom spray workers, the use of the arithmetic mean rather than some other measure of central tendency, like the geometric mean, has no marked effect on the risk assessment.

3.2.2.2. Accidental Exposures – Typical occupational exposures may involve multiple routes of exposure (i.e., oral, dermal, and inhalation); nonetheless, dermal exposure is generally the predominant route for herbicide applicators (Ecobichon 1998; van Hemmen 1992). Typical multi-route exposures are encompassed by the methods used in Section 3.2.2.1 on general exposures. Accidental exposures, on the other hand, are most likely to involve splashing a solution of herbicides into the eyes or to involve various dermal exposure scenarios.

Chlorsulfuron is classified as a moderate eye irritant and as non-irritant to the skin (see Section 3.1.11). The available literature does not include quantitative methods for characterizing exposure or responses associated with splashing a solution of a chemical into the eyes; furthermore, there appear to be no reasonable approaches to modeling this type of exposure scenario quantitatively. Consequently, accidental exposure scenarios of this type are considered qualitatively in the risk characterization (Section 3.4).

There are various methods for estimating absorbed doses associated with accidental dermal exposure (U.S. EPA/ORD 1992, SERA 2001). Two general types of exposure are modeled: those involving direct contact with a solution of the herbicide and those associated with accidental spills of the herbicide onto the surface of the skin. Any number of specific exposure scenarios could be developed for direct contact or accidental spills by varying the amount or concentration of the chemical on or in contact with the surface of the skin and by varying the surface area of the skin that is contaminated.

For this risk assessment, two exposure scenarios are developed for each of the two types of dermal exposure, and the estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Both sets of exposure scenarios are summarize in Worksheet E01, which references other worksheets in which the specific calculations are detailed.

Exposure scenarios involving direct contact with solutions of the chemical are characterized by immersion of the hands for 1 minute or wearing contaminated gloves for 1 hour. Generally, it is not reasonable to assume or postulate that the hands or any other part of a worker will be immersed in a solution of a herbicide for any period of time. On the other hand, contamination of gloves or other clothing is quite plausible. For these exposure scenarios, the key element is the assumption that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in a solution. In either case, the concentration of the chemical in solution that is in contact with the surface of the skin and the resulting dermal absorption rate are essentially constant.

For both scenarios (the hand immersion and the contaminated glove), the assumption of zero-order absorption kinetics is appropriate. Following the general recommendations of U.S. EPA/ORD (1992), Fick's first law is used to estimate dermal exposure. As discussed in Section 3.1.3, an experimental dermal permeability coefficient (Kp) for chlorsulfuron is not available. Thus, the Kp for chlorsulfuron is estimated using the algorithm from U.S. EPA/ORD (1992), which is detailed in Worksheet A07b. The application of this algorithm to chlorsulfuron, based on molecular weight and the $k_{o/w}$, is given in Worksheet B04.

Exposure scenarios involving chemical spills onto the skin are characterized by a spill on to the lower legs as well as a spill on to the hands. In these scenarios, it is assumed that a solution of the chemical is spilled on to a given surface area of skin and that a certain amount of the chemical adheres to the skin. The absorbed dose is then calculated as the product of the amount of the chemical on the surface of the skin (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the concentration of the chemical in the liquid) the first-order absorption rate, and the duration of exposure.

For both scenarios, it is assumed that the contaminated skin is effectively cleaned after 1 hour. As with the exposure assessments based on Fick's first law, this product (mg of absorbed dose) is divided by body weight (kg) to yield an estimated dose in units of mg chemical/kg body weight. The specific equation used in these exposure assessments is specified in Worksheet B03.

Confidence in these exposure assessments is diminished by the lack of experimental data on the dermal absorption of chlorsulfuron. Nonetheless, as summarized in Worksheet E01, there is a noteworthy similarity between the exposure scenario in which contaminated gloves are worn for 1 hour (Worksheet C02b) and the exposure scenario in which a chemical solution is spilled on to the skin surface of the hands and cleaned after 1 hour (Worksheet C03a). Confidence in these assessments is enhanced somewhat by the fact that two similar scenarios based on different empirical relationships yield similar estimates of exposure.

3.2.3. General Public.

3.2.3.1. General Considerations – Under normal conditions, members of the general public should not be exposed to substantial levels of chlorsulfuron. Nonetheless, any number of exposure scenarios can be constructed for the general public, depending on various assumptions regarding application rates, dispersion, canopy interception, and human activity. Several scenarios are developed for this risk assessment which should tend to over-estimate exposures in general.

The two types of exposure scenarios developed for the general public include acute exposure and longer-term or chronic exposure. All of the acute exposure scenarios are primarily accidental. They assume that an individual is exposed to the compound either during or shortly after its application. Specific scenarios are developed for direct spray, dermal contact with contaminated vegetation, as well as the consumption of contaminated fruit, water, and fish. Most of these scenarios should be regarded as extreme, some to the point of limited plausibility. The longer-term or chronic exposure scenarios parallel the acute exposure scenarios for the consumption of contaminated fruit, water, and fish but are based on estimated levels of exposure for longer periods after application.

The exposure scenarios developed for the general public are summarized in Worksheet E03. As with the worker exposure scenarios, details of the assumptions and calculations involved in these exposure assessments are given in the worksheets that accompany this risk assessment (Worksheets D01–D09). The remainder of this section focuses on a qualitative description of the rationale for and quality of the data supporting each of the assessments.

3.2.3.2. Direct Spray – Direct sprays involving ground applications are modeled in a manner similar to accidental spills for workers (Section 3.2.2.2). In other words, it is assumed that the individual is sprayed with a solution containing the compound and that an amount of the compound remains on the skin and is absorbed by first-order kinetics. For these exposure scenarios, it is assumed that during a ground application, a naked child is sprayed directly with chlorsulfuron. These scenarios also assume that the child is completely covered (that is, 100% of the surface area of the body is exposed). These exposure scenarios are likely to represent upper limits of plausible exposure. An additional set of scenarios are included involving a young woman who is accidentally sprayed over the feet and legs. For each of these scenarios, some assumptions are made regarding the surface area of the skin and body weight, as detailed in Worksheet A03.

3.2.3.3. Dermal Exposure from Contaminated Vegetation – In this exposure scenario, it is assumed that the herbicide is sprayed at a given application rate and that an individual comes in contact with sprayed vegetation or other contaminated surfaces at some period after the spray operation. For these exposure scenarios, some estimates of dislodgeable residue and the rate of transfer from the contaminated vegetation to the surface of the skin must be available. No such data are available on dermal transfer rates for chlorsulfuron and the estimation methods of Durkin et al. (1995) are used as defined in Worksheet D02. The exposure scenario assumes a contact period of one hour and assumes that the chemical is not effectively removed by washing for 24 hours. Other estimates used in this exposure scenario involve estimates of body weight, skin surface area, and first-order dermal absorption rates, as discussed in the previous section.

3.2.3.4. Contaminated Water – Water can be contaminated from runoff, as a result of leaching from contaminated soil, from a direct spill, or from unintentional contamination from aerial applications. For this risk assessment, the two types of estimates made for the concentration of chlorsulfuron in ambient water are acute/accidental exposure from an accidental spill and longer-term exposure to chlorsulfuron in ambient water that could be associated with the application of this compound to a 10 acre block that is adjacent to and drains into a small stream or pond.

3.2.3.4.1. ACUTE EXPOSURE –

Two exposure scenarios are presented for the acute consumption of contaminated water: an accidental spill into a small pond (0.25 acres in surface area and 1 meter deep) and the contamination of a small stream by runoff or percolation.

The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill into a small pond. The specifics of this scenarios are given in Worksheet D05. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation of chlorsulfuron is considered. This scenario is dominated by arbitrary variability and the specific assumptions used will generally overestimate exposure. The actual concentrations in the water would depend heavily on the amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs relative to the time of the spill, and the amount of contaminated water that is consumed. Based on the spill scenario used in this risk assessment, the concentration of chlorsulfuron in a small pond is estimated to range from about 0.015 mg/L to 0.76 mg/L with a central estimate of about 0.076 mg/L (Worksheet D05).

The other acute exposure scenario for the consumption of contaminated water involves runoff into a small stream. A single study reports monitoring data on chlorsulfuron concentrations in random samples obtained from midwestern streams, rivers, and ground-water in 1998 (Bagglin et al. 1999). Of the 130 samples collected from streams and rivers, chlorsulfuron was detected in only one sample at a concentration of 0.013 µg/L, just slightly above the method reporting limit of 0.01 µg/L. In ground-water, chlorsulfuron was below the method reporting limit in the 25 samples tested.

While monitoring data provide practical and documented instances of water contamination, monitoring studies may not encompass a broad range of conditions which may occur during program applications – e.g., extremely heavy rainfall – or they may reflect atypical applications that do not reflect program practices. Unfortunately, use of the available monitoring data (Bagglin et al. 1999) in the exposure assessment is limited because sampling was random and not associated with a specific application of chlorsulfuron. Consequently, for this component of the exposure assessment, modeled estimates are made based on GLEAMS (Groundwater Loading Effects of Agricultural Management Systems). GLEAMS is a root zone model that can be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions (Knisel and Davis 2000). As with many environmental fate and transport models, the input and output files for GLEAMS can be complex. The general application of the GLEAMS model and the use of the output from this model to estimate concentrations in ambient water are detailed in SERA (2004).

For the current risk assessment, the application site was assumed to consist of a 10 acre square area that drained directly into a small pond or stream. The chemical specific values as well as the details of the pond and stream scenarios used in the GLEAMS modeling are summarized in Table 3-2. The GLEAMS modeling yielded estimates runoff, sediment and percolation that were used to estimate concentrations in the stream adjacent to a treated plot, as detailed in Section 6.4 of SERA (2004). The results of the GLEAMS modeling for the small stream are

summarized in Table 3-3 and the corresponding values for the small pond are summarized in Table 3-4. These estimates are expressed as both average and maximum water contamination rates (WCR) - i.e., the concentration of the compound in water in units of mg/L normalized for an application rate of 1 lb a.e./acre.

As indicated in Table 3-3, no stream contamination is estimated in very arid regions – i.e., annual rainfall of 10 inches of less. The modeled maximum concentrations in the stream range from about less than 1 µg/L to somewhat over 200 µg/L at annual rainfall rates from 15 to 250 inches per year, with the highest concentrations associated with clay. While not detailed in Table 3-3, the losses from clay are associated almost exclusively with runoff (about 90%), with the remaining amount due to sediment loss. For sand, the pesticide loss is associated almost exclusively with percolation. For both clay and sand, the maximum losses occur with the first rainfall after application. For loam, most of the pesticide loss is associated with percolation but time to maximum loss is attenuated due to slower transport in loam and the total loss is less than from sandy soil.

Due to the lack of monitoring data obtained following a known application of chlorsulfuron, comparisons of the modeled maximum concentrations to monitoring data are of limited use. The highest concentration of chlorsulfuron reported by Bagglin et al. (1999) is 0.013 µg/L. The modeled concentrations range from a minimum of 0.00027 µg/L (in sand with 15 inches of rainfall per year) to a maximum of approximately 200 µg/L (in clay with 150 inches of rainfall per year). As shown in Table 3-3, most of the modeled concentrations are well above the measured value of 0.013 µg/L. Thus, while the GLEAMS runs encompass the range reported by Bagglin et al. (1999), the limited nature of the monitoring report is of little use in assessing the quality of the GLEAMS modeling.

The GLEAMS scenarios do not specifically consider the effects of accidental direct spray. For example, the stream modeled using GLEAMS is about 6 feet wide and it is assumed that the herbicide is applied along a 660 foot length of the stream with a flow rate of 4,420,000 L/day. At an application rate of 1 lb/acre, accidental direct spray onto the surface of the stream would deposit about 41,252,800 µg [1 lb/acre = 112,100 µg/m^2 , 6'x660' = 3960 ft^2 = 368 m^2, 112,100 µg/m^2 x 368 m^2 = 41,252,800 µg]. This would result in a downstream concentration of about 10 µg/L [41,252,800 µg/day / 4,420,000 L/day]. As indicated in Table 3-3, the expected peak concentrations from clay are in excess of 10 µg/L at rainfall rates of 10 inches per year and thus the estimates used in this risk assessment (discussed below) encompass the potential effects of accidental direct spray.

For the current risk assessment, the upper range for the short-term water contamination rate will be taken as 200 µg/L per lb/acre, this about the maximum concentration at an annual rainfall rate 150 inches for clay soil. This value, converted to 0.2 mg/L per lb/acre, is entered into Worksheet B06. The central estimated will be taken as 100 µg/L (0.1 mg/L), about the maximum concentration for clay at an annual rainfall rate of 50 inches. The lower range will be taken as 10 µg/L (0.01 mg/L), concentrations that might be expected in relatively arid regions with clay soil – i.e., annual rainfall of 15 inches. Note that lesser concentrations are modeled for loam and sand and this may need to be considered in any site-specific application of GLEAMS.

3.2.3.4.2. LONGER-TERM EXPOSURE – The scenario for chronic exposure to chlorsulfuron from contaminated water is detailed in worksheet D07. This scenario assumes that an adult (70 kg male) consumes contaminated ambient water from a contaminated pond for a lifetime. The estimated concentrations in pond water are based both the modeled estimates from GLEAMS, discussed in the previous section and summarized in Table 3-4. As discussed in Section 3.2.3.4.2, monitoring data are only available from a single report in which chlorsulfuron concentrations were measured in random samples obtained from midwestern streams, rivers, and ground-water in 1998 (Bagglin et al. 1999). As with the acute exposure assessment, this study is of little use in assessing the quality of the GLEAMS modeling.

For this risk assessment, the typical WCR is taken as 0.6 µg/L or 0.0006 mg/L per lb/acre. This is about the average concentration that modeled in lake using GLEAMS at a rainfall rate of 100 inches per year in clay soil. The upper range of the WCR is taken as 0.9 µg/L or 0.0009 mg/L per lb/acre. This is the highest average concentration modeled from sandy soil – i.e., a rainfall rate of 100 inches per year. The lower range is taken as 0.1 µg/L or 0.0001 mg/L per lb/acre. This selection is somewhat arbitrary but would tend to encompass concentrations that might be found in relatively arid areas.

The WCR values discussed in this section summarized in Worksheet B06 and used for all longer term exposure assessments involving contaminated water. As with the corresponding values for a small stream, these estimates are expressed as the water contamination rates (WCR) in units of mg/L per lb/acre.

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

The potential for accumulation of chlorsulfuron in fish was studied in bluegill fish exposed to 0.01 and 1.0 mg/L (Han 1981c) and channel catfish exposed to 0.5 mg/L ^{14}C-chlorsulfuron for 28 days (Priester et al. 1991b). Both studies examined the bioconcentration of ^{14}C-chlorsulfuron in muscle (edible tissue), liver and viscera during a 28-day exposure period. Details of these studies are provided in Appendix 9. Following 1 day of exposure, no bioconcentration of chlorsulfuron in edible tissue occurred in bluegill sunfish (BCF = 1) or channel catfish (BCF = 0.12). Over the 28-day exposure period, the highest BCF observed in edible tissue was 1.5 in channel catfish on days 7 and 14 of exposure. For this risk assessment, a bioconcentration factor for edible tissue in fish will be taken as 1 L/kg for acute exposure and a BCF of 1.5 L/kg is used for chronic exposure. These assumptions will over-estimate exposure but this over-estimate has no substantial impact on the risk assessment (Section 3.4).

For both the acute and longer-term exposure scenarios involving the consumption of contaminated fish, the water concentrations of chlorsulfuron used are identical to the concentrations used in the contaminated water scenarios (see Section 3.2.3.4). The acute exposure scenario is based on the assumption that an adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. No dissipation or degradation is considered. Because of the available and well-documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations, separate exposure estimates are made for these two groups, as illustrated in worksheet D08. The chronic exposure scenario is constructed in a similar way, as detailed in worksheet D09, except that estimates of chlorsulfuron concentrations in ambient water are based on GLEAMS modeling as discussed in Section 3.2.3.4.

3.2.3.6. Oral Exposure from Contaminated Vegetation – None of the Forest Service applications of chlorsulfuron will involve the treatment of crops. Thus, under normal circumstances and in most types of applications conducted as part of Forest Service programs, the consumption by humans of vegetation contaminated with chlorsulfuron is unlikely. Nonetheless, any number of scenarios could be developed involving either accidental spraying of crops or the spraying of edible wild vegetation, like berries. In most instances, and particularly for longer-term scenarios, treated vegetation would probably show signs of damage from exposure to chlorsulfuron (Section 4.3.2.4), thereby reducing the likelihood of consumption that would lead to significant levels of human exposure. Notwithstanding that assertion, it is conceivable that individuals could consume contaminated vegetation. One of the more plausible scenarios involves the consumption of contaminated berries after treatment of a right-of-way or some other area in which wild berries grow.

The two accidental exposure scenarios developed for this exposure assessment include one scenario for acute exposure, as defined in Worksheet D03 and one scenario for longer-term exposure, as defined in Worksheet D04. In both scenarios, the concentration of chlorsulfuron on contaminated vegetation is estimated using the empirical relationships between application rate and concentration on vegetation developed by Fletcher et al. (1994) which is in turn based on a re-analysis of data from Hoerger and Kenaga (1972). These relationships are defined in worksheet A04. For the acute exposure scenario, the estimated residue level is taken as the product of the application rate and the residue rate (Worksheet D03).

For the longer-term exposure scenario (D04), a duration of 90 days is used. The rate of decrease in the residues over time is taken from the vegetation half-time of 30 days reported by Knisel and Davis (2000). Although the duration of exposure of 90 days is somewhat arbitrarily chosen, this duration is intended to represent the consumption of contaminated fruit that might be available over one season. Longer durations could be used for certain kinds of vegetation but would lower the estimated dose (i.e., would reduce the estimate of risk).

For the longer-term exposure scenarios, the time-weighted average concentration on fruit is calculated from the equation for first-order dissipation. Assuming a first-order decrease in

concentrations in contaminated vegetation, the concentration in the vegetation at time t after spray, C_t, can be calculated based on the initial concentration, C_0, as:

$$C_t = C_0 \text{ x } e^{-kt}$$

where k is the first-order decay coefficient [$k=\ln(2) / t_{50}$]. Time-weighted average concentration (C_{TWA}) over time t can be calculated as the integral of C_t (De Sapio 1976, p. p. 97 ff) divided by the duration (t):

$$C_{TWA} = C_0 (1 - e^{-k\ t}) / (k\ t).$$

A separate scenario involving the consumption of contaminated vegetation by drift rather than direct spray is not developed in this risk assessment. As detailed further in Section 3.4, this elaboration is not necessary because the direct spray scenario leads to estimates of risk that are below a level of concern. Thus, considering spray drift and a buffer zone quantitatively would have no impact on the characterization of risk.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The Office of Pesticide Programs of the U.S. EPA has derived a chronic RfD of 0.02 mg/kg/day for chlorsulfuron. This RfD is based on a chronic rat NOAEL of 5 mg/kg/day (Wood et al. 1980a) and an uncertainty factor of 300. In the same study, the LOAEL was 25 mg/kg/day and the effect noted was a weight loss and decreased weight gain. No frank signs of toxicity were seen at this or higher dose levels. This NOAEL for chronic toxic effects is below the NOAEL of 25 mg/kg/day for reproductive effects (Wood et al. 1981a). Thus, doses at or below the RfD will be below the level of concern for reproductive effects. For acute/incidental exposures, the U.S. EPA uses an acute NOAEL of 75 mg/kg/day with an uncertainty factor of 300 resulting in an acute RfD of 0.25 mg/kg/day [75 mg/kg/day / 300]. Both of these values are used in the current risk assessment for characterizing risks associated with exposures to chlorsulfuron.

3.3.2. Existing Guidelines for Chlorsulfuron. The U.S. EPA derived an agency-wide chronic RfD for chlorsulfuron of 0.05 mg/kg/day (U.S. EPA 1990) and this RfD is currently listed at the U.S. EPA web site for RfDs, http://www.epa.gov/ngispgm3/iris/ . This RfD is based on a NOAEL of 5 mg/kg/day from a two-year rat feeding study (Wood et al. 1981a). As summarized in Section 3.1.5 and in Appendix 2, rats were exposed to dietary concentrations of chlorsulfuron (~95% pure) of 100, 500 and 2500 ppm for two years. Based on a reduction in body weights and weight gains in male rats at 500 ppm or 2500 ppm chlorsulfuron, the U.S. EPA (1990) classified 100 ppm as the NOAEL. Using a conversion factor of 1 ppm dietary equal to 0.05 mg/kg body weight/day, the U.S. EPA (1990) converted the dietary NOAEL of 100 ppm to a daily dose of 5 mg/kg/day. The dose conversion factor used by U.S. EPA (1990) is not referenced but the conversion factor is consistent with the estimated daily doses given by Wood et al. 1981a in Table IX (males) and Table X (females). The RfD of 0.05 mg/kg/day was derived with an uncertainty factor of 100. This uncertainty factor consists of two components: a factor of 10 for extrapolating from animals to humans and a factor of 10 for extrapolating to sensitive individuals within the human population. Using the same conversion factor, the 500 ppm LOAEL based on body weight would correspond to a dose of 25 mg/kg/day.

The U.S. EPA Office of Pesticide Programs has recently proposed a lower chronic RfD of 0.02 mg/kg/day (U.S. EPA 2002). While the U.S. EPA (2002) does not specifically identify the study on which the RfD is based, the study is described as a "rat chronic toxicity/carcinogenicity study" with a NOAEL of 5 mg/kg/day and a LOAEL based on reduced body weight of 25 mg/kg/day. This appears to be identical to the Wood et al. (1981a) study used by U.S. EPA (1990).

The difference in the two RfDs – i.e., 0.02 mg/kg/day from U.S. EPA (2002) and 0.05 mg/kg/day from U.S. EPA (1990) – is accounted for by a different uncertainty factor required by the Food Quality Protection Act (FQPA). FQPA requires the U.S. EPA to use an additional uncertainty factor of 10 to encompasses concerns for exposures involving children unless the available toxicologic demonstrate that such an uncertainty factor is unnecessary. U.S. EPA (2002) cites a three-generation reproduction study in which effects "...considered of questionable toxicological significance..." were noted at 125 mg/kg/day. Again, the U.S. EPA (2002) does not specifically identify the three-generation reproduction study but it appears to be the study by Wood (1980). As summarized in Appendix 2, this was a three generation reproduction study in

which rats were given dietary concentrations of 0, 100, 500, or 2500 ppm and slight alterations in the reproductive and lactation performance observed in the F_{1B} generation rats in the 2500 ppm dose group. Using the same dose conversion as used by U.S. EPA for the RfD – i.e., 1 ppm dietary equal to 0.05 mg/kg body weight/day – the dietary exposure of 2500 ppm would correspond to a dose of 125 mg/kg/day. Given the questionable significance of the endpoint observed at 125 mg/kg/day, the U.S. EPA (2002) elected to reduce the FQPA uncertainty factor from 10 to 3. Thus, the chronic NOAEL 5 mg/kg/day was divided by 300 – factors of 10 for extrapolating from animals to humans, 10 for extrapolating to sensitive individuals within the human population, and 3 for FQPA – resulting in 0.0166... mg/kg/day. This value was rounded to one significant decimal to yield the RfD of 0.02 mg/kg/day. For this risk assessment, the lower and more recent RfD of 0.02 mg/kg/day will be used to characterize all risks involving chronic or longer-term exposures.

3.3.3. Acute RfD.

The U.S. EPA (2002) did not explicitly derive an acute/single dose RfD for chlorsulfuron. Nonetheless, for several short-term exposure scenarios – i.e., incidental short-term and intermediate term exposures for dermal and oral routes – the U.S. EPA (2002) recommends NOAEL of 75 mg/kg/day with an uncertainty factor of 300. Basis for the uncertainty factor of 300 is identical to that cited above for chronic RfD. Thus, the functional acute RfD would be 0.25 mg/kg/day [75 mg/kg/day / 300]. While the U.S. EPA (2002) does not explicitly identify the study on which this short term RfD is based, the derivation of the short term criteria refers to a developmental study in rabbits in which the NOAEL was 75 mg/kg/day and the LOAEL was 200 mg/kg/day based on decreased body weight gain. This appears to refer to the study by Alvarez (1991b) which is documented in Appendix 2. Consistent with U.S. EPA (2002), this risk assessment will use the short term RfD of 0.25 mg/kg/day to characterize all risks acute or short-term exposures.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. For both workers and members of the general public, typical exposures to chlorsulfuron do not lead to estimated doses that exceed a level of concern. For workers, the upper range of hazard quotients is below the level of concern for backpack and aerial applications but somewhat above the level of concern for ground broadcast applications at the highest application rate. For ground broadcast applications, the level of concern is reached at an application rate of 0.14 lb/acre. For members of the general public, the upper limits for hazard quotients are below a level of concern except for the accidental spill of a large amount of chlorsulfuron into a very small pond. Even this exposure scenario results in only a small excursion above the acute RfD and is not likely to be toxicologically significant, because of the short duration of exposure relative to those considered in the derivation of the RfD.

Mild irritation to the skin and eyes can result from exposure to relatively high levels of 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.

3.4.2. Workers. A quantitative summary of the risk characterization for workers associated with exposure to chlorsulfuron is presented in Worksheet E02 (Supplement 1). The quantitative risk characterization is expressed as the hazard quotient, the ratio of the estimated doses from Worksheet E01 to the RfD. For acute exposures – i.e., accidental or incidental exposures – the acute RfD of 0.25 mg/kg/day is used (Section 3.3.3). For general exposures – i.e., daily exposures that might occur over the course of an application season – the chronic RfD of 0.02 mg/kg/day is used (Section 3.3.2).

As indicated in Section 2, the exposures in Worksheet E01 and the subsequent hazard quotients in Worksheet E02 are based on the typical application rate of 0.056 lb a.e./acre and the "level of concern" is one – i.e., if the hazard quotient is below 1.0, the exposure is less than the RfD. For all exposure scenarios, the estimated dose scales linearly with application rate. Thus, at an application rate of 0.25 lb a.e./acre, the highest application rate contemplated by the Forest Service, the level of concern would be 0.224 – i.e., 0.056 lb/acre divided by 0.25 lb/acre. The highest hazard quotient for workers (Worksheet E02) is 0.4 – the upper range for directed ground spray. Thus, at the highest application rate that might be used in Forest Service programs, the upper range of hazard quotients is below the level of concern for backpack and aerial applications but somewhat above the level of concern for ground broadcast applications at the highest application rate. For ground broadcast applications, the level of concern is reached at an application rate of 0.14 lb/acre [0.056 lb/acre x 1/0.4].

While the accidental exposure scenarios are not the most severe one might imagine (e.g., complete immersion of the worker or contamination of the entire body surface for a prolonged period of time) they are representative of reasonable accidental exposures. None of these hazard quotients approach a level of concern at the upper ranges, even when considering the level of concern associated with an application rate of 0.25 lbs a.e./acre – i.e., a level of concern of 0.224. The simple verbal interpretation of this quantitative characterization of risk is that under the most protective set of exposure assumptions, workers would not be exposed to levels of

chlorsulfuron that are regarded as unacceptable so long as reasonable and prudent handling practices are followed.

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 quantitative hazard characterization for the general public associated with exposure to chlorsulfuron is summarized in Worksheet E04 (Supplement 1). Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the acute RfD of 0.25 mg/kg/day for acute/short term exposure scenarios and the the chronic RfD of 0.02 mg/kg/day chronic or longer term exposures.

Although there are several uncertainties in the longer-term exposure assessments for the general public, as discussed in Section 3.2.3, the upper limits for hazard quotients associated with the longer-term exposures are sufficiently below a level of concern that the risk characterization is relatively unambiguous: based on the available information and under the foreseeable conditions of application, there is no route of exposure or scenario suggesting that the general public will be at any substantial risk from longer-term exposure to chlorsulfuron methyl even if the level of concern is set to 0.224 – i.e., that associated with the maximum application rate that will be used in Forest Service programs. The upper range of the hazard quotient for the consumption of contaminated vegetation is 0.2 and does approach a level of concern at the upper range of the application rates.

For the acute/accidental scenarios, the none of the central estimates representing typical exposures exceed the RfD. Exposure resulting from the consumption of contaminated water is of greatest concern; exposure resulting from the consumption of contaminated vegetation or fish is of marginal concern. The estimate of the upper range of exposure resulting from the consumption by a child of contaminated water from a small pond immediately after an accidental spill (Section 3.2.3.4.1) does exceed the level of concern at the upper range of the application rate – i.e., a hazard quotient of 0.3 and a level of concern of 0.224. It does not seem likely that this exposure would result in any frank adverse effects. As noted in Section 3.3.3, the acute NOAEL 75 mg/kg/day used to derive the acute RfD is a factor of about 3 below LOAEL of 200 mg/kg/day. As summarized in Worksheet E01, the upper range of exposure for the consumption of contaminated water at the typical application rate of 0.056 lb/acre is associated with a dose of 0.0854 mg/kg/day. Adjusted for an application rate of 0.25 lb/acre, the corresponding dose would be about 0.4 mg/kg/day [0.0854 mg/kg/day x 0.25 lb/acre / 0.056 lb/acre = 0.38125 mg/kg/day], a factor of about 200 below the animal NOAEL and 525 below the animal LOAEL. In addition, the exposure scenario for the consumption of contaminated water is an arbitrary scenario: scenarios that are more or less severe, all of which may be equally probable or improbable, easily could be constructed. All of the specific assumptions used to develop this scenario have a simple linear relationship to the resulting hazard quotient (Section

3.2.3.4.1). Thus, if the accidental spill were to involve 20 rather than 200 gallons of a field solution of chlorsulfuron, all of the hazard quotients would be a factor of 10 less.

Each of the hazard quotients 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 hazard quotients for each exposure scenario. For chlorsulfuron, considerations of multiple exposure scenarios has little impact on the risk assessment. For example, based on the upper ranges for typical levels of acute/accidental exposure for being directly sprayed on the lower legs, staying in contact with contaminated vegetation, eating contaminated fruit, drinking contaminated water from a stream, and consuming contaminated fish at rates characteristic of subsistence populations leads to a combined hazard quotient of 0.0764 (0.001 + 0.0004 + 0.04 + 0.005 + 0.03). Similarly, for all of the chronic exposure scenarios, the addition of all possible pathways lead to hazard quotients that are below the level of concern of 0.224 – i.e., the level of concern at the maximum application rate.

3.4.4. Sensitive Subgroups. There is no information to suggest that specific groups or individuals may be especially sensitive to the systemic effects of chlorsulfuron. Due to the lack of data in humans, the likely critical effect of chlorsulfuron in humans cannot be identified clearly. As indicated in Section 3.1.3, in animals the most sensitive effect of chlorsulfuron appears to be weight loss. There is also some evidence that chlorsulfuron may produce alterations hematological parameters. However, it is unclear if individuals with pre-existing diseases of the hematological system or metabolic disorders would be particularly sensitive to chlorsulfuron exposure. Individuals with any severe disease condition could be considered more sensitive to many toxic agents.

3.4.5. Connected Actions. As noted in Section 2.2, the manufacturers recommend that chlorsulfuron formulations be mixed with a non-ionic surfactant. There is no published literature or information in the FIFRA files that would permit an assessment of toxicological effects or risk assessment of chlorsulfuron mixed with a surfactant. According to the product label, Telar may be applied in combination with other herbicides, such as 2,4-D or glyphosate. However, there are no animal data to assess whether chlorsulfuron will interact, either synergistically or antagonistically with 2,4-D or any other herbicide.

3.4.6. Cumulative Effects. As noted above, this risk assessment specifically considers the effect of both single and repeated exposures. Based on the hazard quotients summarized in Worksheet E04, as discussed above, there is no indication that repeated exposures will exceed the threshold for toxicity.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. The mammalian toxicity of chlorsulfuron is relatively well characterized in experimental mammals; however, there is relatively little information regarding nontarget wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., weight loss and decreased body weight gain). Results of acute toxicity and reproduction studies in birds indicate that birds appear to be no more sensitive than experimental mammals to the toxic effects of chlorsulfuron. There is very little information on the effects of chlorsulfuron in terrestrial invertebrates. No significant change in mortality rate was observed following exposure of *Gastrophysa ploygoni* larvae by direct spray or in feeding studies using chlorsulfuron treated leaves, although survival from egg hatch to imago was significantly decreased by chlorsulfuron applied to the host plant.

The toxicity of chlorsulfuron to terrestrial plants was studied extensively and is well characterized. Chlorsulfuron inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. This effect is considered quantitatively in the dose-response assessment and is one of the primary effects of concern in this risk assessment. The lowest EC_{50} value reported following direct spray is 0.000023 lbs/acre in cherries. The lowest NOEL reported was in onion (0.0000088 lb/acre).

Terrestrial microorganisms also have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. However, chlorsulfuron appears to be only mildly toxic to terrestrial microorganisms and the results of a field study suggest that effects are transient.

Acute toxicity studies have been conducted in several species of fish. A single study investigated the effects of chronic exposure of to chlorsulfuron in rainbow trout. Due to limited water solubililty of chlorsulfuron, full dose-response curves could not be generated. However, fish do not appear particularly susceptible to chlorsulfuron, with LC_{50} values in most species exceeding the limit of solubility for chlorsulfuron (250 to 980 ppm). Based on 96 hour LC_{50} values, the most susceptible species is the brown trout, with an LC_{50} value of 40 mg/L. Chlorsulfuron also appears to be relatively non-toxic to aquatic invertebrates. Standard toxicity bioassays to assess the effects of chlorsulfuron on aquatic invertebrates were conducted in daphnia and mysid shrimp. Similar LC_{50} values are reported for both species. For reproductive effects, an NOEC of 20 mg/L was reported in a 21-day exposure study in *D. magna*.

The available data suggest that chlorsulfuron, like many other herbicides, is much more toxic to aquatic plants than to aquatic animals. The toxicity of chlorsulfuron has been examined in both algae and aquatic macrophytes. Studies on the mechanism of action of chlorsulfuron in aquatic plants were not identified. However, chlorsulfuron is assumed to have the same mechanism of action in aquatic plants as in terrestrial plants. Based on the results of several studies in algae, the species-dependent variation in sensitivity based on EC_{50} values for growth inhibition is very large, ranging from 0.011 mg/L in *Synechococcus leopoliensis* to 359 mg/L in *Porphyridium cruentum*. Results of a mesocosm study suggest chlorsulfuron can cause changes in

phytoplankton communities at concentrations as low as 1 µg/L. Only three studies were identified regarding the toxicity of chlorsulfuron to aquatic plants, two studies in duckweed and one study in sago pondweed. Comparison of 96-hour EC_{50} values for sago pondweed (0.25 µg/L) and duckweed (0.7 µg/L) show that pondweed is slightly more sensitive than duckweed.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals – As summarized in the human health risk assessment (see Section 3.1), the mode of action of chlorsulfuron in mammals is not well understood. There are several standard toxicity studies in experimental mammals that were conducted as part of the registration process. The most consistent toxic effects observed in mammals after exposure to chlorsulfuron are body 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 a clear or specific target organ toxicity in mammals. Since chlorsulfuron is a sulfonylurea, the potential exists for chlorsulfuron to alter glucose metabolism. However, there is no information available on the effects of chlorsulfuron on glucose metabolism or insulin release.

No field studies are available in which the impact of chlorsulfuron applications were assessed on mammalian wildlife communities. In standard experimental toxicity studies, chlorsulfuron has low acute oral toxicity. A common measure of acute oral toxicity is the LD_{50}, the estimate of the dose that may be lethal to 50% of the exposed animals. As summarized in Section 3.1.4, in rats the acute oral LD_{50} for chlorsulfuron is greater than 5000 mg/kg, which indicates a low order of toxicity (Tirvits 1979). Nevertheless, oral administration of 2200 mg/kg/day to rats for 10 days caused 20% mortality (Henry 1977). The acute LD_{50} values derived from experimental mammals are several orders of magnitude higher than any plausible exposures and have no practical impact on the risk assessment.

The subchronic and chronic toxicity studies on chlorsulfuron were conducted in dogs, mice, and rats. As discussed in Section 3.1.5., the most sensitive effects involve weight loss and decreased weight gain. The current U.S. EPA chronic 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 (~95% pure) was administered at dietary concentrations that resulted in daily doses of 5, 25, and 125 mg/kg/day (Wood et al. 1980b). 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. No effect on body weight or weight gain was observed for female rats in any treatment group. Thus, the NOEL for weight loss and decreased weight gain in this study was 5 mg/kg/day. In addition to weight loss and decreased weight gain, dose related hematologic effects have been observed following subchronic exposure to mice (Smith et al. 1980), and dogs (Schneider et al. 1992) and chronic exposure to rats (Wood et al. 1980b) and dogs (Atkinson 1991). Results of these studies are discussed in more detail in Section 3.1.7 (Effects on Immune System).

4.1.2.2. ***Birds*** – As summarized in Appendix 5, acute and subchronic toxicity studies on chlorsulfuron have been conducted in bobwhite quail (Hinkle and Twig 1980, Hinkle 1979, Fink et al. 1981, Beavers et al. 1992a) and mallard ducks (Hinkle and Bristol 1980, Hinkle and Wentz 1979, Beavers et al. 1992b). In quail, the acute oral LD_{50} of chlorsulfuron administered by

gavage is >5000 mg/kg (Hinkle and Twigg 1980), as it is in mammals. Exposure of adult bobwhite quail to concentrations of chlorsulfuron up to 5000 ppm in the diet for five days did not result in mortalities of any signs of toxicity (Hinkle 1979). In a 5-day feeding study in 14-day old bobwhite quail to dietary concentrations of chlorsulfuron up to 5620 ppm, exposure did not result in any mortality or signs of toxicity other than slightly decreased body weight gain that did not appear to be dose-related (Fink et al. 1981). Similar results were observed for mallard ducks, with an acute oral LD_{50} for chlorsulfuron of > 5000 mg/kg; neither single dose (Hinkle and Bristol 1980) or 5-day dietary exposure (Hinkle and Wentz 1979) at concentrations up to 5000 ppm caused weight loss or other signs of toxicity in mallard ducks.

The most relevant studies for this risk assessment are the 22- week feeding study in bobwhite quail and the 20-week feeding study in mallard ducks conducted by Beavers et al. (1992a,b). No treatment related mortalities, signs of toxicity (including weight loss) or effects on reproductive parameters were observed in ducks fed chlorsulfuron in the diet at concentrations up to 1000 ppm (Beavers et al. 1992b). A slight and transient decreased body weight gain during the first 8 weeks of exposure was observed in female bobwhite quail exposed to chlorsulfuron at dietary concentrations of 1000 ppm (Beavers et al. 1992a). However, there were no other differences in body weight gain for during any other exposure period for any test group. No other signs of toxicity were observed and reproductive function was unaffected following dietary exposure to chlorsulfuron at concentrations up to 1000 ppm for 20 weeks.

4.1.2.3. Terrestrial Invertebrates– There is very little data on the toxicity of chlorsulfuron to terrestrial invertebrates. Although acute toxicity studies using bees is often required by the U.S. EPA in the registration of pesticides (e.g., Guideline 850.3020, Honey bee acute contact toxicity, available at http://www.epa.gov/opptsfrs/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/index.html), toxicity studies in honey bees were not identified for chlorsulfuron in a complete search of the U.S. EPA FIFRA files – i.e., studies submitted to U.S. EPA in support of the registration of chlorsulfuron. Tomlin (2003) reports an LD_{50} value of >25 mg/kg for honey bees.

The open literature includes two toxicity studies involving other terrestrial invertebrates exposed to chlorsulfuron (Kjaer and Elmegaard 1996 and Kjaer and Heimbach 2001); studies are summarized in Appendix 12. 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/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* two days after plants were sprayed with sublethal doses of chlorsulfuron (Kjaer and Elmegaard 1996). Survival from egg hatch to imago was significantly decreased by chlorsulfuron applied to the host plant at rates of 0.0012 and 0.0024 lb/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.

A study assessing the relationship between chlorsulfuron treated plants and insect survival and growth was conducted using the specific insect:plant pairs *Pieris brassicae:Brassica napa* (large white butterfly:oilseed rape) and *Gastrophysa polygoni:Polygonum convolvulus* (beetle:black-bindweed) (Kjaer and Heimbach 2001). No significant effects on survival or growth were observed for either insect:plant pair when plants were treated with chlorsulfuron for four consecutive days at a rate ranging from 0.025 to 0.8 g ai/ha. However, host plants had a significant reduction in root growth rate.

Relatively little information is available on the toxicity of chlorsulfuron to soil invertebrates. In two species of nematodes, no effects were observed on movement, reproductive success or mortality at chlorsulfuron concentrations up to 10,000 ppm in soil (Rovesti and Desco 1990).

4.1.2.4. Terrestrial Plants (Macrophytes)–Chlorsulfuron acts by inhibiting the enzyme acetolactate synthetase resulting in the decreased synthesis of the branched-chain amino acids valine, leucine, and isoleucine, which are essential for plant growth (Bestman et al. 1880, Blair and Martin 1988, Brown 1990, Bhatti et al. 1992a, Chaleff and Mauvais 1984). Other ALS inhibiting herbicides include other sulfonylureas such as sulfometuron methyl as well as imidazolinones, triazolopyrimidines, and pyrimidinylthiobenzoates. Limited information is available regarding the uptake of chlorsulfuron in terrestrial plants. Results of direct foliar application studies show that rate and extent of uptake exhibits species variability(Al-Khatib 1992m, Bestman et al. 1990). In addition, environmental conditions, such as humidity and dew, can alter the degree of chlorsulfuron absorption (Al-Khatib 1992c). Efficacy studies in target plants show that chlorsulfuron is toxic to broadleaf weeds, but that perennial grasses are fairly resistant to the effects of chlorsulfuron (Beck et al. 1990, Blackshaw et al. 1990b, Mayer and Bovey 1990, Moore 1993, Moyer et al. 1990b). As might be expected, the results of greenhouse and field studies on target plants yield low EC_{50} values, which range from 0.00011 lb/acre in chickweed 0.0015 lb/acre in redroot pigweed (Moyer et al. 1995, Olofsdotter et la. 1994).

The toxicity of chlorsulfuron to nontarget plants has been extensively studied in many plant species, as detailed in Appendix 11. With the exception of the study by McKelvey and Kuratle (1991), all studies were identified from the published literature. As such, there are many variations in study protocols and experimental conditions, including type of exposure (soil, direct spray, hydroponic solutions), application rates, timing of application (plant reproductive stage), number of applications (single or multiple exposure), and specific endpoints evaluated (plant weight, plant height, root length).

Standard plant bioassays examining the effect of chlorsulfuron on seedling emergence and vegetative vigor are summarized in Appendix 11. Based on the results of a seedling emergence study summarized in Table 4-1, onion appears to be the most sensitive species tested, with an NOEL of 0.000562 lb/acre and tomato and sorghum were the most tolerant species, both with NOEL values of 0.022 lb/acre (McKelvey and Kuratle 1991).

The most relevant laboratory bioassays regarding the toxicity of chlorsulfuron to terrestrial plants by direct spray are summarized in Appendix 11 (Davison et al. 1987, Fletcher et al. 1996, McKelvey and Kurtle 1991). Table 4-2 summarizes the results the vegetative vigor bioassay

study by McKelvey and Kurtle (1991), which shows a large variation in species sensitivity in nontarget plant species. For vegetative vigor, the lowest EC_{50} value reported is 0.0003 lb/acre in soybean and the lowest NOEC is 0.0000088 lb/acre in sugar beet and onion. Wheat was very tolerant to post-emergent application, with an EC_{50} value of 0.36 lb/acre and an NOEC of 0.0011 lb/acre. The response of grasses to chlorsulfuron was variable. As reported by Davison et al. (1987), crested wheat and Russian wildrye were tolerant to chlorsulfuron at application rates up to 0.14 lb/acre, whereas severe damage or plant death were observed alkaligrass and tall fescue following both pre- and post-emergence applications at rates as low as 0.023 lb/acre. At application rates of 0.000021 to 0.00016 lb/acre, over 1000 time lower than the manufacturers' recommended maximum application rate (0.0234 lb/acre, Section 2.4), dose-dependent decreases in plant yield were observed in canola, smartweed, soybean, and sunflower (Fletcher et al. 1996). Other greenhouse studies examining the effects of chlorsulfuron on plant growth by exposures other than direct spray (in hyponic water media and in soil) are detailed in Appendix 11 (Gunther et al. 1989, Jettner et al. 1999).

For comparison, Obrigawitch et al. (1998) summarizes a large number of 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 (Table 4-2), 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 0.000037 in the onion noted by McKelvey and Kuratle (1991). Based on the results of field studies using foliar application, as detailed in Appendix 11, 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). Wine grapes are highly resistant to chlorsulfuron, with no effects of toxicity at application rates as high as 0.16 lb/acre (Moore and Elliott 1989). This is similar to the range of sensitivities reported in the review by Obrigawitch et al. (1998).

4.1.2.5. Terrestrial Microorganisms– As summarized in Appendix 10, 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. In a laboratory study examining the effects of a chlorsulfuron exposure of 0.1 µmol/agar plate (35.8 µg/plate) on growth in 17 fungal species, growth was inhibited in three species (Belai and Oros 1996). No bactericidal effects were observed in culture assays at chlorsulfuron concentrations up to 1000 mg/L (Julis 1980). Chlorsulfuron in soil at concentrations of 0.1 to 100 µg/g soil to silt loam and clay loam soils had no effect on populations of actinomycetes, bacteria, or fungi during an 8-week post-application period (Julis 1980). In four of the 18 species of fungi tested, growth reduction greater than 50% was observed at chlorsulfuron concentrations of 1000 µg/mL. However, this concentration is >10,000 times the maximum recommended use rate (Julis 1980). 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).

Results of a single field study shows that chlorsulfuron does not produce significant toxicity to 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./acre for two growing seasons (Junnila et al. 1994). In sandy soil, a small, but statistically significant

reduction in soil nitrification was observed one day after chlorsulfuron application. However, no decreases in soil nitrification were 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. However, these effects could be due to other factors, including the death of weeds. In sandy soil, dehydrogenase activity was inhibited at the end of the first growing season for the highest application rate.

The mechanism of toxicity of chlorsulfuron to microorganisms has not been identified. Terrestrial microorganisms have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. However, no studies specifically investigating the effects of chlorsulfuron on this enzyme in microorganisms were identified.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish– Standard toxicity bioassays to assess the effects of exposure of fish to chlorsulfuron are summarized in Appendix 6. Acute toxicity studies have been conducted in bluegill sunfish (Smith 1979a), rainbow trout (Smith et al 1979b), brown trout (Grande et al. 1994), fathead minnow (Smith et al. 1979c), sheepshead minnow (Ward and Boeri 1991a), and channel catfish. (Smith 1979d). A single study investigated the effects of chronic exposure of to chlorsulfuron in rainbow trout (Pierson 1991). No field studies on the effect of chlorsulfuron in fish were identified published literature or the U.S. EPA files.

As with terrestrial species, the acute lethal potency of chlorsulfuron is typically defined based on time-specific LC_x values, where *x* is the estimate of the proportion of fish that die – e.g., 96 hour LC_{50}. For all except two studies (Pierson 1991, Ward and Boeri 1991a), the maximum concentrations of chlorsulfuron tested were limited to 250 to 300 ppm. Pierson (1991) and Ward and Boeri (1991a) tested chlorsulfuron concentrations up to 980 ppm. However, the authors do not specify whether the increase in chlorsulfuron solubility was due to the addition of a solvent or discuss how the addition of such a solvent could alter the results. Based on 96 hour LC_{50} values, the most susceptible species is the brown trout, with an LC_{50} value of 40 mg/L (or 40 ppm) (Grande et al. 1994). In all other acute toxicity studies, the 96 hour LC_{50} values were not determined, as no deaths were observed at the highest chlorsulfuron concentrations tested; the LC_{50} values ranged from > 250 ppm in rainbow trout (Smith 1979b) to >980 ppm in sheepshead minnow (Ward and Boeri 1991a).

Pierson (1991) is the only study available regarding the toxicity of long-term exposure of chlorsulfuron to fish or fry. As detailed in Appendix 6, results of a 77-day exposure study in rainbow trout show that survival of embryos and alevins was not affected at chlorsulfuron concentrations up to 900 mg/L. However, fingerlings appear to be more sensitive than embryos and alevins, with 40% mortality at in the 900 mg/L exposure group; no mortality in fingerlings was observed at chlorsulfuron concentrations < 900 mg/L. Based on assessment of trout length (the most sensitive effect) performed at the completion of the study, the NOEC value of 32 mg/L was determined and an LOEC value of 66 mg/L was determined.

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

***4.1.3.3. Aquatic* Invertebrates**– Standard toxicity bioassays to assess the effects of chlorsulfuron on aquatic invertebrates, which are summarized in Appendix 7, were conducted in daphnia (Goodman 1979, Ward and Boeri 1989), mysids (Ward and Boeri 1991b), and oysters (Ward and Boeri 1991c). No field studies are available on the toxicity of chlorsulfuron to aquatic invertebrates. Chlorsulfuron appears to be relatively non-toxic to aquatic invertebrates. Similar LC_{50} values are reported for mysids and daphnia, with a 96-hour LC_{50} of 89 mg/L and NOEC value (for lethality) of 35 mg/L in *Mysidopsis bahia* (Ward and Boeri 1991b) and a 48-hour LC_{50} value in *Daphnia pulex* between 32 and 100 mg/L and an NOEC (for lethality) of 32 mg/L (Hessen et al. 1994). *D. magna* appear to be more resistant to chlorsulfuron toxicity based on a 48-hour LC_{50} value range of > 100 to 370.9 mg/L and an NOEC for lethality of 10 mg/L (Goodman 1979). For reproductive effects, an NOEC of 20 mg/L was reported in a 21-day exposure study in *D. magna* (Ward and Boeri 1989).

Only a single study examining the effects of chlorsulfuron in mollusks was identified. Acute exposure of oyster embryos and larvae assessing normal versus abnormal appearance of animals yields an EC_{50} value of 385 mg/L and a NOEC value of 200 mg/L (Ward and Boeri 1991c). Although an EC_{50} value was not determined, 48-hour exposure resulted in approximately 25% lethality at a chlorsulfuron concentration of 905 mg/L. No mortality was observed at chlorsulfuron concentrations up to 200 mg/L.

***4.1.3.4. Aquatic Plants*–** The toxicity of chlorsulfuron has been examined in both algae and aquatic macrophytes. Study results are summarized in Appendix 8. As might be expected for a herbicide, aquatic plants are far more sensitive than aquatic animals to the effects of chlorsulfuron. Studies on the mechanism of action of chlorsulfuron in aquatic plants were not identified. However, chlorsulfuron is assumed to have the same mechanism of action in aquatic plants as in terrestrial plants (i.e., the inhibition of ALS as described in Section 4.1.2.4).

As summarized in Appendix 8, substantial differences are apparent in the response of algae and various cyanobacteria to chlorsulfuron. With the exception of the study by Blasberg et al. (1991), all studies were identified from the open literature. Due to the many variations in experimental protocols, including the duration of exposure and the specific variables used to determine EC_{50} values, it is difficult to identify the species most sensitive and most resistant to chlorsulfuron toxicity. In addition to *Synechococcus leopoliensis, Selenastrum capricornutum* also appear fairly sensitive to chlorsulfuron toxicity, with reported EC_{50} values ranging from 0.05 mg/L to 0.8 mg/L (Asbel-Hamid 1996, Blasberg et al. 1991, Fairchild et al. 1997, Kalliquist and Romstad 1994). Results of a standard toxicity bioassay in *S. capricornutum* yield an NOEC of 0.01 mg/L (exposure duration of 120 hours) (Blasberg et al. 1991), which is consistent with the NOEC of < 0.019 mg/L reported by Fairchild et al. (1997) in the open literature. Fairchild et al. also reported an LOEC in *S. capricornutum* of 0.019 mg/L. In addition to the high EC_{50} value of to 359 mg/L in *Porphyridium cruentum,* high EC_{50} values were reported for *Cryptomonas pyrenoidifera* (213 mg/L), *Phaeodactylum tricornutum* (181 mg/L), and *Rhodomonas lens* (179 mg/L) (Nystrom et al. 1999). The longest chlorsulfuron exposure duration for laboratory studies in algae was 92 hours; no laboratory studies with longer exposure durations were identified.

Results of a mesocosm study suggest chlorsulfuron can cause changes in phytoplankton communities at concentrations as low as 10 µg/L (Kallqvist et al .1994). A decrease in biomass

development was observed following exposure to chlorsulfuron concentrations of 10 µg/L for 13 days. In addition, a dose-dependent decrease in species diversity (based on the Shannon-Weiner diversity index) was observed, with the lowest values recorded on the second and last days of the exposure period.

Only three studies were identified regarding the toxicity of chlorsulfuron to aquatic macrophytes – one 96-hour exposure study and one 7-day exposure study in duckweed (Fairchild et al. 1997, Peterson et al. 1994) and one 4-week exposure study in sago pondweed (Coyner et al. 2001). The 96-hour EC_{50} value for growth inhibition based on biomass in duckweed is reported as 0.7 µg/L, with an NOEC value of 0.4 µg/L and an LOEC of 0.7 µg/L (Fairchild et al. 1997). Exposure of duckweed to 20 µg/L for 7 days resulted in 86% inhibition of growth (Peterson et al. 1994). Results of the 4-week exposure in sago pondweed yield an LC_{50} value of 1.0 µg/L, with 100% plant death following a 96-hour exposure to 2.0 µg/L (Coyner et al. 2001). No field studies assessing the effects of chlorsulfuron in aquatic plants were identified.

Very little information is available regarding the toxicity of chlorsulfuron degradation products to aquatic plants or algae. Based on a single study comparing chlorsulfuron and two chlorsulfuron degradation products in *Chlorella pyrenoidosa,* chlorsulfuron breakdown products appear to be considerably less toxic than chlorsulfuron; EC_{50} values for the degradation products are at least 100-fold greater than for chlorsulfuron (Wei et al. 1998).

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview. Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or contact with contaminated vegetation. In acute exposure scenarios, the highest exposures for small terrestrial vertebrates will occur after a direct spray and could reach up to about 1.36 mg/kg under typical exposure conditions. There is a wide range of exposures anticipated from the consumption of contaminated vegetation by terrestrial animals: central estimates range from 0.07 mg/kg for a small mammal to 1.51 mg/kg for a large bird under typical exposure conditions, with upper ranges of about 15 mg/kg for a small mammal and 42 mg/kg for a large bird. The consumption of contaminated water will generally lead to much lower levels of exposure. A similar pattern is seen for chronic exposures. Estimated daily doses for the a small mammal from the consumption of contaminated vegetation at the application site are in the range of about 0.003 mg/kg to 0.01 mg/kg. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, which range from 0.0000008 mg/kg/day to 0.000007 mg/kg/day for a small mammal. Based on general relationships of body size to body volume, larger vertebrates receive lower doses and smaller animals, such as insects, will receive much higher doses than small vertebrates under comparable exposure conditions. Because of the apparently low toxicity of chlorsulfuron to animals, the rather substantial variations in the different exposure assessments have little impact on the assessment of risk to terrestrial animals.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion and the use of contaminated irrigation water. Unintended direct spray is expressed simply as the application rate considered in this risk assessment, 0.056 lb a.e./acre and should be regarded as an extreme/accidental form of exposure that is not likely to occur in most Forest Service applications. Estimates for the other routes of exposure are much less. All of these exposure scenarios are dominated by situational variability because the levels of exposure are highly dependent on site-specific conditions. Thus, the exposure estimates are intended to represent conservative but plausible ranges that could occur but these ranges may over-estimate or under-estimate actual exposures in some cases. Spray drift is based on estimates from AGDRIFT. The proportion of the applied amount transported off-site from runoff is based on GLEAMS modeling of clay, loam, and sand. The amount of chlorsulfuron that might be transported off-site from wind erosion is based on estimates of annual soil loss associated with wind erosion and the assumption that the herbicide is incorporated into the top 1 cm of soil. Exposure from the use of contaminated irrigation water is based on the same data used to estimate human exposure from the consumption of contaminated ambient water and involves both monitoring studies as well as GLEAMS modeling.

Exposures to aquatic plants and animals is based on essentially the same information used to assess the exposure to terrestrial species from contaminated water. The peak estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.01 (0.01 to 0.2) mg a.e./L at an application rate of 1 lb a.e./acre. For longer-term exposures, average estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.0006 (0.0009 to 0.0001) mg a.e./L at an application rate of 1 lb a.e./acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application rates considered in this risk assessment.

4.2.2. Terrestrial Animals. Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or contact with contaminated vegetation.

In this exposure assessment, estimates of oral exposure are expressed in the same units as the available toxicity data. As in the human health risk assessment, these units are usually expressed as mg of agent per kg of body weight and abbreviated as mg/kg. For dermal exposure, the units of measure usually are expressed in mg of agent per cm of surface area of the organism and abbreviated as mg/cm^2. In estimating dose, however, a distinction is made between the exposure dose and the absorbed dose. The *exposure dose* is the amount of material on the organism (i.e., the product of the residue level in mg/cm^2 and the amount of surface area exposed), which can be expressed either as mg/organism or mg/kg body weight. The *absorbed dose* is the proportion of the exposure dose that is actually taken in or absorbed by the animal.

The exposure assessments for terrestrial animals are summarized in Worksheet G01. As with the human health exposure assessment, the computational details for each exposure assessment presented in this section are provided scenario specific worksheets (Worksheets F01 through F16b). Given the large number of species that could be exposed to herbicides and the varied diets in each of these species, a very large number of different exposure scenarios could be generated. For this generic – i.e., not site- or species-specific – risk assessment, an attempt is made to limit the number of exposure scenarios.

Because of the relationship of body weight to surface area as well as the consumption of food and water, small animals will generally receive a higher dose, in terms of mg/kg body weight, than large animals will receive for a given type of exposure. Consequently, most general exposure scenarios for mammals and birds are based on a small mammal or bird. For mammals, the body weight is taken as 20 grams, typical of mice, and exposure assessments are conducted for direct spray (F01 and F02a), consumption of contaminated fruit (F03, F04a, F04b), and contaminated water (F05, F06, F07). Grasses will generally have higher concentrations of herbicides than fruits and other types of vegetation (Fletcher et al. 1994; Hoerger and Kenaga 1972). Because small mammals do not generally consume large amounts of grass, the scenario for the assessment of contaminated grass is based on a large mammal – a deer (Worksheets F10, F11a, and F11b). Other exposure scenarios for a mammals involve the consumption of contaminated insects by a small mammal (Worksheet F14a) and the consumption of small mammals contaminated by direct spray by a large mammalian carnivore (Worksheet F16a). Exposure scenarios for birds involve the consumption of contaminated insects by a small bird (Worksheet F14b), the consumption of contaminated fish by a predatory bird (Worksheets F08 and F09), the consumption of consumption of small mammals contaminated by direct spray by a predatory bird and the consumption of contaminated grasses by a large bird (F12, F13a, and F13b).

While a very large number of other exposure scenarios could be generated, the specific exposure scenarios developed in this section are designed as conservative screening scenarios that may serve as guides for more detailed site-specific assessments by identifying the groups and routes of exposure that are of greatest concern.

4.2.2.1. Direct Spray – In the broadcast application of any herbicide, wildlife species may be sprayed directly. This scenario is similar to the accidental exposure scenarios for the general public discussed in Section 3.2.3.2. In a scenario involving exposure to direct spray, the amount absorbed depends on the application rate, the surface area of the organism, and the rate of absorption.

For this risk assessment, three groups of direct spray exposure assessments are conducted. The first, which is defined in Worksheet F01, involves a 20 g mammal that is sprayed directly over one half of the body surface as the chemical is being applied. The range of application rates as well as the typical application rate is used to define the amount deposited on the organism. The absorbed dose over the first day (i.e., a 24-hour period) is estimated using the assumption of first-order dermal absorption. In the absence of any data regarding dermal absorption in a small mammal, the estimated absorption rate for humans is used (see Section 3.1.3). An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal. The estimates of absorbed doses in this scenario may bracket plausible levels of exposure for small mammals based on uncertainties in the dermal absorption rate of chlorsulfuron.

Other, perhaps more substantial, uncertainties affect the estimates for absorbed dose. For example, the estimate based on first-order dermal absorption does not consider fugitive losses from the surface of the animal and may overestimate the absorbed dose. Conversely, some animals, particularly birds and mammals, groom frequently, and grooming may contribute to the total absorbed dose by direct ingestion of the compound residing on fur or feathers. Furthermore, other vertebrates, particularly amphibians, may have skin that is far more permeable than the skin of most mammals. Quantitative methods for considering the effects of grooming or increased dermal permeability are not available. As a conservative upper limit, the second exposure scenario, detailed in Worksheet F02, is developed in which complete absorption over day 1 of exposure is assumed.

Because of the relationship of body size to surface area, very small organisms, such as terrestrial insects, might be exposed to much greater amounts of chlorsulfuron per unit body weight, compared with small mammals. Because of the relationship of body size to surface area, very small organisms, such as terrestrial insects, might be exposed to much greater amounts of chlorsulfuron per unit body weight, compared with small mammals. Consequently, a third exposure assessment is developed using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993) and the equation above for body surface area proposed by Boxenbaum and D'Souza (1990). Because there is no information regarding the dermal absorption rate of chlorsulfuron by bees or other invertebrates, this exposure scenario, detailed in Worksheet F02b, also assumes complete absorption over the first day of exposure. In addition, the study by Kjaer and Elmegaard (1996) in *Gastrophysa polygoni* may be used to characterize risk. As indicated in Section 4.1.2.3, this study involved the direct spray of the insect in units comparable to application rates – i.e., mass of chemical per unit surface area.

Direct spray scenarios are not given for large mammals. As noted above, allometric relationships dictate that large mammals will be exposed to lesser amounts of a compound in any direct spray scenario than smaller mammals. As detailed further in Section 4.4, the direct spray

scenarios for the small mammal are substantially below a level of concern. Consequently, elaborating direct spray scenarios for a large mammal would have no impact on the characterization of risk.

4.2.2.2. Indirect Contact – As in the human health risk assessment (see Section 3.2.3.3), the only approach for estimating the potential significance of indirect dermal contact is to assume a relationship between the application rate and dislodgeable foliar residue. The study by Harris and Solomon (1992) (Worksheet A04) is used to estimate that the dislodgeable residue will be approximately 10 times less than the nominal application rate.

Unlike the human health risk assessment in which transfer rates for humans are available, there are no transfer rates available for wildlife species. As discussed in Durkin et al. (1995), the transfer rates for humans are based on brief (e.g., 0.5 to 1-hour) exposures that measure the transfer from contaminated soil to uncontaminated skin. Wildlife, compared with humans, are likely to spend longer periods of time in contact with contaminated vegetation.

It is reasonable to assume that for prolonged exposures an equilibrium may be reached between levels on the skin, rates of absorption, and levels on contaminated vegetation, although there are no data regarding the kinetics of such a process. Although the bioconcentration data on chlorsulfuron suggest that chlorsulfuron accumulate in certain tissue compartments of the fish (e.g., viscera), it does not accumulate to any substantial degree in others (e.g., muscle) (Section 3.2.3.5) . However, the low water solubility and low octanol/water partition coefficient for chlorsulfuron suggest that chlorsulfuron is not likely to partition from the surface of contaminated vegetation to the surface of skin, feathers, or fur. Thus, a plausible partition coefficient is unity (i.e., the concentration of the chemical on the surface of the animal will be equal to the dislodgeable residue on the vegetation).

Under these assumptions, the absorbed dose resulting from contact with contaminated vegetation will be one-tenth that associated with comparable direct spray scenarios. As discussed in the risk characterization for ecological effects (Section 4.4), the direct spray scenarios result in exposure levels below the estimated NOAEL (i.e., hazard quotients below one). Consequently, details of the indirect exposure scenarios for contaminated vegetation are not further elaborated in this document.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey – Since chlorsulfuron will be applied to vegetation, the consumption of contaminated vegetation is an obvious concern and separate exposure scenarios are developed for acute and chronic exposure scenarios for a small mammal (Worksheets F04a and F04b) and large mammal (Worksheets F10, F11a, and F11b) as well as large birds (Worksheets F12, F13a, and F13b).

For the consumption of contaminated vegetation, a small mammal is used because allometric relationships indicate that small mammals will ingest greater amounts of food per unit body weight, compared with large mammals. The amount of food consumed per day by a small mammal (i.e., an animal weighing approximately 20 g) is equal to about 15% of the mammal's total body weight (U.S. EPA/ORD 1989). When applied generally, this value may overestimate or underestimate exposure in some circumstances. For example, a 20 g herbivore has a caloric

requirement of about 13.5 kcal/day. If the diet of the herbivore consists largely of seeds (4.92 kcal/g), the animal would have to consume a daily amount of food equivalent to approximately 14% of its body weight [(13.5 kcal/day / 4.92 kcal/g) / 20g = 0.137]. Conversely, if the diet of the herbivore consists largely of vegetation (2.46 kcal/g), the animal would have to consume a daily amount of food equivalent to approximately 27% of its body weight [(13.5 kcal/day / 2.46 kcal/g) / 20g = 0.274] (U.S. EPA/ORD 1993, pp.3-5 to 3-6). For this exposure assessment (Worksheet F03), the amount of food consumed per day by a small mammal weighing 20 g is estimated at about 3.6 g/day or about 18% of body weight per day from the general allometric relationship for food consumption in rodents (U.S. EPA/ORD 1993, p. 3-6).

A large herbivorous mammal is included because empirical relationships of concentrations of pesticides in vegetation, discussed below, indicate that grasses may have substantially higher pesticide residues than other types of vegetation such as forage crops or fruits (Worksheet A04). Grasses are an important part of the diet for some large herbivores, but most small mammals do not consume grasses as a substantial proportion of their diet. Thus, even though using residues from grass to model exposure for a small mammal is the most conservative approach, it is not generally applicable to the assessment of potential adverse effects. Hence, in the exposure scenarios for large mammals, the consumption of contaminated range grass is modeled for a 70 kg herbivore, such as a deer. Caloric requirements for herbivores and the caloric content of vegetation are used to estimate food consumption based on data from U.S. EPA/ORD (1993). Details of these exposure scenarios are given in worksheets F10 for acute exposures as well as Worksheets F11a and F11b for longer-term exposures.

For the acute exposures, the assumption is made that the vegetation is sprayed directly – i.e., the animal grazes on site – and that 100% of the animals diet is contaminated. While appropriately conservative for acute exposures, neither of these assumptions are plausible for longer-term exposures. Thus, for the longer-term exposure scenarios for the large mammal, two sub-scenarios are given. The first is an on-site scenario that assumes that a 70 kg herbivore consumes short grass for a 90 day period after application of the chemical. In the worksheets, the contaminated vegetation is assumed to account for 30% of the diet with a range of 10% to 100% of the diet. These are essentially arbitrary assumptions reflecting grazing time at the application site by the animal. Because the animal is assumed to be feeding at the application site, drift is set to unity - i.e., direct spray. This scenario is detailed in Worksheet 11a. The second sub-scenario is similar except the assumption is made that the animal is grazing at distances of 25 to 100 feet from the application site (lowing risk) but that the animal consumes 100% of the diet from the contaminated area (increasing risk). For this scenario, detailed in Worksheet F12b, AgDRIFT is used to estimate deposition on the off-site vegetation. Drift estimates from AgDrift are summarized in Worksheet A06 and this model is discussed further in Section 4.2.3.2.

The consumption of contaminated vegetation is also modeled for a large bird. For these exposure scenarios, the consumption of range grass by a 4 kg herbivorous bird, like a Canada Goose, is modeled for both acute (Worksheet F12) and chronic exposures (Worksheets F13a and F13b). As with the large mammal, the two chronic exposure scenarios involve sub-scenarios for on-site as well as off-site exposure.

For this component of the exposure assessment, the estimated amounts of pesticide residue in vegetation are based on the relationship between application rate and residue rates on different types of vegetation. As summarized in Worksheet A04, these residue rates are based on estimated residue rates from Fletcher et al. (1994).

Similarly, the consumption of contaminated insects is modeled for a small (10g) bird and a small (20g) mammal. No monitoring data have been encountered on the concentrations of chlorsulfuron in insects after applications of chlorsulfuron. The empirical relationships recommended by Fletcher et al. (1994) are used as surrogates as detailed in Worksheets F14a and F14b. To be conservative, the residue rates from small insects are used – i.e., 45 to 135 ppm per lb/ac – rather than the residue rates from large insects – i.e., 7 to 15 ppm per lb/ac.

A similar set of scenarios are provided for the consumption of small mammals by either a predatory mammal (Worksheet 16a) or a predatory bird (Worksheet 16a). Each of these scenarios assume that the small mammal is directly sprayed at the specified application and the concentration of the compound in the small mammal is taken from the worksheet for direct spray of a small mammal under the assumption of 100% absorption (Worksheet F02a).

In addition to the consumption of contaminated vegetation and insects, chlorsulfuron may reach ambient water and fish. Thus, a separate exposure scenario is developed for the consumption of contaminated fish by a predatory bird in both acute (Worksheet F08) and chronic (Worksheet F09) exposures. Because predatory birds usually consume more food per unit body weight than do predatory mammals (U.S. EPA 1993, pp. 3-4 to 3-6), separate exposure scenarios for the consumption of contaminated fish by predatory mammals are not developed. As detailed in Worksheet B02, the BCF values used in the wildlife risk assessment are based on whole body measurements rather than concentrations in the edible tissue. The acute BCF is for sunfish on Day 1 from the study by Han (1981c) and the chronic BCF is for catfish on Day 12 from the study by Priester et al. (1991b).

4.2.2.4. Ingestion of Contaminated Water – Estimated concentrations of chlorsulfuron in water are identical to those used in the human health risk assessment (Worksheet B06). The only major differences involve the weight of the animal and the amount of water consumed. There are well-established relationships between body weight and water consumption across a wide range of mammalian species (e.g., U.S. EPA 1989). Mice, weighing about 0.02 kg, consume approximately 0.005 L of water/day (i.e., 0.25 L/kg body weight/day). These values are used in the exposure assessment for the small (20 g) mammal. Unlike the human health risk assessment, estimates of the variability of water consumption are not available. Thus, for the acute scenario, the only factors affecting the variability of the ingested dose estimates include the field dilution rates (i.e., the concentration of the chemical in the solution that is spilled) and the amount of solution that is spilled. As in the acute exposure scenario for the human health risk assessment, the amount of the spilled solution is taken as 200 gallons. In the exposure scenario involving contaminated ponds or streams due to contamination by runoff or percolation, the factors that affect the variability are the water contamination rate, (see Section 3.2.3.4.2) and the application rate. Details regarding these calculations are summarized in Worksheets F06 and Worksheet F07.

4.2.3. Terrestrial Plants. In general, 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 or runoff or by wind erosion of soil.

4.2.3.1. Direct Spray – Unintended direct spray will result in an exposure level equivalent to the application rate. For many types of herbicide applications – e.g., rights-of-way management – it is plausible that some nontarget plants immediately adjacent to the application site could be sprayed directly. This type of scenario is modeled in the human health risk assessment for the consumption of contaminated vegetation.

4.2.3.2. Off-Site Drift – Because off-site drift is more or less a physical process that depends on droplet size and meteorological conditions rather than the specific properties of the herbicide, estimates of off-site drift can be modeled using AgDRIFT (Teske et al. 2001). AGDRIFT is a model developed as a joint effort by the EPA Office of Research and Development and the Spray Drift Task Force, a coalition of pesticide registrants. AGDRIFT is based on the algorithms in FSCBG (Teske and Curbishley. 1990), a drift model previously used by USDA.

For aerial applications, AGDRIFT permits very detailed modeling of drift based on the chemical and physical properties of the applied product, the configuration of the aircraft, as well as wind speed and temperature. For ground applications, AGDRIFT provides estimates of drift based solely on distance downwind as well as the types of ground application: low boom spray, high boom spray, and orchard airblast. Representative estimates based on AGDRIFT (Version 1.16) are given in Worksheet A06. For the current risk assessment, the AGDRIFT estimates are used for consistency with comparable exposure assessments conducted by the U.S. EPA. In addition, AGDRIFT represents a detailed evaluation of a very large number of field studies and is likely to provide more reliable estimates of drift. Further details of AGDRIFT are available at http://www.agdrift.com/.

Estimates of drift for ground and aerial applications is given in Worksheet A06. In ground broadcast applications, chlorsulfuron will typically be applied by low boom ground spray and thus these estimates are used in the current risk assessment.

Drift associated with backpack (directed foliar applications) are likely to be much less although studies quantitatively assessing drift after backpack applications have not been encountered. Drift distance can be estimated using Stoke's law, which describes the viscous drag on a moving sphere. According to Stoke's law:

$$v = \frac{D^2 \cdot g}{18n}$$

or

$$v = 2.87 \cdot 10^5 \cdot D^2$$

where v is the velocity of fall (cm sec^{-1}), D is the diameter of the sphere (cm), g is the force of gravity (980 cm sec^{-2}), and n is the viscosity of air ($1.9 \cdot 10^{-4}$ g sec^{-1} cm^{-1} at 20°C) (Goldstein et al. 1974).

In typical backpack ground sprays, droplet sizes are greater than 100 μ, and the distance from the spray nozzle to the ground is 3 feet or less. In mechanical sprays, raindrop nozzles might be used. These nozzles generate droplets that are usually greater than 400 μ, and the maximum distance above the ground is about 6 feet. In both cases, the sprays are directed downward.

Thus, the amount of time required for a 100 micro droplet to fall 3 feet (91.4 cm) is approximately 3.2 seconds,

$$91.4 \ / \ (2.87 \cdot 10^5 (0.01)^2).$$

The comparable time for a 400 micron droplet to fall 6 feet (182.8 cm) is approximately 0.4 seconds,

$$182.8 \ / \ (2.87 \cdot 10^5 (0.04)^2).$$

For most applications, the wind velocity will be no more than 5 miles/hour, which is equivalent to approximately 7.5 feet/second (1 mile/hour = 1.467 feet/second). Assuming a wind direction perpendicular to the line of application, 100 μ particles falling from 3 feet above the surface could drift as far as 23 feet (3 seconds · 7.5 feet/second). A raindrop or 400 μ particle applied at 6 feet above the surface could drift about 3 feet (0.4 seconds · 7.5 feet/second).

For backpack applications, wind speeds of up to 15 miles/hour are allowed in Forest Service programs. At this wind speed, a 100 μ droplet can drift as far as 68 feet (3 seconds · 15 · 1.5 feet/second). Smaller droplets will of course drift further, and the proportion of the smaller droplets in the spray as well as the wind speed and turbulence will affect the proportion of the applied herbicide that drifts off-site.

4.2.3.3. Runoff – Chlorsulfuron or any other herbicide may be transported to off-site soil by runoff or percolation. Both runoff and percolation are considered in estimating contamination of ambient water. For assessing off-site soil contamination, however, only runoff is considered. This approach is reasonable because off-site runoff will contaminate the off-site soil surface and could impact nontarget plants. Percolation, on the other hand, represents the amount of the herbicide that is transported below the root zone and thus may impact water quality but should not affect off-site vegetation.

Based on the results of the GLEAMS modeling (Section 3.2.3.4.2), the proportion of the applied chlorsulfuron lost by runoff was estimated for clay, loam, and sand at rainfall rates ranging from 5 inches to 250 inches per year. These results are summarized in Worksheet G04 and indicate that runoff will be negligible in relatively arid environments as well as sandy or loam soils. In clay soils, which have the highest runoff potential, off-site loss may reach up to about 55% of the applied amount in regions with very high rainfall rates.

4.2.3.4. Contaminated Irrigation Water – Unintended direct exposures of nontarget plant species may occur through the use of contaminated ambient water for irrigation. Although there are no studies in the literature addressing the impact of chlorsulfuron in contaminated irrigation water, the effects of such exposure scenarios on nontarget vegetation have been observed with

other herbicides (e.g., Bhandary et al. 1991). Furthermore, given the mobility of chlorsulfuron, the contamination of irrigation water is a plausible scenario.

The levels of exposure associated with this scenario will depend on the concentration of chlorsulfuron in the ambient water used for irrigation and the amount of irrigation water that is applied. As detailed in Section 3.2.3.4, chlorsulfuron is relatively mobile and contamination of ambient water may be anticipated and can be quantified (i.e., 0.1 [0.01 to 0.2] mg a.e./L at an application rate of 1 lb a.e./acre [Worksheet B06]).

The amount of irrigation water that may be applied will be highly dependent on the climate, soil type, topography, and plant species under cultivation. Thus, the selection of an irrigation rate is somewhat arbitrary. Typically, plants require 0.1 to 0.3 inch of water per day (Delaware Cooperative Extension Service 1999). In the absence of any general approach of determining and expressing the variability of irrigation rates, the application of one inch of irrigation water will be used in this risk assessment. This is somewhat higher than the maximum daily irrigation rate for sandy soil (0.75 inches/day) and substantially higher than the maximum daily irrigation rate for clay (0.15 inches/day) (Delaware Cooperative Extension Service 1999). This variability is addressed further in the risk characterization (Section 4.4.2.2).

Based on the estimated concentrations of chlorsulfuron in ambient water and an irrigation rate of 1 inch per day, the estimated functional application rate of chlorsulfuron to the irrigated area is 1.27×10^{-4} (1.27×10^{-5} – 2.53×10^{-4}) lb a.e./acre (see Worksheet F15 for details of these calculations). This level of exposure is inconsequential relative to off-site drift and runoff. Specifically, off-site movement from runoff can result in functional offsite application rates of 3.37×10^{-2} lb a.e./acre (Worksheet G04) and offsite movement from drift can result in functional offsite application rates of about 1×10^{-3} lb a.e./acre after ground broadcast applications (Worksheet G05a).

4.2.3.5. Wind Erosion – Wind erosion is a major transport mechanism for soil (e.g., Winegardner 1996). Although no specific incidents of nontarget damage from wind erosion have been encountered in the literature for chlorsulfuron, this mechanism has been associated with the environmental transport of other herbicides (Buser 1990). Numerous models have been developed for wind erosion (e.g., Strek and Spaan 1997; Strek and Stein 1997) and the quantitative aspects of soil erosion by wind are extremely complex and site specific. Field studies conducted on agricultural sites found that wind erosion may account for annual soil losses ranging from 2 to 6.5 metric tons/ha (Allen and Fryrear 1977). The upper range reported by Allen and Fryrear (1977) is nearly the same as the rate of 2.2 tons/acre (5.4 tons/ha) recently reported by the USDA (1998). The temporal sequence of soil loss (i.e., the amount lost after a specific storm event involving high winds) depends heavily on soil characteristics as well as meteorological and topographical conditions.

To estimate the potential transport of chlorsulfuron by wind erosion, this risk assessment uses average soil losses ranging from 1 to 10 tons/ha·year, with a typical value of 5 tons/ha·year. The value of 5 tons/ha·year is equivalent to 500 g/m^2 (1 ton=1000 kg and 1 ha = 10,000 m^2) or 0.05 g/cm^2 (1m^2=10,000 cm^2). Using a soil density of 2 g/cm^3, the depth of soil removed from the surface per year would be 0.025 cm [(0.05 g/cm^2) / (2 g/cm^3)]. The average amount per day

would be about 0.00007 cm/day (0.025 cm per year / 365 days/year). This central estimate is based on a typical soil loss rate of 5 tons/ha·year. Since the range of plausible rates of annual soil loss is 1 to 10 tons/ha·year, the range of soil loss per day may be calculated as 0.00001 cm/day (0.00007 / 5 = 0.000014) to 0.0001 cm/day (0.00007×2 = 0.00014).

The amount of chlorsulfuron that might be transported by wind erosion depends on several factors, including the application method, the depth of incorporation into the soil, the persistence in the soil, the wind speed, and the topographical and surface conditions of the soil. Under desirable conditions, like relatively deep (10 cm) soil incorporation, low wind speed, and surface conditions that inhibit wind erosion, it is likely that wind transport of chlorsulfuron would be neither substantial or nor significant. For this risk assessment, it will be assumed that chlorsulfuron is incorporated into the top 1 cm of soil. Thus, daily soil losses expressed as a proportion of applied amount would be 0.00007 with a range of 0.00001 to 0.001.

As with the deposition of chlorsulfuron in runoff, the deposition of the chlorsulfuron contaminated soil from wind erosion will vary substantially with local conditions and, for this risk assessment, neither concentration nor dispersion is considered quantitatively. Nonetheless, these factors together with the general and substantial uncertainties in the exposure assessment are considered in the risk characterization (see Section 4.4).

4.2.4. Soil Organisms. Limited data are available on the toxicity of chlorsulfuron to soil invertebrates (Section 4.1.2.3) as well as soil microorganisms (Section 4.1.2.5). For both groups, the toxicity data are expressed in units of soil concentration – i.e., mg chlorsulfuron/kg soil which is equivalent to parts per million (ppm) concentrations in soil. The GLEAMS modeling discussed in Section 3.2.3.4 provides estimates of concentration in soil as well as estimates of off-site movement (runoff, sediment, and percolation). Based on the GLEAMS modeling, concentrations in clay, loam, and sand over a wide range of rainfall rates are summarized in Table 4-3. As indicated in this table, peak soil concentrations in the range of about 0.2 to 0.3 ppm are likely in relatively arid soils at an application rate of 1 lb a.e./acre. As rainfall rate increases, maximum soil concentrations are substantially reduced in sand and, to a lesser extent, in loam because of losses from soil through percolation. The potential consequences of such exposures are discussed in Section 4.4 (Risk Characterization).

4.2.5. Aquatic Organisms. The potential for effects on aquatic species are based on estimated concentrations of chlorsulfuron in water that are identical to those used in the human health risk assessment (Worksheet B06). As summarized in Worksheet B06, the peak estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.1 (0.01 to 0.2) mg a.e./L at an application rate of 1 lb a.e./acre. For longer-term exposures, average estimated rate of contamination of ambient water associated with the normal application of chlorsulfuron is 0.0006 (0.0001 to 0.0009) mg a.e./L at an application rate of 1 lb a.e./acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application considered in this risk assessment – i.e., 0.056 lb a.e./acre. The consequences of using higher application rates is discussed in the risk characterization (Section 4.4).

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview. For terrestrial mammals, the dose-response assessment is based on the same data as the human health risk assessment (i.e., an acute NOAEL of 75 mg/kg/day and a chronic NOAEL of 5 mg/kg/day). None of the exposure scenarios, acute or longer term, result in exposure estimates that exceed this NOAEL. Birds appear to be substantially less sensitive to chlorsulfuron than mammals with an acute NOAEL 1686 mg/kg/day of from a 5-day feeding study and a longer-term NOAEL from a reproduction study of 140 mg/kg/day. Toxicity data on terrestrial invertebrates are not extensive. An LD_{50} value of >25 mg/kg has been reported in honeybees. Based on direct spray studies, no mortality would be expected at application rates of up to 107 lb/acre. Indirect effects to herbivorous insects associated with sublethal effects on treated vegetation have been noted at a very low application rates – i.e., about 0.001 lb/acre to 0.002 lb/acre. Soil microorganisms do not appear to be sensitive to chlorsulfuron with an NOEC of 10 ppm (or 10 µg/g soil).

The toxicity of chlorsulfuron to terrestrial plants can be characterized relatively well. A very broad range of sensitivities for various types of plants is apparent, with grasses appearing far more tolerant than most other species. For assessing the potential consequences of exposure to nontarget plants via runoff, an NOEC for seedling emergence of 0.000035 lb/acre is used for sensitive species and the corresponding value for tolerant species is 0.022 lb/acre. For assessing the impact of drift, an NOEC for vegetative vigor of 0.0000088 lb/acre is used for sensitive species and the corresponding value for tolerant species is 0.14 lb/acre.

The data on toxicity to fish and aquatic invertebrates are limited. For acute exposures, the NOEC of 30 mg/L in brown trout is used for the most sensitive species and the NOEC of 300 mg/L in rainbow trout is used for the most tolerant species. Toxicity values for chronic toxicity may be based on the available egg-and-fry/early life stage studies; only one study of chronic exposure in fish, a 77-day exposure of rainbow trout with an NOEC of 32 mg/L. This value is used directly as a longer term NOEC in tolerant species because the rainbow trout appears to be a relatively tolerant species in acute toxicity assays. Using the relative potency for acute exposures of 10 (brown trout relative to rainbow trout), NOEC for sensitive species is estimated at 3.2 mg/L. The lowest NOEC value for acute exposure in an aquatic invertebrate is 10 mg/L in *Daphnia magna* and the highest NOEC is 35 mg/L in *Mysidopsis bahia* , a mysid shrimp. Although mysid shrimp are saltwater species, the assumption is made that some freshwater species may be as tolerant as the most tolerant saltwater species. For long-term exposure of aquatic invertebrates, only one study was identified in the available literature – a 21-day exposure study in *Daphnia magna* reporting an NOEC for mortality of 20 mg/L. Since *Daphnia magna* were identified as the most sensitive species in acute exposure studies, they will also be considered as the most sensitive species for chronic exposure. In the absence of data in a more tolerant species, the relative potency comparing *Daphnia magna* to *Mysidopsis bahia* is used to estimate a chronic exposure NOEC for *Mysidopsis bahia*, the most tolerant species in acute exposure studies. Based on a relative potency factor of 3.5 and a chronic NOEC of 20 mg/L in *Daphnia magna*, the NOEC in *Mysidopsis bahia* is estimated to be 70 mg/L.

Aquatic plants, particularly macrophytes, appear to be much more sensitive to chlorsulfuron than aquatic animals. An NOEC of 0.00047 mg/L in *Lemna minor* is used for quantifying effects in aquatic macrophytes. This value is comparable to other studies in aquatic macrophytes. Thus,

there is no basis for differentiating sensitive and tolerant species of aquatic macrophytes. There is, however, a wide range of toxicity values for aquatic algae. The most sensitive algal species appears to be *Selenastrum capricornutum*, with a 96-hour EC_{50} of 0.05 mg/L and a corresponding NOEC of 0.01 mg/L. The most tolerant species of freshwater algae appears to be *Cyclotella crypitica*, with an EC_{50} value of 276 mg/L.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals – As summarized in the dose-response assessment for the human health risk assessment (Section 3), the Office of Pesticide Programs of the U.S. EPA used an acute NOAEL of 75 mg/kg/day as the basis for the acute RfD (Section 3.3.3) and a chronic NOAEL of 5 mg/kg/day as the basis of the chronic RfD (Section 3.3.2). All of the estimated mammalian acute exposures are below the acute NOEL of 75 mg/kg/day and all of all of the estimated mammalian chronic exposures are below the chronic NOEL of 5 mg/kg/day. Consequently, these acute and chronic NOAELs are used directly and without elaboration.

4.3.2.2. Birds – As discussed in Section 4.1.2.2, results of all acute exposure studies in birds show that chlorsulfuron has very low toxicity, with LD_{50} values exceeding 5000 mg/kg. Results of a 5-day feeding study in 14-day-old bobwhite quail show that body weight gain was slightly decreased following exposure to dietary concentrations of chlorsulfuron of 1780 ppm and 5620 ppm chlorsulfuron, but decreased weight gain was not observed at a chlorsulfuron concentration of 3169 ppm (Fink et al. 1981). Since the degree of decreased weight gain was modest (< 10%) and no signs of toxicity are reported in these birds or in adult birds exposed to 5000 ppm, the NOAEL for acute exposure to birds is taken as 5620 ppm (1686 mg/kg/day). Conversion of dietary concentrations of chlorsulfuron to a daily dose of chlorsulfuron was made by multiplying the average fractional weight of food consumption per bird (0.3) by the concentration of chlorsulfuron in food (5620 ppm or mg/kg). The average fractional weight of food consumption of 0.3 was determined by dividing the average food consumption/bird/day (9.1 g) by average body weight (30.6 g). 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.

For chronic exposure, chlorsulfuron does not appear to be toxic to birds at dietary concentrations up to 1000 ppm for up to 22 weeks (Section 4.1.2.2). Although a slight and transient decrease in body weight gain (<10%) during the first 8 weeks of exposure was observed in female bobwhite quail exposed to chlorsulfuron at dietary concentrations of 1000 ppm, there were no other differences in body weight gain during any other exposure period for any test group (Beavers et al. 1992a). In a similar study in mallard ducks, no signs of toxicity were observed. Thus, for this risk assessment, the NOAEL of 1000 ppm (140 mg/kg/day) is used to characterize risks from chronic exposures. To convert the concentration of 1000 ppm to units of mg/kg/day, the average fractional weight of food consumption per bird (0.14) was multiplied by the concentration of chlorsulfuron in food (1000 ppm or mg/kg). 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). Since acute and chronic NOAELs for birds greatly exceed all exposure scenarios, it is not necessary to elaborate this dose-response assessment.

4.3.2.3. Terrestrial Invertebrates **–** As discussed in Section 4.1.2.3, there is little information on the toxicity of chlorsulfuron to terrestrial invertebrates compared to the more extensive studies available in mammals. Standard acute toxicity studies using bees were not identified for chlorsulfuron in a complete search of the studies submitted to U.S. EPA under FIFRA. Based on a secondary source (Tomlin 2003), the reported honey bee LD_{50} of >25 mg/kg is used for characterizing the risk to terrestrial invertebrates after direct spray.

In addition, no increase in mortality was noted following direct spray of a folivorous beetle – i.e., a beetle that consumes leaves – with chlorsulfuron at application rates up to 1.2 mg/cm^2, a rate corresponding to 107 lb/acre (Kjaer and Elmegaard 1996). For the purposes of this risk assessment, the application rate of 107 lb/acre will be used as a NOAEL for risk characterization. This extremely high application rate exceed the typical application rate of 0.056 lb/acre by a factor of nearly 2000.

As discussed in Section 4.1.2.3 and summarized in Appendix 12, Kjaer and Elmegaard (1996) also conducted two additional and bioassays: a feeding study and a growth and survival study. In the feeding experiment, beetles feeding on vegetation that had been treated with chlorsulfuron treated at 1.6 g a.i./ha (about 0.0014 lb/acre) evidenced no signs of toxicity. However, when eggs were placed on vegetation that had been treated with 1.32 g/ha or 2.68 g/ha (about 0.001 lb/acre and 0.002 lb/acre, respectively) increased mortality was observed in the first two instars over a 42 day period. As discussed by Kjaer and Elmegaard (1996), this effect does not appear to be due directly to chlorsulfuron but may be attributed to changes in host plant. This is discussed further in the risk characterization.

4.3.2.4. Terrestrial Plants (Macrophytes) **–** Chlorsulfuron is a herbicide and causes adverse effects in a variety of nontarget plant species. As discussed in Section 4.1.2.4, there is an enormous range of sensitivities for various types of plants, with grasses appearing far more tolerant than most other species. For assessing the potential consequences of exposure to nontarget plants via runoff, results of seedling emergence studies are used. As summarized in Table 4-1, results of the seedling emergence study by McKelvey and Kuratle (1991) identify onion as the most sensitive species, with a NOEL of 0.000035 lb/acre. In this same study, the most tolerant species were sorghum and tomato, both with NOELS of 0.022 lb/acre. Thus, for assessing the potential consequences of exposures to nontarget plants via runoff, the NOEL for seed emergence in onion of 0.000035 lb/acre is used for the most sensitive species and the NOEL for seed emergence in tomato and sorghum of 0.022 lb/acre is used for the most tolerant species (Worksheet G04).

For assessing the impact of drift, bioassays on vegetative vigor will be used – i.e., studies in the herbicide is applied to the growing plant. The most relevant studies for assessing the effects of direct spray or drift are the series of bioassays conducted by McKelvey and Kuratle (1991), with additional supplemental information provided by Bhatti et al. (1995), Davison et al. (1987), Fletcher et al. (1996), and Moore and Elliott (1989). In this type of assay, the most sensitive species appear to be onion and sugarbeet, with NOELs of 0.0000088 lb/acre. This value is used

in Worksheets G05a and G05b for characterizing risks to sensitive plant species associated with drift. The highest reported NOEC from a greenhouse vegetative vigor assay is 0.14 lb/acre for Crested wheat, Russian wildrye, bermudagrass and alkali sacaton (Davison et al 1987). Although a slightly higher NOEL of 0.16 lb/acre was reported in a field study of wine grapes (Moore and Elliott 1989), this value will not be used for this risk assessment due to the lack of controlled conditions associated with field studies. Therefore, the application rate of 0.14 lb/acre is used in Worksheets G05a and G05b for characterizing risks to tolerant plant species associated with drift.

4.3.2.5. Terrestrial Microorganisms – Two different approaches may be used in the dose-response analysis and subsequent risk characterization for soil microorganisms – studies in which exposures are expressed as application rates or studies in which exposures are expressed as soil concentrations. Results of the laboratory study by Julis et al. (1980) show that population of bacteria, actinomycetes and fungi were unaffected by exposure to chlorsulfuron at concentrations up to 100 µg/g soil. The lower NOEC of 10 ppm (or 10 µg/g soil) is reported by Rapisarda et al. (1981a). For this risk assessment, the NOEC for soil microbes for chlorsulfuron is taken as 10 µg/g soil. Application of chlorsulfuron at rate of 10.7 lb/acre to barley plots in sandy soil produced a transient decrease in soil nitrification during the first day after application, but no effects were observed at the lower application rate of 3.67 lb/acre (Junnila et al. 1994). Other effects observed in this study were most likely not related to chlorsulfuron exposure. For field application, the NOEC for chlorsulfuron is 3.67 lb/acre, an application rate that is over 50-fold greater than the typical rate used by for Forest Service applications. It is anticipated that if effects on soil microbes did occur following chlorsulfuron exposure, they would be transient.

4.3.3. Aquatic Organisms.

The toxicity values used in this risk assessment are summarized in Worksheet G03 based on the information presented in Section 4.1.3.

4.3.3.1. Fish – It should be noted that the use of LD_{50} and LC_{50} values for risk characterization is generally avoided because a common concern with this approach is that more subtle non-lethal effects, that may impact the stability of fish populations in the field, may not be properly assessed. In some respects, this concern is somewhat misguided. Most acute fish toxicity studies report the results as LC_{50} values and there are sound statistical reasons for this approach (e.g., Finney 1971). In addition, as used by the U.S. EPA/OPP, levels of concern for hazard quotients based on LC_{50} values may be as low as 0.05. In other words, if the expected exposure is equal to one-twentieth (0.05) of the LC_{50}, the Agency may judge that there is a cause for concern at least in sensitive or endangered species. This is essentially similar to the use of an uncertainty factor as in the human health risk assessments. For chlorsulfuron, the sublethal effects associated with acute exposures must be assessed based on NOEC values for no mortality because this is the only type of information that is available and this information is relevant for assessing risk, as discussed in Section 4.4.3.

As discussed in Section 4.3.1.3, investigations of the toxicity of chlorsulfuron to fish have been somewhat hampered by the limited water solubility of chlorsulfuron; in most studies the LC_{50} values could not be determined because 50% mortality did not occur at the highest chlorsulfuron concentrations studied. For acute exposures, the most sensitive species was the brown trout,

with a 96-hour LC_{50} value of 40 mg/L and an NOEC for mortality of 30 mg/L (Grande et al. 1994). For acute exposure, the most tolerant species appear to be bluegill sunfish and rainbow trout. In bluegill sunfish exposed to chlorsulfuron concentrations of 115 to 300 mg/L, Smith (1979a) reports a 96-hour LC_{50} value of > 300 mg/L and an NOEC for mortality of 217 mg/L (Smith 1979a). In this study, 10% mortality was observed at a concentration of 266 mg/L, but no mortality was observed at any other exposure level. In rainbow trout exposed to chlorsulfuron concentrations of 95 to 350 mg/L, no mortalities were observed at any exposure level (Smith 1979b). Thus, for this risk assessment, the NOEC of 30 mg/L in brown trout is used for the most sensitive species and the NOEC of 300 mg/L in rainbow trout is used for the most tolerant species. Based on the results of acute exposure studies, brown trout appear to be approximately 10 times more sensitive to chlorsulfuron toxicity, or have a relative potency of 10, compared to rainbow trout.

Toxicity values for chronic toxicity may be based on the available egg-and-fry/early life stage studies; only one study of chronic exposure in fish, a 77-day exposure of rainbow trout, was identified in the available literature (Pierson 1991). For this risk assessment, the most conservative approach is to consider rainbow trout to be the most tolerant species, although it is recognized that other species may be more tolerant. Based on the results of this study, the NOEC of 32 mg/L based on based trout growth is used for chronic exposure of the most tolerant species. Although no data are available to determine the most sensitive species for chronic exposures, parallels can be drawn to the acute exposure studies. As discussed above, the relative potency factor comparing brown trout to rainbow trout is 10, i.e., brown trout are 10-times more sensitive to chlorsulfuron toxicity than rainbow trout. Using the relative potency for acute exposures of 10 and the chronic NOEC in rainbow trout of 32 mg/L, and NOEC for brown trout is estimated to be 3.2 mg/L. Thus, in the absence of data, a surrogate NOEC for chronic exposure can be estimated in what may be the most sensitive species.

4.3.3.2. Invertebrates – As detailed in Section 4.1.3.3, the lowest NOEC value for acute exposure in an aquatic invertebrate is 10 mg/L in *Daphnia magna* exposed to chlorsulfuron for 48 hours (Hessen et al. 1994) and the highest NOEC is 35 mg/L in *Mysidopsis bahia*, a mysid shrimp, exposed to chlorsulfuron for 96 hours (Ward and Boeri 1991b). Although mysid shrimp are saltwater species, the conservative assumption is made that some freshwater species may be as sensitive as the most sensitive saltwater species. For this risk assessment, the NOEC values for daphnids and mysids are used to bracket a plausible range of sensitivities for invertebrates after acute exposures to chlorsulfuron. Based on the results of acute exposure studies, dahpnids appear to be approximately 3.5 times more sensitive to chlorsulfuron toxicity, or have a relative potency of 3.5, compared to mysids. For long-term exposure of aquatic invertebrates, only one study was identified in the available literature – a 21-day exposure study in *Daphnia magna* reporting an NOEC for mortality of 20 mg/L (Ward and Boeri 1989). Since *Daphnia magna* were identified as the most sensitive species in acute exposure studies, they will also be considered as the most sensitive species for chronic exposure, although it is recognized that other species may be more sensitive. In the absence of data in a more tolerant species, the relative potency comparing *Daphnia magna* to *Mysidopsis bahia* can be used to estimate a chronic exposure NOEC for *Mysidopsis bahia*, the most tolerant species in acute exposure studies. Based on a relative potency factor of 3.5 and a chronic NOEC of 20 mg/L in *Daphnia magna*,

the NOEC in *Mysidopsis bahia* is estimated to be 70 mg/L. Thus, in this risk assessment, the estimated NOEC of 70 mg/L will be used for chronic exposure of the most tolerant species.

4.3.3.3. Aquatic Plants – The relevant data on the toxicity of chlorsulfuron to aquatic plants is summarized in Appendix 8. The most sensitive algal species appears to be *Selenastrum capricornutum*, with a 96-hour EC_{50} of 0.05 mg/L (50 µg/L) with a corresponding NOEC of 0.01 mg/L (10 µg/L) based on a reduction in cell count relative to controls (Blasberg et al. 1991). Somewhat higher toxicity values for this species have been reported by Fairchild et al. (1997) but the differences are not substantial – i.e., an EC_{50} of 123 µg/L with an NOEC of <19 µg/L reported by Fairchild et al. (1997). The most tolerant species of freshwater algae appears to be *Cyclotella crypitica*, with an EC_{50} value of 276 mg/L.

For this risk assessment, 10 µg/L will be used as the NOEC for sensitive algal species. As noted in Section 4.1.3.4, Kallqvist et al . (1994) noted changes in phytoplankton communities in a mesocosm study at 10 µg/L. The changes involved a decrease in chlorophyll concentrations that was accompanied by a decrease in photosynthesis. The much higher concentration of 276 mg/L will be used for risk characterization in more tolerant species of algae.

The three studies available on the effects of chlorsulfuron on aquatic macrophytes, all indicate that macrophytes appear to be more sensitive than algae with LOEC values in the range of 0.25 µg/L (Coyner et al. 2001) to 0.7 µg/L (Fairchild et al. 1997). While differences in sensitivity among aquatic macrophytes seem likely, there are no data available for quantifying these differences. Thus, for this risk assessment, the NOEC of 0.47 µg/L in *Lemna minor* (Fairchild et al. 1997) will be used for quantifying effects in aquatic macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. Chlorsulfuron is an effective and potent herbicide and adverse effects on some nontarget plant species, both terrestrial and aquatic, are plausible 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, 0.056 lb/acre, is over 6000 times higher than the NOEC determined in a vegetative vigor (direct spray) assay of the most sensitive nontarget species – i.e, 0.0000088 lb/acre in onions and sugar beets – and only a factor of 2.5 below the NOEC for the most tolerant species in the same assay – i.e., 0.14 lb/acre in wheat, wild rye, and some other grasses. The highest application rate that may be considered in Forest Service programs – i.e., 0.25 lb/acre – is over 25,000 times the NOEC in sensitive species and about a factor of 2 above the NOEC in tolerant species. Given these relationships, damage to nontarget plant species after ground broadcast applications could extend to distances of greater than 900 feet from the application site. This risk characterization applies only to ground broadcast applications. When used in directed foliar applications (i.e., backpack), offsite drift could be reduced substantially but the extent of this reduction cannot be quantified.

The NOEC values for soil exposures (assayed in the seedling emergence test) are 0.000035 lb/acre for sensitive species and 0.022 lb/acre for tolerant species, values that are substantially higher than those in the vegetative vigor assay. Nonetheless, the offsite movement of chlorosulfuron via runoff could be substantial under conditions that favor runoff – i.e., clay soils – and hazard quotients in the range of 75 to nearly 1000 are estimated for sensitive species over a wide range of rainfall rates – i.e., 15 inches to 250 inches per year. In very arid regions in which runoff might not be substantial, wind erosion could result in damage to nontarget plant species. The plausibility of observing such damage would, however, be highly dependent on local conditions. This risk characterization would be applicable to either broadcast ground or directed foliar applications.

The probability of damage to aquatic plants, particularly macrophytes, is less substantial but still noteworthy. At the typical application rate, peak concentrations of chlorsulfuron in water could result in damage to aquatic macrophytes – i.e., hazard quotients ranging from 1.2 to about 24 based on an EC_{50} for growth inhibition. Thus, if chlorsulfuron is applied in areas where transport to water containing aquatic macrophytes is likely, it would be plausible that detectable damage could be observed.

Aquatic algae do not appear to be as sensitive to chlorsulfuron and the hazard quotient is only modestly above the level of concern based on an acute NOEC. Thus, it is not clear if any substantial damage would be likely in aquatic algae. At the upper range of the application rate covered in this risk assessment, the hazard quotient would exceed the level of concern by a factor of about 3. Again, it is not certain that this would result in any substantial adverse effect.

Just as there is little reason to doubt that adverse effects on some plant species are plausible, 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 using typical or worst-case exposure assumptions at the typical application rate of 0.056 lb a.e./acre or the maximum application rate of 0.25 lb a.e./acre. One study has suggested

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 and this effect has not been noted in subsequent studies by the same group of investigators using other plant-insect pairs. As with the human health risk assessment, this characterization of risk must be qualified. Chlorsulfuron has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging nontarget species. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects are anticipated in terrestrial animals that no adverse effects are anticipated in terrestrial animals that do not directly depend on the weeds that are targeted.

Similarly, the risk characterization for aquatic animals is relatively simple and unambiguous. Chlorsulfuron appears to have a very low potential to cause any adverse effects in aquatic animals. All of the hazard quotients for aquatic animals are extremely low, ranging from 0.00000008 (longer term exposures in tolerant invertebrates) to 0.001 (acute exposures to sensitive aquatic invertebrates). At the maximum application rate of 0.25 lbs/acre, the risk characterization is unchanged: the highest hazard quotient 0.001 would be increased to 0.005, below the level of concern by a factor of 200.

4.4.2. Terrestrial Organisms.

4.4.2.1. Terrestrial Vertebrates – The quantitative risk characterization for mammals and birds is summarized in Worksheet G02. The toxicity values used for each group of animals is summarized at the bottom of Worksheet G02 and refer to values derived in the dose-response assessment (Sections 4.3.2.1 and 4.3.2.2). In this worksheet, risk is characterized as the estimated dose, taken from Worksheet G01, divided by toxicity value. This ratio is referred to as the hazard quotient (HQ). All exposures summarized in Worksheet G01 are based on the typical application rate of 0.056 lb a.e./acre. At this application rate, an HQ of 1.0 or less indicates that the estimated exposure is less than the toxicity value. When this is the case, there is no basis for asserting that adverse effects are plausible.

As discussed in Section 2 (Program Description), the maximum application rate that might be used in Forest Service programs is 0.25 lb a.e./acre. Because exposure is directly related to application rate, the level of concern for the hazard quotients given in Worksheet G02 for an application rate of 0.25 lb a.e./acre is 0.224 [0.056 lb a.e./acre / 0.25 lb a.e./acre = 0.224].

As indicated in Worksheet G02, the highest hazard quotient for any acute exposure is 0.05 [5e-02], the upper range of the hazard quotient for the consumption of contaminated insects by a small mammal. Thus, there is no basis for asserting that adverse effects are likely from the application of chlorsulfuron at any application rate that might be used in Forest Service programs. For chronic exposures, all hazard quotients are below 1.0. Thus, at the typical application rate of 0.056 lb a.e./acre, there is also no basis for asserting that adverse effects are likely.

The hazard quotients for the chronic consumption of contaminated vegetation by a large bird feeding exclusively on treated vegetation (i.e., labeled “on-site” in Worksheet G02) yields a hazard quotient of 0.01. This is substantially below the level of concern at an application rate of

0.25 lb a.e./acre and would correspond to a hazard quotient of 0.04 [0.01 / 0.224 = 0.04464]. This scenario, as well as the similar exposure scenario for mammals consuming vegetation on-site, is used in these risk assessments as a very conservative/extreme screening scenario. The scenarios assume that the vegetation is treated and that the animal stays in the treated area consuming nothing but the contaminated vegetation. Given that most forms of vegetation treated at an effective (i.e., herbicidal) application rate would likely die or at least be substantially damaged, this exposure scenario is implausible. It is, however, routinely used in Forest Service risk assessments as a very conservative upper estimate of potential exposures and risks. Based on this highly protective exposure scenario, no longer-term risk to birds is apparent.

The simple verbal interpretation of this quantitative risk characterization is that no adverse effects in mammals or birds appear to be plausible using exposure assumptions at the typical application rate of 0.056 lb a.e./acre or the maximum application rate of 0.25 lb a.e./acre. As with the human health risk assessment, this characterization of risk must be qualified. Chlorsulfuron has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging nontarget terrestrial mammals or birds. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects are anticipated in terrestrial mammals or birds.

No toxicity data are available for reptiles or amphibians. Thus, no quantitative risk characterization for these animals can be made.

4.4.2.2. Terrestrial Invertebrates – Quantitative risk characterizations may be made for the direct spray of a honey bee, the direct spray of a herbivorous beetle, and soil insects.

Based on the reported LD_{50} value of >25 mg/kg given in Tomlin (2003) and the estimated exposures to a honey bee after a direct spray at an application rate of 0.056 lb/acre (Worksheet F02b), the hazard quotient would be below the level of concern – i.e., 0.4 as summarized in Worksheet G02. However, as noted above, the level of concern at the maximum application rate, application rate of 0.25 lb a.e./acre, is 0.224. In other words, the risk quotient that would be associated with the maximum application rate would be 1.8 [0.25 lb/acre / 0.056 lb/acre x 0.4]. Because the LD_{50} value is reported as >25 mg/kg (i.e., the LD_{50} is greater than 25 mg/kg), it is not clear that the maximum application rate would result in any adverse effects.

Based on the study by Kjaer and Elmegaard (1996), direct spray of a herbivorous beetle at an application rate of 107 lb/acre resulted in no mortality. The hazard quotient of 0.002 may be calculated as the ratio of the maximum application rate (0.25 lb/acre) to this NOEC for lethality. Thus, there is no basis to assert that direct spray of chlorsulfuron is likely cause lethal effects in insects.

Kjaer and Elmegaard (1996) conducted two additional and bioassays: a feeding study and a growth and survival study. While the feeding study suggested that no toxicity was likely at low application rates (about 0.0014 lb/acre) mortality was observed in larvae after eggs were placed on vegetation that had been treated with chlorsulfuron at about 0.001 lb/acre and 0.002 lb/acre. At an application rate of 0.056 lb/acre (the typical application rate) these values correspond to hazard quotients of 28 [0.056 lb/acre / 0.002 lb/acre] to 56 [0.056 lb/acre / 0.001 lb/acre]. The

extent to which mortality might be observed in the field is unclear. As discussed by Kjaer and Elmegaard (1996), this effect does not appear to be due directly to chlorsulfuron but may be attributed to changes in host plant. In a subsequent study conducted at lower application rate (Appendix 11), Kjaer and Heimbach (2001) found no indication that chlorsulfuron would cause substantial effects on herbivorous insects and that the effect noted in the study by Kjaer and Elmegaard (1996) may be specific only to the test insect (*Gastrophysa ploygoni*) and plant species (*Polygonum convolutus*) assayed by Kjaer and Elmegaard (1996).

The only other data on terrestrial invertebrates involves a standard soil assay in which no effects were seen on reproduction, viability and movement in two species of nematodes at chlorsulfuron concentrations of 10,000 mg/kg soil (Rovesti and Desco 1990). As summarized in Table 4-3, an application rate of 1 lb/acre results in maximum soil concentrations for chlorsulfuron of about 0.3 mg/kg soil, far below the soil NOEC.

As with mammals and birds, the risk characterization for terrestrial invertebrates is based on data covering very few species relative to the large number of terrestrial invertebrates that might be exposed to chlorsulfuron.

4.4.2.3. Soil Microorganisms – As noted above, maximum concentration of chlorsulfuron in soil at an application rate of 1 lb/acre is about 0.3 mg/kg soil. At the maximum application rate of 0.25 lb/acre, the corresponding concentration in soil would be 0.075 mg/kg soil [0.3 mg/kg soil x 0.25 lb/acre / 1 lb/acre]. These projected maximum concentrations in soil are far below concentrations that appear to be toxic – i.e., the NOEC of 10 mg/kg based on cellulose and protein degradation reported by Rapisarda et al. (1981a) (Section 4.3.2.5). Using the 10 mg/kg NOEC, the hazard quotient for soil microorganisms can be calculated at 0.0075. An alternative approach to expressing risk in soil microorganisms can be based on the study by Junnila et al. (1994) in which no effects were noted on soil nitrification at an application rate of 3.67 lb/acre with a corresponding LOEC of 10.7 lb/acre associated with a transient decrease in soil nitrification. Using the maximum anticipated application rate of 0.25 lb/acre as the exposure estimate, the resulting hazard quotient is 0.07 [0.25 lb/acre / 3.67 lb/acre = 0.0681]. Using either approach, there is no basis for asserting that chlorsulfuron is likely to cause adverse effects in soil microorganisms under the conditions of application covered in this risk assessment.

4.4.2.4. Terrestrial Plants – A quantitative summary of the risk characterization for terrestrial plants is presented in Worksheet G04 for runoff and Worksheets G05a and G05b for drift. Analogous to the approach taken for terrestrial animals, risk in these worksheets is characterized as a ratio of the estimated exposure to a benchmark exposure (i.e., exposure associated with a defined response). For both worksheets, the benchmark exposure is a NOEC, as derived in Section 4.3.2.2, for both sensitive and tolerant species.

Chlorsulfuron is an effective and potent herbicide and adverse effects on some nontarget plant species due to drift are likely under certain application conditions and circumstances. As indicated in Worksheets G05a, off-site drift of chlorsulfuron associated with ground broadcast applications may cause damage to sensitive plant species at distances of greater than 900 feet from the application site. The closer that the nontarget species is to the application site, the greater is the likelihood of damage. Whether or not damage due to drift would actually be

observed after the application of chlorsulfuron would depend on a several site-specific conditions, including wind speed and foliar interception by the target vegetation. In other words, in some right-of-way applications conducted at low wind speeds and under conditions in which vegetation at or immediately adjacent to the application site would limit off-site drift, damage due to drift would probably be inconsequential or limited to the area immediately adjacent to the application site. Tolerant plant species would probably not be impacted by the drift of chlorsulfuron and might show relatively little damage unless they were directly sprayed.

As summarized in Worksheet G04, runoff could pose a substantial risk to sensitive nontarget plant species under conditions in which runoff is favored – i.e., clay soil over a very wide range of rainfall rates. Some tolerant plants species could also be adversely affected under conditions which favor runoff and in regions with high rainfall rates.

The situational variability in the exposure assessments for runoff, wind erosion, and irrigation water does have a substantial impact on the characterization of risk for sensitive nontarget plant species. All of these scenarios may overestimate or underestimate risk under certain conditions. For example, the exposure conditions involving runoff and contaminated irrigation water are plausible for applications in which relatively substantial rainfall occurs shortly after application and in which local topographic and/or hydrological conditions favor either runoff or percolation. less than that in arid regions.

As summarized in Section 4.2.3.5, daily soil losses due to wind erosion, expressed as a proportion of an application rate, could be in the range of 0.00001 to 0.001. This is substantially less than off-site losses associated with runoff from clay (Worksheet G04) and similar to off-site losses associated with drift at a distance of 500 feet or more from the application site (Worksheet G05a). As with the drift scenarios, wind erosion could lead to adverse effects in sensitive plant species. Wind erosion of soil contaminated with chlorsulfuron is most plausible in relatively arid environments and if local soil surface and topographic conditions favor wind erosion.

The simple verbal interpretation for this quantitative risk characterization is that sensitive plant species could be adversely affected by the off-site drift or runoff of chlorsulfuron under a variety of different scenarios depending on local site-specific conditions. If chlorsulfuron is applied in the proximity of sensitive crops or other desirable plant species, site-specific conditions and anticipated weather patterns will need to be considered if unintended damage is to be avoided.

It should be noted that the conclusions reached in this risk assessment are not consistent with the conclusions reached in the review by Obrigawitch et al. (1998). As noted in Section 4.1.2.4, however, the range of plant toxicity data cited by Obrigawitch et al. (1998) are consistent with studies summarized in the current risk assessment. Citing the field study by Marrs et al. (1989), Obrigawitch et al. (1998) concluded that: *a buffer zone of only 5-10 m surrounding nature reserves would be required to protect sensitive vegetation from annual sulfonylurea applications* (Obrigawitch et al. 1998, p. 213). It should be noted, however, that the study by Marrs et al. (1989) involved a relatively low application rate for chlorsulfuron – i.e., 0.013 lb/acre compared to the typical Forest Service application rate of 0.056 lb/acre. In addition, Marrs et al. (1989) study is a field study in which a number of different species were tested but these species do not appear to be the most sensitive species. As detailed in Worksheet G05a, more tolerant species

are not expected to be at risk at distances of 25 feet or less from the application site. Thus, for tolerant plant species, relatively narrow buffers may be adequate. For sensitive plant species, however, much wider buffers and/or conditions that do not favor drift may be required.

4.4.3. Aquatic Organisms.

4.4.3.1. Aquatic Animals – The risk characterization for aquatic animals is relatively simple and unambiguous. Chlorsulfuron appears to have a very low potential to cause any adverse effects in aquatic animals. As detailed in Section 4.2.3 and summarized in Worksheet G03, concentrations of chlorsulfuron in ambient water over prolonged periods of time are estimated to be no greater than 0.00005 mg/L and peak concentration of chlorsulfuron associated with runoff or percolation are estimated to be no more than 0.011 mg/L. As summarized in Worksheet G03, all of the hazard quotients for aquatic animals are extremely low, ranging from 0.00000008 (longer term exposures in tolerant invertebrates) to 0.001 (acute exposures to sensitive aquatic invertebrates). Thus, there is no basis for asserting that effects on nontarget aquatic species are likely. As detailed in Section 4.3.3.1, confidence in this risk characterization is reduced by the lack of chronic toxicity studies in potentially sensitive fish – i.e., brown trout. Based on the use of the relative potency method to account for the potential magnitude of the higher sensitivity in brown trout, the upper range of the hazard quotient is 0.00001, a factor of 100,000 below the level of concern.

As with other risk characterization worksheets, Worksheet G03 is based on the typical application rate of 0.056 lbs/acre. At the maximum application rate of 0.25 lbs/acre, all of the hazard quotients would be increased by a factor of about 5 [0.25 lbs/acre / 0.056 lbs/acre = 4.46]. This difference would have no impact on the risk characterization for aquatic animals – i.e., the highest hazard quotient 0.001 in Worksheet G03 would be increased to 0.005, below the level of concern by a factor of 200.

4.4.3.2. Aquatic Plants – The risk assessment for aquatic plants differs substantially from that of aquatic animals, particularly for macrophytes. For acute exposures based on the peak concentrations of chlorsulfuron, aquatic macrophytes appear to be at risk, even at the lower range of plausible exposures. It should be noted that the risk characterization is based on an EC_{50} value rather than a NOEC. Thus, the lower range of the hazard quotient for acute exposure to chlorsulfuron indicates that the estimated concentration would exceed the EC_{50} for growth inhibition. The the upper range of exposure, the EC_{50} value is exceeded by a factor of 24. For longer term exposures, the upper range of the hazard quotient is 0.1.

Some species of algae appear to be much less sensitive to chlorsulfuron than macrophytes and tolerant species of algae would not be at risk in either chronic or acute exposures. Sensitive species of algae, however, have a hazard index that modestly exceeds 1.0 at the upper range of acute exposure. No algal species appear to be a risk based on estimated longer term concentrations of chlorsulfuron in water.

Thus, as with terrestrial plants, aquatic macrophytes appear to be at substantial risk if chlorsulfuron is applied near bodies of water containing aquatic macrophytes. In such applications, it would be desirable to take measures that would substantially reduce the anticipated levels of exposure.

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Table 2-1. Identification and physical/chemical properties of chlorsulfuron.

Property	Value	Reference
Synonyms	2-chloro-N-[(4-methoxy-6-methyl-1,3,5-trizin-2-yl)aminocarbonyl] benzenesulfonamide Formulations: Telar (DuPont), Glean (DuPont), Corsair (Riverdale) Other names for chlorsulfuron: DPX-4189, DPX-W4189-165, INW-4189-19, INW-4189-22	C&P Press 2003 Trivits 1979
CAS Number	64903-72-3	USDA/ARS 1995
U.S. EPA Registration Number	532-522 (Telar DF and Glean) Corsair (228-375)	DuPont 1998a,b,c C&P Press 2003
MW	357.8	USDA/ARS 1998
Henry's Law Constant (atm m^3/mole)	6.8×10^{-10} 1.58×10^{-13}	USDA/ARS 1998 RAIS 2003
pK_a	3.6 3.4	USDA/ARS 1998 Schmuckler and Moore 1992
Vapor pressure (mPa) at 25°C	3.07×10^{-10} 4.6×10^{-7} 4.6×10^{-6} $<1\times10^{-10}$ 2.33×10^{-11}	USDA/ARS 1998 Du Pont de Nemours 1977a Du Pont de Nemours 1983j Schmuckler and Moore 1992 Montgomery 1993
Water solubility (ppm)	at pH, 5,587 at pH 7, 3.18×10^{5} at 25°C, 125 at 22°C, 100-120 at 25°C, 430 at 25°C, pH 7, 27,900	USDA/ARS 1998 USDA/ARS 1998, Schmuckler 1992a Du Pont de Nemours 1977a, 1983j Rapisarda et al. 1978 Neary et al. 1993, WSSA 1989 Bergstrom and Strenstrom 1998, Alvarez-Benedi et al. 1998
$K_{o/w}$	at pH 5, log K_{ow} = 0.33 At pH 5, K_{ow} = 2.13 at pH 7, log K_{ow} = -1.0 at pH 9, log K_{ow} = -1.4 at pH 9, K_{ow} = 0.0387 at 24-2 °C (pH not specified), K_{ow} = 13	USDA/ARS 1998 Schmuckler and Moore 1992 Schmuckler and Moore 1992 USDA/ARS 1998 Schmuckler and Moore 1992 Rapisarda et al. 1978

Table 2-1. Identification and physical/chemical properties of chlorsulfuron *(continued)*.

Property	Value	Reference
$K_{o/c}$ (ml/g)	36 (14-60)	USDA/ARS 1998
	1.02	Montgomery 1993
	pH 7, 40 (soil type not specified)	Bergstrom and Strenstrom 1998
	in silt loam, 17-20	Strek 1998a
	in sandy loam, 13	Strek 1998a
Foliar $t_{1/2}$ (field dissipation)	no information available	
Water $t_{1/2}$ (field dissipation)	4-6 weeks (under growing season conditions)	Tomlin 1997
Water $t_{1/2}$	203 [0.0034 day^{-1}]	USDA/ARS 1998
	198 days	Strek 1998b
	exposed to light, 80 days	Strek 1998b
	69 days at pH 7.1	Sarmah et al. 2000
Soil, aerobic $t_{1/2}$ in days	32 (13-88)	USDA/ARS 1998
	in clay, 168	Smith 1986
	in loam, 37	Anderson and Barrett 1985
	in sand, 47	Sarmah 1999
Soil, hydrolysis $t_{1/2}$ in days	in sterile sandy clay solution, 53	Sarmah 2000
Soil $t_{1/2}$ (field dissipation)	56 (10-185)	USDA/ARS 1998
	28-56 days	Alvarez-Benedi et al. 1998

Table 2-2: Use of Chlorsulfuron by the Forest Service in 2001 Sorted by Region (USDA/FS 2002).

Region	Forest	Use	Pounds	Acres	Lbs/acre	Proportion of Use by lbs	Proportion of Use by Acres
1	**12**	**Noxious Weed Control**	**28.2**	**402.5**	**0.070**	0.839	0.671
2	4	Noxious Weed Control	0.47	10.06	0.047		
2	6	Noxious Weed Control	1.06	17	0.062		
2	12	Noxious Weed Control	0.93	67.5	0.014		
2	13	Noxious Weed Control	0.94	10	0.094		
2	15	Noxious Weed Control	0.55	11.8	0.047		
Region 2 Totals and Average Application Rate			**3.95**	**116.36**	**0.034**	0.117	0.194
4	2	Noxious Weed Control	0.1	1	0.100		
4	17	Noxious Weed Control	0.38	50	0.008		
4	19	Noxious Weed Control	1	30	0.033		
Region 4 Totals and Average Application Rate			**1.48**	**81**	**0.018**	0.044	0.135
Grand Totals and Average Application Rate			**33.63**	**599.86**	**0.056**	1	1

Table 3-1: Summary of LD_{50} values for chlorsulfuron and chlorsulfuron formulations in rats

Material tested (Reference)	**LD_{50} of material expressed as amount of material tested (mg/kg)**	**LD_{50} of material expressed as amount of active ingredient (mg a.i./kg)**
chlorsulfuron - 95% pure (Tirvits 1979)	Males: 5545 Females: 6293	Males: 5268 Females: 5978
chlorsulfuron formulation containing 80% a.i. (Hinckle and Dashiell 1980)	Males: 7699 Females: 8891	Males: 6159 Females: 7113
chlorsulfuron formulation containing 75% a.i. (Dashiell and Hinckle 1981)	Males: 3053 Females: 2341	Males: 2290 Females: 1756

Table 3-2: Chemical and site parameters used in GLEAMS Modeling for chlorsulfuron.

Chemical Specific Parameters

Parameter	Clay	Loam	Sand	Comment/ Reference
Halftimes (days)				
Aquatic Sediment		154		Note 1
Foliar		30		Knisel and Davis 2000
Soil	168	37	47	Note 2
Water	200	200	200	Note 3
Ko/c, mL/g	40	40	40	Note 4
K_d, mL/g	0.24	0.18	0.12	Note 5
Water Solubility, mg/L		27,900		Note 6
Foliar wash-off fraction		0.75		Knisel and Davis 2000

Note 1 The value of 154 days is taken from the upper range reported by Chrzanowski (1980a). Other reported halftimes range from 109 days (Chrzanowski and Priester 1991) to >365 days (Strek 1998a).

Note 2 Soil halftimes are based on neutral soil (pH ≈ 7) at an ambient temperature of about 77°F (20°C). Much shorter halftimes reported in acidic soils (pH ≈ 6) as well as soils at a higher temperatures. Degradation in soil is highly dependant on microbial activity (Priester 1991a) and may vary substantially within a given type of soil. Values listed above are taken from Smith (1986) for clay, Anderson and Barrett (1985) for loam, Sarmah (1999) for sand.

Note 3 Chlorsulfuron is chemically stable in water at pH 7 but the hydrolysis halftime as pH 5 is 24 days (Strek 1998a). Value of 200 days is based on aqueous photolysis of 198 days from Strek (1998b). Lesser halftimes are likely (e.g., 80 days) with more intense irradiation.

Note 4 Reported by Bergstrom and Strenstrom (1998). Identical to value recommended by Knisel and Davis 2000.

Note 5 Values for clay and sand taken from Sharmah (1999). Value for loam taken as mid-point. Values of 0.16 ml/g for sandy loam and 0.27 ml/g for clay loam reported by Sharmah (1999)

Note 6 Reported by Bergstrom and Strenstrom (1998) at pH 7. Similar to 31,800 mg/L reported by Schmuckler (1992a) at pH 7. Much lower water solubility at acidic pH – e.g., 300 mg/L at pH 5 (Sarmah 1998).

Site Parameters

(see SERA 2003, SERA AT 2003-02d dated for details)

Pond	1 acre pond, 2 meters deep, with a 0.01 sediment fraction. 10 acre square field (660' by 660') with a root zone of 60 inches and four soil layers.
Stream	Base flow rate of 4,420,000 L/day with a flow velocity of 0.08 m/second or 6912 meters/day. Stream width of 2 meters (about 6.6 feet') and depth of about 1 foot. 10 acre square field (660' by 660') with a root zone of 60 inches and four soil layers.

Table 3-3: Summary of modeled concentrations of chlorsulfuron in streams (all units are µg/L or ppb per lb/acre)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
10	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
15	0.11477	12.45998	0.00000	0.00000	0.00000	0.00027
20	0.19412	26.81967	0.00000	0.00000	0.03075	0.49905
25	0.26292	42.45427	0.00000	0.00000	0.10770	1.56313
50	0.47589	112.90105	0.02819	0.43011	0.57214	13.18334
100	0.61241	198.91349	0.14713	2.61717	0.88306	34.19460
150	0.61859	201.76430	0.20963	4.29446	0.86684	44.88269
200	0.59069	193.08031	0.23235	5.26545	0.79782	49.83249
250	0.55414	181.37922	0.23576	5.69884	0.72501	52.57532

Table 3-4: Summary of modeled concentrations of chlorsulfuron in ponds (all units are µg/L or ppb per lb/acre)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
10	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
15	8.49276	15.18346	0.00000	0.00000	0.00008	0.00019
20	9.19275	26.49647	0.00000	0.00000	1.03004	1.54850
25	9.68024	36.77989	0.00000	0.00000	2.91460	4.33955
50	10.26978	76.75120	0.33985	0.50953	9.04627	23.75894
100	9.57092	140.44917	1.33507	2.78968	10.33769	43.78458
150	8.51752	155.48776	1.61368	4.10148	9.30003	51.61099
200	7.62310	158.58237	1.63149	4.64787	8.23028	54.70676
250	6.88085	156.33192	1.56499	4.73363	7.32781	55.75912

Table 4-1: Influence of soil surface application of chlorsulfuron on seedling emergence of several terrestrial plants *

Plant	Exposure in oz a.i./acre [lb a.i./acre]				
	NOEL	EC_{25}	95% CI	EC_{50}	95% CI
Onion	0.000562 [0.000035]	0.0066 [0.00041]	0.000008-0.018 [0.0000005 - 0.0011]	0.024 [0.0015]	0.0043-0.17 [0.00027 - 0.011]
Corn	0.0702 [0.0044]	0.80 [0.05]	not determined	2.3 [0.14]	not determined
Sorghum	> 0.351 [> 0.022]	not determined		not determined	
Sugarbeet	0.00281 [0.00018]	0.014 [0.000875]	0.00075-0.071 [0.000047 - 0.0044]	0.078 [0.0049]	0.022-> 10 [0.0014 - > 0.63]
Soybean	> 0.0702 [> 0.0044]	not determined		not determined	
Pea	0.00281 [0.00017]	0.0045 [0.00028]	0.0016-0.0074 [0.0001 - 0.00046]	0.008 [0.0005]	0.0042-0.013 [0.00026 - 0.00081]
Tomato	> 0.351 [> 0.022]	not determined		not determined	
Rape	> 0.0702 [> 0.0044]	not determined		not determined	
Cucumber	> 0.0702 [0.0044]	not determined		not determined	

*Source: McKelvey and Kuratle 1991 (MRID 42201001) and McKelvey and Kuratle 1992 (MRID 42587201). These appear to be the same studies submitted twice to U.S. EPA.

Table 4-2: Influence of foliar application of chlorsulfuron on ***vegetative vigor*** of several terrestrial plants [responses for plant height during Tier 2 emergence testing]*

Plant	NOEL	Exposure in oz a.i./acre [lb a.i./acre]			
		EC_{25}	95% CI	EC_{50}	95% CI
Onion	0.000140 [0.0000088]	0.00059 [0.000037]	0.00014-0.0014 [0.0000088 - 0.0.000088]	0.011 [0.00069]	0.0055-0.021 [0.00034 - 0.0013]
Corn	0.00360 [0.000225]	0.010 [0.00062]	0.0045-0.018 [0.0028 - 0.0011]	0.073 [0.0046]	0.046-0.11 [0.0029 - 0.0069]
Wheat	0.0180 [0.0011]	0.89 [0.056]	0.57-1.2 [0.035 - 0.075]	5.8 [0.36]	3.5->10 [0.22 - >0.62]
Sorghum	0.00360 [0.00022]	0.042 [0.0027]	0.030-0.055 [0.0019 - 0.0034]	0.21 [0.013]	0.17-0.25 [0.011 - 0.016]
Sugarbeet	0.000140 [0.0000088]	0.0033 [0.0002]	0.0012-0.0066 [0.000075 - 0.00071]	0.072 [0.0045]	0.036-0.20 [0.0022 - 0.012]
Soybean	0.000720 [0.000045]	0.00071 [0.000044]	0.00023-0.0015 [0.000014 - 0.000094]	0.0048 [0.0003]	0.0025-0.0082 [0.00016 - 0.00051]
Pea	0.000720 [0.000045]	1.004 [0.063]	0.00062-0.011 [0.000039 - 0.00069]	0.082 [0.005]	0.035-0.22 [0.0022 - 0.014]
Tomato	0.000720 [0.000045]	0.032 [0.002]	0.010-0.057 [0.00062 - 0.0036]	0.15 [0.0094]	0.096-0.20 [0.006 - 0.012]
Rape	0.000720 [0.000045]	0.0016 [0.0001]	0.00081-0.0028 [0.000051 - 0.00018]	0.012 [0.00075]	0.0083-0.018 [0.00052 - 0.0011]
Cucumber	0.00360 [0.00022]	0.03 [0.0019]	0.020-0.044 [0.0012]	0.26 [0.016]	0.15-0.73 [0.0094 - 0.046]

*Source: McKelvey and Kuratle 1991 (MRID 42201001) and McKelvey and Kuratle 1992 (MRID 42587201). These appear to be the same studies submitted twice to U.S. EPA.

Table 4-3: Summary of model concentrations in soil (all units are mg chemical/kg soil or ppm) at an application rate of 1 lb a.e./acre

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.20127	0.32350	0.21567	0.36332	0.13994	0.32189
10	0.16770	0.33243	0.08856	0.26837	0.04887	0.24578
15	0.15302	0.32909	0.05914	0.25631	0.04438	0.23497
20	0.14440	0.32185	0.04991	0.24595	0.03695	0.22403
25	0.13633	0.31568	0.04481	0.25072	0.03100	0.21489
50	0.10852	0.27837	0.03248	0.23971	0.01683	0.18266
100	0.08026	0.24936	0.02283	0.21233	0.00870	0.14299
150	0.06473	0.20179	0.01889	0.19822	0.00588	0.11711
200	0.05452	0.17030	0.01674	0.18978	0.00446	0.09886
250	0.04717	0.14753	0.01540	0.18407	0.00362	0.08572

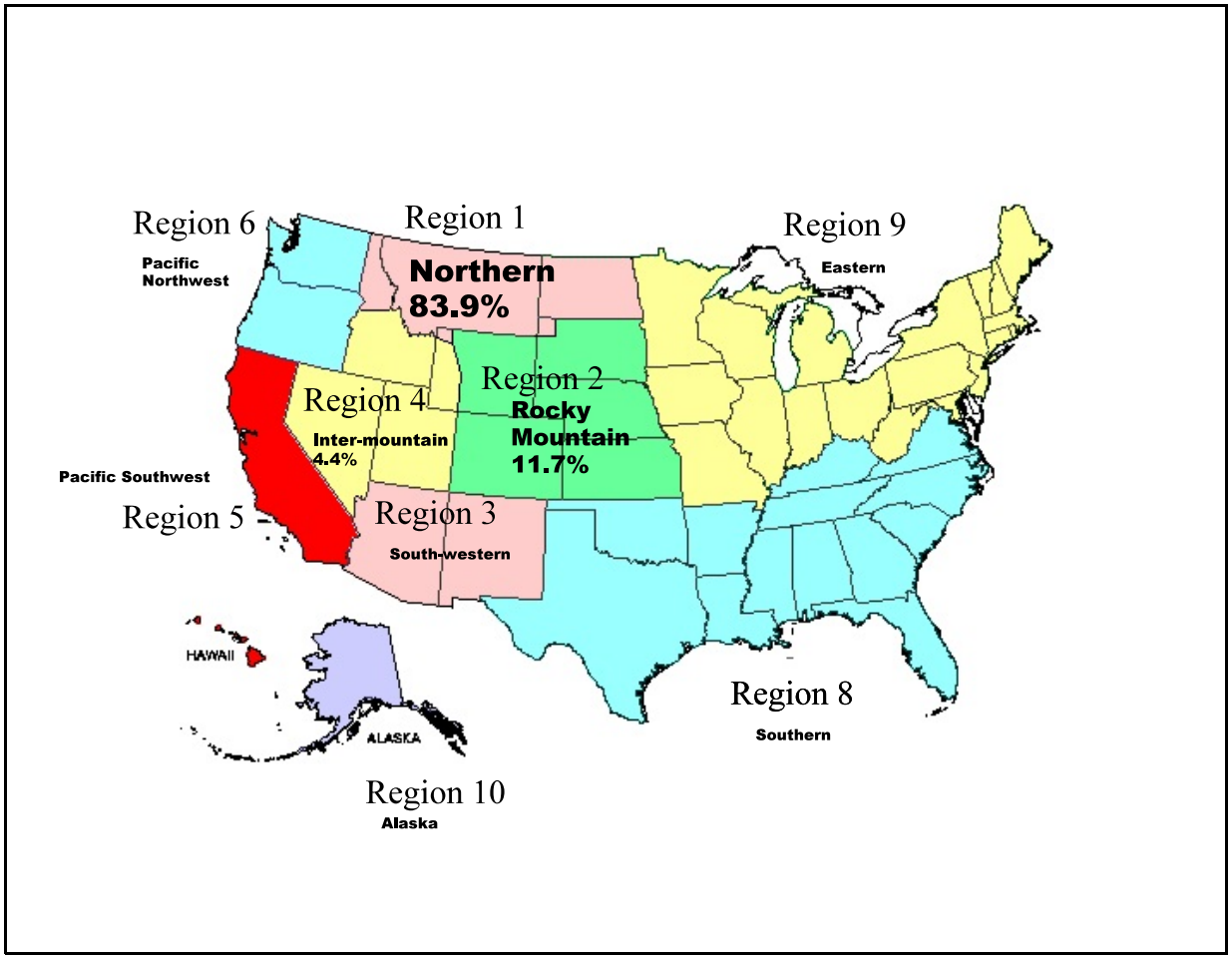

Figure 2-1. Use of Chlorsulfuron by the USDA Forest Service in various regions of the United States based on percentages of total use by FS.

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Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
		ORAL	
Rats, ChR-CD strain, young adult males (4 groups of 10) and females(6 groups of 10), fasted 20 hours prior to dosing and observed for 14 days	single gavage dose of 4000-10,000 mg/kg bw benzenesulfonmide (DPX-4189, INW-4189-19, Haskell #12,361)(~95% a.i.) suspended in corn oil	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)	Trivits 1979 MRID 00031406
Rats, ChR-CD strain, young adult males (4 groups of 10) fasted 20 hours prior to dosing and observed for 14 days	single gavage dose of 4000, 5000, 6000, or 7000 mg/kg bw benzenesulfonmide (DPX-4189, INW-4189-19, Haskell #12,361)(~95% a.i.) suspended in corn oil	All dose levels resulted in humped posture and stained faces and perineal areas; common effects not observed at all dose levels included half-shut eyes, lethargy, chromodacryorrhea, salivation and diarrhea; frequently observed signs of toxicity included prostration, hematuria, weakness, piloerection, lacrimation, and stained undersides of feet and bodies. Mortality occurred 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 were observed in the following organs at 4000-7000 mg/kg bw: thymus, liver, lungs, brain, heart, spleen, kidney, eye, pancreas, testis, GI tract, skin, and stomach	Trivits 1979 MRID 00031406
Rats, ChR-CD strain, young adult males (4 groups of 10) and females(5 groups of 10), fasted approximately 24 hours prior to dosing and observed for 14 days	single gavage dose of 5000-9000 mg/kg benzenesulfonamide (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)	Hinckle and Dashiell 1980 MRID 00031407

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
Rats, ChR-CD strain, young adult males (4 groups of 10) fasted approximately 24 hours prior to dosing and observed for 14 days	single gavage dose of 5000, 6000, 7000, or 9000 mg/kg bw benzene-sulfonamide (DPX-4189, Haskell #13,402) (80% a.i.) suspended in corn oil	Most frequently observed clinical signs included stained and wet perineal area, stained face, weakness, and slight to moderate weight loss. Mortality occurred within 1-4 days of dosing. Gross pathology indicated changes to lungs, thymus, spleen, kidneys, stomach, liver, testes, brain, and eyes.	Hinckle and Dashiell 1980 MRID 00031407
Rats, ChR-CD strain, young adult females (5 groups of 10) fasted approximately 24 hours prior to dosing and observed for 14 days	single gavage dose of 5000, 6000, 7000, 8000, or 9000 mg/kg bw benzene-sulfonamide (DPX-4189) (80% a.i.) suspended in corn oil	Most frequently observed clinical signs included stained and wet perineal area, stained face, weakness, and slight to moderate weight loss;mortality occurred within 1-4 days of dosing; gross pathology indicated changes to lungs, thymus, spleen, kidneys, stomach, liver, brain, and eyes.	Hinckle and Dashiell 1980 MRID 00031407
Rats, Crl:CD strain, fasted young adult males, 10/dose group (weighing 214-225 g) and 6 groups of 10 fasted females(weight of 149-177g)	single gavage dose of 3000, 3200, 3500, or 4000 mg/kg benzenesulfonamide (INW-4189-83) (Haskell #13,808) (DPX-4189,**75% dry flowable**) (75% a.i., 25% inerts) in corn oil suspension.	LD_{50} =3053 mg/kg bw (95% CI =1123-3342 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. Range-finding study produced death at ≥5000 ppm when conducted from 200-7500 mg/kg, 1 rat/dose level.	Dashiell and Hinckle 1981 MRID 00083958

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
Rats, Crl:CD strain, fasted young adult females, 10/dose group (weight of 214-225 g)	single gavage dose of 1000, 2000, 2500, 3000, 4000 or 5000 mg/kg benzenesulfonamide (INW-4189-83) (Haskell #13,808) (composition: 75% a.i., 25% inerts) in corn oil suspension	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; 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.	Hinckle and Dashiell 1981 MRID 00083958
Rats, 10 young adult males; positive control group of 10 young adult males; observed for 14 days	gavage doses of 2200 mg/kg/day benzene-sulfonamide (INW-4189-4) 30% suspension in corn oil 5 times/week for 2 weeks	Mortality: 2/10 (deaths occurred after 5th and 9th doses). No treatment related gross or histopathological effects were observed.	Henry 1977 MRID 00031409
Guinea pigs, young adult males (3 groups of 10) observed for 14 days	single gavage doses of 1000, 1500, or 2000 mg/kg bw benzenesulfonamide (INW-4189-57) (91.9% by analysis) suspended in corn oil	LD_{50} =1363 mg/kg bw 95% confidence limits not defined 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

DERMAL

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
Rabbits, 5 males for 2000 mg/kg dose; 10 adult males and 10 adult females for 3400 mg/kg dose; observed for 14-day recovery period and sacrificed	single doses of 2000 and 3400 mg/kg *as received* benzenesulfonamide (INW-4189-19) (*composition about 100%*) (moistened with physiological saline) applied to abraded skin of shaved back and trunk. Treated areas covered with gauze pads, layer of saran wrap, and Elastoplast adhesive bandage for 24 hours. Treated sites washed with water and dried after exposure. Necropsy performed on 2 rabbits from each dose group	LD_{50} > 3400 mg/kg (males and females) No clinical signs or deaths were observed in any of the treatment groups.	Edwards 1979a MRID 00031411
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 mg/kg and 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 2 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. Majority of males had slight skin irritation in abraded area on day ?? after treatment. No clinical signs of toxicity observed in females throughout duration of study.	Edwards 1979b MRID 00083956 Edwards 1979c MRID 00086824 [Appear to be same studies]

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
Rabbits, albino, 5 adult males and 5 adult females observed for 14-day recovery period and sacrificed	single dose of 2000 mg/kg *as received* 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
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 [Appear to be same studies]
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

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
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	Results of scoring according to Draize technique indicate that benzenesulfonamide *as received* is 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, albino, 10 males, average weight = 763 g	**Primary irritation test** involved application via *lightly rubbing* of 1 drop (~0.05 mL) each of 30% and 3% suspension (wt/vol) of benzene-sulfonamide (INW-4189-3, Haskell #10,539) in propylene glycol on shaved intact shoulder skin.	No irritation observed	Goodman 1976 MRID 00031417
Guinea pigs, albino, 10 males (treatment group) 10 males (control group received similar applications at time of challenge), average weight = 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 (wt/vol) 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 (wt/vol) of benzene-sulfonamide (INW-4189-3) in propylene glycol on shaved intact shoulder skin	No sensitization response was observed	Goodman 1976 MRID 00031417

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
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)	Negative results for skin irritation at 60% in DMP This is a range finding study	Dashiell and Silber 1981 MRID 00083962
Guinea pigs, Duncan-Hartley males, /dose group	**Primary irritation test** conducted by applying and lightly rubbing 0.05 mL of 6% or 60% benzenesulfon-amide (INW-4189-83; **DPX-4189,75% dry flowable**; Haskell #13,808) (75% a.i.) in dimethyl phthalate (DMP) on shaved, intact shoulder skin	No skin irritation observed at 6 of 60% 24 or 48 hours after exposure	Dashiell and Silber 1981 MRID 00083962
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

INTRAPERITONEAL

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
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 benzenesulfonamide (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. Mortality ratio at 2500 mg/kg ratio was 10/10. 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.	Hinckle 1979 MRID 00031410

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
		INHALATION	
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. Chen 1980 reports a concentration of 5 mg/L	No systemic pathological findings believed to be compound induced. All animals had chronic rhinitis which may account for the retaplastic changes that were observed. 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.	Chen 1980 MRID 00083963 Fereuz and Chen 1980 MRID 00031413 Ferenz 1980b MRID 00086825 Fereuz 1980a MRID 00083957 [Appear to be same studies]
		OCULAR	
Rabbits, albino, 9 males	0.1 mL (~ 30 mg) of a 80% formualtion 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, 14and 19 after treatment.	Unwashed eyes: transient local to moderate areas of slight corneal clouding and mild to no conjuctival irritation. Washed eyes: transient small to local areas of slight corneal clouding and mild to no conjuctival irritaiton . No *iritic involvement* observed in washed or unwashed eyes. All eyes were normal 3-4 days after treatment.	Silber 1980 MRID 00031415

Appendix 1: Acute toxicity of chlorsulfuron and chlorsulfuron formulations to experimental mammals.

Species	Exposure	Response	Reference
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 with bright artificial light and ophthalmoscope on 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

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Dogs, young adult purebred beagles, males and females, 4/sex/dose group	Exposure: In the diet at concentrations of 0, 100, 500, or 2500 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) (~95% a.i.) for 26 weeks. Response: 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)	Schneider et al. 1992 MRID 00031420 Du Pont de Nemours 1977b MRID 00032101
Dogs, beagles, 6 ½ months old, males (mean wgt = 9.3 kg) and females (mean wgt = 8.2 kg), 5/sex/dose group	Exposure: In the diet concentrations of 100, 2000 or 7500 ppm chlorsulfuron (DPX-W4189) (~97.5% a.i.) (beige powder) for at least 1 year. Response: Hematological changes and slight body weight changes in females at 7500 ppm; NOEL = 2000 ppm. No treatment-related mortality; the greatest treatment-related effect on body weight occurred 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.	Atkinson 1991 MRID 41862601

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rabbits, New Zealand white 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	Exposure: corn oil (controls) or 10, 25, or 75 mg/kg bw of Haskell #12,700 (off-white powder) (*purity assumed to be 100% for purposes of dose calculations)* in corn oil vehicle administered by gavage on days 6-19 of gestation. Response: Two rabbits, one at 25 mg/kg bw and one at 75 mg/kg died on 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 **Significant increase in the incidence of resorptions at 75 mg/kg bw indicates embryotoxicity.**	Hoberman 1980 MRID 00083945 Hoberman et al. 1980 MRID 00086827 [Appear to be same studies]

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rabbits, New Zealand white, nulliparous females, wgt = 2491.3-3671.8 g, mean wgt = 3055.1 g ± 23.35 g, 20/dose group	Exposure: daily dose levels of 0, 25, 75, 200, or 400 mg/kg chlorsulfuron (DPX-W4189-165) (98.2% purity) by gavage on days 7-19 of gestation. Response: No overt maternal or fetal toxicity at any dose level. **Due to the lack of toxic response, a supplementary study was conducted in which DPX-W4189-165 was administered at daily dose levels of 0, 400, and 1000 mg/kg and all other study conditions remained the same.** Response: 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. **In the original study, a significant trend also was detected for this parameter, but no significant differences were seen. No other maternal toxic effects were seen at any dose level.** No evidence of fetal toxicity was observed in either study. NOAEL = 200 mg/kg/day for dams NOAEL > 1000 mg/kg for conceptus	Alvarez 1991b MRID 41983101
Rats, weanling, males and females, 10/sex/dose group	Exposure: In the diet at concentrations of 0, 100, 500, or 2500 ppm benzensulfonamide (INW-4189, Haskell #12,700) (~95% pure) for approximately 90 days. Response: 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)	Wood et al. 1980a MRID 00031418 Du Pont de Nemours 1977b MRID 00032101

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, weanling, males and females, 80/sex/dose group	Exposure: In the diet at concentrations of 0, 100, 500, or 2500 ppm benzensulfonamide (INW-4189-22, Haskell #12,700) (~95% pure) for approximately 52 weeks. Response: 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 Du Pont de Nemours 1977b MRID 00032101

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, CD, males and females, 80/sex dose group	Exposure: In diet concentrations of 0, 100, 500, or 2500 ppm technical grade benzenesulfonamide (INW-4189) for 2 years. *The test material (INW-4189-22 and INW-4189-57) was supplied in two shipments as a white crystalline material, stated to be approximately 95% and 91.9% pure, respectively.* Response: NOEL = 100 ppm 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.	Wood et al. 1981a MRID 00086003

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, females, nulliparous 64 days old, wgt = 245.1-38.0 g, mean wgt =291.9 g ± 1.12 g, 25/dose group	Exposure: daily dose levels of 0, 55, 165, 500 or 1500 mg/kg chlorsulfuron (DPX-W4189-165) (98.2% pure) by gavage on days 7-16 of gestation. Response: 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 copora lutea counts. NOAEL = 165 mg/kg/day for dams NOAEL = 500 mg/kg/day for conceptus.	Alvarez 1991a MRID 41976406
Rats, 20 males and 20 females taken from each treatment level in the 2-year feeding study described above.	Exposure: 3-Generation reproduction study in which the F_0 generation rats taken from the 2-year feeding study described above received 0, 100, 500, or 2500 ppm chlorsulfuron (98.2% pure) for 98 days. Response: NOEL = 500 ppm 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 F_{3B} litters.	Wood et al. 1981a MRID 00086003

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, males and females, 20/sex/dose group	Exposure: Three-generation, six-litter feeding study using in diet concentrations of 0, 100, 500, or 2500 ppm benzene- sulfonamide (INW-4189). Response: 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 related to the dietary presence of the test compound.	Wood 1980 MRID 00031423
Rats, Charles River, 2- to 3-days pregnant	Exposure: In the diet concentrations of 0,100, 500, or 2500 ppm benzenesulfonamide (INW-4189-13)(in the form of white crystals) (~100% pure) on days 6 through 15 of gestation. Response: No embyrotoxic 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
Mice, weanling, males and females, 10/sex/dose group	Exposure: In the diet at concentrations of 0, 500, 2500, 5000, or 7500 ppm sulfonamide (INW-4189-19) (100% a.i.) for approximately 3 months. Response: No mortality; no adverse effects on weight gain, food consumption, or food efficiency; at 5000 or 7500 ppm, males had lower erythrocyte counts and higher mean corpuscular volumes and mean corpuscular hemoglobin values, compared with male controls; at 5000 or 7500 ppm, females 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)	Smith et al. 1980 MRID 00031421 Du Pont de Nemours 1977b MRID 00032101

Appendix 2: Toxicity of chlorsulfuron and chlorsulfuron formulations after repeated oral administrations.

Species	Exposure/Response	Reference
Mice, weanling, males and females, 80/sex/dose group	Exposure: In the diet at concentrations of 0, 500, 2500, or 5000 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) (~95% pure) for 52 weeks. Response: 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. **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
Mice, CD, males and females, 80/sex/dose group	Exposure: In the diet concentrations of 0, 100, 500, or 5000 ppm benzenesulfonamide [INW-4189-22; Haskell #12,700-01 (95% pure) and INW-4189-57; Haskell #12,700-02 (91.9% pure)] for 2 years. Response: 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	Wood et al. 1981b MRID 00090030

Appendix 3: Mutagenicity studies on chlorsulfuron.

Organism	Exposure Level	Assay System	Effects	Reference
Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100	up to 30 μg/petri plate	microbial assays in the presence or absence of a liver microsomal system (S-9)	no significant increase in spontaneous mutation frequency	Russell 1977 MRID 00031425
Hamster	20-60 μL benzenesulfonamide (INW-4189-22, Haskell #12,700)(about 95% a.i.) with or without S-9 activation	CHO/HGPRT assay	no dose-related cytotoxicity either with or without S-9 activation	Krahn and Waterer 1980a MRID 00083943 Krahn and Waterer 1980b MRID 00086828 [Appear to bet same studies]
Hamster	≤5 mg/mL benzene-sulfonamide (Haskell #12,700) with or with metabolic activation	CHO/HGRPT assay	did not induce aberrations in CHO cells with or without metabolic activation	Galloway and Lebowitz 1981a MRID 00086830 Galloway and Lebowitz 1981b MRID 00086830 [Appear to be same studies]

Appendix 3: Mutagenicity studies on chlorsulfuron.

Organism	Exposure Level	Assay System	Effects	Reference
Rats, Sprague-Dawley, males, 49-days-old, average weights 192-279 g, 10 controls and 10/dose group	in diet 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	dominant lethal mutations assay	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 Hoberman and Fieser 1980b MRID 00086829 [Appear to be same studies]
Rat	≤2.0 mg/mL Haskell #12,700 dissolved in DMSO	HPC/DNA repair assay	test compound negative for genotoxic effects	Williams et al. 1981 MRID 00090008
Rat	0-3750 μg/mL IN W4189-165 dissolved in DMSO	unscheduled DNA synthesis with rat hepatocytes	test compound negative for unscheduled DNA synthesis	Vincent 1990 MRID 42545601

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
^{14}C-phenyl-labeled DPX-4189 or ^{14}C-triazine-labeled DPX-4189 applied to post emergence spring wheat at 70 g/ha (1 oz/acre). The soil in the field was Keyport silt loam.	^{14}C residues in wheat grain (sample size = 50 g) were 0.008 ppm (triazine) and 0.016 ppm (phenyl) (limit of detection = 0.01 ppm); ^{14}C residues in dry straw (sample size = 10 g) were 0.036 ppm (triazine) and 0.053 ppm (phenyl) (limit of detection = 0.05 ppm) No intact DPX-4189 or degradation products were present in the grain or straw extracts. NOTE: The 1980 study refers to an addendum (not included on this fiche) that describes "how wheat rapidly metabolizes DPX-4189 to the polar product Metabolite A, characterized a the O-glycoside of 5-hydroxylated DPX-4189.	Du Pont de Nemours 1980f MRID 00032567 (summary) Du Pont de Nemours 1979a MRID 00032568
^{14}C-phenyl-labeled DPX-4189 or ^{14}C-triazine-labeled DPX-4189 applied to young wheat plants (1- to 2-weeks old) at rates equivalent to ~20-200 g a.i./ha. Treated leaves were washed with acetone 24 hours after treatment.	Metabolite A, a glucose conjugate of the 5-hydroxyphenyl analog of DXP-W4189 was the major radioactive component; small amounts of DPX-4189, the acid hydrolysis products of DPX-4189 and Metabolite A, were also present.	Sweetser 1980 MRID 00097395
Greenhouse study in which postemergence wheat planted in Fallsington sandy loam soil was treated with 0.125 kg/ha (1.8 oz/acre) or 0.0313 kg/ha (0.45 oz/acre) ^{14}C-DPX-4189	^{14}C residue in wheat grain was < 0.01 ppm (limit of detection); ^{14}C residue in dry straw ranged from 0.10 to 0.13 ppm (limit of detection = 0.05 ppm)	Du Pont de Nemours 1980f MRID 00032567 (summary) Du Pont de Nemours 1979a MRID 00032568
Greenhouse study in which Waldron Spring wheat was planted in each of three flats filled with Fallsington sandy loam soil from Stanton, Delaware. At 4-leaf stage, wheat was sprayed with 70 g/ha (1.23 mg, 7.4 μCi/13 mL/flat) ^{14}C-phenyl-labeled DPX-4189 (> 99% radiochemical purity) **without surfactant** dissolved in water and methanol (10:1, v/v). Wheat samples were collected at 1 day and 1,2, and 4 weeks after treatment and at maturity.	Total ^{14}C-residue in wehat foliage decreased from 1.51 ppm on day to 0.045 ppm at maturity; ~0.0072 ppm ^{14}C-residue was detected in dry wheat grain; treated foliage had much higher ^{14}C-residues, compared with new growth; treatment produced < 3% of metabolite A, a glucose conjugate of the 5-hydroxyphenyl analog of DXP-W4189 in the total residue shortly after treatment.	Han 1981d MRID 00086833

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Broadcast spray application of Telar at rate of 1.0 oz a.i./acre made to grass at forgeable stage just prior to booting at one treatment site and one control site in Minnesota, South Dakota, North Dakota, and Texas.	Chlorsulfuron residues in pasture grass forage samples collected at day 0 after application ranged from 1.9 to 7.7 ppm; chlorsulfuron residues in pasture grass hay samples collected at day 0 after application ranged from 4.5-15 ppm; at approximately 7 days after application, chlorsulfuron residues in pasture grass hay samples ranged from undetectable to 0.36 ppm.	Du Pont de Nemours 2001 MRID 45630001
Field study in which Winter wheat was planted the third week of September 1980 in Newark, Delaware. The soil in the field was Keyport silt loam. When seedling were about 12" high with 5th leaf fully expanded (May 5, 1981), the plot (100 ft^2) was treated with ^{14}C-phenyl-labeled DPX at a rate of 100 g/ha. Approximately 92.9 mg (558 μCi) of the ^{14}C-phenyl-labeled DPX was formulated as **Glean 75 DF** before mixing with 1.5 L distilled water. 3.75 g (0.25%) **Surfactant WK** (Du Pont)(maximum recommended amount) was added to the spray solution. Two hours after treatment, the plot was covered with clear polyethylene film to protect the crop from rain for the first 5 days.	Total ^{14}C- residues were 1.41-2.16 ppm in fresh samples and 9.2-10.8 ppm in air-dried samples during the first 6 days after treatment; total ^{14}C-residue decreased to 0.38 ppm (dry weight basis) at maturity; foliage that grew after treatment contained very little residue (0.063 and 0.061) at 2 week and 1 month respectively; ~0.03 ppm ^{14}C- residue was detected in mature grain. Treatment with maximum recommended surfactant added produced > 50% of metabolite A , a glucose conjugate of the 5-hydroxyphenyl analog of DXP-W4189 in the short-term residue, which gradually hydrolyzed to metabolite B, a glucose conjugate of 2-chloro-5-hydroxybenzenesulfonamide, in the wheat foliage; little or no intact DPX-W4189 and its hydrolysis products were detected in the foliage that grew after treatment.	Han 1981d MRID 00086833

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Post-emergence (3rd leaf stage) spring barley (Rapidan) planted in a field of Keyport silt loam in Newark Delaware on April 2, 1981 was treated on May 15, 1981 (seedlings about 6" high) with ^{14}C-phenyl-labeled DPX at a rate of 40 g/ha. Approximately 6.0 mg (36 μCi) of the ^{14}C-phenyl-labeled DPX was formulated as **Glean 75 DF** before mixing with 300 mL distilled water. 0.75 g (0.25%) **Surfactant WK** (Du Pont) was added to the spray solution. The first rainfall (0.5") was measured about 36 hours after treatment.	Little or no (< 0.005 ppm) intact DPX-W4189 was detected in the straw and grain at maturity; total ^{14}C-residues were 0.023 ppm in dry straw and 0.0004 ppm in grain; metabolite A , a glucose conjugate of the 5-hydroxyphenyl analog of DXP-W4189 accounted for more than 50% of the total residue in treated foliage 1 week after spraying and gradually hydrolyzed to metabolite B, a glucose conjugate of 2-chloro-5-hydroxybenzene-sulfonamide; a small amount of ntact DPX-W4189 was detected on the surface and inside of the 1-week treated foliage and gradually became undetectable after several weeks.	Han 1981e MRID 00086834
^{14}C-phenyl-labeled DPX-4189 or ^{14}C-triazine-labeled DPX-W4189 applied to two field plots of Keyport silt loam at a rate of 70 g/ha. One year after treatment, soybean and rape were planted and the crops were grown to maturity and analyzed for ^{14}C-content and extractable ^{14}C-content.	1 ppb intact DPX-W4189 remained in the soil at the time of planting; total ^{14}C-residues were 2-3 ppb in harvested soybeans and 1 ppb in rape seed; total ^{14}C-residues in mature foliage from soybeans and rapes were 7-9 and 1 ppb, respectively. No (< 1 ppb) intact DPX-W4189, metabolites, or decomposition products were detected in any crop.	Han 1981b MRID 00086818
Greenhouse study in which wheat, sugar beets, and rape plants were grown in Keyport silt loam treated with 1 oz/acre of ^{14}C–DPX-W4189 and field aged for 4- and 12-month periods.	At planting, total ^{14}C-residues in the 4- and 12-month aged soil were 12 and 9 ppb respectively, but the parent compound was present at only about 0.1 ppb. In 4-month aged soil, wheat grew unaffected; sugar beets and rape sustained some injury; sugar beet seedlings showed about 50% survival, compared with controls, and exhibited additional growth retardation in the follow 2-3 months after which time the surviving plants were thinned and developed as well as the controls; rape showed about 75% survival of seedlings with some mild chlorosis, were thinned at 3 months and developed as well as controls. In the 12-month aged soil, all three crops grew uneventfully with no sign of injury.	Rapisarda 1981c MRID 00086819

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Chlorsulfuron applied to three field plots by spray (30 g ai./ha). On the day of application and at 14 day intervals, soil samples were collected for 20 weeks.	Soil type: sandy loam Half-life decreased with increasing temperature and moisture content. In persistence studies, half-life of chlorsulfuron was 40 days. After 140 days, 5% of applied chlorsulfuron was recovered.	Walker and Brown 1983
Chlorsulfuron herbicide applied to 8 test locations (two at Akron, CO; Carrington, ND; Clay Center, NB; Fargo, ND; Kimberly ID; Newark, DE; and Rochelle IL) at 100 g a.i./ha and at one test location (Madera, CA) at 158 g a.i./ha. Application rates used represent 4-8 times the maximum label use for Glean FC and up to the maximum label use for Telar.	Rapid degradation of residues under actual field use conditions. Half-lives = 24-72 days, depending on soil and weather conditions. Residues of chlorsulfuron were only detected in the 0-6" soil indicating a lack of soil mobility and low potential for leaching. Observed major soil metabolites of chlorsulfuron included chlorosulfonamide, triazine amine, and ring-opened chlorsulfuron. No significant concentrations of chlorsulfuron or its metabolites were detected below a soil depth of 24".	Djanegara 1991a MRID 42214201

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Greenhouse study involving crops of wheat, sugar beets, and rape grown in Keyport silt loam previously treated with ^{14}C-DPX-W4189 at 1 oz/acre and field-aged 4 and 12 months (approximately 5.3 times greater than the rate used).	Average total ^{14}C soil residues were 12 and 9 ppb at 4 and 12 months of aging, respectively. Wheat grew uneventfully in both aged soils; sugar beets and rape exhibited some injury on the 4-month-aged soil: sugar beet seedlings showed ~50% reduced stand, compared with controls and some initial growth retardation; rape seedlings showed ~25% reduced stand and some initial chlorosis. Both crops recovered by 2-3 months and developed as well as controls. Chlorsulfuron degraded fairly rapidly in soil and only very low levels of chlorsulfuron residues were detected. A year after treatment, the degradation products were detected as 0.001 ppm intact chlorsulfuron; 0.003 ppm chlorosulfonamide; and 0.004 ppm triazine amine, all of which disappeared after two years. At 2.7-8.0 times normal use rate, wheat straw was the only crop sample containing significant chlorsulfuron equivalent residues (0.041 ppm) at harvest, with no significant amounts of individual components present; intact chlorsulfuron residues in root crops (sugar beets) or small grains (wheat straw) were below the analytical detection limit (< 0.0002 ppm) at the 120-day rotational interval.	Djanegara 1991b MRID 42214203
Greenhouse and field study involving foliar applications of ^{14}C labeled chlorsulfuron (phenyl and triazine moiety) to wheat and barley.	Results indicate limited systemic absorption and translocation; most of the deposited radioactivity remained at the application sites (i.e., was localized on foliar surfaces) and was recoverable as surface-dislodgeable residues by simple solvent washing.	Lee 1992a MRID 42248701
Foliar uptake and translocation of chlorsulfuron studied for chlorsulfuron applied to plants (leaves) as aqueous solution (pea, alfalfa and grapes) and soil.	Significant amounts of chlorsulfuron adsorbed by pea, alfalfa and grapes when applied as an aqueous solution to leaves; limited adsorption of herbicide treated soil. Chlorsulfuron readily translocated in all three plants.	Al-Khatib et al. 1992a
Pre-emergent application of chlorsulfuron at 0, 10, 20, and 40 g a.i./ha to wheat grown in three soils (sandy loam, sandy clay loam, and silty clay loam) and pH (7.9, 4.7, and 7.6)	Residual leaching increased with increasing application rates. In sandy loam soil, sunflower, lentil and sugarbeets sown 8 months after application (all rates) were injured. Only lentil and sugarbeet were injured by chlorsulfuron in silty clay loam. No crops injured when sown 8 months after application in sandy clay loam.	Kotoula-Syka et al. 1993a

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Glean herbicide applied as post emergence broadcast spray to wheat (flag leaf just visible, which is the latest application timing tolerable to the plant and represents the shortest pre-harvest interval) at 0.62 oz a.i./acre (2 times use rate), 0.93 oz a.i./acre (3 times use rate), or 1.55 oz a.i./acre (5 times use rate) in Mississippi test site.	Residues of chlorsulfuron and its metabolite, 5-hydroxychlorsulfuron were < 0.050 (limit of quantitation) in all wheat grain samples and in all of the processed samples.	Klemens and Tomic 1993 MRID 42900601
Field study to measure the persistence and mobility of chlorsulfuron at four field location in Italy. Chlorsulfuron applied at rate 30 g ai/ha.	Degradation rates followed first-order kinetics. Dissipation rates were slower with increasing rainfall Half-life in sandy loam: 51 and 149* days Half-life in clay: 70 days Half-life in silty clay: 59 days *2 locations tested	Vicari et al. 1994
Field study to monitor leaching and degradation of chlorsulfuron on a gradually textured alkaline cropping soil	Following boom spray application of 19 g ai/ha in May 1991, 46% (est.) of chlorsulfuron was leached beyond 50 cm by late winter. Half-life = 80 days. Leaching took place again the following growing season, between late autumn and mid-spring, where trace quantities of chlorsulfuron moved from shallower depths. Residues were in the range of 0.1-0.4 ng/g	Stork 1996

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Field study on the fate and mobility of ^{14}C-chlorsulfuron at several sites following fall and spring treatments of ~ 100 g ai/ha.	In sandy loam soil, chlorsulfuron demonstrated rapid dissipation (pseudo-first-order half-life of 18 days). No intact chlorsulfuron at 120 days. Major metabolites were chlorobenzenesulfonamide and triazine amine. Average DT_{50} of fall application: 192 days Average DT_{50} of spring application: 49 days sandy loam (pH 6.3-6.9, OM% 0.3-0.3, soil temp ^{o}C): pseudo-first-order half-life of 18 days, no chlorsulfuron detected below 0-15 cm, ^{14}C-residues detected to 60 cm Half-life in silt loam (pH 6.1-6.9, OM% 1.0-2.2, soil temp 8.6 ^{o}C): biphasic dissipation, initial half-life of 18 days, half-life of slower second phase 109 days, no chlorsulfuron detected below 0-15 cm, ^{14}C-residues detected to 50 cm	Strek 1998b

Appendix 4: Summary of field or field simulation studies on chlorsulfuron formulations.

Application	Observations	Reference
Foliar broadcast spray of DPX-W4189 (dry flowable formulation containing 75% a.i.) applied to 28 test sites (9 established on pasture grass and 19 established on wheat) at rates of 0.50, 1.0, or 2.25 oz a.i./acre	At 0.50 a.i./acre, chlorsulfuron residues were as follows on day 0 after application: pasture grass forage: 0.75-3.9 ppm pasture grass hay: 0.80-11 ppm wheat forage: 0.66-5.0 ppm wheat hay: 0-56-12 ppm At1.0 a.i./acre, chlorsulfuron residues were as follows on day 0 after application: pasture grass forage: 1.2-11 ppm pasture grass hay: 1.0-19 ppm At1.0 a.i./acre, chlorsulfuron residues were as follows on day 7 after application: pasture grass forage: <0.05-1.4 ppm pasture grass hay: 0.098-3.6 ppm At1.0 a.i./acre, chlorsulfuron residues were as follows on day 14 after application: pasture grass forage: <0.05-0.77 ppm pasture grass hay: <0.05-1.4 ppm At 2.25 a.i./acre, chlorsulfuron residues were as follows on day 7 after application: pasture grass forage: 0.090-3.0 ppm pasture grass hay: 0.26-10 ppm	Brill 1998 MRID 44705401

Appendix 5. Acute toxicity of chlorsulfuron to birds

Species	Nature of Exposure	Exposure Time	Effects	Reference
Bobwhite quail (*Colinus virginianus*), males (initial body weight 176-234g) and females (initial body weight 179-238 g), 5/sex /dose group	acute oral exposure to 312.5-5000 mg/kg H-12361(white crystalline powder; *100% a.i. was assumed*) suspended in 0.5% methyl-cellulose; controls received 10 mL/kg 0.5% methlycellulose alone	single dose (gavage)	LD_{50} > 5000 mg/kg bw (males and females)	Hinkle and Twigg 1980 MRID 00035263
Bobwhite quail (*Colinus virginianus*), 10/dose group (NOS)	in the diet concentrations of 156.25-5000 ppm H-12361(white crystalline powder)(*value of 100% a.i. used for purposes of dose calculations*); basal diet used as control material	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 1979 MRID 00035265
Bobwhite quail (*Colinus virginianus*), 14-days old, 10 birds/dose group	in diet concentrations of 0, 562, 1000, 1780, 3160, and 5620 ppm Haskell #12,700 (light gray powder, *100% a.i. was assumed*) dissolved in corn oil	5 days on test diet followed by 3 days on basal diet	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.	Fink et al. 1981 MRID 00090009

Appendix 5. Acute toxicity of chlorsulfuron to birds

Species	Nature of Exposure	Exposure Time	Effects	Reference
Bobwhite quail (*Colinus virginianus*), males and females, 25 weeks old, 16/sex/dose group	in diet concentrations of 0, 40, 200, or 1000 ppm chlorsulfuron (Haskell# 18,053) (purity of compound was not indicated)	22 weeks (1-generation reproduction study)	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. NOEC = 200 ppm (*and my have been as high as 1000 ppm*)	Beavers et al. 1992a MRID 42634001
Mallard ducks, males (initial weight 960-1280 g) and females (initial weight 900-1255 g), 5/sex/dose group	acute oral exposure to 312.5-5000 mg/kg H-12361 (100% a.i. was assumed) suspended in corn oil; controls received 20 mL/kg corn oil	single dose (gavage)	LD_{50} > 5000 mg/kg bw (males and females)	Hinkle and Bristol 1980 MRID 00035264
Mallard ducks, ~2-weeks old, 10/dose group (NOS)	in the diet concentrations of 156.25-5000 ppm H-12361(white crystalline powder) (purity of compound was not indicated); basal diet used as control material	5 days on test diet followed by 3 days on basal diet	LC_{50} > 5000 ppm (estimated)	Hinkle and Wentz 1979 MRID 00032566

Appendix 5. Acute toxicity of chlorsulfuron to birds

Species	Nature of Exposure	Exposure Time	Effects	Reference
Mallard ducks, males and females, 16/sex/dose group	in diet concentrations of 0, 40, 200, or 1000 ppm chlorsulfuron (Haskell# 18,053) (purity of compound not indicated	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	Beavers et al. 1992b MRID 42634002

NOS = Not otherwise specified.

Appendix 6. Toxicity of chlorsulfuron to fish

Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Bluegill sunfish (*Lepomis macrochirus*)	115-300 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent) under static, unaerated conditions (*no information provided on chlorsulfuron purity*)	96 hours	Effects assessed only by % mortality. With the exception of the 255 ppm concentration, no mortality was observed in any test group. In the 255 ppm group, 10% mortality was observer. However, no deaths were observed in the 300 ppm exposure group. LC_{50} > 300 ppm test material poorly soluble in water; higher concentrations could not be tested due to possible toxicity associated with dimethulformamide (DMF) as carrier solvent	Smith 1979a MRID 00035258
Rainbow trout (*Salmo gairdneri*)	95-250 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent) under static unaerated conditions (*no information provided on chlorsulfuron purity*)	96 hours	Effects assessed only by % mortality. No mortality was observed in any test group. LC_{50} > 250 ppm test material poorly soluble in water; higher concentrations could not be tested due to possible toxicity associated with DMF as carrier solvent	Smith 1979b MRID 00035259

Appendix 6. Toxicity of chlorsulfuron to fish

Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Rainbow trout (*Oncorhynchus mykiss*), embryos, alevins, and fingerlings	mean measured concentrations of 18-900 mg/L (nominal concentrations of 15.6-1000 mg/L) chlorsulfuron (DPX-W4189-170) (97.9% pure) under flow-through conditions	77 days	Survival of embryos and alevins did not differ from controls. Survival of fingerlings significantly reduced in 900 mg/L dose group (40% mortality). Not deaths were observed at any other exposure level. NOEC = 32 mg/L LOEC = 66 mg/L MATC = 46 mg/L based on standard length of the trout at test conclusion. LC_{50} values not determined since 50% mortality was not observed. length showed the greatest sensitivity to exposure	Pierson 1991 MRID 41976405
Brown trout (*Salmo trutta*)	Chlorsulfuron tested as Gleam (75% formulation) at concentrations ranging from 10 to 100 mg/L	4 days	LC_{50} = 40 mg/L	Grande et al. 1994 MRID 45202909
Fathead minow (*Pimephales promelas*)	115-300 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent) under static, unaerated conditions (*no information provided on chlorsulfuron purity*)	96 hours	Effects assessed only by % mortality. 10% mortality observed in the 185 ppm and 300 ppm groups. No mortalities observed in the 217 and 255 ppm groups or at concentrations below 186 ppm. LC_{50} > 300 ppm test material poorly soluble in water; higher concentrations could not be tested due to possible toxicity associated with DMF as carrier solvent	Smith 1979c MRID 00035260

Appendix 6. Toxicity of chlorsulfuron to fish

Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Channel catfish (*Ictalurus punctatus*)	1-50 ppm benzenesulfonamide (INW-4189-22, Haskell #12,700) in DMF (carrier solvent) under static, unaerated conditions	96 hours	Effects assessed only by % mortality. No mortality was observed in any test group. LC_{50} > 50 ppm due to insolubility of test material in water, concentrations greater than 50 ppm were not tested to comply with EPA recommendations regarding maximum allowable concentration of carrier solvents in exposure solutions	Smith 1979d MRID 00035261
Sheepshead minnow (*Cyprinodon variegatus*), juveniles	mean measured concentrations of 132-980 mg/L (nominal concentrations of 133-1025 mg/L) chlorsulfuron (DPX-W4189-165) (98.2% pure) under static conditions	96 hours	Effects assessed only by % mortality. No mortality was observed in any test group. LC_{50} > 980 mg/L NOEC for morality = 980 mg/L	Ward and Boeri 1991a MRID 41976401

[a] Values in parentheses are the 95% confidence limits.

Appendix 7. Toxicity of chlorsulfuron to aquatic invertebrates

Species	Exposure	Effects[a]	Reference
Daphnids (*Daphnia magna*)	benzenesulfonamide (DPX-4189, INW-4189-22, Haskell #12,700)(*purity not indicated*) concentrations ranging from 188 to 500 ppm for 48 hours under static unaerated conditions.	LC_{50} = 370.9 ppm (346.4-400.2 ppm) 90% mortality in 500 ppm exposure group.	Goodman 1979 MRID 00035262
Daphnia magna, less than 24-hours old, no solvent control was used.	chlorsulfuron (DXP-W4189-94) (95.4% pure) at test concentrations of 9.3, 20, 36, 79, 140, or 300 mg/L for 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 MATC = between 20 and 36 mg/L	Ward and Boeri 1989 MRID 41976404 Hutton 1992 MRID 42309701 (***correction of incorrect reference to use of a solvent control***)
Mysids (*Mysidopsis bahia*)	chlorsulfuron (DPX-W4189-165)(98.2% pure) mean measured concentrations of 12-99 mg/L (nominal concentrations of 13-100 mg/L) under static, unaerated conditions for 96 hours	Assessments made by % mortality LC_{50} =89 mg/L (359-414 mg/L) NOEC = 35 mg/L	Ward and Boeri 1991b MRID 41976402
Eastern oyster (*Crassostrea virginica*) bivalve mollusc 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 under static, unaerated conditions for 48 hours	Acute toxicity test in embryos and larvae. Assessments made based on % normal and abnormal oysters. 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) LC_{25} = 905 mg/L NOEC not reported, although normal of 98% of animals appeared normal in the 200 mg/L group.	Ward and Boeri 1991c MRID 41976403 Ward and Boeri 1991d MRID 41976403 Appear to be the same study.

Appendix 7. Toxicity of chlorsulfuron to aquatic invertebrates

Species	Exposure	Effects[a]	Reference
Daphnia magna and *Daphnia pulex*	Chlorsulfuron (purity not specified) concentrations range from 0.01 to 100 mg/L for 48 hours	In *D. magna*, LC_{50} > 100 mg/L. Estimated mortality of 30% at 100 mg/L concentration. NOEC = 10 mg/L In *D pulex*, LC_{50} between 32 and 100 mg/L. No mortality at 32 mg/L, 100% mortality at 100 mg/L concentration. NOEC = 32 mg/L	Hessen et al. 1994

[a] Values in parentheses are 95% confidence limits.

Appendix 8: Toxicity of chlorsulfuron to aquatic algae and macrophytes

Species	Exposure	Effects [a]	Reference
AQUATIC ALGAE			
Selenastrum capricornutum, green algae	measured test concentrations of 9.6, 17, 34, 61, or 104 μg/L chlorsulfuron (DPV-W4189-165) (99/7% pure chlorsulfuron) for 120 hours	Results based on cell counts EC_{50} = 50 μg/L (40-60 μg/L) NOEL = 10 μg/L	Blasberg et al. 1991 MRID 42186801
Selenstrum capricornumtum, 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/L for 96 hours. Tests conducted free cells, immobilized cells and bottle test	Results based on inhibition of algal growth (algal dry weight) Free algae: EC_{50} = 0.68mg/L Immobilized cultures: EC_{50} = 0.81mg/L bottle test assay: EC_{50} = 0.7 mg/L	Abdel-Hamid 1996
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/L or 1.6 μmol/L (1.39-1.77) EC_{50} (Inhibition of cell reproduction) = 0.40 mg/L or 1.1 μmol/L (1.04-1.22) Bioconentration Factor: at pH 6.0 = 8 (6-9) at pH 5.3 = 36 (30-41) at pH 5.0 = 53 (28-32)	Fahl et al. 1995
Selenstrum capricornumtum	Exposure for 96 hours, chlorsulfuron concentration range not specified, chlorsulfuron purity not specified	Growth inhibition was determined based on biomass. EC_{50} = 123 µg/L (109-161) NOEC < 19 µg/L LOEC = 19 µg/L	Fairchild et al. 1997

Appendix 8: Toxicity of chlorsulfuron to aquatic algae and macrophytes

Species	Exposure	Effects [a]	Reference
6 species of phytoplankton *Selenstrum capricornumtum, Chlamydomonas noctigama, Cyclotella sp., Crytomonas purindoifera, Microcystis aeruginosa, Synechococcus leopoliensis*	Chlorsulfuron (75% formulation) concentrations ranging from 0.032 to 320 mg/L for 72 hours	EC_{50} for growth rate, expressed as mg/L for the active ingredient: *Selenstrum capricornumtum,* 0.8 *Chlamydomonas noctigama, 0.6* *Cyclotella sp.,* 1.0 *Crytomonas purindoifera,* 60 *Microcystis aeruginosa,* 10 *Synechococcus leopoliensis*, 0.15	Kalliquist and Romstad 1994
Field study (Specific species not identified). Study conducted in enclosures in a lake in Sweden.	chlorsulfuron (purity not specified) concentrations of 1, 10, and 100 µg/L for up to 13 days	Decreases in biomass development (as measured by chlorophyll-a) observed at10 and100 µg/L concentrations. NOEC = 1 µg/L LOEC = 10 µg/L At all exposure levels, species diversity was decreased. No effects observed on photosynthsis or rate of nitrated assimilation at any concentration.	Kalliquist et al. 1994

Appendix 8: Toxicity of chlorsulfuron to aquatic algae and macrophytes

Species	Exposure	Effects [a]	Reference
16 species of fresh water and 20 species of marine algae	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	Range of EC_{50} for growth inhibition in fresh water species: < 1 µM (0.358 mg/L) in *Stuarastrum gracile* to 770 µM (276 mg/L) in *Cyclotella cryptica* Range of EC_{50} for growth inhibition in marine species: 0.032 µM (0.011 mg/L) in *Synechococcus leopoliensis* to approximately 1000 µM(358 mg/L) in *Porphyridium cruentum* In almost all species tested, 100% mortality was observed at the 1000 µM (358 mg/L) concentration. In *S. leopoliensis*, 100% mortality was observed at 0.32 µM(0.11 mg/L)	Nystrom et al. 1999
4 species of algae, 6 species of cyanobactiera	Studied the phytoxicity of the expected environmental concentrations (EEC) of several chemicals in aquatic test organisms. For chlorsulfuron, EC = 0.02 mg/L. Exposure duration: 22 hours	Examined toxicity of chlorsulfuron at EEC on % inhibition of ^{14}C uptake in 4 species of algae (no inhibition observed), 6 species of cynobacteria (statistically significant reduction of 23% in *Microcystis aeruginosa*, but no change in 5 other species).	Peterson et al. 1994
Three species of freshwater phytoplankton - *Cholorella saccharophila, Scenedesmus acutus, Pseudanabaena galeata*	Chlorsulfuron (95% pure) concentrations ranging from 0.07 to 184.7 ppm (mg/L) for 96 hours	NOEC values in ppm (mg/L) for growth inhibition: *Cholorella* 9.3 *Scenedesmus* 0.07 *Pseudanabaena* 3.9 EC_{50} for growth (ppm) *Cholorella* 54.0 (41.5-66.9) *Scenedesmus* 0.22 (0.19-0.26 *Pseudanabaena* 16.3 (13.7-19.0)	Sabater and Carrasco 1997

Appendix 8: Toxicity of chlorsulfuron to aquatic algae and macrophytes

Species	Exposure	Effects [a]	Reference
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	log EC_{50} for growth inhibition: chlorsufuron = -0.39 degredation product #1: 2.06 degredation product #2: 1.97	Wei et al. 1998
AQUATIC MACROPHYTES			
Aquatic macrophyte *Potamogeton pectinatus* (sago pondweed)	Plants exposed to chorsulfuron at 0.25, 0.5, 1.0 or 2.0 ppb (µg/L) in an environmental growth chamber for 4 weeks.	At 0.25 µg/L, reduction in leaf length (76%) and number of leaves (50%), number of stems (50%). At doses $\geq$0.5 µg/L, reduction in length of stems (47%). At doses $\geq$1.0 µg/L, significant reductions in wet and dry weights and increased mortality. 50% of plants died at 1.0 µg/L; 100% death at 2 µg/L.	Coyner et al. 2001
Lemna minor (duckweed)	Exposure for 96 hours, under static conditions. Chlorsulfuron concentrations not specified	Growth inhibition was determined based on biomass. EC_{50} = 0.7 µg/L (0.5-0.9) NOEC = 0.4 µg/L LOEC = 0.7 µg/L	Fairchild et al. 1997
lemna minor (duckweed)	Studied the phytoxicity of the expected environmental concentrations (EEC) of several chemicals. For chlorsulfuron, exposure level based in EEC was 0.02 mg/L. Exposure duration: 7 days	86% inhibition of 7-day growth (based on increase in number of leaves).	Peterson et al. 1994

[a]Values in parentheses are 95% Confidence Intervals.

Data Summary	Reference
Aquatic Sediments	
Degradation of DPX-W1849 (formerly DPX-4189), the active ingredient in Glean Weed Killer, in anaerobic aquatic environments and under flooded soil conditions.	Chrzanowski 1980a MRID 00086815
^{14}C-phenyl and ^{14}C-triazine labeled DPS-W4189 decomposed slowly (**$t_{1/2}$ = 20-22 weeks**) in anaerobic aquatic environments and more rapidly in flooded soils (**$t_{1/2}$ = 7-8 weeks**) to 2-chlorobenzenesulfonamide, 2-chlorophenylsulfonylurea, and 2-amino-4-methoxy-6-methyl-1,3,5-triazine. The rate of decomposition increased with increasing acidity and increasing amounts of oxygen in the system.	
Sediment and water collected from a spring-fed pon. Degradation of ^{14}C-phenyl and ^{14}C-triazine labeled chlorsulfuron studied Half-life >365 days	Strek 1998a
Metabolic fate of chlorsulfuron in the anaerobic aquatic environment under laboratory conditions examined using ^{14}C-phenyl and ^{14}C-triazine labeled chlorsulfuron. Anaerobic aquatic half-life = 109-263 days flooded soil half-life = 47-86 days Degradation rate was apparently not affected by active anaerobic microorganisms but was significantly influenced by increasing the level of dissolved oxygen in the aquatic test systems.	Chrzanowski and Priester 1991 MRID 42156704
Bioconcentration	
100 bluegill sunfish (*Lepomis macrochirus*), 2-3 g, 4-5 cm 0.01 or 1.0 ppm ^{14}C-phenyl labeled DPX-4189 (specific activity, 0.15 µCi/mg; >99% radiochemical purity)for 4 weeks in dynamic study residues in edible tissue reached plateau in 1 day **BCF: <1 in edible tissue** average residues in edible tissue were 0.006 ppm at 0.01 ppm exposure and 0.5 ppm at 1.0 ppm exposure low accumulation factors (4-6) detected in viscera and liver during 2-week depuration period, residues levels dropped 70-90% no adverse effects on fish during study	Han 19?? MRID 00083951
150 channel catfish (*Ictalurus punctatus*), ~5 g, mean length = 8 cm exposed for 4-weeks in a tank containing ^{14}C-DPX-W4189 treated soil (0.5 ppm) that was aerobically aged for 29 days and flooded for 2 weeks prior to initiation of fish exposure study. during aerobic aging period, ~30 of DPX-W4189 degraded to 2-chlorobenzenesulfonamide, major degradation product residue levels in fish reached plateau in 2 weeks: **BCF 1.5 in edible muscle and BCF<12 in viscera and liver**. during 2-week depuration period, residue levels decreased >90% no adverse effects on fish were observed during the course of the experiment.	Han 1981c MRID 00086820
Hydrolysis	

Data Summary	Reference
Rate of hydrolylsis of ^{14}C-DPX-4189 in 0.01M pH 4,7, and 9 aqueous buffers. Total loss of radioactivity in all samples <5% after 4 weeks; DPX-4189 stable for 4 weeks at pH 7 and 9 (<3% relative decomposition), but degraded in the acidic buffer solution (pH 4) to 2-chlorobenzene sulfonamide and 2-amino-4-methoxy-6-methyl-1,3,5-triazine. After 1 week, ~50% of the test compound decomposed at pH 4, and no intact material was detected after 4 weeks.	Han 1960a MRID 00035270
Rate of hydrolysis of ^{14}C-DPX-W4189 (both phenyl and triazine labeled) in 1.0 or 10.0 ppm at pH 4, 7, and 9 aqueous buffers at 10°C. Total loss of radioactivity from any sample was <5% after 4 weeks. Stable at pH 7 and 9 for at least 4 weeks Hydrolysis extensive at pH 4: $t_{1/2}$ = 1 week at 20°C and ~10-14 days at 10°C Hydrolysis products included 2-chlorobenzene sulfonamide and 2-amino-4-methoxy-6-methyl-1,3,5-triazine.	Han 19?? MRID 00083946
Rate of hydrolysis of ^{14}C-DPX-W4189 (both phenyl and triazine labeled) in initial concentration of approximately 5 ppm at pH 5, 7, and 9 in sterilized buffered aqueous solution kept in darkness at 24 ± 1°C for 31 days.	Dietrich and McAleer 1989b MRID 41408102
Hydrolysis was measurable only at pH 5 with a first-order half-life of approximately 23 days.	Dietrich and McAleer 1989c MRID 42156701
Chlorsulfuron was stable to hydrolysis at pH 7 and 9 comprising 96-99% of total radioactivity after 33 days of incubation at ~25°C.	Studies appear to be identical
Pseudo-first-order hydrolysis rate contant (k) at different pHs and temperatures (all values x10^{-2}/day): pH 4, 22°C, k = 14.89; pH 4, 40°C, k = 138.69; pH7, 40°C, k = 0.66; pH10, 40°C, k = 1.26 At lower pH, hydrolysis becomes more important. Pseudo-first-order disappearance rate constants in two water sediment systems (all values x10^{-2}/day): Cherokee Park (native): 0.78; Cherokee Park (sterile): 0.23; Beaver Dam (native): 0.38; Beaver Dam (sterile): 0.68	Berger and Wolfe 1996
Aqueous hydrolysis was pH-dependent and followed pseudo-first-order degredation kinetics at 25°C, with faster hydrolysis occurring at pH5 (half-life 24 days) than at either pH7 or 9 (half-lives > 365d) Degradation occurred primarily by cleavage of the sulfonylyurea bridge to form the major metabolites chlorbenzenesulfonamide and triazine amine. This is the major route in both water and soil.	Strek 1998a
Photolysis	
When DPX-4189 (1 and 100 ppm aqueous solutions) was degraded in distilled water under laboratory conditions water, only 10% of intact test compound remained after 4 weeks of exposure. Major degradation products included 2-chlorobenzene sulfonamide and 2-amino-4-methoxy-6-methyl-1,3,5-triazine. 2-Chlorophenylsulfonylurea (minor degradation product) and a polar unidentified product were detected at the origin of the TLC plate. Loss of total radioactivity during the course of the study was 62% (1 ppm solution) and 36% (100 ppm solution).	Han 1960a MRID 00035270

Data Summary	Reference
After 1 month, >95% of 10 mg ^{14}C-DPX-4189 dissolved in methyl chloride was recovered as the intact compounds. 2-Chlorobenzene sulfonamide accounted for 1-2% of the radioactivity. Loss of total radioactivity after 1 month of exposure was ~2%	Han 1960a MRID 00035270
Under the conditions of natural sunlight, solutions of 0.1 ppm ^{14}C-phenyl labeled DPX-4189 or 2-^{14}C-triazine labeled DPX-4189 in distilled water, standard reference water, or Brandywine Creek water with or without sediments were used to study the photodegradation of ^{14}C-DPX-4189 in water. Results of TLC analysis indicated that DPX-4189 in aquesous solutions exposed to natural sunlight degraded to the same compounds observed in the laboratory photolysis studies (see above). In distilled water, <10% of intact compound was recovered after 8 weeks; in Brandywine Creek water (with or without sediments), DPX-4189 accounted for 30-55% of radioactivity after 8 weeks; in standard reference water, ~40% decomposition occurred. Loss of total radioactivity from the water samples was ≤20%, except for the loss of 73% of ^{14}C-phenyl labeled DPX-4189 in distilled water.	Han 1960a MRID 00035270
Photodegredation of chlorsulfuron in methanol, distilled water, natural creek water, on silica gel and on montomorillonit surfaces in outdoor and indoor conditions. In all experiments, 2 main photoproducts identified: 2-chloro-benzene-sulfonamide and 2-methoxy-4-methyl-6-amino-1,3,5-triazine. Wide range in degradation rates in different media (pH not specified, temperature range: 10-25°C): t1/2 in pure water: 18 hr; in creek water: 18 hr.	Herrmann et al. 1985
Photodegradation is not a major degradation process for chlorsulfuron in sterile buffered water at pH 5, 7, or 9 at 25° C. At pH 7 and 9, chlorsulfuron was relatively stable with >95% of recovered radioactivity present as parent compound after 31 days. At pH 5, average half-life = 23 day in nonirradiated samples and 18 days in irradiated samples (differences may be partly due to slight differences in sample temperature). *In both irradiated and nonirradiated samples, hydrolysis is the major contributing factor to chlorsulfuron degradation at pH 5.*	Dietrich and McAleer 1989a MRID 41408101 Dietrich and McAleer 1989d MRID 42156702 Studies appear to be identical
Aqueous photolysis occurred slowly (half-life 198 days). Photolysis not a significant contributor to degradation. However, hydrolysis in thin-layer plates exposed to light (half-life 80 days) progressed faster than in the dark (half-life 130 days).	Strek 1998a
On irradiated soil (Nora silty clay loam), the half-life = ~65 days under study conditions, equivalent to approximately 158 days of natural (latitude 52° N) sunlight. Half-life on dark control soil estimated to be >300days.	Hawkins et al. 1990a MRID 41721001 Hawkins et al. 1990b MRID 42156703 Studies appear to be identical

Data Summary	Reference
Soil Degradation/Transport	
$t_{1/2}$ of intact ^{14}C-DPX-W4189 = 1 month under field conditions in slightly acidic soils [Delaware, North Dakota, Illinois, and Versailles(France)] treated with 100 g a.i./ha	Han 1981a MRID 00086817
$t_{1/2}$ of intact ^{14}C-DPX-W4189 = 2-3 months under field conditions in alkaline soil (Rosetown, Saskatchewan, Canada) treated with 100 g a.i./ha.	
The degradation products, which included 2-chlorobenzene sulfonamide and 2-amino-4-methoxy-6-methyl-1,3,5-triazine, were detected in all soils a few days after application. Intact DPX-W4189 and its degradation products steadily decreased throughout the course of the field studies.	
Aerobic soil degradation under greenhouse conditions. light soil = Fallsington sandy loam heavier soil = Keyport silt loam **$t_{1/2}$ of ^{14}C-DPX-4189 = ~2 months** (no major differences in rate of degradation in Fallsington sandy loam *vs* Keyport silt loam) 2-chlorobenzenesulfonamide = major degradation product in both soils accounted for 30-35% of residual radioactivity after 3 months; decreased to 12-13% after about 9 months minor metabolite, 2-chlorophenylsulfonylurea	Han 19??a MRID 00035273
^{14}C-Chlorsulfuron (both phenyl and triazine labeled)a pplied at the maximum use rate of Telar herbicide (2.2.5 oz a.i./acre; 158 g a.i./ha) resulting in an initial concentration of approximately 0.060 ppm in the upper 6" of soil (sandy-loam/loamy-sand). The application was made to bare ground without an intercepting canopy and regular irrigation, where leaching behavior os fhclorsulfuron and it degradation products would be accentuated.	Dietrich and Taylor 1990 MRID 41714401
Rapid degradation of chlorsulfuron in Madera, CA soil with approximate half-life of 3 weeks.	
After 6 months, approximately 5% of applied of ^{14}C-phenyl labeled chlorsulfuron was converted to $^{14}CO_2$ and >20% of the initial ^{14}C-triazine labeled chlorsulfuron was converted to $^{14}CO_2$	
^{14}C-chlorsulfuron was only detected in the 0-6" soil segments, indicating a lack of soil mobility and low potential for groundwater contamination under actual field conditions. The mobility of ^{14}C-phenyl labeled chlorsulfuron was limited to the top 24" and ^{14}C-triazine labeled degradation products to the top 12" of soil.	
Fallsington sandy loam and Keyport silt loam treated with ^{14}C-phenyl labeled DPX-W4189 (1 ppm) and exposed to simulated sunlight.	Han 1960b MRID 00083947
Cleavage of the carbamoyl bond to form 2-chlorobenzenesulfonamide appeared to be the major route of degradation in both soil types. **$t_{1/2}$ of ^{14}C-phenyl labled WDPX-4189 = ~2 weeks**	Han ?? MRID 00086813 (This study is identical to Han 1960b)

Appendix 9: Laboratory and simulation studies on the environmental fate of chlorsulfuron.

Data Summary	Reference
Laboratory and greenhouse studies on the adsorption and movement of chlorsulfuron in 4 soil types (silt loam, clay loam, sandy loam and loamy sand). Organic carbon was the predominant adsorbent in all soils studied. Clorsulfuron had low affinity for clay. Chlorsulfuron was most mobile in soils containing low organic matter and nonacidic soils.	Mersie and Foy 1986
Chlorsulfuron persistence studied in loam and sandy loam. Calculated half-life in loam soil was 37.0 days Increasing soil temperature significantly reduced chlorsulfuron persistence. Increasing soil water also reduced persistence.	Anderson and Barrett 1985
Influence of soil pH on the uptake, degradation, and movement of chlorsulfuron in silty loam soil in laboratory setting. Soil pH strongly influenced degradation rate of chlorsulfuron. Half-life at pH 5.6 = 1.9 we4eks; Half-life at pH 7.5 = 10 weeks.	Friedrickson and Shea 1986
^{14}C-Chlorsulfuron applied (23.4 µg chlorsulfuron/50 g soil) to screened clay soil (pH 7.5) with moisture content below 10% of field capacity. Half-life = 168 days	Smith 1986
Chlorsulfuron applied on alkaline soil (pH 8.0) at rate of 125 g a.i./ha. Response of alfalfa roots in growth chamber was monitored for 28 months after application. Estimated months to 50% dissipation (MT_{50}) = 0.22. MT_{90} = 8.4, MT_{99} = 24.8. Rates of dissipation were estimated following 25 g a.i./ha as follows: 2 years = 0.23 ng/g; 3 years = 0.04 mg/g; 4 years = 0.01 mg/g. Residues from 25 g a.i./ha were toxic to alfalfa in the field until 4 years after application (or until >99% chlorsulfuron had dissipate). Estimated half-life = 0.22 months	Moyer et al 1989
Adsorption of chlorsulfuron studied in several soils. Chlorsulfuron adsorption was highly correlated with organic matter content of soils. Adsorption was pH dependent, decreasing with increasing pH, with negligible absorption at pH > 7-8. Range of Kds: at pH4.2, 0.24-3.56; at pH 7, 0.04-0.36	Boggaard and Streibig 1989
In sandy loam (pH 5.8), Langmuir K = 0.44 mL/µg Half-life decreased with increasing temperature and increasing pH uv radiation increased loss of herbicide from sand	Blacklow and Pheloung 1991

Data Summary	Reference
Degradation of chlorsulfuron investigated in three soil types, with 2 depths for each type. Soil type: Typic Haplorthox Depth of 0-30 cm, half-life at 25°C = 7.32 days, at 40°C = 2.41days Depth of 50-200 cm, half-life at 25°C = 8.23 days, at 40°C = 1.19days Soil type: Typic Acrohumox Depth of 0-40 cm, half-life at 25°C = 10.18 days, at 40°C = 2.35days Depth of 100-200 cm, half-life at 25°C = 29.05 days, at 40°C = 5.04 days Soil type: Typic Haplohumox Depth of 0-15 cm, half-life at 25°C = 8.20 days, at 40°C = 3.48 days Depth of 70-150 cm, half-life at 25°C = 25.67 days, at 40°C = 4.66 days In all cases, half-life decreased with increasing moisture content. Sterilization decreased degradation rates in some soil types. Half-life increased as soil pH increased.	Ravelli et la. 1997
Secondary reference chlorsulfuron Kd: 3.0 kg/L chlorsulfuron half-life: 42-112	Sorensen et al. 1998
Aerobic soil metabolism In Keyport silt loam soil (pH6.4, 2.8% OM) was rapid (half-life 20 days). Adsorption and desoprtion K values given as L/Kg. No units specified for Koc. Dissipation in an anaerobic sediment/water system (initial pH of 6.7, final pH of 7.4) progressed more slowly (half-life > 365 days) than in aerobic soil. Major soil degradation products were chlorbenzenesulfonamide and triazine amine (same as aqueous hydolysis) Batch equilibrium adsorption studies conducted on 4 soils (1 sandy loam, 1 loam, 2 silt loam) was low in this system. Adsorption Koc in sandy loam = 13; in loam = 54; in silt loam = 17 and 20. Kom, Kads values for each soil type also provided (Table 5, p. 45). Desorption Koc in sandy loam = 52; in loam = 520 in silt loam = 33 and 44. Kom, Kads values for each soil type also provided (Table 5, p. 45).	Strek 1998a
A Review - the following parameters were given for chlorsulfuron: Koc: 40 mL/g(pH 7) half-life: 40 days (soil type not specified) water solubility: 27.9 g/L (pH 7)	Bergstrom and Stenstrom 1998

Data Summary	Reference
Kd values (mL/g) and half-lives (weeks) in four soil types, at three depths for each soil type: Soakwaters 0-20 cm: Kd = 0.259; t1/2 = 3.0 20-40 cm: Kd = 0.187; t1/2 = 3.1 40-60 cm: Kd = 0.053; t1/2 > 31 Wharf Ground 0-20 cm: Kd = 0.157; t1/2 =8.4 20-40 cm: Kd = 0.114; t1/2 = 8.2 40-60 cm: Kd = 0.069; t1/2 = 13.0 Cottage Field 0-20 cm: Kd = 0.200; t1/2 = 7.6 20-40 cm: Kd = 0.098; t1/2 = 13.4 40-60 cm: Kd = 0.048; t1/2 = 17.5 Hunts Mill 0-20 cm: Kd = 0.163; t1/2 = 6.5 20-40 cm: Kd = 0.107; t1/2 = 8.2 40-60 cm: Kd = 0.047; t1/2 = 21.0 A positive correlation observed between chlorsulfuron sorption and organic carbon content.	Sarmah et al. 1998
Degradation of chlorsulfuron in alkaline soils (pH 7.1-9.4) spikes with 40 µg a.i./kg under laboratory conditions at 25°C and a moisture content corresponding to 70% field capacity (25°C -33kPa). sandy loam (Walpeup): Kd = 0.16 mL/g; DT_{50} = 19 days clay loam (Halbury): Kd = 0.37 mL/g; DT_{50} = 34 days sand (Tepko): Kd = 0.12 mL/g; DT_{50} = 47 days clay (Dooen): Kd = 0.24 mL/g; DT_{50} = 62 days calcareious sandy loam (Avon): Kd = 0.11 mL/g; DT_{50} = 26 days Disappearance of chlorsulfuron was faster in non-sterile than in sterile soil, demonstrating the importance of microbes in the degradation process. Persistence of chlorsulfuron increased in increasing depth, most likely due to a decline in microbial populations.	Sarmah et al. 1999
^{14}C-chlorsulfuron applied to loamy soil composed of 2.14% organic matter, 39% silt, 43% sand, 18% clay; soil pH of 7.7. After 10 days, 40.9% of ^{14}C was extractable and 35.4% was in the bound residue form. After 150 days, 25.1% of ^{14}C was extractable and 47.1% was in the bound residue form. For bound ^{14}C, most was bound to fulvic acid and humin.	Guo and Sum 2002

Data Summary	Reference
Field soil disappearance studies with ^{14}C-DPX-4189 several sites encompassing a wide variety of soil types and climatic conditions data indicate that radioactivity traveled downward, but that more radioactivity remained in upper increments than was found in the lower increments major degradation products were 2-chlorobenzenesulfonamide from ^{14}C-phenyl labeled DPX-4189 and 2-amino-4-methoxy-6-methyl-1,3,5-triazine from 2-^{14}C-triazine labeled DPX-4189 unidentified polar material consisting of radioactivity appeared in the water phases and remained at the origin of the TLC plates after development **$t_{1/2}$ of ^{14}C-DPX-4189 = ~1 month** no major differences were found with respect to soil characteristics or climates in either the rate of degradation or the degradation products formed.	Du Pont de Nemou rs 1979b MRID 00035274
Keyport silt loam, sterile and nonsterile treated with ^{14}C-DPX-4189 at rates of 0.1, 1, and 10 ppm biodegradation of ^{14}C-DPX-4189 to $^{14}CO_2$ in ***nonsterile*** soil was ~5% for all three treatment rates over the duration of the study biodegradation of ^{14}C-DPX-4189 to $^{14}CO_2$ in *sterile* soil was <1% Total ^{14}C recoveries averaged ≥97% **$t_{1/2}$ of ^{14}C-DPX-4189 = <2 weeks in *nonsterile* soil** major degradation products were 2-chlorobenzenesulfonamide and 2-amino-4-methoxy-6-methyl-1,3,5-triazine with unidentified, smaller amounts of more polar metabolites	Rapisarda 1965 MRID 00035275
Keyport silt loam, sterile and nonsterile, treated with 0.1, 1, or 10 ppm ^{14}C-phenyl(U) labeled WDPX-4189 and 0.1 or 1 ppm ^{14}C-triazine labeled WDPX-4189 and incubated at 25°C in the dark for 6-7 months. **$t_{1/2}$ of ^{14}C-DPX-4189 =** between 1 and 2 weeks easily degraded to polar material(part of which became incorporated into soil organic matter and part of which was released as $^{14}CO_2$) microbial degradation to $^{14}CO_2$ was temperature and moisture sensitive occurring mostly at 25°C and 70% of moisture retention capacity. DPX-4189 had no effect on soil microorganisms regarding ability to degrade complex molecules like cellulose and protein.	Rapisarda 1981a MRID 00083950 Rapisarda 1981b MRID 00086814
Aerobic soil metabolism under laboratory conditions. Calculated half-lives ranged from ~6 days (1 week) on sterile and non-sterile Flanagan silt loam at 40°C (pH 6.1) to 881 days (27 months) on sterile Utah silt loam at 25°C (pH 9) . Chlorsulfuron degrades rapidly to biologically inactive substances in soils that have a pH <7 and at a low use rate of 0.125-2.25 oz/acre.	Priester 1991a MRID 42214201
Degradation and leaching of ^{14}C-chlorsulfuron was investigated in three soil types: very heavy clay, medium fine sand, and organic soils at 10-11°C. Application of 4 g a.i./ha was used. No degradation to $^{14}CO_2$ was seen in any soil type. Chlorsulfuron leached (after precipitation) to depths of 42 cm in sand, 24 cm in organic soil, and 12 cm in clay	Iivanainen and Heinonen-Tanski 1991

Appendix 9: Laboratory and simulation studies on the environmental fate of chlorsulfuron.

Data Summary	Reference
Degradation of chlorsulfuron studied in acidic and alkaline soils. Soil sterilization significantly reduced breakdown; ability for breakdown restored bu reinnoculation of soil with indigenous microbes. Chemical hydrolysis also contributed to disappearance of chlorsulfuron from soil; hydrolysis more rapid in acid soil..	Joshi et al. 1985
Degradation rates of chlorsulfuron determined after 2 applications rates (15 and 30 a.i./ha) in sandy loam soil (pH 5.7, 7.3% o.m.) of volcanic origin under controlled and field conditions. Chlorsulfuron degraded rapidly according to first-order kinetics. Half-life under varying controlled conditions: range of 22-38 days Half-life under field conditions: 13-14 days In New Zealand acidic soil, chlorsulfuron disappeared within 11-15 weeks	James at al. 1999
^{14}C-Chlorsulfuron application of 2.25 oz a.i./acre to silt loam field in Moscow, Idaho. average half-life = 16 days test substance and its metabolites found in the top 4" of soil ^{14}C-residues = 0.09 ppm at day 0 and day 571 conclusion: minimal soil mobility and relatively short half-life	Rhodes 1994 MRID 43421401

Appendix 10. Effects of chlorsulfuron on microorganism and microbial populations in soil

Application	Observations	Reference
Paper discs containing $1x10^{-7}$ mol were placed centrally onto the surface of agar plates containing $1x10^{5}$ of one of 17 fungal species	Tested 17 fungal species for inhibition of growth (expressed as % of control, based on diameters of growth inhibition zones). Growth of three species inhibited by chlorsulfuron: *Penicillium oxalicum* (7.7%) *Fusarium oxysporum* (23.9%) *Thielaviopsis basicola* (33.4%)	Belai and Oros 1996
Technical grade DPX-4189 applied to Harney silt loam from Hays, Kansas, Keyport silt loam from Newark, Delaware, and Renohill clay loam from Plattesville, Colorado at concentrations of 0.1, 1.0, 10, or 100 μg/g of soil. Soils were sampled at 2, 4, 6, and 8 weeks to determine populations of actinomycetes, bacteria, and fungi.	No effects on populations of actinomycetes, bacteria, or fungi during the 8-week post-treatment period. No significant differences or trends between treated soils and controls. No effects on the distribution of the fungi recovered.	Julis 1980 MRID 00035277
DPX-4189 at rates of 1.0, 10, 100 or 1000 μg/mL in monexenic culture assay in broth of representative soilborne saprophytic and plant pathogenic bacteria and fungi.	No bactericidal or fungicidal effects at $\leq$100 μg/mL. None of the 18 fungi were completely inhibited at 1000μg/mL. Growth reduction $>$50% recorded for four fungi at 1000 μg/mL. Inhibitory concentrations of DPX-4189 for fungi were found to be $>$10,000 times the maximum recommended use rate.	Julis 1980 MRID 00035277

Appendix 10. Effects of chlorsulfuron on microorganism and microbial populations in soil

Application	Observations	Reference
Field plots grown with barley were sprayed with 4 and 12 g a.i./ha (corresponding to 3.67 and 10.7 kb.acre) at the tillering stage for 2 growing seasons	Observations made in three soil types (sandy, clay, and organic) 1 day after application, 1 month after application, at the end of the first growing season, at the beginning of the next growing season, at the end of the 2nd growing season, and the beginning of the third growing season. In sandy soil: a small, but statistically significant inhibition observed for soil nitrification 1 day after the highest application rate. Nitrification not affected at other time points. Soil dehydrogenase activity inhibited only at the end of the growing season for the highest application rate. In clay soil: small, but statistically significant increase in soil nitrification observed at the end of the second growing season for both application rates. Authors suggest this difference may not be due to treatment, but may be an effect of plant death. Soil dehydrogenase activity not assessed. In organic soil: Small, but statistically significant increase in soil nitrification observed at the end of the first growing season for highest application rate. Soil dehydrogenase activity not assessed.	Junnila et al. 1994
Keyport silt loam, sterile and nonsterile, treated with 0.1, 1, or 10 ppm ^{14}C-phenyl(U) labeled WDPX-4189 and 0.1 or 1 ppm ^{14}C-triazine labeled WDPX-4189 and incubated at 25°C in the dark for 6-7 months.	microbial degradation to $^{14}CO_2$ was temperature and moisture sensitive occurring mostly at 25°C and 70% of moisture retention capacity. DPX-4189 had no effect on soil microorganisms regarding ability to degrade complex molecules like cellulose and protein.	Rapisarda 1981a MRID 00083950

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
alfalfa, grape, and pea	Greenhouse study. ^{14}C-Chlorsulfuron applied to soil and directly to leaves. Chlorsulfuron was applied at a rate of 23g/ha (0.023 lb/acre)	Chlorsulfuron applied to leaves: absorption increased gradually over 7 days, but most absorption took place within 24 days. ^{14}C-Chlorsulfuron taken up most rapidly by alfalfa; In 7 days, alfalfa absorbed 92.8%, grape absorbed 96.2% and pea absorbed 56.3& of applied ^{14}C. Increased in relative humidity produces a small increase in absorption by grape leaves. Simulated dew also increased absorption by grape leaves. Absorption of chlorsulfuron was increased by plants grown in greenhouse vs field conditions. Application of soil containing ^{14}C-chlorsulfuron: only small amounts (< 5%) of ^{14}C-chlorsulfuron were absorbed when herbicide treated soil was applied to leaves (similar results in all three species). Translocation of chlorsulfuron applied to leaves of all three species was acropetal.	Al-Khatib 1992
field pennycress (*Thlaspi arvense*)	Grreenhouse study. Spot application of 1 µg chlorsulfuron (98.9% pure) applied in 8-10 droplets of 10 µL per leaf.	Chlorsulfuron was absorbed slowly after application (24% absorbed after 24 hours). Compared to controls, chlorsulfuron treated leaves exported only 60-70% of assimilates (12 and 24 hrs after exposure). No affect observed 6 hours after treatment. Chlorsulfuron effects were abolished by supplying branched-chain amino acids prior to chlorsulfuron.	Bestman et al. 1990

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
Prunus avium (sweet cherries); three different cultivars: Rainier, Chinook, and Bing	Field study of simulated chlorsulfuron drift at different reproductive growth stages. Branches were treated at side-green, full-bloom, post-bloom, and pit-hardening stages with chlorsulfuron solutions with concentrations ranging from 0.31 to 25.11 µM (corresponding to application rates of 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". 10 mL of spray used for each treatment. Single exposures made at each growth stage. In one experiment in Chinook at the full-bloom stage, 3 sequential applications of the 3 lowest chlorsulfuron concentrations were made on the same branch at 3-day intervals.	For foliar symptoms, all assessments made on a 0-7 scale (0 = normal leaf development; 7 = necrotic and dead leaves). For evaluation of reproductive effects, fruit yield was determined as the percentage of potential fruit harvested. Fruit quality was assessed by size, color, firmness, and soluble solids. Dose-dependent increase in symptom severity in all cultivars. Effects observed at all application rates. Full-bloom and post-bloom stages most sensitive; side-green and pit-hardening stages least sensitive. Dose-dependent decreased in fruit yield. Full-bloom stage most sensitive. Dose-dependent decrease in fruit quality. For all endpoints, variations were observed between cultivars, although the dose-dependent effect pattern was observed for all cultivars. Chinook was the most susceptible cultivar; Bing was the least sensitive. Conclusions: Severity of injury is dependent upon the cultivar, number of exposures, growth stage, and chlorsulfuron exposure level.	Bhatti et al. 1995

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
6 species of grass: crested wheatgrass, Russian wildrye, alkaligrass, tall fescue, bernudagrass, alkali sacaton	Incubated seeds and greenhouse plants were treated pre- and post-emergence with chlorsulfuron at rates of 0.023, 0.047, 0.093, and 0.14 lb/acre. Pre-emergence applications were immediately after planting, Post-emergence applications when grasses had reached the four- to five-leaf stage.	EC_{50} values were not determined Seed response was measured as % germination; plant response was measured as % mortality and dry weight production at the four- to five-leaf stage. No affect on germination in any grass for any chlorsulfuron exposure level. Crested wheat grass and Russian wildrye tolerant to all pre- and post-emergence applications. For post-emergent applications, no effects seen at any dose for Crested wheatgrass, Russian wildrye, bermudagrass, and alkali sacaton. Dry weight production of bermudagrass not affected by any post-emergence application but significantly reduced by all pre-emergence applications. Survival and dry weight production of alkali sacaton significantly reduced by all pre-emergence applications. Alkaligrass and Alta tall fescue were killed or severely damaged at all rates regardless of timing.	Davison et al. 1987
canola, smartweed, soybean, sunflower	Single application at one of three different stages of reproductive development (pre-flower, and 2 intervals after pre-flower, but before flower stage). 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) Very low exposure levels (approximately 1000 times less than recommended application rate).	Effects determined by measuring height and yield of mature plants. Chlorsulfuron produced a dose-dependent reduction in yield of all plants tested. Degree of reduction also dependent upon time of application. 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 $1.8\ 10^{-4}$kg/ha (0.00016 lb/acre) reduced total seed weight to 1% of control.	Fletcher et al. 1996

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
Brassica rapa (turnip)	Greenhouse study on 3 different soil types and vermiculite. Chlorsulfuron concentrations in soil ranged from 0.010 to 40 µg ai/kg soil. Details of how chlorsulfuron was applied appear to be provided in an earlier publication.	Soil types: loamy sand, pH 6, Organic C(%) 1.27 clay loam, pH 7.2, Organic C(%) 1.85 sandy loam, pH 4.9, Organic C(%) 7.62 Availability of chlorsulfuron in various soils assessed by comparison of ED_{50} values based on plant fresh weight). Visual symptoms observed within 1-2 days of application. ED_{50} (based on fresh weight) vermiculite = 0.2 µg/L loamy sand = 0.3 clay loam = 0.58 sandy loam = 0.61.	Gunther et al. 1989

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
22 plants	Greenhouse test using a soil-free bioassay system (hyponics). Chlorsulfuron (Glean, a 75% formulation) concentrations in the hyponics system ranged from 0 to 1000 µg a.i./L	ID_{10} for seedling growth (µg a.i./L) (based on seedling fresh weight) sunflower: 0.27 Soyabean: 0.10 Sorghum:0.34 cotton: 0.31 chickpea: 0.13 and 0.19 barley: 5.93 wheat: 7.47 navy bean: 0.14 peanut: 0.45 mung bean:0.48 lablab: 0.21 cowpea: 0.40 lucerne: 0.06 snail medic: 0.14 oilseed rape: 1.13 oat: 0.69 triticale: 0.95 *Rapistrum rugosum*: 0.36 *Phalaris paradoxa*: 0.43 linseed: 0.24 canary grass: 0.23 maize: range of 0.08 to 0.27 ID_{50} for seedling growth (µg a.i./L) sunflower: 0.54 (0.48-0.61) Soyabean: 0.85 (0.64-1.12) Sorghum: 1.55 (1.29-1.88) cotton: 1.81 (1.56-2.09) chickpea: 0.94 (0.53-1.68), 1.57 (0.87-2.82) barley: 28.5 (12.7-63.7) wheat: 102 (37.1-280) navy bean: 0.75 (0.61-0.92) peanut: 0.99 (0.81-1.21) mung bean: 1.21 (0.91-1.61) lablab: 1.38 (1.09-1.76) cowpea: 2.42 (2.00-2.93) lucerne: 0.19 (0.14-0.24) snail medic: 0.21 (0.19-0.23) oilseed rape: 2.01 (1.57-2.56) oat: 4.67 (no CI reported) triticale:5.86 (3.67-9.35) *Rapistrum rugosum*: 0.55 (0.39-0.79) *Phalaris paradoxa*: 1.47 (0.99-2.18) linseed: 0.57 (0.46-0.71) canary grass: 1.47 (1.07-2.01) maize: range of 0.46 (0.38-0.55) to 1.29 (0.80-2.08)	Jettner et al. 1999

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
Brassic napa (Oilseed rape) and *Fallopia convolvulus* (black bind-weed)	Two insect-plant interactions tested for effects of chlorsulfuron. Species pairs tested were *Pieris brassicae/Brassic napa*, *Gastrophysa polygoni/Fallopia convolvulus* Chlorsulfuron (Glean, a 75% formulation) was applied to plants on 4 consecutive days at a rate ranging from 0.025 to 0.8 g ai/ha (0.000022 to0.00071 lb/acre)	Plants had significantly reduced root growth rate, but not shoot growth rate. Qualitative description only; EC_{50} value not determined	Kjaer and Heimbach 2001
non-target plants: onion, corn, wheat, sorghum, sugarbeet, soybean, pea, tomato, rape, and cucumber	chlorsulfuron (98.2% pure), maximum rate tested was the maximum labeled rate of 2.25 oz/acre (0.14 lb/acre) for non-crop land. Range of application rates tested varied depending upon species tested. The lowest application rate used was in onions (0.0000088 lb/acre). For seed emergence studies, test solutions applied as a pre-emergence soil surface application; for vegetative vigor, single application of chlorsulfuron mixed wiht 0.25%X-77 surfactant	All values given in oz/acre. See Tables 4-1 and 4-2 in report Section 4-1 for complete results in all species and for conversion of EC_{50} values from oz/acre to lb/acre. For seed emergence: most sensitive species was onion [NOEL = 0.000562; EC_{25} = 0.0066 (0.000008-0.018); EC_{50} = 0.024 (0.0043-0.17)]; most resistant species were sorghum,[NOEL $>$0.351, EC_{25} and EC_{50} not determined] and tomato [NOEL $>$0.351, EC_{25} and EC_{50} not determined]. Growth inhibition occurred from soil applications occurred in 9 of the species tested when applied at a rate of 2.25oz/acre. For vegetative vigor based on plant height: most sensitive species were onion [NOEL = 0.000140; EC_{25} = 0.00059 (0.00014-0.0014); EC_{50} = 0.011 (0.0055-0.021)] and sugarbeet [NOEL = 0.000140; EC_{25}= 0.0033 = (0.0012-0.0066); EC_{50} 0.072 = (0.036-0.20)]; most resistant species was wheat,[NOEL = 0.0180, EC_{25} = 0.89 (0.57-1.2) and EC_{50}= 5.8 (3.5-$>$10)].	McKelvey and Kuratle 1991 MRID 42587201

Appendix 11: Toxicity of chlorsulfuron to terrestrial plants

Plant	Exposure	Response	Reference
wine grapes (22 varieties)	Field study - Foliar application of Glean (a 75% formulation) at rate of 60 and 180g/ha (0.054 and 0.16 lb/acre) applied at the pre-bud burst stage. Report does not indicate if chlorsulfuron application rate is in terms of a.i.	Compared to control plants, no evidence of toxicity based on a phytotoxicity rating scale of 0 (no symptoms) to 5 (severe symptoms), pruning weight, fruit yield or number of grape bunches.	Moore and Elliott 1989
alfalfa and redroot pigweed	Field experiment with applications of chlorsulfuron 0.12 to 9.6 g/ha (amount of a.i. not specified) (corresponds to 00.00011 to 0.0086 lb/acre)	GR_{50} value (rate required to reduce growth by 50% by visual assessment) for alfalfa = 0.35 g/ha (0.00031 lb/acre) and 0.39 g/ha (0.00035 lb/acre); for redroot pigweed = 1.67g/ha (0.0015 lb/acre).	Moyer 1995
Review: includes serveral species of non-target fruit, grain and fiber and several species of crops grown for forage and pasture	Review: variable exposures (not specified)	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
Daucus carota (carrot), *Stellaria media* (chickweed), *Chemopodium album* (pigweed)	Dose-response curves for chlorsulfuron (commercial formulation, not specified). Full range of application rates were not specified. Whole plants sprayed after emergence.	Fresh and dry weight determined. Low doses stimulated growth in both assays. ED_{50} (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] *Chemopodium* album, 1.21 g/ha (95%CI 0.49-1.94) [0.00019 lb/acre]	Olofsdotter et al. 1994

[a] Values in parentheses are 95% Confidence Intervals.

Appendix 12. Effects of chlorsulfuron terrestrial invertebrates

Application	Observations	Reference
Direct spray studies: first-instar larva of *Gastrophysa polygoni* sprayed with 0 - 1.2 mg/cm^2 (recommended field rate corresponds to 4x10^{-5} mg/cm^2). No indication that surfactant was added. **Growth and survival studies:** Effect of sub-lethal treatment of the annual weed *Polygonum convolvuvus* on growth and survival of the beetle *Gastrophysa ploygoni*. Plants sprayed with chlorsulfuron at rates corresponding to 0.32, 0.67, 1.32, and 2.68 g/ha (surfactant added). Eggs place on plant leaves 2 days after chlorsulfuron application. **Feeding experiments**: Feeding experiments with leaves treated with chlorsulfuron applied at a rate corresponding to 1.6 g a.i./ha. Larvae fed for 6 days. Experiments conducted 11, 24, and 42 days after spraying. No indication that surfactant was added.	**Direct spray studies:** no significant changes in mortality rate were observed for any exposure level. **Growth and survival studies:** 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). **Feeding experiments**: weight of larvae unchanged for chlorsulfuron sprayed leaves compared to larvae feeding on control leaves.	Kjaer and Elmegaard 1996
Two insect-plant interactions tested for effects of chlorsulfuron. Species pairs tested were *Pieris brassicae/Brassic napa*, *Gastrophysa polygoni/Fallopia convolvulus* Chlorsulfuron (Glean, a 75% formulation) was applied to plants on 4 consecutive days at a rate ranging from 0.025 to 0.8 g ai/ha. 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. Authors conclude that chlorsulfuron is unlikely to cause widespread effects on herbivorous insects.	Kjaer and Heimbach 2001
Steinernema carpocapsae and *Steinernema feltiae* (nematodes) exposed to chlorsulfuron in soil (purity not specified) at concentrations ranging from 312 to 10,000 ppm for 72 hours	Assessed reproduction, viability and movement No effect observed on any parameter at any concentration tested. NOECs (for both species) = 10,000 ppm	Rovesti and Desco 1990